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Scripta Varia

110

# *The Signs of Death*

*The Proceedings of the Working Group  
11-12 September 2006*



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2007

Thus, when the functions of the brain which are, so to speak, at the service of the soul, cease completely because of some defect or perturbation – since the messengers of the sensations and the agents of movement no longer act –, it is as if the soul was no longer present and was not [in the body], and it has gone away. *Denique, dum haec eius tamquam ministeria vitio quolibet seu perturbatione omni modo deficiunt desistentibus nuntiis sentiendi et ministris movendi, tamquam non habens cur adsit abscedit [anima].*

Saint Augustine, *De Gen. ad lit.*, L. VII, chap. 19; PL 34, 365

## THE SIGNS OF DEATH

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*Working Group on*

# THE SIGNS OF DEATH

*11-12 September 2006*

Edited by  
H.E. Msgr. Marcelo Sánchez Sorondo



EX AEDIBVS ACADEMICIS IN CIVITATE VATICANA

MMVII

The opinions expressed with absolute freedom during the presentation of the papers of this meeting, although published by the Academy, represent only the points of view of the participants and not those of the Academy.

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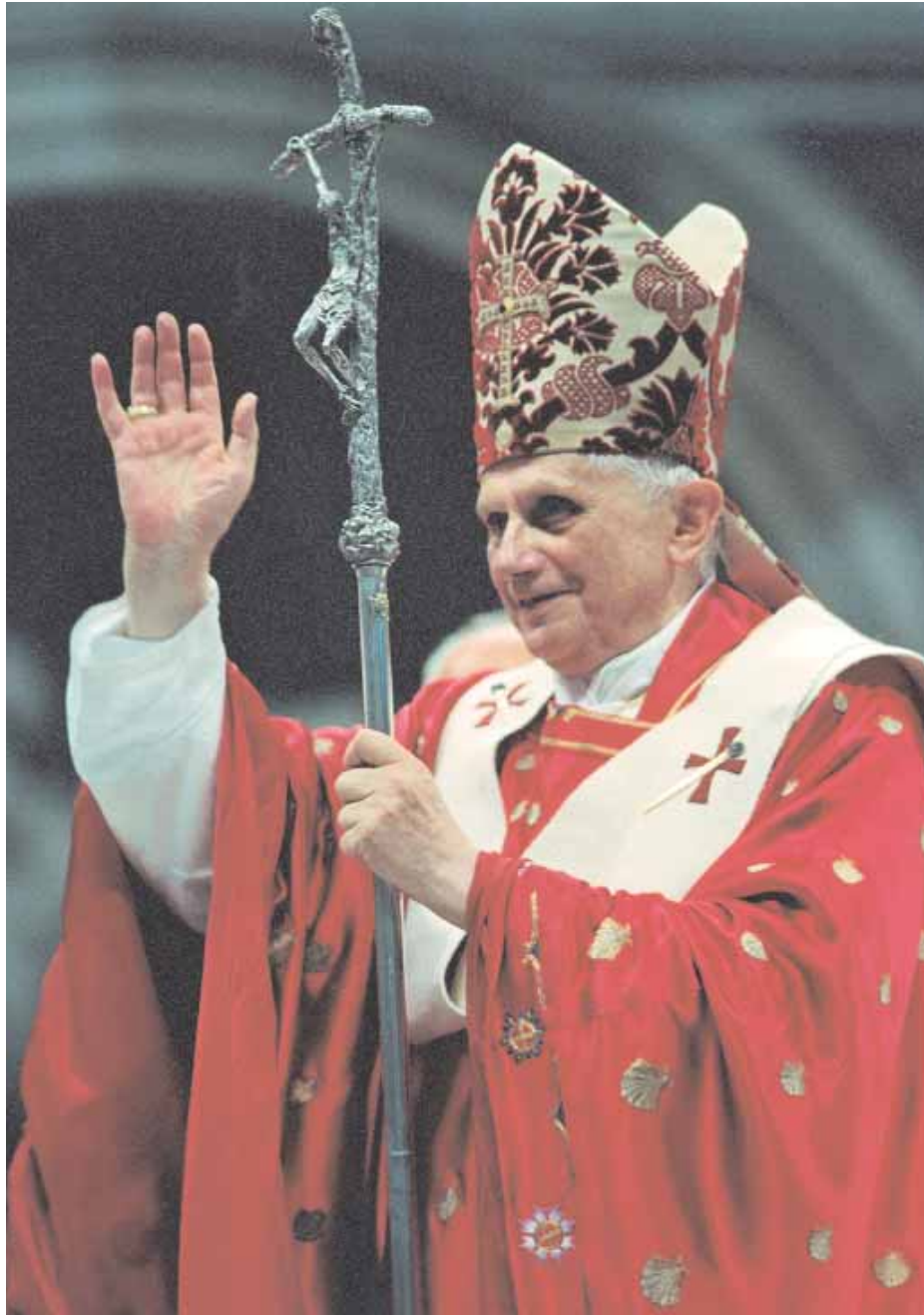
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PONTIFICIA ACADEMIA SCIENTIARVM  
VATICAN CITY



His Holiness Pope Benedict XVI



The Participants of the Working Group of 11-12 September 2006





The Participants of the Working Group of 11-12 September 2006





The Participants of the Working Group of 11-12 September 2006

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## PREFACE

This publication begins with the 'Letter of His Holiness Benedict XVI to Our Venerable Brother Msgr. Marcelo Sánchez Sorondo Chancellor of the Pontifical Academy of Sciences on the Occasion of the Working Group' (pp. xiv-xv). An introduction then explains the purpose of the meeting organised by the Pontifical Academy of Sciences on 'The Signs of Death' held in September 2006 (pp. xvi-xx). In addition, the reader will find a statement by distinguished neurologists and other important thinkers on 'Why the Concept of Brain Death is Valid as a Definition of Death', signed by nearly all of those taking part in the meeting (pp. xxi-xxix). This is followed by a list of 'Questions for Neurologists and Others about Brain Death as the Criterion for Death', which also contains the answers to these questions (pp. xxx-lxxxvii). The volume then continues with the papers of the speakers at the meeting and the discussion of their contents, as well as a general discussion. The volume also includes a paper (read with attention by the participants) by Dr. D.A. Shewmon who was not able to take part in the meeting (pp. 292-333). To help the reader, brief biographies of the participants are presented, as well as the programme of the meeting. This publication also offers the reader three appendixes. The first contains comments on the discussion by Dr. Shewmon (pp. 371-381). The second is a 'Dissenting Statement' by Dr. Shewmon and Prof. R. Spaemann which has been published as an appendix because one of its authors was not present at the meeting (pp. 382-387). The third is a response by nearly all of the participants to the dissenting statement of Prof. Spaemann and Dr. Shewmon and the comments of this last, an appendix made necessary, in part, by the same circumstance (pp. 388-394). Through these appendixes this volume wishes to continue the dialogue, at least at a distance, of the participants. At the end an index is provided to help the reader consult a volume which addresses a very complex and delicate subject.

The reader should note that the views expressed in the papers, the statement, and elsewhere, are those of the respective signatories and not necessarily those of the Pontifical Academy of Sciences.

I would like to take this opportunity to express my gratitude to all those who took part in this event which, as they themselves have observed, constitutes an initiative marked by high scientific quality, by authentic and interdisciplinary dialogue, and by a contribution that expresses the views of scholars from different parts of the world. A special word of thanks goes to the staff of the Chancellery of the Academy for their contribution to this volume, and in particular for the work they dedicated with diligence and precision to the transcribing of the recordings of the discussions.

Lastly, it is incumbent upon me to thank the Holy Father Benedict XVI for the trust he has reposed in the Pontifical Academy of Sciences and the participants. We hope that this meeting constitutes a contribution to a profound reflection on the very important subject of 'The Signs of Death' and a suitable response to the trust that has been reposed in us by His Holiness.

Bishop Marcelo Sánchez Sorondo  
Chancellor of the Pontifical Academy of Sciences





Al venerato Fratello  
Mons. MARCELLO SÁNCHEZ SORONDO  
Cancelliere della Pontificia Accademia delle Scienze

Nei prossimi giorni 11 e 12 settembre codesta Pontificia Accademia organizza un seminario di studio per approfondire ulteriormente lo studio delle tematiche correlate con l'ultima fase della vita umana sulla terra. Tale significativo incontro si colloca nel solco della plurisecolare tradizione della Pontificia Accademia delle Scienze, il cui compito è stato e continua ad essere quello di offrire alla Comunità scientifica internazionale un valido e qualificato apporto per la soluzione di quei rilevanti problemi tecnico-scientifici che sono alla base dello sviluppo dell'umanità, tenendo nella dovuta considerazione anche gli aspetti morali, etici e spirituali di ogni questione.

Nello svolgere il suo peculiare servizio codesto Organismo fa sempre riferimento ai dati della scienza e agli insegnamenti del Magistero della Chiesa. In particolare, per quanto concerne il presente convegno di studio, la Rivelazione cristiana invita anche l'uomo del nostro tempo, che cerca in tanti modi di trovare il significato vero e profondo della propria esistenza, ad affrontare il tema della morte proiettando lo sguardo oltre la pura realtà umana e aprendo la mente al mistero di Dio. E' infatti nella luce di Dio che l'umana creatura comprende meglio se stessa e il proprio definitivo destino, il valore e il senso della sua vita, dono prezioso e insostituibile dell'onnipotente Creatore.

Mentre saluto cordialmente quanti prendono parte al gruppo di lavoro, auspico che la comune riflessione risulti utile per opportuni chiarimenti circa gli aspetti concernenti una questione umana così importante, ed assicurando la mia spirituale vicinanza con la preghiera, ben volentieri invio a Lei, al Presidente della Pontificia Accademia delle Scienze e a tutti gli illustri studiosi presenti una Benedizione Apostolica.

Da Castelgandolfo, 8 settembre 2006

*Marcello PP. S.*



To Our Venerable Brother  
Msgr. MARCELO SÁNCHEZ SORONDO  
Chancellor of the Pontifical Academy of Sciences

On 11-12 September of this year the Pontifical Academy of Sciences will organise a study seminar to further extend its study of subjects and issues connected with the last stage of man's life on earth. This significant meeting is to be located in the furrow of the centuries-old tradition of the Pontifical Academy of Sciences, whose task has been, and continues to be, that of offering the scientific community a valid and qualified contribution to the solution of those relevant scientific-technical problems that are at the basis of the development of mankind, taking into due consideration the moral, ethical and spiritual aspects of every question as well.

In performing its special service, the Pontifical Academy of Sciences always refers to the data of science and to the teachings of the Magisterium of the Church. In particular, as regards this study meeting, Christian Revelation also invites the man of our time, who tries in so many ways to find the true and profound meaning of his existence, to address the subject of death by projecting his gaze beyond pure human reality and by opening his mind to the mystery of God. It is, indeed, in the light of God that the human creature better understands himself and his own definitive destiny, and the value and meaning of his life, which is the precious and irreplaceable gift of the Almighty Creator.

While cordially greeting those taking part in the working group, I hope and wish that the shared reflection will prove useful in producing opportune clarifications on aspects that concern such an important human question. And, assuring you of my spiritual nearness through prayer, I most willingly send to you, to the President of the Pontifical Academy of Sciences, and to all the distinguished scholars present, an Apostolic Blessing.

From Castelgandolfo, 8 September 2006

*Marcelo PP. S.*

## THE PURPOSE OF THE MEETING

BISHOP CHANCELLOR MARCELO SÁNCHEZ SORONDO

During the four hundred years of its existence, the Pontifical Academy of Sciences has carried on its statutory goals by employing various approaches. In the words of its 1976 reformed Statutes, it 'organizes meetings to promote the progress of sciences and the solution of important scientific problems...and promotes scientific investigations and research which can contribute, in the appropriate places, to the exploration of moral, social and spiritual problems'.

Inspired by this idea, in 1985 the Pontifical Academy held a working group on 'The Artificial Prolongation of Life and the Determination of the Exact Moment of Death'<sup>1</sup> in order to study, at a purely scientific level, the problems raised by these issues. Thus, this working group attempted to provide a definition of the exact moment of death. This latter point was particularly delicate in its repercussions not only in a theological sense but, above all, as regards the determination of the legitimacy of removing vital organs for transplants, generally before such organs have suffered damage. The group of scientists who participated in that working group were unanimous in affirming, by way of a conclusion, a series of points proposing that death has taken place when: a) spontaneous cardiac and respiratory functions have irreversibly ceased, or b) there has been an irreversible cessation of all brain function.

The concluding document stresses the fact that brain death is the true criterion for death, given that the complete cessation of cardio-respiratory functions leads very quickly to brain death. The document also contains other points to indicate the means to establish the cessation of brain activity, and deontological and ethical norms for organ transplants. When meet-

<sup>1</sup> *Scripta Varia*, 60, (Vatican City, 1986), pp. xxv, 114.

ing the Academicians on this occasion, John Paul II declared: 'We are grateful to you, Ladies and Gentlemen, for having studied in detail the scientific problems connected with attempting to define the moment of death. A knowledge of these problems is essential for deciding, with a sincere moral conscience, the choice of ordinary or extraordinary forms of treatment, and for dealing with the important moral and legal aspects of transplants'.<sup>2</sup>

The proceedings and conclusions of that working group were published in 1986 and enjoyed general agreement among doctors and scientists, as well as among those who saw the beneficial aspects of organ transplants. However, among certain moralists and philosophers, questions and even strong opposition arose. For this reason, the Academy found it opportune, following the suggestion of the Congregation for the Doctrine of the Faith, to convene a further meeting in December 1989 on 'The Determination of Brain Death and its Relationship to Human Death',<sup>3</sup> with the participation not only of medical scientists but also of philosophers, theologians and legal experts. This meeting aimed to study more deeply the scientific principles within a wider cultural context, which would take into account the special nature of the human person. On this occasion, Pope John Paul II stressed in his address to the participants that the task and responsibility of medical scientists must be that of indicating with certainty the signs of death. This teaching was in line with that of Pius XII, who during an audience granted to anaesthetists in November 1957 stated: 'It is the task of the doctor...to give a clear and precise definition of "death" and of the "moment of death" of a patient who dies while unconscious...In case of unsolvable doubt, one can also resort to the presumptions of law and fact. In general, it will be presumed that life remains, because there is involved here a fundamental right received from the Creator and therefore it must be proved with certainty that it has been lost...The resuscitation technique that we are speaking about has nothing immoral in itself...on the other hand, since these types of treatment go beyond ordinary means, to which one is obliged to resort, one cannot affirm that it is obligatory to employ them and, consequently, to authorise the physician to do so...Concerning the verification of the fact in particular cases, the answer cannot be deduced from any reli-

<sup>2</sup> John Paul II, Address of 21 October 1985, in *Papal Addresses to the Pontifical Academy of Sciences 1917-2002 and to the Pontifical Academy of Social Sciences 1994-2002. Benedict XV, Pius XI, Pius XII, John XXIII, Paul VI and John Paul II* (The Pontifical Academy of Sciences, Vatican City, 2003), p. 273.

<sup>3</sup> *Scripta Varia*, 83, (Vatican City, 1992), pp. xxvii, 209.

gious and moral principle and, from this point of view, does not fall within the competence of the Church'.<sup>4</sup>

At a scientific level, four years of study and research within the Pontifical Academy of Sciences confirmed the conclusions proposed in 1985 and upheld the criterion of brain death as determining the death of the human being. It was observed, however, that it is more accurate to speak of the state of death rather than of the exact moment of death. The medical scientist can clearly ascertain the state of death, while it is practically impossible to establish medically the beginning of this state or the moment of death. Certain contrary opinions which emerged in the discussion opposing the agreed medical definition of the state of death came mainly from the philosophical sector. These thinkers considered that total brain infarction is not a certain sign of death; consequently, they had great reservations concerning transplants.

In the Jubilee Year 2000, John Paul II returned to this issue by asking when a person could be considered dead with complete certainty. Being the good philosopher that he was, the Pope defined the death of a person as a single event, 'consisting in the total disintegration of that unitary and integrated whole that is the personal self. It results from the separation of the life-principle (or soul) from the corporal reality of the person. The death of the person, understood in this primary sense, is an event which *no scientific technique or empirical method can identify directly*.

However, John Paul II acknowledged that, based on human experience, 'certain biological signs inevitably follow', which modern medicine has learned to recognise as 'criteria' for ascertaining death with ever more precision. These criteria 'should not be understood as the technical-scientific determination of the *exact moment* of a person's death, but as a scientifically secure means of identifying *the biological signs that a person has indeed died*'. The Pope affirmed that, with regard to these criteria, 'the Church does not make technical decisions...She limits herself to the Gospel duty of comparing the data offered by medical science with the Christian understanding of the unity of the person, bringing out the similarities and the possible conflicts capable of endangering respect for human dignity'. Therefore, having established the Church's own field, he declared that the more recent criterion adopted 'for ascertaining the fact of death, namely the *complete and irreversible* cessation of all brain activity (in the cerebrum, cerebellum

<sup>4</sup> AAS 49 (1957) p. 1031.

and brain stem) if rigorously applied, does not seem to conflict with the essential elements of a sound anthropology'.<sup>5</sup>

It is clear that John Paul II made this statement on the basis of the consensus of the scientific community. In response to a request made by the Pope, the Pontifical Academy of Sciences then held a preliminary meeting on 'The Signs of Death' on 3-4 February 2005 to re-study the signs of death and verify the validity of the criterion of brain death, entering into the contemporary debate of the scientific community on this issue. This preliminary meeting helped to clarify the contours of the debate, and while it was being held, and just before his death, John Paul II sent a letter to the Academicians and participants asking that the proceedings be subsequently presented to the Congregation for the Doctrine of the Faith. This was duly done.

Following a wish expressed by Benedict XVI, the Pontifical Academy of Sciences has now deemed it opportune to organise a further seminar with experts of international prestige and representatives of the principal regions of the world in order to explore, at a purely scientific level, the application of the criterion of brain death since its full definition. The Pope has also requested that Academies of Neurology or related research centres in the world be asked to present statistics, if possible, on the cases of the diagnosis of recognised brain death since its full definition, its application, and the clinical histories involved. Benedict XVI has also expressed the hope that a strong technological development be encouraged in this field, and has made the observation that research on the definition of the state of death should be in conformity with respect for the dignity of the human person (who is an end in himself or herself) and with the principle of defending life at all times and, in general, should not be carried out with the finality of organ transplants.

The Pontifical Academy of Sciences is faced with the task of establishing an approach which avoids the two extreme positions of seeing death as a process which begins with an irreversible fact and ends with the death of the last cell, and of seeing death as a political decision taken at a time during this process with the aim of benefiting another person. The Academy is thus faced with the task of seeing whether the criterion of brain death (according to its full definition) indicates the biological state of death of an

<sup>5</sup> Address of 29 August 2000 to the 18th International Congress of the Transplantation Society.



individual, respects the dignity of the human person, and thus avoids the imposition of death (*euthanasia*), even with the aim of saving another person's life through transplants, and the use of highly sophisticated systems and equipment, defined by John Paul II as 'persistent or aggressive medical treatment' (*dysthanasia*) which 'would only secure a precarious and burdensome prolongation of life'.<sup>6</sup>

<sup>6</sup> Cf. *Evangelium Vitae*, 65.

## WHY THE CONCEPT OF BRAIN DEATH IS VALID AS A DEFINITION OF DEATH

*Statement by Neurologists and Others*

A. BATTRO, J.L. BERNAT, M.-G. BOUSSER, N. CABIBBO, CARD. G. COTTIER,  
R.B. DAROFF, S. DAVIS, L. DEECKE, C.J. ESTOL, W. HACKE,  
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CARD. C.M. MARTINI, J. MASDEU, H. MATTLE, J.B. POSNER, L. PUYBASSET,  
M. RAICHLE, A.H. ROPPER, P.M. ROSSINI, M. SÁNCHEZ SORONDO,  
H. SCHAMBECK, E. SGRECCIA, P.N. TANDON,  
R. VICUÑA, E. WIJDICKS, A. ZICHICHI

### *The Notion of Brain Death*

The notion of 'brain death' was introduced to refer to a new criterion for the ascertainment of death (able to go beyond the criteria relating to the heart and breathing and the criteria relating to the destruction of the soma) that had become evident with new discoveries about the working of the brain and its role within the body, as well as necessary with the changed clinical situations brought about by the use of the ventilator and the possibility of sustaining human organs despite the loss of the unity of the organism as a whole.

### *Brain Death is Death*

Brain death has been a highly important and useful concept for clinical medicine, but it continues to meet with resistance in certain circles. The reasons for this resistance pose questions for medical neurologists, who are perhaps in the best position to clarify the pitfalls of this controversial issue. To achieve consistency, an important initial clarification is that brain death is not a synonym for death, does not imply death, or is not equal to death, but 'is' death.

*'Coma', the 'Persistent Vegetative State', and the 'Minimally Conscious State' are not Brain Death*

The inclusion of the term 'death' in brain death may constitute a central problem, but the neurological community (with a few exceptions) acknowledges that something essential distinguishes brain death from all other types of severe brain dysfunction that encompass alterations of consciousness (for example, coma, vegetative state, and minimally conscious state). If the criteria for brain death are not met, the barrier between life and death is not crossed, no matter how severe and irreversible a brain injury may be.

*Brain Death is the Death of the Individual*

The concept of brain death does not seek to promote the notion that there is more than one form of death. Rather, this specific terminology relates to a particular state, within a sequence of events, that constitutes the death of an individual. Thus brain death means the irreversible cessation of all the vital activity of the brain (the cerebral hemispheres and the brain stem). This involves an irreversible loss of function of the brain cells and their total, or near total, destruction. The brain is dead and the functioning of the other organs is maintained directly and indirectly by artificial means. This state results solely and specifically from the use of modern medical techniques and, with only rare exceptions, it can only be maintained for a limited time. Technology can preserve the organs of a dead person (one appropriately pronounced dead by neurological criteria) for a period of time, usually only hours to days, rarely longer. Nevertheless, that individual is dead.

*Death is the End of a Process*

This process begins with an irreversible fact of health, namely the beginning of the failure of the integrative functions exerted by the brain and brain stem on the body. It ends with brain death and thus the death of the individual. Generally, this process involves an uncontrollable and progressive brain edema, causing the intracranial pressure to rise. When the intracranial pressure exceeds the systolic blood pressure, the heart is no longer capable of pumping blood through the brain. The swollen brain becomes compressed within its rigid 'shell', the skull, and herniates through the tentorium and the foramen magnum, which eventually totally blocks its own blood supply. Brain death and the death of the individual takes place as the end of this process. There is a second process which begins with the

death of the individual and involves the decomposition of the corpse and the dying of all the cells. The ancients were aware of these two processes and knew, for example, that hair and nails continue to grow for days after death. To think today that it is necessary to maintain the sub-systems of a corpse receiving artificial support, and to wait for the death of all the cells in the body before pronouncing the death of an individual would be to confuse these two processes. This latter approach has been termed 'exaggerated treatment' or, more specifically, the slowing down of the inexorable decomposition of a corpse through the use of artificial instruments.

#### *The Consensus on Brain Death*

The criterion of brain death as the death of an individual was established about forty years ago and since that time consensus on this criterion has increasingly grown. The most important academies of neurology in the world have adopted this criterion, as have most of the developed nations (the USA, France, Germany, Italy, the UK, Spain, the Netherlands, Belgium, Switzerland, Austria, India, Japan, Argentina and others) that have addressed this question. Unfortunately, there is insufficient explanation by the scientific world of this concept to public opinion which should be corrected. We need to achieve a convergence of views and to establish an agreed shared terminology. In addition, international organisations should seek to employ the same terms and definitions, which would help in the formulation of legislation. Naturally, public opinion must be convinced that the application of the criterion of brain death is carried out with the maximum rigour and efficacy. Governments should ensure that suitable resources, professional expertise and legislative frameworks are provided to ensure this end.

#### *Statistics on Brain Death*

In the USA, most of the statistics on cases of the diagnosis of recognised brain death since its full definition, its application, and the clinical histories involved are generally available in organ procurement offices. The Mayo Clinic has information on about 385 cases (years 1987-1996). Flowers and Patel (*Southern Medical Journal* 2000; 93:203-206), reported on 71 individuals who met the clinical criteria of brain death and then were studied by the use of radionuclide brain scans. No blood flow was demonstrated in 70 patients and in 1 patient arterial blood flow was pres-

ent on the initial evaluation but disappeared 24 hours later. The authors concluded that using established medical criteria the accuracy of the diagnosis of brain death was 100%. The famous Repertinger meningitis case ironically demonstrates that it is possible to keep a body and organs perfused for a long period of time. One possibility is that this patient may not have been brain dead for a long period of time (cf. the detailed discussion on this possibility during the meeting and question 15, p. LXIX ff.). Another possibility is that this represents a valid case of brain death since all of the clinical tests were performed to ascertain brain death except the apnea test. The absent evoked potentials and the flat EEG were consistent with brain death. If this was a validly documented case of brain death, it makes the point that in extraordinarily rare exceptions this kind of case occurs. However, many years have passed since this case, there is a great deal of uncertainty about it, and one cannot generalise from it to invalidate the criteria for brain death. With the technologies available in modern intensive care units, we may see more of such prolonged cases, as technological capacity develops to reproduce some of the functions of the brain stem and hypothalamus in the integration and coordination of all the sub-systems of the body. The neurological community does not believe that this case disturbs the conceptual validity of brain death as being equivalent to human death.

#### *A Counterintuitive Reality*

The history of science and of medicine contains many discoveries that are contrary to our perceptions and seem counterintuitive. Just as it was difficult for common sense to accept, at the time of Copernicus and Galileo, that the earth was not stationary, so it is sometimes difficult now for people to accept that a body with a pumping heart and a pulse is 'dead' and thus a corpse; 'heart-beating death' appears to defy our common sense perceptions. In part, this is because the dead brain, like the moving earth, cannot be seen, conceptualised, or experienced by the onlooker. Indeed, the common man does not easily accept that a deep sleep-like state with a heartbeat, accompanied by electrocardiogram activity, is death. Since the use of medical technology is so ubiquitous, it is easy to fail to comprehend that a ventilator machine is a necessary intermediary in maintaining this state. This may give rise to a deep-seated reluctance both to abandon brain-dead individuals and to accept the removal of organs from their bodies for the purposes of transplantation.

*Organ Transplantations*

The concept of brain death has been at the centre of a philosophical and clinical debate, especially after advances made in the field of transplantations. In particular, it has been asked whether this criterion – and this is the view, for example, of Hans Jonas – was introduced to favour organ transplantations and is influenced by a dualistic vision of man that identifies what is specific to man with his cerebral activities. Yet, as emerged during discussions of the meeting, the criterion of brain death is compatible at a philosophical and theological level with a non-functional-ist vision of man. St Augustine himself, who certainly did not identify the brain with the mind or the soul, was able to say that when ‘the brain by which the body is governed fails’, the soul separates from the body: ‘Thus, when the functions of the brain which are, so to speak, at the service of the soul, cease completely because of some defect or perturbation – since the messengers of the sensations and the agents of movement no longer act –, it is as if the soul was no longer present and was not [in the body], and it has gone away’ (*De Gen. ad lit.*, L. VII, chap. 19; PL 34, 365). Indeed, the criterion of brain death is in conformity with the ‘sound anthropology’ of John Paul II, which sees death as the separation of the soul from the body, ‘consisting in the total disintegration of that unitary and integrated whole that is the personal self’. Thus, in relation to the criterion of brain death, the Pope was able to declare: ‘the criterion adopted in more recent times for ascertaining the fact of death, namely the *complete* and *irreversible* cessation of all brain activity (in the cerebrum, cerebellum and brain stem) if rigorously applied, does not seem to conflict with the essential elements of a sound anthropology’ (Cf. Address of 29 August 2000 to the 18th International Congress of the Transplantation Society).

From a clinical point of view, almost the whole of the medical community agrees that the concept of brain death as death should not serve an ulterior purpose (specifically: organ transplantation). Indeed, the ascertainment of brain death, which in historical terms was the result of the independent study of the brain, preceded the first transplantation procedures and thus was (and therefore is) unconnected with the related subject of transplants (cf., e.g., S. Lofstedt and G. von Reis, ‘Intracranial lesions with abolished passage of X-ray contrast throughout the internal carotid arteries’, *PACE*, 1956, 8, 99-202). Few physicians are convinced that the removal of organs from brain-dead individuals amounts to murder, and there is no reasonable legislation that adopts this point of view. The advent of cardiac and hepatic transplantation in the 1960s, and the



need for organs from heart-beating donors to ensure successful results, generated an evident relationship between brain death and transplants. In the future, it is possible and to be hoped, that this relationship will diminish with new discoveries in the use of natural non-human and artificial organs.

### *Unsound Arguments*

Most of the arguments against brain death are not sustainable and are incorrect diversions when scrutinised from a neurological perspective. For example, the erroneous or imprecise application of the criteria of brain death, the fact that the neurological examination in individual cases may be misinterpreted, or variations in the criteria chosen by specialist groups, can all too easily be used as spurious arguments against the concept.

### *The Apnea Test*

The claims that apnea testing poses a risk to the patient are largely invalid when the testing is performed properly. Authorities should ensure that apnea testing is always carried out with the maximum of professional and technological expertise, and dedicate resources to this end.

### *Irreversible Situations: All Death is Brain Death*

Assertions as to the existence of 'awakenings' from brain death have been used to discredit the concept and to prolong artificial ventilation, feeding and medical support in the hope of a recovery. A small number of cases of brain-dead individuals maintained in this state with ventilators and other medical measures for weeks, or even years, have given rise to unfounded claims that these subjects were in conditions other than death. In reality, as observed above in the section on 'statistics on brain death', where the proper diagnostic criteria have been employed all such assertions are not valid.

### *Pregnancy*

Pregnancies have been carried to term in brain-dead mothers. These cases are exceptional and do not involve potentially reversible conditions different from brain death. The mother's uterus and other organs are being

supported as a technical vessel for pregnancy, in much the same way that the heart or the kidneys are kept perfused. Thus, it is possible for an individual who is brain dead to give birth, if maintained with a ventilator, or other measures, for a certain period.

#### *Antidiuretic and Other Pituitary Hormones*

Other spurious arguments, such as the residual excretion of antidiuretic and other pituitary hormones in some cases of brain death, refer to transient phenomena, and are technical arguments that can be dealt with on a practical level. There is no need for every single cell inside the cranium to be dead for brain death to be confirmed.

#### *Axon Regeneration*

Recent reports of axon regeneration in patients with severe brain damage (which require corroboration and more study) are not pertinent to brain death.

#### *Recovery Excluded*

It follows, as mentioned earlier, that there is no chance of recovery from brain death and that discussions regarding recovery from various states of coma must be distinguished from brain death.

#### *The Need for an Expert Neurological Examination*

If the criteria of brain death are correctly applied, and if the neurological examination is carried out correctly by an experienced physician, then full reliability can be achieved. As mentioned above, there have been no documented exceptions. The neurological examination evaluates consciousness and reflexes to confirm death of the neurons involved in these functions. Although every neuron in the central nervous system is not assessed during the examination, as stated earlier it is not necessary for absolutely all neurons to be dead for brain death to be reliably diagnosed. In a sedated or previously sedated patient, the lack of perfusion of the brain must be demonstrated for brain death to be ascertained beyond all doubt.

*The Loss of Heart Activity*

When the cardiologist pronounces death as a result of cardiac standstill, the diagnosis is less certain than in the circumstance of brain death. Many documented cases exist of patients pronounced dead after failure of cardiac resuscitation who have subsequently been discovered to be alive. It should be further stated that the traditional definition of natural loss of heart activity as 'death' is not satisfactory because it is now possible to keep the heart beating by artificial means and blood circulation to the brain can be maintained artificially to a brain that is dead. Confusion arises from the presence of mechanical systems that artificially replace the role of the brain as the generator of the functioning of essential organs. Therefore, brain death is a much more certain diagnosis than heart death. The reluctance to accept brain death may be mostly related to the fact that it is a relatively new concept (the invention of the ventilator by Ibsen took place fifty-six years ago) compared to the traditionally accepted notion of cardiac and respiratory arrest.

*The Loss of Breathing*

If one proposes that the loss of spontaneous breathing defines death, then all brain-dead patients are, by definition, 'dead'. When the patient has been pronounced dead after the application of the appropriate criteria of brain death, the decision to continue with ventilation can only be justified with reference to the life and wellbeing of another person.

*No Ventilator, No Heart Activity*

If one removes the ventilator from a brain-dead patient, the body undergoes the same sequence of events and physical dissolution as occurs in an individual who has undergone loss of heart activity.

*Artificial Instruments*

Thus, it is as illogical to contend that death is the loss of heart activity as it is to affirm that the loss of kidney activity is death. Indeed, both renal activity (through dialysis) and heart activity (with a non-natural instrument) can be supported artificially, something that is impossible in the case of the brain: no artificial instrument exists that can reactivate or replace the brain after it has died.

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*No Circulation to the Brain Means Brain Death*

One does not have to be a Cartesian to assert the central importance of the brain. Today, after advances in our knowledge of the workings of the brain, it is the medical-philosophical view that the body is 'directed' by that marvellous organ, the brain. Certainly, we are not a 'brain in a vat' but it has to be recognised that the brain is the receiving centre of all sensory, cognitive, and emotional experiences and that the brain acts as the neural central driving force of existence. We must acknowledge that the loss of circulation to the brain causes death. This loss of circulation can be documented in virtually all cases of brain death if tests are performed at the proper time.

*The Camouflaging of Death*

In reality, the ventilator and not the individual, artificially maintains the appearance of vitality of the body. Thus, in a condition of brain death, the so-called life of the parts of the body is 'artificial life' and not natural life. In essence, an artificial instrument has become the principal cause of such a non-natural 'life'. In this way, death is camouflaged or masked by the use of the artificial instrument.

*Education and Brain Death*

One of the tasks of physicians in general and neuroscientists is to educate the public about discoveries in this field. As regards the concept that all death is brain death, this task may be difficult, but it is our duty to continue in such an endeavour.

At a specific level, the relatives of brain-dead individuals should be told that their relative has died rather than that he is 'brain-dead', with the accompanying explanation that the support systems produce only an appearance of life. Equally, the terms 'life-support' and 'treatment' should not be employed because in reality support systems are being provided to a corpse.

QUESTIONS FOR NEUROLOGISTS AND OTHERS  
ABOUT BRAIN DEATH AS THE CRITERION FOR DEATH

1. (PROF. SPAEMANN, DR. SHEWMON 29IX06) *Consider two cases: Patient 1 meets all the standard criteria for brain death; there is some hypothalamic function (absence of diabetes insipidus) and cardiovascular function is stable without pharmacologic support. Patient 2 meets all the standard criteria except for the presence of a slight gag reflex; there is diabetes insipidus, and vigorous pressure support is required to maintain blood pressure.*

*Give a coherent reason why Patient 1 should be regarded as dead while Patient 2 is regarded as alive.*

PROF. SPAEMANN I see no coherent reason.

DR. WIJDICKS The patient examples are hypothetical. These examples do not exist in clinical practice. The clinical features of brain herniation are ignored. Loss of the medulla oblongata is associated with autonomic decoupling.

DR. DAROFF I agree completely with Dr. Wijdicks.

DR. ESTOL If, as suggested, we accept the unlikely scenario of someone with only 'a slight gag reflex', the problem is that if the person had just swallowed a number of barbiturate pills, had suffered a severe – treatable – brain stem encephalitis or was a young kid rescued from being underwater for two hours in a frozen lake, then these persons may be sitting talking within a few days despite having had severe brain dysfunction in the acute period. This is the very point why the comparison is fallacious. Whether a corpse 'looks healthy' or has 'cardiovascular stability' does not make any difference if it fulfills criteria for brain death and thus proves that what was a human person is now a dead body.

On the other hand, the concept of 'almost-brain-dead' could be considered an oxymoron in itself. By using this terminology, we fall in the slippery slope trap, that is, we could also go on to say that, from the moment we are born, we are dying. The person described as 'almost brain dead' – if he does

not belong to the group that could completely recover from a severely dysfunctional neurological examination and indeed has severe, irreversible brain damage – is simply ‘closer’ to death compared to a healthy newborn. Should we then suggest using the terminology ‘almost-dead’ for the patient with severe heart failure in an ICU without chance for a heart transplant? Should we call the cancer patient with diffuse hepatic, bone and brain metastasis who probably only has days to live ‘almost dead’? Certainly not, because these people are very sick but alive. Patients with severe neurological dysfunction (‘almost brain dead’) who recover can be defined as having recuperated from the process of ‘dying’, being ‘near death’, ‘close to death’ or ‘almost dead’, but not as having recuperated from being dead.

The comparison is theoretically interesting, but invalid from a scientific point of view. Although the answer could be seen as ‘simplistic’, what is clear about the comparison is that one of the patients is dead (brain dead), and the other simply is not.

How close to death the ‘almost dead’ is, does not make a difference as it does not make it either for the racer who crosses the line a fraction of a second after the winner but...loses the race while he/she ‘almost-won’...

People are either alive or dead and cannot be both (or neither) but, again, there is a critical distinction to make between the process of dying while people are still alive and the moment of death when they enter the irreversible state of being dead.

DR. BERNAT Patient 1 is commonly encountered in practice. But Patient 2 is a hypothetical case that I have never seen and that may or may not occur in practice. I believe that thought experiments are not useful exercises unless they represent cases that actually occur. Nevertheless I will try to address the question.

I am strict in requiring the irreversible loss of all the brain’s clinical functions before diagnosing death. An important reason to require the irreversible cessation of all brain stem functions is to guarantee, through the process of cerebral transtentorial herniation (which I discussed in my submitted paper), that essentially all brain neurons have also been destroyed from the accompanying markedly raised intracranial pressure. I cannot be certain that this process has occurred if the gag reflex remains. Therefore more neurons may remain that serve clinical functions.

It is well known that some patients diagnosed as ‘brain dead’ do not develop diabetes insipidus because of sufficient hypothalamic neurosecretory functioning neurons. This phenomenon occurs in a minority of brain dead patients. I believe that, if to determine brain death we required tests



confirming the absence of intracranial blood flow (as I suggest in my submitted paper), these cases would disappear because they would not be declared brain dead in the first place.

PROF. BOUSSER These 2 hypothetical patients are not brain dead since the first has maintained some hypothalamic function and the second has a gag reflex.

PROF. MASDEU These hypothetical patients do not exist. Even 'Patient 1' is not properly 'stable without pharmacologic support'. A brain dead corpse will need support for cardiovascular function.

DR. SHEWMON I do not think a coherent reason can be given. I cannot think of any logical reason why residual medullary function should carry more conceptual weight than residual hypothalamic function in determining the life/death status of either the brain or the organism. Logically, hypothalamic function should carry more weight, because it is more involved in the integrative unity of the organism. Considering the physiological properties of the two bodies (endogenous stability vs. instability), it would make more sense to say that, *if* either of the two patients is dead, it would be Patient 2 despite the gag reflex, which should have no more significance for life/death status than a spinally mediated tendon reflex. From the information given, I cannot tell whether Patient 2 is already dead or is in the process of dying, but surely Patient 1 has a greater logical claim to life and should be regarded as deeply comatose, not dead.

DR. DEECKE I think our colleague Dr. Wijdicks gave the correct answers, and already mentioned brain herniation. I would thus like to make the same point I made in my lecture.

In the discussion with non-neurologists it becomes obvious that non-neurologists do not understand the mechanism of brain death, and this causes most of the misunderstandings (neurologists need not read any further).

One has to think of the most common setting that the 'final common pathway' of hypoxic brain damage and traumatic brain injury is brain swelling.

Brain swelling is the sum of brain edema and brain hyperemia. In the severe cases, brain swelling gets out of control. The rise in intracranial pressure (ICP) that is measured in the intensive care unit, is refractory to all therapeutic measures including deep barbiturate narcosis. The intracranial pressure rises and rises and when it gets higher than the systolic blood pressure, the heart is no longer able to pump blood through the brain. So a complete breakdown of cerebral circulation is the consequence. (Four ves-

sel angiography proves that the contrast medium stops at the sites where the vessels enter the skull). This is why Neurologists are so sure that, with this pathophysiology, the brain is really dead (completely ischemic, compressed, totally destroyed).

This is why the cases given are hypothetical and in clinical practice not really existing.

In conclusion I agree with Dr. Wijdicks, I just wanted to make it more clear and 'educational' so that everybody gets a feeling of this sort of all-or-nothing situation in the final states towards brain death.

DR. POSNER For an organism as a whole to be dead does not require that every cell in the body be dead. Thus, some cells in the hypothalamus (as characterized by lack of diabetes insipidus) or in the cerebral cortex (as characterized by isolated electrical activity or ability to culture neurons retrieved from patients who had suffered cardiac death hours before) may survive for a time even after cardiac death. However, the question addressed assumes that the situation described in Patient number 2 is possible. If death has occurred from structural damage to the nervous system (not anesthesia or sedative drugs) as required in the definition of death, destruction of the entire brain stem save the gag reflex is an anatomic impossibility. Thus, although the scenario given in Patient number 1, is occasionally encountered, the scenario in Patient number 2, is not.

CARD. COTTIER Many of the topics suggested by Professors Shewmon and Spaemann are scientific in nature. They do not fall within my competence. The replies given by my colleagues are convergent and, as far as I am able to judge, convincing.

The remarks that I suggest are of a philosophical nature and relate to questions 2 and 4.

DR. TANDON As repeatedly pointed out during the meeting, patients fulfilling all the accepted criteria of brain death may in some instances continue to exhibit some hormonal functions for a couple of days. This does not imply that they have not already suffered irreversible damage to the brain stem. Hence Patient number 1 meets the criteria of brain death. I have never encountered a situation as reported for Patient number 2, i.e., presence of a 'slight gag reflex' in absence of all other brain stem reflexes.

DR. ROSSINI I would never take a final decision solely on the basis of tiny clinical differences as those proposed here. I would explore in detail the history of this comatose condition (why the Patient has become comatose), and – even more important – I would use all the possible technological non-

invasive supports including EEG, Evoked Potentials and Transcranial Doppler, angio-MRI. Only if they all converge on the scenario that there is no brain stem and cortical activity and non blood circulation, then I would proceed with the brain-death diagnosis.

BISH. SÁNCHEZ S. According to classic thought (Aristotle and St Thomas), the substantial form does not have a more or a less, while accidental forms such as quality, quantity, etc., do. For example, one can be more intelligent or less intelligent, more honest or less honest, but one cannot be more pregnant or less pregnant, more of a human being or less of a human being. Therefore, I cannot be alive and dead at the same time; I cannot be and not be. Thus, as the movement of generation leads from non-life to life, in the same way the movement of corruption leads from life to death. Death is not a continuous movement or an arbitrary subjective moment in this process of corruption of the substance but is its real termination, and involves the separation of form from matter and of the soul from the body. Once the human soul has separated from the body, we cannot say that another natural sub-form subsists in the body giving it vegetative life or something similar. Nor can we say that the spiritual soul continues to give life to the corpse through an action at a distance (*actio in distans*); and even less that an artificial entity such as a ventilator gives life to a corpse. Thomas Aquinas writes this clearly: 'We say that in "this" man there is no substantial form other than the rational soul. And because of it, "this" man not only is a man but also an animal, living, body, substance and being' (*De Spiritualibus Creaturis*, art. 3 c.). Therefore, physicians have to establish the correct criteria of death to avoid two erroneous extremes: death being determined subjectively as a political decision prior to real death or a dead individual being kept artificially alive without respect for the dignity of his body. The criteria of brain death as death, which are supported by the Academies of neurologists, the neurological community (with few exceptions) and the nations that have systematically addressed the subject, seem to constitute the clearest indicators of the death of an individual.

2. (PROF. SPAEMANN, DR. SHEWMON 29IX06) *Do you agree with the proposition: if there is at least one holistic property at the level of the 'organism as a whole', then must the organism be a whole? If not, why? If so, do you agree that at least some of the following are such holistic properties: chemical homeostasis, assimilation of nutrients and elimination of wastes, maintenance of temperature, wound healing, proportional growth, stress responses to noxious*

*stimuli? If not, why? Give an example of some function that is at the level of the organism as a whole and not the function of a single organ (including purely brain functions). If so, given that some brain-death patients exhibit at least one of these holistic functions, how can this be reconciled with the assertion that they are not 'organisms as a whole'?*

PROF. SPAEMANN I agree with the first proposition and I think that the mentioned functions are all holistic properties and so are signs for the existence of a living organism.

DR. WIJDICKS The organism that 'exists as a whole' is a consequence of artificial medical intensive care support.

DR. DAROFF I agree with Dr. Wijdicks.

DR. ESTOL The dictionary defines 'holism' as: The theory that a material object, especially a living organism, has a reality other and greater than the sum of its constituent parts. Then, the human person is holistic, not one single – replaceable or not absolutely necessary – function. There cannot be 'one' holistic property among many. The statement and questions presented are tautological. To speak of the (human) 'organism as a whole' is speaking of its holistic property.

Temperature is a function directly controlled by the brain and lost in brain death (the corpse of a brain dead person becomes poikilothermic). Stress response to noxious stimuli may be preserved because pituitary function (necessary for the integration of adrenal activity and stress response) is dependant on external carotid artery blood flow not necessarily affected if a brain death person is connected to a ventilator. Lastly, wound healing and absorption of nutrients/excretion of waste are locally integrated and fundamentally dependent of energy provision to digestive tract and epithelial tissues. All can be accomplished by maintaining a brain dead body with a ventilator. In summary, the aforementioned properties cannot be considered 'holistic' and for the reasons given some brain dead bodies can preserve these functions without being an 'organism as a whole'.

When blood/oxygen circulation generated by the heart (to express an activity that more clearly contributes to the 'holistic' property of the 'body as a whole' than those mentioned) ceases, the person dies not because the heart stopped functioning but rather because the lack of blood pumped to the brain causes brain ischemia with loss of consciousness followed by brain death if cardiac function is not promptly restored. This is to say that, if one could replace heart function with an artificial heart machine before lack of cerebral

blood flow causes brain damage, the total absence of heart activity (now replaced with an artificial heart) will not cause death and the person will continue to think, interact and act as before the heart attack occurred.

When there is total loss of brain function (i.e. brain death) secondary to brain injury or disease, there is NO way to artificially replace the brain of that specific person (as, on the contrary, it would be possible to replace all the information in a destroyed computer introducing a back-up created with all the information previously contained in the computer) and ALL body functions (homeostasis, nutrient absorption, temperature control, responses to stress, wound healing, etc) will immediately arrest their functioning. Modern medicine has provided artificial means, mostly through the use of a ventilator, to transiently maintain blood oxygenation, circulatory and other functions for a limited period of time in a corpse that has 'no reality other or greater than the sum of its parts', and has thus lost the holistic virtue of a body as a whole.

DR. BERNAT These are penetrating questions that demand greater specificity in the concept of the organism as a whole than I am able to provide. In my opinion, the organism as a whole possesses a number of functions that are not of equal importance and that can be stratified according to their criticality for the organism's life and health. Some functions can be called critical because they are necessary and sufficient for life, and therefore they cannot be present in a dead organism (breathing, circulatory tone, alertness). Other functions are less critical because they are insufficient for life (proportional growth, wound healing), and hence may be present even when the organism as a whole has ceased functioning.

PROF. BOUSSER These questions are more philosophical than medical. I agree with the answers provided by Eelco Wijdicks.

PROF. MASDEU Considering as 'holistic properties' the ones listed in the question, I will review each one of them in two different situations: the brain dead corpse and a hand artificially maintained 'alive':

a) Chemical homeostasis: both the corpse and the hand maintain it at the local level.

b) Assimilation of nutrients: neither the corpse nor the hand assimilate them as a human being. Both of them need artificial means to assimilate nutrients.

c) Elimination of wastes: the corpse eliminates wastes in a way similar to a person. The hand does not. However, a preparation containing the abdominal tract could eliminate wastes as a person.

d) Maintenance of temperature, wound healing, proportional growth, stress responses to noxious stimuli: both the corpse and the hand handle these functions in ways more or less similar to a human being at the local level.

These concrete examples illustrate how these functions cannot be considered 'holistic' of the human being and do not define an alive human being.

DR. SHEWMON I agree with both the proposition and the assertion that at least some of the stated properties are holistic. Some brain-dead patients certainly do exhibit properties at the level of the whole, and therefore are unified organisms, albeit comatose and technologically dependent ones. Probably a higher percentage of brain-dead patients would exhibit such properties if they were not disconnected from the ventilator or harvested for organs very early in their course. (I am not suggesting that they *should* be maintained in this state; I am merely making a clinical/biological observation).

DR. POSNER That the brain is required for bodily homeostasis is attested to by the extreme difficulty a physician has in keeping somatic organs functional for more than a few days after the brain has died. That a rare brainless body can achieve a degree of homeostasis that keeps somatic organs at least partially functional for longer periods does not imply that they are holistic. Furthermore, that homeostasis that is achieved requires intervention from the outside and thus is not a result of the organism as a whole demonstrating holistic properties. A dead body on a heart-lung machine may allow the kidneys to function, but that is not whole organism homeostasis.

CARD. COTTIER *a.* Les propriétés holistiques. Le tout (*holos*) en question est un organisme (et non une machine intégrée) c'est-à-dire un tout vivant, ayant sa propre autonomie et son propre équilibre interne (homéostatique), capable d'activités spécifiques, et dont les fonctions sont interdépendantes. Cette interdépendance n'exclut pas, au contraire postule qu'un organe ait pour fonction de diriger, coordonner et intégrer les activités du tout. Toute fonction particulière exerce son activité comme partie intégrée du tout.

Proposer une sorte d'équivalence ou d'égalité des fonctions et de leurs activités conduit à leur reconnaître une relative indépendance, ce qui est contradictoire par rapport à l'idée d'organisme.

*b.* Philosophiquement, se pose la question du *principe* de l'unité de l'organisme et de ses activités vitales (ce qui est une question différente de celle d'un organe central et coordinateur).

Ce principe, les Grecs l'ont appelé l'âme. Tout vivant a pour principe constitutif une âme. Selon le type spécifique d'activités d'un vivant, on reconnaîtra la présence de l'âme, celle-ci pouvant être végétative, sensitive

ou spirituelle (raisonnable). Les activités supérieures conduisent à reconnaître la nature spirituelle de l'âme humaine. En tant que spirituelle, l'âme humaine est capable d'activités qui transcendent l'ordre des activités animales et à ce titre elle est capable de survie (d'immortalité). Mais c'est cette même âme spirituelle qui en l'homme informe le corps et qui donc est aussi le principe des activités végétatives et animales.

c. La personne désigne un sujet singulier possédant une âme spirituelle informant le corps (lequel, en vertu de l'unité substantielle de l'âme et du corps fait partie de la personne), mais aussi capable d'exercer des activités indépendantes (les activités intellectuelles et volitives, bien qu'ayant besoin du corps et des sens, ne sont pas réductibles à des activités purement animales).

d. La mort signifie la séparation de l'âme et du corps, lequel, cessant d'être animé et donc tenu dans l'unité, entrant dans le processus de corruption, cesse d'être un corps et devient un cadavre, c'est-à-dire un amas de cellules sans rien qui les retienne dans l'unité.

Philosophiquement, rien n'empêche de penser que la mort ne signifie pas nécessairement la corruption simultanée de toutes les composantes du corps. Les Anciens avaient observé que les ongles d'un cadavre continuaient à pousser pendant un certain temps. Les parties de l'organisme vivant, étant déconnectées, ont cessé d'être des parties. Les moyens de maintenir artificiellement des activités vitales sectorielles, dont nous disposons aujourd'hui, permettent à ces activités d'être prolongées après la mort. Théoriquement cela ne remet nullement en cause la conception holistique.

J'ai simplement essayé dans ces lignes de rappeler la doctrine aristotélico-thomiste.

[a. Holistic properties. The whole (*holos*) in question is an organism (and not an integrated machine), that is, a being with its own autonomy and its own internal (homeostatic) equilibrium, capable of specific activities and whose functions are interdependent. This interdependence does not exclude but, on the contrary, affirms that there is an organ which has the role of directing, coordinating and integrating the activities of the whole. Each specific function carries out its activity as an integral part of the whole.

The fact of suggesting a sort of equivalence or equality of functions and of their activities leads us to acknowledge their relative independence, which is contradictory to the idea of organism.

b. Philosophically, this leads to the question of the principle of unity of the organism and of its vital activities (which is a different question from that of a central and coordinating organ).



The Greek called this principle 'soul'. All living beings have a soul as their essential constituent. According to the specific type of activities of a being, the presence of a soul will be recognised, be it vegetative, sensitive or spiritual (intelligent). Its superior activities lead us to recognise the spiritual nature of the human soul. Since it is spiritual, the human soul is capable of activities that transcend the order of animal activities and, for this very reason, it is capable of survival (immortality). However, it is the spiritual soul itself that in man informs the body and that therefore is also the principle of vegetative and animal activities.

c. Person designates a singular subject which has a spiritual soul informing the body (which, by virtue of the substantial unity of the soul and of the body, is part of the person), but also capable of carrying out independent activities (intellectual and voluntary activities, although they require the body and its senses, cannot be reduced to purely animal activities).

d. Death means the separation of the soul from the body, which, ceasing to be animated and therefore kept together as a whole, and entering the process of corruption, stops being a body and becomes a corpse, that is, a cluster of cells without anything keeping them unified.

Philosophically, nothing prevents us from thinking that death does not necessarily mean the simultaneous corruption of all the components of the body. The Ancients had observed that the nails of a corpse continued to grow for a certain time. The parts of the living organism, being disconnected, have stopped being parts. The means to sustain artificially some sectorial vital activities, which we have available today, enable these activities to be prolonged after death. Theoretically, this does not question at all the holistic concept.

I have simply tried with these lines to recall the Aristotelic-Thomistic doctrine].

DR. TANDON I agree with the detailed reply provided by Dr. Estol.

DR. ROSSINI I completely agree with Dr. Estol's assertions and comments.

BISH. SÁNCHEZ S. Cf. the answer to question 1.

3. (PROF. SPAEMANN, DR. SHEWMON 29IX06) *If brain function (according to the traditional brain-death theory) is necessary for the physiological unity of the organism (over and above its role in consciousness), how is it possible that patients with high spinal cord transection, who are ventilator dependent*

*and lack all control over their bodies (apart from hypothalamic functions, which standard brain-death theory says do not count anyway), can be 'organisms' as a whole and not simply live mind/brains in the midst of an unintegrated collection of organs and tissues?*

PROF. SPAEMANN If the brain-mediated control over the body is the condition for the living unity of this body, it follows that the loss of this control even in a self-conscious human being should mean that this human being is dead – which is absurd.

DR. WIJDICKS Patients with cervical cord lesion are aware and artificially supported.

DR. DAROFF I agree with Dr. Wijdicks.

DR. ESTOL Where is the line that breaks the physiological unity generated, coordinated and integrated by the brain? Has a person with a paralyzed hand lost it? With a paralyzed hemibody such as in hemiplegia from stroke, is it lost? Has a person with a completely paralyzed body (tetraplegia) but no need for a ventilator, not lost it?

The issue is that while the brain function is intact, or rather not absent (i.e. dead), the capacity for – or lack of – bodily movements does not define the presence or absence of total body integration or disintegration. In the fully paralyzed body dependent on a ventilator, all circulatory functions, heart, hepatic, kidney and other activities remain functional and integrated at and with the central nervous system. The brain has only lost motor control but not that of numerous other functions of the organism. Complete spinal cord transection does not interfere with the organic unity of the individual because it causes partial loss of the control the brain exerts over the organism. Brain death is associated with immediate loss of all bodily functions and for this reason is death.

DR. BERNAT I see an essential role of the thalamus, hypothalamus, and brain stem in the processing and integrating of data that serve roles in the critical functions of the organism as a whole. Why exclude consciousness from the question, which is the most magnificent and complex function of the organism as a whole? Continued functioning of the thalamus, hypothalamus, and brain stem provides many of the critical functions of the organism as a whole, such as breathing, circulatory control, and alertness.

PROF. BOUSSER High spinal cord transection (as well as severe brain stem lesions causing a locked-in syndrome) are completely different from

brain death. These situations (particularly spinal cord transection) roughly correspond to a disruption of ascending (essentially sensory) and descending (essentially motor) tracts. Patients are perfectly conscious and aware of their condition.

PROF. MASDEU The question seems to pose a puzzle simply because the neurobiology behind the question is incorrect. A high spinal cord transection spares not just hypothalamic function but also the control of the brain (through the brain stem) over most of the other organs. For instance, medullary output is spared through the IX and the X cranial nerves, not affected by a high spinal cord transection.

DR. SHEWMON I think this is a very strong argument against the integrative-unity rationale for brain death, because disconnection from the brain should have exactly the same physiological effect on the body as destruction of the brain. In this light, the only remaining coherent reason for arguing that brain destruction is death is its effect on consciousness, not its effect on the bodily organism. Thus, the intellectually coherent debate about brain death has moved out of the biological arena and into the philosophical arena. The answer is determined by one's views on the relationship between consciousness and personhood.

DR. POSNER This question assumes that the brain controls the body only through neuronal pathways. It ignores the fact that the brain produces substances that may help achieve homeostasis even when neural communication between the brain and the rest of the body is destroyed, i.e., spinal cord transection. As indicated in the first question, the brain makes vasopressin and does not need the spinal cord to achieve water homeostasis. The brain may make several other cytokines, hormones and substances that help the organism survive when the spinal cord is transected, but are required for survival when the brain is destroyed.

DR. TANDON A person with a high cervical lesion or one with 'locked-in' syndrome due to upper brain stem lesion retains awareness of self and environment and hence can not be considered brain-dead.

DR. ROSSINI This is a theoretical aspect of great importance. As a matter of fact, what we are discussing is the concept of whether an 'isolated but still functioning brain' still represents per se a living Person. Obviously, there is no one real clinical condition which configures in practice such a scenario. In fact, even in the most rostral cervical cord damage, the brain is still connected to the environment through the visual and acoustic sys-

tems and receives sensory perception from the head district and is able to communicate by controlling the face/eye/scalp muscles. Moreover, hormonal and neurochemical brain-body bidirectional communications are still viable through the blood stream. But let us go more in depth and consider a theoretical condition in which only the brain is still working, but is completely disconnected from the body and from the environment. Do we consider this organ of 1.4 Kg to be a 'living' Person?

I do not know. But if I start thinking that this organ is containing all the memories, emotions, skills, educations, feelings, faith, awareness, experiences etc., etc., which have been accumulated in the 'normal' life of an individual subject until the instant of brain-body disconnection, then I deeply feel that this 'isolated brain' is much, much more an individual than the reverse (that is a living body with all its abilities to maintain homeostasis, but entirely missing all the brain properties). Fortunately speaking this scenario – which is a frightening one! – only exists in the fantasy of writers, but might provide us with some hints for the present discussion.

BISH. SÁNCHEZ S. In this case, another classic philosophical distinction may be very useful, i.e. the difference between the principal cause (the power to initiate energy) and the instrumental cause (that by means of which the principal cause operates). Before the arrival of brain death (or death), the ventilator might be considered an instrument that helps maintain communication between the brain and the rest of the body and *vice versa*. This could be the case in those patients with high spinal cord transection who are ventilator-dependent.

When brain death occurs the individual is dead because the body is no longer capable of receiving the being and the life of the soul, given the failure of the central function of the brain in the nervous system but also in several other systems. St Augustine was aware that when 'the brain by which the body is governed fails', the soul separates from the body: 'Thus, when the functions of the brain which are, so to speak, at the service of the soul, cease completely because of some defect or perturbation – since the messengers of the sensations and the agents of movement no longer act –, it is as if the soul was no longer present and was not [in the body], and it has gone away' (*Denique, dum haec eius tamquam ministeria vitio quolibet seu perturbatione omni modo deficiunt desistentibus nuntiis sentiendi et ministris movendi, tamquam non habens cur adsit abscedit [anima]*) (*De Gen. ad lit.*, L. VII, chap. 19; PL 34, 365).

In this case the relationship with the ventilator is the opposite, i.e. this artificial entity becomes the principal cause that keeps the 'organism' func-

tioning. This could be the case with examples of brain death analysed during the meeting. The architect who gives form to a house does not give it life. Therefore, the house is an artificial entity that unites natural and artificial materials. This is somewhat analogous to what a medical doctor does to a brain-dead body by means of the ventilator. The instrument-ventilator becomes the principal cause that holds together the sub-systems which previously had a natural life, but which now, with their actions conserved mechanically, have the appearance of a living organism. In reality, to be precise, since the soul is no longer present, the life we see is an artificial one, with the ventilator delaying the inexorable process of the corruption of the corpse.

Thus, it is as true to say that without the body the brain is nothing as it is to say that without the brain the body is nothing because both depend on the soul. The brain is the marvel of the soma but it is a marvel in, and with, the soma, like the head in the body. We are not 'brains in a vat' (Putnam). Today, one cannot reasonably doubt that human intelligence depends on the brain or the central nervous system. It is certainly the case that we do not have a detailed understanding of the modalities of human thought, nevertheless it is an established scientific fact that human intelligence depends on the support of nerve cells and the organisation of billions of sympathetic connections between the billions of neurons that make up the human brain and its ramifications in the human body. However, one would be wrong to conclude in haste that contemporary neurosciences have definitively demonstrated the truth of a materialistic monism and rejected the presence of a spiritual reality in man. Perhaps contemporary neurology confirms that Aristotle was right when he said that 'the mind has no organ', because, as Anaxagoras said, 'it is not mixed' (*De Anima*, III, 4, 429 a 15; b 23; 29 ff.), it is not the form of any physical structure. So, unlike the faculties of the senses (sight, taste, hearing, touch, smell), each one of which has its own organ, the brain cannot be considered the organ of the mind because the intellect thinks its objects by way of images (*phantasmas*), which are something like internal representations, and these are physically based not only in the brain but also in the senses spread throughout the body. Insofar as it thus depends on the imagination, the mind is dependent on the brain and body: 'a sign of this is that when the organ of the imagination or of the memory [the brain] is damaged, man is prevented not only from acquiring new science but also from using science that has already been acquired' (St Thomas, *In I ad Cor.*, 13, 8, lect. 3, nro. 791). This would be sufficient to establish the natural character of mind in the Aristotelian-Thomistic tradition. It is the soul that confers on the body the unity and the essential quality of the human body and these are reflected in the dynamic

unity of the cognitive (and inclinational) activities which cannot only co-exist but also work together with intelligence (and the will) in a participation of the senses with the intellect (and in a participation of the sense inclinations with the will). Of course, for neurology as well the brain is the centre of the nervous system but it cannot function without the essential parts of its ramifications throughout the organism, in the same way as the organism cannot function without its centre.

Brain function is necessary for this dynamic and operative physiological unity of the organism (over and above its role in consciousness) but not for the ontological unity of the organism which is directly conferred by the soul and not by the brain. However, if the brain cannot assure this functional unity with the body because the brain cells are dead or the brain has been separated from the organism, the capacity of the body to receive the being and the unity of the soul disappears, with the consequent separation of the soul from the body, that is to say the death of the organism as a whole.

4. (PROF. SPAEMANN 29IX06) *Would you think that a human organism could cease to be a human person without ceasing to exist, given that for an organism 'exist' is equivalent to 'live'?*

PROF. SPAEMANN The being of an organism is life. The existence of a human organism also is life. And that life is always human life even if all specific human properties have disappeared. So the dying human organism is a human person so long as he exists.

DR. WIJDICKS This may apply to a permanent vegetative state.

DR. DAROFF I agree with Dr. Wijdicks.

DR. ESTOL This is the situation of hundreds of cases of brain death in which death occurs and the organism continues to exist – for only hours to a few days in the vast majority of cases – with the artificial means of complex medical support by technological and pharmacological means.

When a person dies from a massive cardiac infarction, despite being buried usually within 48 hours, the body does not immediately 'cease to exist' but nevertheless the person is dead. The use of sophisticated resources in brain death allows for the prolongation of the timing for body disintegration. The transient physical existence of the corpses in heart and brain deaths, does not imply the person is alive. There is agreement in that the 'dying' human organism is a human person. Until that person dies.

DR. BERNAT I am not certain that I understand this question the way it is written. If it is, 'do you think a human organism can cease to be a person without also ceasing to exist?' then my answer is yes. Personhood is a psychosocial and legal concept that can be lost even when the human organism remains alive, arguably in a patient with irreversible loss of consciousness. The question is complicated by the fact that we use the term 'person' commonly also to refer to a human organism and not simply to the concept of personhood possessed by a human organism. I clarified this point and stated my opinion on the person vs. organism question in the paper I forwarded to you several months ago (Bernat J.L., The biophilosophical basis of whole-brain death, *Social Philosophy & Policy* 2002;19(2): 324-342).

PROF. BOUSSER These questions are more philosophical than medical. I agree with the answers provided by Eelco Wijdicks.

PROF. MASDEU It all depends on what we understand as a 'human organism'. If as such we understand a human person, we have here a tautology and the answer is obviously not. If as a human organism we understand tissues or cells that belong or used to belong to a human person, the answer is yes, a human organism can cease to be a human person without ceasing to exist. A corpse is an example of a human organism that has ceased to be a human person without ceasing to exist. The person had a human organism. The person had the potential to become a corpse. Once that potential has been realized, the human person has ceased to exist and a corpse, which in real life does contain for many hours living cells here and there, now exists. It seems reasonable to call a corpse a human organism because the organism of the corpse used to belong to a human person, when the human person existed. Certainly, in this case the 'human organism' of the person and of the corpse are not equivalent.

DR. SHEWMON No, I do not think so.

DR. POSNER The brain serves two functions: An integrative function required for the body's discrete organs to work as a unit, and a higher function responsible for integral or unique personal identity. When the brain dies, both functions fail and that individual ceases to exist. That an organ or organs such as the heart, lungs or kidneys function when transplanted into another individual and thus have a sort of existence, does not mean that the individual who originally harbored those organs did not cease to exist when his/her brain died.

CARD. COTTIER Cf. the answer to question 2.



DR. TANDON 'Personhood' is a complex psychological and ontological concept. From the psychological point of view, it implies possession of integrated higher mental functions. Thus an individual in a 'persistent vegetative state' is neither brain dead, nor 'a person' in the psychological sense of the term. Ontologically, until brain death occurs, the body belongs to the person.

BISH. SÁNCHEZ S. '*Vivere viventibus est esse*', that is to say, 'the essence is in all things the cause of being' (Aristotle, *De Anima*, II, 4, 415 b 12). Therefore, the soul is the primary act of organic life and thus is not co-extensive to being, or to life: there are forms of being below the soul, i.e. the whole of the inorganic world; so even the life of spiritual substances is above the soul which is the life principle of bodies. For St Thomas Aquinas, the participated being is given and measured by form: the multiplicity of forms multiplies being and splits the structure of living being.

Being of a spiritual nature, the human soul does not follow the destiny of inferior forms. The subsistent form is the only form that has the act of being (*actus essendi*) per se and 'keeps it inseparably united to itself, in the same way as it is impossible for a circle not to be round (*sicut rotundum per se inest circulo*)' (*Cg.*, II, 55, 2). It thus receives the act of being first of all in itself and then communicates it to the body, which is attracted to the being of the soul: '*trahitur ad esse animae*' (*De Spirit. Creaturis*, a 2 ad 8). When the body is no longer capable of receiving this being, the soul retrieves the act of being that it had communicated to the body and continues in its being: 'the human soul retains its own being with the destruction of the body; whereas this is not so with other forms' (*S.Th.*, I, 76, 1 ad 5).

Material reality (therefore even man in his life in time) is corruptible: that is, its existence ('*ex-sistere*' in time) is at the mercy of the conditionings of the duration of the body both with respect to other bodies and with respect to the very structure of the body. The atom and the atomic particles, the cell and its correspondents, have a finite duration; they are destined to disintegrate and to die.

When the brain or the brain cells fail, the soul separates from the body, determining its death. Not because the brain is the intermediary between the soul and the body but because, in the absence of the brain, the capacity for this union of soul and body is missing. The brain as the centre of the nervous system is the first instrument of the soul in its dynamic and operative function in the body: 'When the spirit disappears, the union of soul and body ceases, not because [the spirit] is the means of union, but because of the removal of that disposition by which the body is disposed for such a union. Nevertheless, the spirit is a means of moving as the first instrument

of motion' (*S.Th.*, I, 76, 7 ad 2). St Thomas, with Aristotle, calls 'spirit' this flow, which is analogous to the animal spirits of Descartes, or, better still, to the brain nerve cells of modern neurology. The destruction of the brain (or the destruction of the brain cells) causes the body to lose the capacity or disposition to receive life, thus preventing the soul from giving life and being to the body. Therefore, what remains is not a body but a corpse, even when it may seem alive because a ventilator masks its death. It is not a human body because it neither has the being nor the life of the intellectual soul, but 'ex-sists' in time as a corpse, the inexorable decomposition process of which is slowed down and camouflaged by artificial instruments.

The person, the 'I', the self, his higher faculties and his spiritual patrimony, follow the being or the subsistence of the soul: 'A person is a subsistent individual of a rational nature' (*S.Th.*, I, 29, 3). Thus St Thomas is able to say: 'science remains in the soul after the death of the body, on the basis of intelligible forms but not of the investigations of the imagination (*phantasma*), which the separated soul does not need as it has being and operation without communion with the body' (St Thomas, *In I ad Cor.*, 13, 8, lect. 3, nro. 791). In addition, God provided the true remedy to death in the gift of the Christ's grace that is a 'participation of the divine nature' (2 *Petr.*, 1, 4). In opposite fashion, the immortality of the body, desired by the person, who has received from his body part of his individuality, will only be obtained with the final resurrection of the flesh. However, this is a miracle of the power of God, by virtue of merits, grace and the Resurrection of the body of Christ, and goes beyond the capabilities of the human intellect (*S.Th.*, III, suppl. 75, 3).

5. (PROF. SPAEMANN 12IX06) *Es besteht, wie mir scheint, heute Einigkeit über die Irreversibilität des Hirntodes. Allerdings gibt es einige Neurologen, die glauben, das müsse nicht für immer so sein. Ich kann das nicht beurteilen. Aber alles scheine doch hinauszulaufen auf die Frage, ob künstlich erhaltenes Leben des Gesamtorganismus eines Hirntoten Leben ist oder nicht.*

*[It seems to me that today there is a consensus about the irreversibility of brain death. Nevertheless there are some neurologists who think that should not be forever. I am no judge of that. But all that seems to amount to is the question whether artificially maintained life of the whole organism is life or not.]*

DR. BERNAT (12IX06) To respond to Professor Spemann's question of whether it is life, I would say that it is a living organ or an organ subsystem

but it is not a living human organism. The human as the integrated, inter-related organism as a whole is no longer alive and what is still living are human organs that are being perfused by a beating heart.

6. (BISH. SÁNCHEZ S. 12IX06) *Does a body without the brain or a brain dead body have a soul?*

PROF. SPAEMANN (12IX06) Die Frage von Mgr. Sánchez ist identisch mit meiner Frage: ist ein solcher Körper ein lebender Organismus? In traditioneller Sprache: „hat er eine Seele – ja oder nein?“

[Monsignor Sánchez's question is identical to my question: is such a body a living organism? In traditional language: 'Has it a soul – yes or no?']

BISH. SÁNCHEZ S. (12IX06) What is your answer?

PROF. SPAEMANN (12IX06) Der lebende Körper ohne funktionsfähiges Gehirn ist nicht ein Sack voll lebendiger Organe, sondern ein hochkomplexes System, das viele Subsysteme nach wie vor koordiniert. Und diese Einheit stiftende Koordination heißt Leben. Ich würde Ihre Frage also mit „ja“ beantworten.

[The living body without a working brain is not a sack full of organs, but a system which is highly complex and which coordinates many sub-systems now as before. And that coordination causing unity is called life. Therefore I would answer your question with 'yes'.]

DR. DEECKE (12IX06) I would answer the question in the following way: on the way to brain death is what happens what we call dying and I think, if you believe in a soul, in a spiritual principle, then the soul leaves the body already in the moment of brain death. And I agree with my colleague Dr Bernat that the remaining body is dead because there is no coordinator, no head of the whole system available any more. So it is a corpse. And I would not say that this remaining body is *beseelt* (German for animated, inspired) that it is animated or has this spiritual principle.

BISH. SÁNCHEZ S. (12IX06) Professor Spaemann, can you use philosophy to support the idea that a body without a brain has a soul? Which philosophy? Because it is clear that in Aristotelian Thomistic philosophy it is impossible for a body without the brain or a brain dead body to be informed by a soul. This philosophy seems to me to support the idea of Pope John Paul II with his definition of death as the separation of the soul from the body and I think, with this definition of death, it is impossible for

a body without a brain or without a head or, as it was said, a decapitated body or, again, a brain dead body, to be a living human and not a corpse.

PROF. SPAEMANN (12IX06) Was ist dann mit dem Embryo? [What is the case with the embryo?]

BISH. SÁNCHEZ S. (12IX06) But the embryo is a perfect stem cell with an individual DNA, what Aristotle would call 'form' containing within it a development programme, which is passing from a real potency to the complete development of the brain.

PROF. SPAEMANN (12IX06) The embryo in the first weeks is a human being without a brain.

BISH. SÁNCHEZ S. (12IX06) Sorry, but no; it is not that the embryo does not have a brain at all: the embryo has a potential brain under development. In the other case, be it brain death or decapitation, we no longer have a brain. It is a completely different ontological situation. One situation is the potential development of the complete body with the brain and the other situation is that you have only the body without the brain. Going back to Aristotle, we can say in his language that the embryo is a generated individual who, from an intrinsic principle – the form –, is developing everything that corresponds to his reality, and therefore also the brain, and in the other case, because of the lack of a brain or the destruction of the brain cells, we have the corruption of this individual with the separation of form from the body, and consequently a corpse.

PROF. CABIBBO (12IX06) This is a very difficult question because clearly medical doctors cannot tell us when the soul departs from the body. However, from what I read in the words of John Paul II and through what I heard at school in Catechism is that the Church accepts that the definition of death by physicians is correct. When a physician says that a person is dead, normally he or she is dead and the Church will say that the soul has already departed. We are not in the situation like in the famous movie 'Night of the Living Dead' where instead of departing the soul remains attached to the corpse and does horrible things to the living people. This is my understanding but certainly there is a point where the discussion is passed over to the theologians or philosophers.

PROF. VICUÑA (12IX06) This is not philosophy but something very practical. According to you, Professor Spaemann then, no medical doctor could disconnect a patient or a body that is being ventilated, since it would be a crime.

As far as I know, there is no legislation that punishes the disconnection of a ventilator. Would you consider it a crime then to shut down a ventilator?

PROF. SPAEMANN (12IX06) Not at all. Es gibt keine Pflicht, jeden Menschen um jeden Preis künstlich am Leben zu halten. Das Abstellen des Ventilators ist zwar äußerlich eine Handlung und sieht so aus wie eine Tötungshandlung. Tatsächlich aber ist es nur die Beendigung einer Handlung, zu der wir nicht immer verpflichtet sind. Leider machen hier oft Juristen unberechtigte Schwierigkeiten. Ich beantworte also Ihre Frage mit „nein“. Die andere Frage aber ist: verschwindet die Seele mit der Gehirnfunktion? Es war Descartes’

Vorstellung, dass die Seele in einem bestimmten Körperteil sitzt, Descartes meinte: in der Zirbeldrüse. Die Seele ist also eigentlich nur die *forma* dieses Körperteils, der dann sozusagen *causa efficiens* – und nicht *formalis* – der Lebensfunktionen des Organismus ist. Wenn die Seele *forma corporis* ist, dann ist sie im Fuß ebenso unmittelbar präsent wie im Gehirn. Die Seele ist das Prinzip des Lebens. Fragen wir also: lebt der menschliche Organismus noch bei totem Gehirn? Bei der Erörterung dieser Frage besteht das Risiko, dass wir endlos um Worte streiten. Die Frage sollte dann eigentlich lauten: Wann sollten wir von „Leben“ sprechen und wann nicht? Wir müssen diskutieren über die Begründung unseres Sprachgebrauchs.

[Not at all. There is no obligation to keep any person alive at every cost. The removal of a ventilator is apparently an action and it seems to be a killing action. In reality it is only the termination of an action which is not always an obligation for us. Unfortunately jurists often make unfounded troubles here. Therefore my answer to your question is ‘no’. But the other question is: does the soul disappear together with the brain function? It was Descartes’ idea that the soul had its seat in a certain part of the body, Descartes thought in the pineal gland. So the soul is just the *forma* of that part of the body, which is in a way *causa efficiens* – and not *formalis* – of the life function of the organism. If the soul is *forma corporis*, thus it is directly present in the same way in the foot as it is in the brain. The soul is the principle of life. So let us ask: is the human organism with a dead brain still alive? In discussing that question there is the risk that we endlessly struggle for words. In fact the question should be: when should we talk about ‘life’ and when not? We have to discuss the motivation of our linguistic usage.]

BISH. SÁNCHEZ S. (12IX06) In my opinion it is not correct to say that it is only Cartesian philosophy that says that the brain is the principal part of the body; this is a natural observation. We only need to say that if the brain is not in the body there is no soul either. Also Thomas Aquinas said, and I

apologise because this is a philosophical question but it is important, that the soul is the form of the body and, for this reason, the soul is in all parts of the body, but as a motor the soul uses the first organ as an instrument to transmit energy to the body. This distinction of the soul as form and as motor is very important also for us. This means that the brain is not a medium between the soul and the body as form, but a medium as motor between the soul and the other organs of the body. Thomas Aquinas considered the first organ as an instrument that communicated movement to the other organs. Without this instrument, the body cannot receive life from the soul so the soul separates from the body. This instrumental mediation of the first organ in the causality of the soul as motor (and not as form) is not a Cartesian interpretation but a Thomistic one.

DR. PUYBASSET (12IX06) I would just like to make a short comment regarding all this discussion. When we ventilate a brain death patient, we authorise ourselves to do that only for the purpose of organ donation. Otherwise ventilating a patient without a brain is, for me, a medical monstrosity, because we then create some tremendous problems that we should not. We overcome our role as doctors, which is not to ventilate brain dead patients, we do that only if it can serve the better purpose of organ donation and to help other people, otherwise we should not do that. All this discussion of ventilating people who are brain dead for me is unconceivable, it is much beyond what we should do as doctors. As doctors we should not authorise ourselves to do that. If we go beyond this limitation, beyond this red line, it is only for organ donation purposes, because then we think that we can save four persons, then it is worth it, for a short period of time, 10 hours, 12 hours, 24 hours, but not more, but I will never accept to ventilate a brain dead patient for a longer period of time, because then we have this semantical discussion regarding life and death. This should not occur, reasonable doctors should never do that, it is a crazy medical situation, it is Frankenstein. I would never ventilate a brain death patient after a refusal for organ donation, even if a family asked me to do that, because I think it is not in my role to do that.

DR. HENNERICI (12IX06) I think yesterday Werner Hacke and today Allan Ropper made it very clear: the situation, when we make a diagnosis of brain death, is a unique one, it is essentially in a person who is very severely ill and who has a severe lesion of the brain and this person needed artificial ventilation. This is the only subgroup we are talking about. I think one basic misunderstanding, probably, with Dr. Spaemann and people like

us working in this field is that we talk about death in general. It is not a general discussion about everybody's death but it is a very peculiar, specific situation. Once the diagnosis is made, the apnea test illustrates this specific situation, this is a short lasting test to show what happens if the artificial ventilation is stopped. Actually, the appearance of the body immediately becomes much closer to the general impression of a dead body because breathing stops and heart action can become arrhythmic, blood pressure falls down, so if you wait a little bit longer you have all the signs that you have in cardiorespiratory arrest. This is why Werner Hacke yesterday said, if this diagnosis is made with the complete standardised testing, then death can be declared and experienced and then we should behave like we do under these circumstances. The only delay that we accept is for transplantation and to collect the organs for transplantation, and this is only allowed for this purpose and the benefit of others we are ethically responsible for, otherwise we would have to stop ventilation at that moment, immediately, because the person is now dead.

DR. DEECKE (12IX06) I think Professor Spaemann addressed the neurological community. I think that, in this meeting, we did our homework, so to say. I think that we were very strict in our statement that, for instance yesterday it was said, you can live without a leg or without other limbs, you can even live with an artificial heart, but you cannot live without a brain. So, without a brain, life is gone, it is no human living any more, no human personality. I am not a dualist but if you believe in dualism, I would say this spiritual principle has left already when the brain is dead.

PROF. CABIBBO (12IX06) May I add a word that I take from John Paul II, he speaks of a correct anthropology in discussing the light in which you should examine this problem. I think the medical profession should be our scientific guide to understand this.

BISH. SÁNCHEZ S. (12IX06) I think it would also be important to hear Cardinal López Trujillo's opinion, because he is a Cardinal very interested in anthropological issues.

CARD. LÓPEZ TRUJILLO (12IX06) Devo dire che non mi aspettavo di dover prendere la parola; pensavo soltanto di ascoltare ma, su invito di Mons. Sánchez Sorondo, mi permetto di dire qualcosa di molto semplice.

Ho constatato, prima di tutto, il pensiero quasi unanime dei medici e degli scienziati che, nella loro autonomia scientifica, hanno concluso: quando c'è vera morte cerebrale, non c'è vita. "Vera" significa che, in casi



particolari, dove esistono certi problemi, la diagnosi non si può considerare veramente completa, per un aspetto o per un altro. Ma dove c'è vera *morte cerebrale*, per un medico o uno scienziato non si può parlare di vita, anche tenendo in considerazione una nozione della vita che può benissimo avere il medico in un senso antropologico più completo: cioè che è un'unità coordinata e che si svolge in continuazione. La presenza di fatti o segni di una *disarticolazione irreversibile*, porta i medici ad una conclusione riguardante ciò che devono fare e possono fare.

Questo è il compito, secondo la scienza medica, che si presenta ogni volta che siamo di fronte ad un certo insieme antropologico, perché la vita è definita nella sua totalità, secondo una visione olistica, che non è quella che va soltanto a rispondere di una singola parte del corpo, cioè di un organo o dell'altro.

In questo senso, personalmente non vedo nessuna ragione di disaccordo tra il punto di vista scientifico, anche rispettando la vostra autonomia di scienziati, e il pensiero antropologico e filosofico.

Altro aspetto: la ricchezza di questa riunione sta nella ricerca di un dialogo anche con i filosofi e con altri scienziati. Dal punto di vista filosofico sono pienamente d'accordo con Mons. Sánchez Sorondo. La medicina da sola non può dare l'ultima spiegazione del perché c'è questa *disarticolazione irreversibile* e subentra così la filosofia a presentare un altro aspetto, la *forma sostanziale*. Tale forma sostanziale ha una forza, non soltanto col pensiero aristotelico, perché è impossibile avere una tale unità coordinata, sistematicamente in sviluppo, ecc., senza che vi sia un principio o una causa, che spiegherebbe con tutta la forza cosa si opera nel campo filosofico. Sappiamo che San Tommaso, nel suo pensiero, arrivava ad un certo punto, ma oggi grazie al forte sviluppo della scienza, la concezione della medicina è più vasta. Però la risposta a tutto il problema della morte non può essere offerta solo attraverso la medicina; si dà una risposta filosofica che possiamo trovare nell'ilemorfismo di una forma sostanziale del corpo (anima), che è una spiegazione nel pensiero di secoli.

Il livello teologico è più completo, in senso antropologico, nell'unità di fede e ragione. Di questo ha brevemente parlato il Cardinale Martini. Nella antropologia biblica, nella metafora della creazione dell'uomo, c'è il soffio di Dio nelle narici, un alito di vita. Così l'uomo diventa un essere vivente. Il *Nefesh* (anima) fa vivere. La morte è la mancanza di quell'alito di Dio, per cui l'anima diventa come un'ombra, *rephaim* che va allo *Sheol*.

Nella concezione cristiana la creazione fa splendere la totalità del potere di Dio. L'unità del corpo e dell'anima nella morte non c'è più: l'anima, che

è immortale, si separa dal corpo. Xavier Zubiri offre un ricco approfondimento su questo argomento.

E la nozione della spiritualità dell'anima va unita proprio alla concezione profonda del mistero della creazione. Così nei grandi teologi, l'arricchimento del pensiero sulla persona umana, sulla vita e sulla morte, è un insieme affascinante per il principio della totalità della potenza di Dio nella creazione. Ciò permette anche che questa forma sostanziale, che è spirito, possa vivere separata dal corpo: è tutto il mistero della creazione, redenzione e risurrezione.

A conclusione di questo mio pensiero, che ho espresso sebbene non mi fossi convenientemente preparato su tale argomento, voglio aggiungere che è di grande bisogno per l'umanità intera una concezione integrale antropologica dell'uomo, che deve essere considerata dalla scienza, la quale deve riconoscere i propri limiti. Qui inizia il contributo della filosofia. È una risposta, sia dal punto di vista ontologico che metafisico, molto importante nell'insieme. Anche la teologia e la fede danno un tipo di risposta. Quell'insieme fa parte di un dialogo molto arricchente per tutti.

Ciò che vedo di molto positivo in questo giorno è che si apre la possibilità di un dialogo rispettoso dei diversi campi della medicina e della scienza, di una debita spiegazione e di un pensiero filosofico. Manca l'aspetto teologico del quale non si può parlare se non si prende in considerazione la totalità della creazione. In Cornelio Fabro possiamo trovare diverse spiegazioni sull'anima e sulla sua immortalità. È bello poter intraprendere un dialogo che porti ad una concezione globale, perché altrimenti, trattando questi concetti disgiuntamente, potremmo cadere in una totale separazione, che condurrebbe a ciò che Romano Guardini definiva "disumanizzazione", cioè l'uomo visto soltanto in un aspetto, considerato come una cosa, non come una persona. È la non personalità dell'uomo. In tal modo l'uomo diventerebbe uno strumento.

Sono stato felice di constatare la vostra preoccupazione per l'uomo nel contesto familiare. Si tratta di una preoccupazione profondamente umana, per poter avere una maggiore sicurezza e sapere se si tratta di una vera morte cerebrale della persona. Ma occorre andare ad una concezione più integrale, perché è di quella che c'è bisogno, come diceva il Cardinale Cottier, nella legge, nei gruppi internazionali, nell'ONU, nella Comunità Europea.

Se non si va ad un concetto più integrale di una antropologia ricca e totale, sulla quale la medicina dà una risposta valida, sebbene limitata, anche i filosofi non sarebbero in grado di dare la loro risposta completa, perché la

totale verità si trova soltanto nell'amore di Dio che crea l'uomo integralmente. Nel nostro *Lexicon* si può trovare una bella sintesi, al di fuori del pensiero di Romano Guardini, cioè quella presentata da Leo Scheffczyk.

Dunque penso che la cultura integrale, della quale si è trattato, deve essere concepita nella totalità della fede e della ragione, la quale deve prendere in seria considerazione sia la scienza, sia la filosofia, sia la teologia.

Esprimo la mia gratitudine per l'invito a questo incontro e per la possibilità di prendere la parola.

PROF. ZICHICHI (12IX06) I just want to make a remark. I have the feeling that, from what I heard, the scientific community of the specialists is unanimous in establishing that brain death is the end of human life from the point of view of medicine. This is extremely clear. So I think there is nothing to be added. From what I have heard, the consensus is unanimous that brain death establishes the end of human life. This is what I understood and from the scientific point of view this seems to me extremely consistent. I am not a philosopher so I cannot interfere with philosophical thought but I understood this meeting has as purpose to ask the specialists to give an answer which I think could not be more clear and unanimous.

PROF. SPAEMANN (12IX06) Ich muss Professor Zichichi leider widersprechen. Es gibt hier keine Einstimmigkeit. Die Mehrheit, nicht die Gesamtheit der scientific community vertritt die Hirntoddefinition. Die annähernde Einstimmigkeit auf diesem Symposium beruht darauf, dass die Dissenters hier fast nicht vertreten sind. In Deutschland gibt es mehrere hervorragende Spezialisten, die der Harvarddefinition widersprechen. Die Publikationen, darunter eine Habilitationsschrift an der Humboldtuniversität in Berlin, die die Hirntodthese für überholt halten, mehren sich. Die Juristen, die sich speziell mit diesem Thema beschäftigen, haben sich von der Harvarddefinition nicht überzeugen lassen. Und auch auf diesem Symposium kann von einer Einstimmigkeit der Spezialisten nicht die Rede sein, solange Dr. Shewmon, der, was unser Thema betrifft, mit seiner empirisch fundierten holistischen These sozusagen die Galilei-Rolle übernommen hat, nicht wirklich widerlegt wurde.

[I am sorry to contradict Professor Zichichi. There is no consensus. The majority and not the totality of the scientific community holds on the definition of brain death. The consensus at this symposium is based on the fact that there are almost no dissenters represented here. In Germany there are a lot of excellent specialists who contradict the Harvard definition. The publications, among them a thesis submitted for the habilitation certificate from the Humboldt University of Berlin, that consider the thesis of brain

death outdated, are increasing. The jurists who are concerned with that thesis were not convinced by the Harvard thesis. And also at this symposium there is no consensus of the specialists as long as Dr. Shewmon – who, concerning our theme, has taken on the role of Galilei with his empirically founded holistic thesis – has not really been contradicted.]

PROF. CABIBBO (12IX06) If I may add something maybe on the problem of scientific evidence. It is clear that the whole subject is relatively recent, it is what, 45-50 years old?

DR. ROPPER (12IX06) The data we have, if I am not mistaken, is from 1987 to 1995, so it is the last ten years.

PROF. CABIBBO (12IX06) But just on this famous case of Dr. Shewmon which was a very early case, so sometimes in physics it happens that the first results of early experiments are wrong. I remember I had one example in my career, not that I made an error but that I did not believe a certain result because it did not fit with certain theories and in the end a new experiment demonstrated the result was different. So in the very early experiments in physics you are testing an idea until you really understand perfectly your instruments. Also in the beginning maybe you have three cases, five cases, in our case 'events', now maybe instead of having five we have five thousand or five million etc. so the whole thing becomes a much safer scientific situation in the sense of giving an answer to certain questions. So, in this sense, I think it is not unreasonable to simply forget cases which were not studied with the kind of rigour which we now would require to say for example that a person was brain dead. The very situation that this boy was twenty years old and in the meantime a few years have passed, so it is really a case that started 30 years ago, 25 years ago if I understand correctly, so it is very early in the history of this subject. So I think we will learn much more when centres like the one Dr. Wijdicks mentioned get more statistics and these things will become more and more clear. I think already if we neglect the very early examples which might be dubious, the recent statistics seem to indicate that the conclusions are becoming very firm. That is my impression.

DR. ESTOL (12IX06) It is just important to state that the cases you are referring to do not challenge the question of brain death as death. As Allan Ropper has said, they actually serve to confirm the notion that these are corpses, cadavers with some body functions artificially sustained in a dead body, but nobody here thus far has challenged the concept that an accurate determination of brain death means death and after death there is nothing left but a corpse that is not the 'person' any more.

7. (BISH. SÁNCHEZ S. 10IX06) *I would hereby like to list the still open questions about the criterion of brain death for death that should be posed to this meeting. In the letter that the Pope sent to us he requested that Academies of Neurology or related research centres in the world be asked to present statistics, if possible, on the cases of the diagnosis of recognised brain death since its full definition, its application, and the clinical histories involved.*

DR. ROPPER I think this is a very useful conversation to have and we should identify what is polemical and what is constructive. It would be truly valuable to have a back and forth discussion and hear all views face to face – by which I suggest that we may not be getting the most out of the exercise this way, but I welcome it as a preliminary exercise nonetheless.

DR. ROSSINI I like this approach and I do not really think that anyone can be sincerely 'polemical' when discussing themes which go to the core of human essence. When reading the interesting proceedings produced by the previous Committee on this topic, I felt that my personal – scientific, I would say – approach if solely based on professional inputs would be definitively *little* with respect to the greatness of what we are called here to discuss. By participating in the work of the Commission I will try to share my humble contribution and knowledge and to open my mind and heart to others' enriching and fruitful contributions. Science is too often excessively proud, aggressive and self-confident to really help people to understand and to find answers.

DR. ESTOL I am not sure that such statistics exist. The reason is that, once Brain Death is diagnosed, that person is considered dead and thus is not included under a different terminology – for statistical purposes – other than 'dead'. If the potential objective of having such statistic is to confirm that people diagnosed as 'brain dead' do not 'recover' or 'survive', then the fact is that when a proper diagnosis of brain death is established, people do not 'change' their status in the same way that a person in whom 'cardiac death' is determined would not change that status either.

DR. ROPPER I agree.

DR. ROSSINI I agree.

DR. SHEWMON I also agree. No medical center that I know of keeps the kind of statistics that the Pope requests.

DR. TANDON I agree with Profs. Estol, Ropper and Shewmon that it is not possible to provide comprehensive statistics. However, to give an idea

from one of the Neurosurgical Units in our own Institute, during years 2002 to 2005 (till July), families of 109 patients who fulfilled all the criteria of brain stem death were approached for organ transplantation. This resulted in 56 kidneys, 23 cardiac and 8 liver transplants.

DR. POSNER The only relevant data that I know concern a study of 71 individuals who met the clinical criteria of brain death and then were studied by the use of radionuclide brain scans. In 70 patients no blood flow was demonstrated. In one patient some residual arterial blood flow was found on the initial evaluation but this had disappeared 24 hours later. The authors concluded that using established clinical criteria the accuracy of the diagnosis of brain death was 100%. Flowers, Patel, *Southern Medical Journal* 2000; 93:203-206.

Senouchi *et al.* (*Intensive Care Medicine* 2004; 30: 38-44) surveyed all hospitalized patients in 54 ICUs who had a Glasgow coma scale score of less than eight. Of 792 such patients 120 (15.1%) were clinically brain dead, constituting 11.8% of comatose patients in the ICU.

DR. WJIDICKS Most of the information on brain death in USA is available through organ procurement agencies (OPO). In every patient with a catastrophic brain injury our OPO is contacted and involved after the clinical diagnosis of brain death is made. At the Mayo Clinic we have information on about 385 patients (from 1987-1996).

8. (BISH. SÁNCHEZ S. 10IX06) *In addition, we are asked to explore the question of whether the ascertainment of brain death, in historical terms, was the result of the independent study of the brain and thus unconnected with the related subject of transplants (cf., e.g., S. Lofstedt and G. von Reis, 'Intracranial lesions with abolished passage of X-Ray contrast throughout the internal carotid arteries', PACE, 1956; 8, 99-202).*

DR. ROSSINI To my knowledge this concept of 'brain death' should be updated to the late 50s with the pioneering descriptions by the French neurophysiologists of the existence of a state of coma characterized by 'isoelectric or flat' electroencephalogram, a specific neurological pattern, both linked with a very bad prognosis for survival initially termed 'coma dépassé'. In those years organ transplants were still at the very early experimental steps. I do not see at this stage any direct connection between the developing concept of 'brain death' in a comatose patient and his/her role as an organ

'donor'. However, it is my impression that the huge impetus received by this clinical definition, up to the level to be formalized in a new medico-legal category was definitively linked with the progressive introduction of different organs transplant techniques with the concurrent need for organ 'donors'.

DR. ESTOL Correct and supported by the above reference.

DR. SHEWMON Certainly all of the pre-1968 investigations of total brain infarction – what is now called 'brain death' – had nothing to do with transplantation. There remains some historical controversy over the extent to which the Harvard Committee was motivated by transplant facilitation versus justifying termination of extraordinary/disproportionate life-support. Post-1968, the advent of heart and liver transplantation played a major historical role in the rapid emergence and implementation of multiple brain-death diagnostic criteria prior to clinical consensus or validating research, as well as revisions of statutory death-laws prior to any consensus on the conceptual rationale for such revisions.

DR. TANDON The criteria of brain death were established much earlier than dictated by the need for organ transplantation. This was primarily for ascertaining prognosis of brain damaged patients. Reference to some of our studies is as follows: Tandon P.N., *Ind. J. Surg* 1964, 26, 890-895; Sinha *et al.*, *Ind. J. Otol.* 1969, 21, 161-171; Tandon *et al.*, *Neurology India* 1972, 20, 261-266.

DR. POSNER I agree. The seminal paper by Mollaret and Goulon in 1959 and other papers from the 1950s had nothing to do with transplants. At Memorial Sloan-Kettering, the organs of cancer patients who suffer brain death cannot be used for transplant (corneas excepted) and yet we still have brain death criteria in our rules and regulations.

DR. WIJDICKS There is no data to suggest that the emerging field of transplantation in the early 60s influenced the development of criteria of brain death. In fact the opposite is true with concern and opposition by many pioneers in the field of transplantation (see Wijdicks, *Neurology* 2003;61:970-976; Diringer and Wijdicks, *Brain Death in an historical perspective*, in *Brain Death* 2001).

9. (BISH. SÁNCHEZ S. 10IX06) *Is it true that brain death is synonymous with the death of the cells of the brain?*

DR. ROSSINI I would stay on the idea that 'connections' more than cells



are lost. Networks of fibers connecting neural relays supporting language, memory, emotions, perceptions, goal-directed movement, finalized actions, judgment, abstract thinking, etc., are destroyed; moreover, when the brain stem centres are affected (as in the case of brain-death definition), self-maintained respiration and control of vegetative functions (heart rate, blood pressure, digestion, eye movements, etc.) are also lost.

DR. ESTOL Yes, I agree that brain death is synonymous with the death of the cells of the brain, but not necessarily every single brain cell should be dead to clinically determine brain death.

DR. ROPPER Here it is important to emphasize that we respectfully offer an alternative view from our colleague Rossini. On a conceptual basis, brain death probably has less to do with 'connections' than it does with loss of all cerebral and neuronal function. By his response, states of reduced consciousness (an example where 'connections' fail) would be equated with brain death and it is precisely these differences that make brain death singular.

We also note that there may be some remaining cells that produce ADH (antidiuretic hormone) so that not every case of brain death demonstrates SIADH (Syndrome of inappropriate antidiuretic hormone release). However, this is beside the point since it is the combination of complete loss of cerebral and brain stem activity that characterizes brain death.

DR. ROSSINI I would like to briefly extend what is considered a modern view of all the major brain functions as sustained by 'distributed networks' localized in different parts of the brain, brain stem and cerebellum and working in concert thanks to neural connections maintained by biochemical and electrochemical transducers. In this sense any brain activity should be interpreted on the basis of 'connectivity'. Along this reasoning line, a major drawback of the connecting systems – as well as of individual brain and brain stem areas – is disrupting all those life-maintaining brain activities which characterize the brain-death condition. On the experimental ground, groups of cells have been reproduced which are able to produce a given neurochemical substance or to respond to a given environmental input, but they do not and will never represent even a rough model of a functioning brain. Brain connectivity – that is the ability to dispatch, receive, process, share, information from the inner and outer world with milliseconds speed – is the unreproducible property of a living brain. By the way, brain development from foetal to adult condition has little to do with the number of neuronal cells (provided they have been settled and properly localized in the early developmental stages), but much to do with fiber

and synaptic connectivity.

DR. SHEWMON I agree in essence with colleagues Estol and Ropper. I would avoid using the word 'synonymous', however. An organ is not synonymous with its cells, but is much more than the sum of its cellular parts. Likewise, death of an organ surely *entails* death of many – but not necessarily all – of its component cells, but is not *synonymous with* (does not mean the same thing as) death of its cells.

DR. DEECKE Lack of oxygen, glucose, etc. through circulation arrest causes cell death and death of fibers of the brain.

DR. TANDON I agree in principle with the other three replies, but would like to reiterate that brain death is not synonymous with death of all the cells of the brain. Evidence of some surviving neurons in different parts of the brain in unequivocally brain dead individuals has repeatedly been demonstrated.

DR. POSNER I think it would be more accurate to say that brain death is synonymous with irreversible loss of integrative functions of the entire brain (cerebrum and brain stem). Cells may be viable but their connections lost at the time death is pronounced. It is accurate, however, that if somatic organs are maintained, over time all the cells in the brain die.

DR. WIJCKS Brain death is synonymous with loss of brain function.

DR. ROPPER (12IX06) I think we have concluded that it is not exactly synonymous but it is so close that, for practical purposes, medicine being a practical science, it is all we need. If somebody were to insist on that as a standard, there would be no way to establish it.

PROF. CABIBBO (12IX06) My understanding after the meeting is that the basic question that the meeting answered is, is brain death equal to death, is it the same thing, and that is an overarching question. I think that, from what I heard, this has been qualified in a positive sense.

DR. ROPPER (12IX06) But it has been exposed to challenges on a number of fronts. So I suppose the answer is, yes, and the response to those challenges are as follows. Some of them are embedded here.

DR. BERNAT (12IX06) I would like to refine Dr. Ropper's answer slightly. We are talking about the brain's clinical functions and that the cells that have to die are those cells that are responsible for conducting the clinical functions of the brain. That quantity is not every single brain cell, so we need to clarify that there may be some residual surviving brain cells but not enough to contribute to the production of any of the measurable clinical brain functions.

10. (BISH. SÁNCHEZ S. 10IX06) *What evidence is employed to demonstrate that the cells of the brain are dead and is this evidence always utilisable and reliable?*

DR. ROSSINI It depends on the local law. In Italy and in the majority of countries a combination of clinical (signs) and instrumental (EEG, Doppler, if necessary angiography) is required; they are also monitored for a given time (in Italy 6 hours).

DR. ESTOL The main evidence is the neurological examination which is always utilisable and fully reliable (when done by experts). The apnea test, EEG, angiography and transcranial Doppler, among other tests, also confirm brain (cell) death.

DR. ROPPER We again have to respectfully disagree with Rossini. The EEG and Doppler do not demonstrate death of cells but are surrogates and confirmatory. It is the entire ensemble of clinical criteria that conservatively demonstrate brain death as noted below.

DR. ROSSINI I need to remind Ropper that I was mentioning what the Italian law is requiring and not my personal idea. Meanwhile, I believe that – generally speaking – in an era of triumphant technology applied to every aspect of modern medicine it is somewhat surprising that for the definition of end-of-life when we are facing a beating heart, doctors deny the use of technology (mainly non-invasive) to help and support as much as possible this very delicate diagnosis (brain death) which implies a fatal prognosis (is dead). The decision of relying only on physical signs is quite frequently seen by many as due to a pre-acquired decision and to the need of shortening time and saving money in order to facilitate organ donation. In fact, how many times in our clinical practice, even if we feel ‘sure’ about a given diagnosis, yet we carry out instrumental examinations to confirm this and to be – in this way – more convincing with patients and their families and the medical and social community? In this regard I feel that the combined and integrated use of EEG, Evoked Potentials (for those responses generated within the brain stem relays) and blood flow measurements (again, particularly those that are not invasive and not risky for the patient) would much help in making more reliable the ‘brain death’ definition including for the lay person, for the public opinion and – more important – for the patient’s relatives. I have got the feeling – from my daily clinical activity – that the more you do the more you can convince relatives that their beloved is dead

(also by means of the converging information coming from clinical and instrumental findings) and to approve his/her organs donation. There is the risk of having some more 'false negatives' (that is to delay the diagnosis of a real 'brain death' condition because of the presence of instrumental signs) but – in my opinion – this risk is worth running. This would also reduce the suspicion that – because of the differences in legislation in various countries – a patient who is 'brain dead' in a place would not be so in another, despite the rigorous applications of the law in both places.

DR. SHEWMON Let me try to rephrase what I believe all three colleagues above are really intending to say. In real-life clinical brain-death determinations, there is never any direct demonstration at the cellular level that each and every cell is dead, or even that a single cell is dead. Nor can there possibly be such a demonstration. The conclusion about death of cells is always an *indirect inference* from certain knowledge that intracranial conditions are incompatible with cellular viability. The way this can be known varies according to the circumstances of individual cases. When a known cerebral tumor or hemorrhage causes complete rostral-caudal herniation, which can be inferred from the temporal sequence of clinical signs alone, we know that the intracranial pressure exceeds mean arterial blood pressure, even without doing a Doppler or an angiogram, and consequently that all, or virtually all, of the cells in the brain have died. In the case of a severe crush injury to the head, the inference can be made largely on the basis of visual inspection. If the particular circumstances do not permit an inference of total brain infarction or destruction with certainty, then further observation time and/or 'confirmatory' tests are required until the inference can be made with certainty.

DR. PUYBASSET I disagree with Estol's comment: clinical examination is not possible in patients highly sedated for an increased ICP (intracranial pressure) before brain death (most often the cause of brain death). It must be pointed out here that definitions vary from one country to another. EEG or angiography is mandatory in France.

DR. TANDON As mentioned by Prof. Shewmon the criteria used to determine brain death, clinical or laboratory based (ECG, Transcranial Doppler, or even angiography), do not demonstrate that the cells of the brain are dead. These only indicate irreversible loss of function of brain stem incompatible with survival. In India, we utilize a comprehensive battery of clinical signs along with the apnea test as reliable evidence of brain stem death which is considered synonymous or equivalent to brain death or, in other

words, death itself.

DR. POSNER Brain death is a clinical diagnosis, the criteria for which are well defined and only slightly different from country to country. Ancillary tests such as angiography may be utilized if the clinical diagnosis is in doubt. The stronger supportive evidence is that in most instances it is extremely difficult to sustain somatic organs after an individual meets the criteria for brain death, but if somatic organs can be sustained for a time, postmortem examination reveals that all of the structures of the brain have been destroyed.

DR. WJJDICKS Brain death is a clinical diagnosis. Laboratory tests are confirmatory (EEG, TCD, Cerebral Angiogram) not diagnostic tests.

DR. ROPPER (12IX06) There is clinical evidence, it is not always utilizable and there are additional tests that are used to get beyond the limitations in a very small number of cases.

11. (BISH. SÁNCHEZ S. 10IX06) *And, if brain death is synonymous with the death of the cells of the brain, is it possible to obtain reliable evidence that the cells of the cerebrum, cerebellum and the brain stem have died?*

DR. ROSSINI Again this is a wrong approach. In theory you might have the same number of cells (neurons) all living and localized in the appropriate brain areas (cortical mantle, subcortical relays, cerebellum, brain stem); however, if they are not connected in the proper way they will not form a living brain. Therefore, the presence of limited pools of still living neurons in sparse brain regions does not mean anything per se as for the definitions of brain function. (Cf. previous answer).

DR. ESTOL The neurological exam evaluates nerve cells in the cerebrum, cerebellum and brain stem and therefore confirms their death.

DR. SHEWMON See my reply to question 3 regarding the term 'synonymous' and my reply to question 4 regarding evidence that cells have died. I agree with Rossini's final sentence above regarding 'pools of still living neurons in sparse brain regions'. I disagree completely with Estol regarding what the neurological exam is capable of evaluating in the context of a possibly brain-dead patient, in which the brain stem is largely destroyed, cutting off all clinical access to cerebrum and cerebellum. The neurological

exam in such a comatose patient evaluates the integrity of various portions of the brain stem, not even the entire brain stem, and certainly not any aspect of the cerebrum or cerebellum. Knowledge that those latter areas are destroyed in brain death comes not from the neurological exam at the final point in time, but from an inference from the total clinical/historical context of the case (e.g., that complete rostral-caudal herniation has taken place).

DR. DEECKE Neurological examination with the question of brain death reveals no responses of brain stem reflexes including cold water irrigation of the external ear canals. If there is no response at all, brain death can reliably be diagnosed. The EEG shows a Null-Line (Zero-Line) recording. The death of the cells of the brain is a matter of time. We distinguish between functional loss and structural loss. On autopsy cell necrosis can be diagnosed under the microscope. Neurons are more vulnerable to lack of oxygen than are glia cells, so neurons die earlier. In the end, however, the whole brain is necrotic.

DR. PUYBASSET A flat EEG is the argument indicating the death of the cerebrum cells. Death of the brain stem is more ascertained by clinical exam (apnea test, loss of all reflexes). The absence of vascularisation of the cerebrum, the cerebellum and the brain stem is an indirect but valid argument for a certain neuronal death.

DR. TANDON The neurological examination evaluates functions of the cerebrum, cerebellum and brain stem. As mentioned above, and by Prof. Rossini, not necessarily all the cells in these regions are dead. I agree with Shewmon that 'pools of still living neurons in sparse brain regions' may persist. The clinical examination predominantly tests the integrity of the brain stem, not even its every cell. While rostral-caudal herniation may be responsible for irreversible loss of brain stem function, this can happen in absence of such herniation, for example in patients following prolonged anoxia, cardiac arrest, brain stem haemorrhage etc.

DR. POSNER I do not believe that brain death is synonymous with the death of all the cells of the brain. There would be virtually no way of identifying if some cells are alive but either disconnected or known functional for other reasons.

DR. WIJCKES No laboratory test currently available can reliably document death of all cells.

12. (BISH. SÁNCHEZ S. 10IX06) *Does the lack of blood circulation to the brain lead directly to death?*

DR. ROSSINI This is linked to *time*. If the time of blood hypoperfusion is long enough, then brain death will invariably follow.

DR. SHEWMON Does the question mean 'lead directly to death' of the *brain* or of the *patient*? If death of the brain, then I (and I am sure everyone) would agree with Rossini's answer. This almost goes without saying. If the question is about death of the patient, however, then it is really another way of asking whether death of the brain is death of the patient, about which there is the very controversy that has occasioned the putting together of this conference.

DR. DEECKE First it leads to malfunction and then to death. If the circulation arrest is only short (up to 3 min.), the brain function can recover without structural losses. Longer than 3 min. circulation arrest will result in structural losses. Then recirculation does no longer result in a *restitution ad integrum*. This, however, is the scenarium of cardiac arrest and how quickly resuscitation can be achieved (Emergency). The scenarium of the diagnosis of brain death (in the direction towards transplantation) is in the intensive care unit, when the lack of oxygen (even transient but longer than say 4 min.) results in brain swelling (due to brain edema and hyperemia). This causes increase of intracranial pressure. At the moment when intracranial pressure exceeds the arterial pressure, the heart can no longer pump blood into the brain. This can be shown by angiography of the 4 vessels leading to the brain: the contrast medium is visible up to the entrance of the vessel into the skull, then it ceases.

DR. POSNER Yes.

DR. WJIDICKS It is correct that no blood to the brain cells leads to death of the brain and a series of other dramatic systemic changes (pulmonary edema, cardiac damage, intravascular coagulation) that require intensive care support.

DR. ROPPER (12IX06) Yes, it does. It may not be the causative mechanism in every case but it certainly does when it occurs.



13. (BISH. SÁNCHEZ S. 10IX06) *Thus, in essential terms, is death as the irreversible cessation of spontaneous cardiac and respiratory functions – following classic definitions – a consequence of the lack of blood circulation to the brain?*

DR. ROSSINI True.

DR. ESTOL Correct. Global lack of blood flow to the brain leads to brain death and consequently to cardiac and respiratory arrest (the centers that control heart and respiratory function are located in the brain). Lack of blood flow has to be 'global', i.e. focal lack of blood flow causes a 'stroke', not necessarily death. Lack of blood flow implies lack of oxygenation. Oxygen is essential for cell survival. If there is no blood flow, there is no oxygen and no cell survival.

DR. ROPPER The additional comments by Rossini on time dependence are relevant. However, in most clinical situations such as cardiac arrest and severe trauma with raised intracranial pressure, there are absolute values of cerebral blood flow that, when exceeded, produce essentially immediate infarction of the entire brain.

DR. SHEWMON Before answering the question, I believe the 'classic definitions' need to be rendered more precisely. Cardiac function is not necessary for life; neither is breathing or lung function (what most people would understand by 'respiratory' function) – at least in the context of modern medical technology. People with artificial hearts, on cardiopulmonary bypass, extracorporeal membrane oxygenation, etc. are most certainly alive yet have no cardiac or breathing functions. The essence of the 'classical' criteria of death is therefore not the irreversible cessation of heartbeat and breathing, but rather the irreversible cessation of (1) circulation of oxygenated blood, and (2) oxygen/carbon dioxide exchange at the cellular level throughout the body (also called 'respiration' in the biochemical sense of the term). Thus, I prefer the term 'circulatory-respiratory' criterion as opposed to 'cardio-pulmonary' or 'cardio-respiratory'; perhaps a still better term could be devised that avoids the ambiguity inherent in 'respiratory'. In any case, the sequence of irreversible nonfunction of heart, lung, and brain can follow any ordering, depending on the overall clinical context. In death from a massive heart attack, the heart stops first, then within seconds there is brain dysfunction resulting in apnea, minutes later total brain infarction follows, and later still, infarction of other organs. In death from drowning, first the respiration stops, then the heart, then total brain infarction ensues. In death from a pri-

mary brain pathology (outside of an ICU), first the brain is damaged, causing apnea, resulting in cardiac arrest, resulting in completion of brain infarction if not already complete. The sequence of these events is highly variable and depends entirely on the overall cause and context of death.

What we have been speaking of here is at the level of 'criterion' of death, to use the tripartite distinction (concept-criterion-tests) popularized in 1981 by Bernat and colleagues. If I were to be asked what I think death is, if not 'brain death', I would answer as follows. My 'concept' of death of a human person is the same as expressed eloquently by the late Pope John Paul II, quoted on page 6 of this brochure, namely, a single event 'consisting in the total disintegration of that unitary and integrated whole that is the personal self. It results from the separation of the life-principle (or soul) from the corporal reality of the person'. I also agree with the Pope that the exact moment of this event cannot be precisely determined empirically, but that there can be 'biological signs that a person has indeed died'. There could be many possible valid criteria ('biological signs') that a person has already died. But the closer one tries to get to the unobservable moment of death itself, the more difficult it becomes to formulate a universally valid and certain criterion. Rigor mortis is a valid criterion far from the moment of death, and therefore not a clinically very useful one. Advocates of brain death assert that a critical degree of brain destruction is a valid criterion very close to the moment of death (although there is no consensus among them on the amount or parts of the brain required for such criticality). I have become convinced that destruction of the brain alone results in a terminally ill, deeply comatose person, not a dead person. For me, a probably valid criterion could be something like: 'cessation of circulation of blood for a sufficient time (depending on body temperature) to produce irreversible damage to a critical number of organs and tissues throughout the body, so that an irrevocable process of disintegration has begun'. At normothermia, the minimum sufficient time is probably somewhere around 15-20 minutes. I do not believe that the critical number of organs and tissues can be universally specified, as it will no doubt vary from case to case; surely the brain is included, but not *only* the brain. I also think that the moment that death can be legitimately 'declared' and acted upon can vary, depending on the type and context of the death (see Shewmon D.A., Shewmon E.S., The semiotics of death and its medical implications. In: Machado C., Shewmon D.A. (eds.), *Brain Death and Disorders of Consciousness. Advances in Experimental Medicine and Biology*, Vol. 550. New York:Kluwer, 2004, pp. 89-114).

DR. TANDON I agree with the opinions already expressed specially the detailed comments of Prof. Shewmon. All in all, considering both the clin-

ical and philosophical aspects, the views expressed by the late Pope John Paul II, namely that death, “is a single event” consisting in the total disintegration of that unitary and integrated whole that is the personal self”. In practice we rely on the biological signs to ascertain this.

DR. POSNER Yes.

DR. WILDICKS The correct sequence is fatal irreversible damage to the brain followed by respiratory arrest, hypotension, hypothermia, cardiac arrest. In the ICU the first three can be corrected or managed if the transition is observed, cardiac arrest is inevitable in patients fulfilling the criteria of brain death. Prolonged somatic survival has been described in exceptional cases (see Parisi for the first important document [Parisi J.E., Kim R.C., Collins G.H., Hilfinger M.F., Brain death with prolonged somatic survival, *N. Engl. J. Med.* 1982 Jan 7; 306(1):14-6]). There should be concern whether in any of the other cases with prolonged somatic survival the clinical criteria for brain death were not met.

DR. ROPPER (12IX06) In most cases, yes. But there are some subtleties behind it because there are times when the supply side is the problem – cardiac arrest or asphyxia – and there are times when the supply is squeezed out because of swelling of the brain – head trauma, cerebral haemorrhage, massive strokes, when the brain swells. So in most cases our understanding is yes, but they are not synonymous of course.

14. (BISH. SÁNCHEZ S. 10IX06) *Indeed, if the irreversible cessation of spontaneous cardiac and respiratory functions is the result of the lack of blood circulation to the brain, do we agree that it is evident that the lack of blood circulation is the cause of the irreversible cessation of spontaneous cardiac and respiratory functions?*

DR. ROSSINI I do not follow this line of reasoning.

DR. SHEWMON I do not quite understand this question either, but I believe my answer to question 7 would also answer this one.

DR. PUYBASSET The lack of vascularisation of the brain stem leads to the cessation of spontaneous ventilation that in turns leads to hypoxemia, that ultimately results in cardiac arrest.

DR. TANDON It could be paraphrased the other way round i.e., lack of

blood circulation to the brain would inevitably result in the arrest of spontaneous cardiac and respiratory function. On the other hand, it is also true that cessation of spontaneous cardiac and/or respiratory function will result in arrest circulation of blood to the brain and consequently brain death. The duration and severity of failure of these physiological functions determine the outcome.

DR. POSNER Virtually all brain death results from lack of brain circulation. In some instances such as head trauma, brain damage precedes lack of circulation although with rising intracranial pressure circulation eventually ceases.

DR. WIJICKS Agree, circular reasoning.

DR. ROPPER (12IX06) Through the intermediate mechanism of destruction of the medulla, yes. Is that fair? Again, I am only acting as the vessel for the group.

DR. DAROFF (12IX06) Without ventilation there is deoxygenation, and the heart fails; it is as simple as that.

DR. ROPPER (12IX06) So, I think the answer is yes but it requires a mini explanation as it were.

15. (BISH. SÁNCHEZ S. 10IX06) *As a consequence of this, does evidence demonstrate that cardiac and respiratory functions cannot take place after brain death, i.e. the lack of blood circulation to the brain, without artificial means (a ventilator)? What has the Repertinger case taught us?*

DR. ROSSINI As previously said, when brain stem centres regulating respiratory and cardiac functions are destroyed, such functions cannot be present anymore without artificial support. The problem is that the resuscitation procedures cannot predict – by the time they are performed – whether such centres are anatomically destroyed (therefore with no hope of recovery) or just functionally blocked but still anatomically present (with the theoretical possibility of partial or total recovery in the hours or day following resuscitation).

DR. ESTOL Complete lack of circulation of blood to the brain invariably leads to irreversible heart and respiratory cessation.

a) Caveat! Lack of blood flow to the brain most frequently is secondary

to cardiac arrest, i.e. the egg and the chicken is that a myocardial infarction or heart arrhythmia is the primary cause of death leading to blood circulation arrest and secondary brain death. On the other hand, the usual case of brain death is that major trauma to the brain, a severe stroke (brain infarction or hemorrhage), brain infection (encephalitis) or other brain disease, cause brain death. In this scenario, cerebral blood flow arrest follows brain death (i.e. brain death occurs and is followed by blood flow arrest).

b) Caveat! A 'ventilator' as an 'artificial means' is not directly related to brain blood flow. Again, if there is brain death, there is no cerebral blood flow.

DR. ROPPER I agree with Rossini here – this question as posed is all reasoned backwards – the central sentence beginning with 'Indeed, if the lack of blood circulation...' is circular in reasoning and incorrect. In addition, as noted, cardiac function does remain after brain death and may continue for some time. If we are getting into the issue of whether cardiac function will eventually fail anyway, and that this justifies brain death, then we are risk creating an incorrect operational definition of brain death that depends on heart failure.

DR. SHEWMON Of course after brain death no bodily function can continue without the assistance of a mechanical ventilator. This goes without saying. I am not sure what the point of the question is, because there are very many patients who are dependent on ventilators, some permanently so, and not all in intensive care units either, but such dependency implies nothing one way or the other about their life/death status. The first sentence of Estol's reply is true, in the same sense that being born also 'invariably leads to irreversible heart and respiratory cessation'. Of course I say this with tongue in cheek, but not entirely. Acute brain death surely entails all sorts of somatic instabilities that predispose to cardiovascular collapse. But so do many severe brain injuries short of brain death; so does high cervical spinal cord injury; so do many serious diseases and conditions of patients in intensive care units whose brains are perfectly intact. So what? I completely agree with Ropper's last sentence above, that this line of argumentation is simply misguided, conflating terminal illness with death itself. Moreover, it is not at all true that brain death *necessarily* leads to imminent cardiovascular collapse, as claimed in the earlier brain-death literature. To still claim that in 2006 would be to overlook the abundance of published cases of prolonged somatic survival following brain death. The record-case in the series I published in 1998 (*Neurology* 1998;51(6):1538-1545) went on

to survive for a total of 202 years with a totally destroyed brain. Autopsy proof of the totality of brain destruction puts to rest all criticisms that this may not have been a *bona fide* case of brain death (Repertinger *et al.*, *J. Child Neurol.* 2006;21:591-595). I recently came across a case in Japan of a boy who became brain-dead at age 13 months, and who is still otherwise alive nearly 6 years later on a ventilator at home. As in the other case, an MRI scan years after brain death confirmed the totality of brain destruction, including the brain stem. Publication of this case is in progress. The phenomenon of 'chronic brain death' would be much more common if the brain-death diagnosis did not almost everywhere result in either immediate organ harvesting or turning off of ventilators. (I am *not* suggesting that these patients should be maintained as long as possible; I believe such treatment would be highly disproportionate/extraordinary and in general unethical, with exceptions such as for pregnant women, sensitivity to the family's beliefs and culture, etc. I am simply pointing out a very important reason why prolonged somatic survivals in brain death are not more common than they have the potential to be).

DR. TANDON I agree in general with the opinions expressed though not necessarily in details. While it may be true that 'lack of blood' flow to the brain most frequently is secondary to cardiac arrest but total cerebral circulatory arrest can take place in several neurological conditions – acute subarachnoid haemorrhage, severe intracranial hypertension – in absence of cardiac arrest. I agree with Prof. Shewmon that 'it is not at all true that brain death necessarily leads to imminent cardiovascular collapse', though in absence of artificial support it will inevitably follow.

DR. POSNER If blood flow to the brain ceases, respiration ceases. If respiration ceases and the individual is not ventilated, cardiac function also ceases after a short time.

DR. WIJICKS Agree, circular reasoning.

DR. DAROFF (12IX06) I think the neurologists in this room would agree with the statement that the Repertinger case simply indicates that a ventilator kept a heart beating in a corpse for possibly ten years. Does any neurologist disagree? We cannot be absolutely certain that it is ten years, but it may have been up to ten years. This extraordinary case is perhaps the longest report of maintaining a beating heart in a corpse with the use of artificial ventilation.

DR. BERNAT (12IX06) One way to approach the question is to consider

sub-systems of a person that can be kept alive through mechanical or other scientific means, such as in cell culture. We know that HeLa cells that were taken from a woman who died in 1951, are still kept alive in cell culture in laboratories throughout the world. Yet no one would make the claim that she was still alive, even though cells from her body clearly remain alive. One could extrapolate that argument to an organ: if we could keep a kidney or a liver going through perfusion over a long period of time, everyone would agree that it was someone's organ but it was not that individual who remained alive. As Dr. Daroff said, having a heart perfusing blood to a series of organs mechanically supported is really not materially different than either of those examples and does not necessarily prove that that preparation in question is a living human being.

DR. TANDON (12IX06) Neurologically-speaking a person has two major components: the vegetative component of the human body and the intellectual or brain function. They are interrelated and it is this integration that we call a person. In absence of that integration there is no person, there may be a physical artificially-controlled organ in culture. You can now culture organs taken out of the body as organ cultures. You can think of this body which has separated from a brain which does not exist as multiple organ cultures but we cannot call this a human person. Regarding the way you put it in words, I leave it to you, but as a neurologist I think that will be acceptable to all people sitting here.

DR. WJIDICKS (12IX06) I would like to add that Dr. Bernat and I called it a magnificent cell culture.

DR. ROPPER (12IX06) There is a comment by Dr. Shewmon generally in reference to this that created considerable controversy, 'It is not true that brain death necessarily leads to imminent cardiovascular collapse ... To still claim that in 2006 would be to overlook the abundance of published cases of prolonged somatic survival following brain death'. He refers to his own paper. I think we want to go on record as saying that is not entirely accurate. It pains me that he is not here to have the conversation, but I do not think he is a critical care neurologist and people who do this for a living would say that is just not true.

DR. ESTOL (12IX06) The famous Repertinger meningitis case demonstrates that it is possible to keep a body and organs perfused for a long – almost two decades – period of time. The patient did not have an apnea test, at a time when it could have been presumed that he was brain dead. At some time, perhaps in a brief epoch before the autopsy, there was necrosis of the



lower brain stem, completing the brain death status, but there is no testing to confirm that. One possibility is that this patient may not have been brain dead for a long period of time (i.e he was vegetative and progressed to brain death at an unknown moment in time). The other possibility is that the neurological community should accept that this represents a valid case of 'chronic' brain death that was confirmed by exhaustive pathology. All of the clinical tests were performed to ascertain brain death except the apnea test. The absent evoked potentials, and the flat EEG were consistent with brain death. However, some persistent movements described in the report and the presence of 'trace' intracranial blood flow detected with magnetic resonance angiography (a test with less imaging resolution than conventional catheter angiography and thus likely to underestimate the degree of blood flow present) are not consistent with accepted brain death criteria. The neurological community should agree to accept that it may be a validly documented case of brain death that was pathologically confirmed. If this is the case, it well serves to make the point that, in extraordinarily rare circumstances, this kind of case can occur. With the technologies that we have in the modern intensive care unit we may be seeing more of this type of case, as physicians develop the technological prowess to reproduce some of the functions of the brain stem and hypothalamus in the integration and coordination of all the sub-systems of the body. However, the neurological community does not believe that this case in any way disturbs the conceptual validity of brain death as being equivalent to human death.

DR. POSNER (12IX06) I think we should go on record saying it is not relevant. In the literature there are patients who have been kept with their body functioning a week, a month, a hundred days. The fact that Shewmon can say that there are some individual bodies that have been kept going for two months or six months is irrelevant. That patient was dead from the time the ventilation was started.

DR. WJJDICKS (12IX06) I think we should say it is not true and not relevant.

16. (BISH. SÁNCHEZ S. 10IX06) *What is the clinical evidence that there is no chance of recovery from brain death and that discussions regarding recovery from various states of coma must be separated entirely from brain death?*

DR. ROSSINI To my knowledge, when the international guidelines for the

definition of brain death have been followed, in no case of the scientific literature was there any recovery.

DR. ESTOL The same clinical evidence that there is no recovery from death – death i.e. brain death is always/invariably associated with cardiac and respiratory arrest (when there is no artificial ventilations) constituting the ‘usual’ concept of death. ‘Confusion’ arose in the 60s with the advent of technology that allowed blood oxygenation and persisting ventilatory and circulatory functions (artificially maintained) after brain death.

Coma is a neurological state of altered consciousness in which a person is alive and thus represents an entirely different condition from that – brain death – in which a person is dead.

DR. ROPPER I agree except that brain death is not associated with cardiac cessation unless there is no artificial ventilation.

DR. SHEWMON It is impossible to recover from brain death, by definition. Any case of apparent recovery would *ipso facto* prove that it was not brain death but a misdiagnosis.

DR. DEECKE As mentioned above, if the *lege artis* neurological examination for the diagnosis of brain death shows complete areflexiveness (See above: ‘... reveals no responses of brain stem reflexes including cold water irrigation of the external ear canals. If there is no response at all, brain death can reliably be diagnosed. The EEG shows a Null-Line [Zero-Line] recording’).

DR. TANDON Extensive experience in dealing with clinically brain dead individuals (as established by strictly following the criteria for such a diagnosis) provides enough proof of their being no chance for recovery from brain death. This also implies careful exclusion of ‘persistent vegetative state’, ‘coma vigil’, ‘locked-in-state’, prolonged hypothermia, drug toxicity, neonates while arriving at the diagnosis of brain death.

DR. POSNER There is to my knowledge no instance, of an individual meeting the clinical criteria for brain death who recovered consciousness. Those whose somatic organs are sustained by artificial means, invariably demonstrate at postmortem examination, death of the brain.

DR. WJJDICKS No patient has recovered any brain function after the clinical diagnosis of brain death has been made. That is the most important distinguishing and defining feature. Clinical acumen trumps any laboratory test.

DR. ROPPER (12IX06) Certainly the latter part of that is true, I think that

has been repeatedly emphasised. The first part is true but tricky to prove. There has never been a recorded case and, in fact, in a way again through a paradox of logic these few prolonged somatic survivals are evidence that there has not been such a case.

DR. BERNAT (12IX06) I would like to make a refinement to that comment also. I suspect that some of the cases of 'prolonged somatic survival' that have been reported were not examined properly. Physicians may not have performed state-of-the-art neurological examinations, including a proper apnea determination. In our institution we had such a case and I was asked to review it. It was clear to me that the physician who performed the brain death determination did it incorrectly. So my mild refinement to Prof. Ropper's answer would be to add the qualification that the brain death determination has been done properly, using the accepted standards of medical practice that we have defined here.

DR. DEECKE (12IX06) We should add for the non-physicians the fact that brain tissue or brain cells cannot regenerate.

DR. WIJDIKES (12IX06) I think it is, in general, correct to say that the clinical examination was incomplete in those cases in which recovery has occurred but I would argue that in practice it is probably far more that preconditions were not met and that these patients recovered because they were intoxicated, rather than have patients who missed some part of their neurological examination then suddenly started to recover. In general, those patients are so severely damaged that there is very little recovery possible. I think that it is perhaps in practice more the failure to recognise the important preconditions, hypothermia and sedative agent and neuromuscular agents and several others were not met or not recognised and therefore the patient had a chance to recover even sometimes dramatically.

DR. POSNER (12IX06) I think it is fair to say that there is no recorded case of a patient awakening from properly diagnosed brain death. On the contrary, there are a number of recorded cases of autoresuscitation of the heart after the cardiologist has given up attempting resuscitation, so that brain death is a much more certain diagnosis than is cardiac death.

17. (BISH. SÁNCHEZ S. 12IX06) *I believe that it is important to make a clear distinction between the brain dead state and the other two states which are very different to death: loss of consciousness (coma, minimally conscious state, vegetative state) and the decomposition process of the corpse. What are*

*your thoughts?*

DR. DAVIS (12IX06) I would just like to say two things. First, I am concerned about the confusion between persistent vegetative state and brain death that has been promoted by some authors on this subject. I think this is an absolutely fundamental issue that has been mentioned by Professor Ropper. We do not regard persistent vegetative state as brain death and this is a confusion that has been introduced that is not consistent with the concept of brain death. The second issue is the issue of perfusion of an individual who has died and the concept of masking of death. This has been alluded to but I wonder whether Professor Spaemann can comment on his view of whether death can be masked. He spent quite some time talking about appearances but, as Werner Hacke pointed out yesterday, this masking is an artefact of the intensive care environment, it is a masking of the death that has occurred and I think the third point that was made very eloquently by Jerry Posner, yesterday, is that there is no recorded instance, ever, of a person who is brain dead, of having revived.

PROF. SPAEMANN (12IX06) Was verstehen Sie, Dr. Davis, unter „Maskierung des Todes“?

[What do you mean, Dr. Davis, by ‘masking of death’?]

DR. DAVIS (12IX06) What does this appearance mean? It is perfusing organs, it is artificially ventilating organs, and produces pink skin and there is a heartbeat for a period of time that will unequivocally cease if the artificial control is removed, so this is an appearance that is not life and by that I think the term of masking is used. It is an artificial appearance when death has occurred.

PROF. SPAEMANN (12IX06) Ich würde nicht von Maskierung sondern von Verhinderung des Todes sprechen. Die Tatsache, dass jemand ein künstliches Herz hat, bedeutet nicht, dass sein Tod maskiert wird sondern dass er mit künstlichem Herzen lebt. Dadurch wird sein Leben nicht künstlich. Es gibt kein künstliches Leben.

[I would not talk about masking of death but about avoiding death. The fact that somebody has an artificial heart does not mean that his death is masked, but that he lives with an artificial heart. His life does not become artificial because of that. There is no artificial life.]

CARD. MARTINI (12IX06) I am not competent on these subjects neither in neurology nor philosophy but, as an incompetent, I would like to say three things. First of all, I was most impressed and convinced by what I heard

yesterday and by the reading of the famous article of Professor Shewmon, although I could not really understand the value of his reasoning. Secondly, I would like to mention the many meanings of death, starting just from the Scripture. In the Scripture death may mean that *nefesh*, that is the breathing, is going out of the body, is taken by God or has disappeared, or it may also mean sociological death, that is, that one is separated from a community, or historical death, one is separated from history, has become nothing in history, or theological death, one is separated from God. Therefore, thirdly, I think I will briefly comment on a sentence that I find in the very interesting speech of Professor Spaemann, at number six, when he says, quoting a German anaesthesiologist, 'brain dead people are not dead but dying'. I could accept this statement if it meant that there is the beginning of an irreversible process which is not capable of integrating the person, and this process can go on and on up to complete disappearance of the body, but in fact when we speak of brain death we speak of the signs of this no longer existence of the principle of unity and of unifying the entire body and the life of the person. Therefore, I think that, although I would not equate verbally brain death with death as such, brain death is a real sign of death being there at work and therefore it is no longer to be considered a living person. That is my remark.

PROF. SPAEMANN (12IX06) Es gibt kein Kontinuum von Sterben und Verwesung. Der Sterbende verwest nicht, und der Verwesende ist tot. Sterben ist ein kurzer Abschnitt des Lebens. Der Sterbende ist „jemand“, der stirbt. Verwesung hat kein Subjekt. Verwesung beginnt, wenn das Subjekt nicht mehr existiert. Die Würde des Sterbens wird ebenso verletzt durch den therapeutischen Fanatismus der künstlichen Lebensverlängerung wie durch die Tötung des Sterbenden.

[There is no continuum of dying and decay. The dying person does not decay and the decaying person is not dead. Dying is a short part of life. The dying person is 'somebody' who dies. Decay has no subject. Decay starts when the subject does not exist anymore. The dignity of dying is hurt by the therapeutic fanaticism of artificial life prolongation in the same way as by killing the dying person.]

CARD. MARTINI (12IX06) *Sterben* is a process but it is also a moment. There is a moment when the process is irreversible and from this moment you can say that a person is dead. Also, dying will continue with corruption of the body, therefore I think it is possible to distinguish between dying as process and death as the moment of beginning of the irreversible process, which, from inside the person, is no longer capable to keep united all the faculties of the person himself.

18. (BISH. SÁNCHEZ S. 10IX06) *What are the clinical evidence and implications of the recent reports on axon regeneration in patients with severe brain damage and what is the relationship of such reports to the criterion of brain death as death?*

DR. ROSSINI It is still a matter of experimental discussion. No real proof of that.

DR. ESTOL I am not aware of data showing axonal regeneration in dead (brain dead) persons. Axonal regeneration in patients with severe brain injury who are alive constitutes a different scenario.

DR. ROPPER This is controversial material in the first place, and there is no prospect of regeneration (or survival of stem cells in reference to below – also controversial in the adult human brain in my opinion).

DR. SHEWMON I completely agree. Axon regeneration requires a living cell body, and there are virtually none in the context of brain death.

DR. DEECKE This is a different scenario. A coma patient or apallic patient is *not* brain dead. In these cases fiber connections can indeed recover, even the ones of the reticular formation in the brain stem and thalamus. This is why patients can wake up from coma after years (in Austria we had a coma patient who woke up after 6 years).

DR. TANDON I agree with the opinions expressed.

DR. POSNER The report suggesting axonal regeneration involves patients who are brain damaged but not brain dead. Regeneration would not be possible in a brain-dead patient.

DR. WIJDICKS No relevance to the discussion of brain death. May not even have relevance to the discussion of persistent vegetative state. Could have some relevance to minimally conscious state or unclear cases in need for longer observation.

DR. ROPPER (12IX06) They are really two different entities, two different circumstances. The notion, particularly when you see the dissolution and liquefaction of the brain, that there would be regeneration of any sort would not be biologically feasible.

DR. DAVIS (12IX06) Just to reiterate, because we are making concluding

remarks, we have all agreed that these patients are not dead, they are severely brain injured. It is a very challenging area in which there are some developments but these people are not dead and we have made that fundamental distinction, so it is not relevant to the criteria or the signs of death.

DR. ROPPER (12IX06) Moreover, there is a societal risk to suggesting that there is a continuum and there might be a relationship. It is at the moment beyond comprehension.

PROF. MASDEU (12IX06) That is very important. The reports of axonal regeneration are on people who are not brain dead, so there is no evidence of any axonal regeneration in brain dead individuals.

DR. TANDON (12IX06) The evidence of axonal regeneration that was claimed in the paper presented by Dr. Davis was not an evidence of axonal regeneration, it was only imaging which showed axonal flow, not necessarily that there was axonal regeneration. So far there has been no demonstrable acceptable proof that such an axonal regeneration will take to the extent that it will overcome the whole brain dead brain.

DR. DAROFF (12IX06) It is an absurdity, and absolutely inconceivable that axons can grow in a brain in the absence of blood flow to the brain.

19. (BISH. SÁNCHEZ S. 10IX06) *In addition, can one demonstrate that adult stem cells in the brains of brain dead people are dead or is it possible to posit that some are still alive and could be used in the future for regenerative purposes?*

DR. ROSSINI Not at the present moment and with the present knowledge.

DR. ESTOL I do not have the specific data to answer. However, even if stem cells survived severe brain injury causing brain death, this would lead to cardiac, circulatory and respiratory arrests ultimately causing stem cell death.

DR. ROPPER It is a great question. As noted, let us not get ahead of ourselves in assuming such cells exist. Several authorities (e.g., Goldman Rakic) are skeptical as I am. However, these would be as or more susceptible to ischemia/hypoxia than the rest of neurons.

DR. SHEWMON Again I agree completely. Even if some stem cells did miraculously survive the general total brain infarction, or if external stem cells were injected into the necrotic brain tissue, they would not be able to regenerate a functioning brain, much less one with the personal character-



istics of the pre-brain-dead patient. But it could make for a good futuristic science fiction movie!

DR. DEECKE In brain death they are also dead. The abundant brain swelling kills them as well. The question, however, is irrelevant because adult stem cells need not to be taken from the brain, they are taken from the peripheral blood. Stem cells are 'omnipotent' and the blood stem cells also contain the genes expressed in brain tissue.

DR. TANDON I agree with the opinions expressed notwithstanding some claims of harvesting and culturing surviving stem cells from cadavers. Let me reiterate, we are concerned with life in the terms defined by the late Pope John Paul II, and not survival of a group of cells or some parts of the body.

DR. POSNER Although the issue has not been directly addressed, post-mortem examinations of individuals whose cardiac and respiratory function is maintained for a time, demonstrates that there are no viable cells in the brain. That includes brain cells. A good example is the report of the individual whose somatic organs were supported 20 years. At autopsy, there were no viable cells, *J. Child Neurol.* 2006;21:591-595.

DR. WJIDICKS I have concern about the cited case distributed by Shewmon. The clinical information is incomplete and the pathology is sloppy. No testing of medulla oblongata function is described, there are 'movements' and I am concerned they did not look at the lower part of the brain stem. May not have recovered it during autopsy. For sure they did not salvage the cervical cord. The journal has a low impact factor and ranked 100 out of 148 clinical neurology journals. Highly suspicious case.

20. (BISH. SÁNCHEZ S. 10IX06) *What is the clinical evidence that the claims that apnea testing poses a risk to the patient are largely invalid when the testing is performed properly?*

DR. ROSSINI There is no scientific support to such claims. When the tests are performed in an Intensive Care Unit there are all the monitoring conditions assuring that they are safely run and cannot by definition provoke any further damage.

DR. ESTOL The apnea test is a confirmatory test of brain death in patients with absent brain stem reflexes. It is performed to confirm the absence of persistent medulla function (lower brain stem). The medulla

controls respiratory function and a positive apnea test (i.e. lack of respiratory efforts during the test) confirms total brain stem death. However, even if a patient showed respiratory efforts during the apnea test suggestive of preserved medulla function, not a single patient has been reported to recover from this state. Hypotension and arrhythmias are potential complications of the apnea test. The indication is to stop the test if one of these complications ensues. Even if they occurred, these complications and related acidosis would not cause brain death in the event that the patient was not brain dead prior to testing. Different strict measures are taken to avoid such complications during the test.

DR. ROPPER The question is posed as if there is data that it is harmful. The proper conduct of the test has safeguards to avoid excessive hypotension or hypoxia.

DR. SHEWMON Regarding Rossini's reply, there is nothing 'definitional' about potential risks of an apnea test. Most studies of the apnea test have reported that a properly done apnea test is safe, but some have reported complications of hypotension and even pneumothorax (e.g., *Arch. Neurol.* 1994;51(6):595-9; *Neurol. India* 2004; 52(3):342-5). Page 553 of Dr. Wijdicks' book *The Clinical Practice of Critical Care Neurology*, 2nd ed., details various possible complications of the apnea test. There can be no 'clinical evidence that [such] claims' are invalid, because such 'claims' are in fact clinical evidence in the other direction, i.e., that a non-negligible risk does in fact exist. Msgr. Sánchez's question does not mention Dr. Cicero Coimbra by name, but I suspect that Msgr. Sánchez is alluding to his work (*Braz. J. Med. Biol. Res.* 1999;32 (12):1479-87). As far as I know, there is no positive *clinical data* supporting Coimbra's theory of 'global ischemic penumbra', which could be pushed over the edge to global infarction by an apnea test. It is a provocative proposal, and it would be difficult to conduct a clinical study that would either prove or disprove it with the usual kind of evidence. But there are good theoretical reasons to be concerned that such a phenomenon could occur in some cases. It is simply a mathematical necessity that as cerebral perfusion pressure decreases, it will pass through a certain range of marginal perfusion which is neither high enough to permit clinically evident brain function nor low enough yet to cause global infarction. This is what Coimbra refers to as the 'global ischemic penumbra'. Such patients would appear clinically brain dead even though their brains are not dead yet (although they soon will be). An apnea test could induce sufficient hypotension (it would not take much) to transform the 'global ischemic penumbra' into global brain infarction before the natural pathophysiology of brain her-

niation would have brought that about. I suspect this is the risk that Msgr. Sánchez is referring to in his question, and the burden of proof is on those who would maintain that such a thing cannot possibly happen, rather than on those who express reasonable concern that it might in some cases.

DR. DEECKE Apnea testing is performed in order to test if a patient is still depending on artificial respiration or regains self-breathing. This question is not of relevance in the setting of brain death.

DR. ROSSINI I am not an expert in this field, but looking at the literature one gets the information that the risks linked with early methods of apnea test have been progressively reduced to a minimal level (see Vivien *et al.*, *Anesthesiology* 2006; Levesque *et al.*, *Crit. Care Med.* 2006; Sharpe *et al.*, *Neurocrit. Care* 2004).

DR. TANDON Apnea test is carried out only after all other clinical signs of irreversible loss of brain stem functions like complete loss of consciousness, fully dilated fixed pupils, absence of oculocephalic and vestibulo-ocular reflex, and loss of corneal reflex are well established. Under these circumstances, apnea test, carried out with appropriate precautions has not been documented to pose any risk. It may be mentioned that persisting with artificial ventilation itself results in progressive encephalomalacia.

DR. POSNER I believe there is no credible evidence that apnea testing poses a risk when properly performed.

DR. WJEDICKS There is a risk to the patient subjected to the apnea test (e.g. cardiac arrest, severe hypotension). In the best of hands it is very low but only if certain measures are taken to prevent those risks. Unexperienced physicians underestimate the risk and do not take sufficient precautions.

21. (BISH. SÁNCHEZ S. 10IX06) *What does the clinical evidence tell us about pregnancies carried to term in brain-dead mothers and what conclusions can we draw from such cases?*

DR. ESTOL Clinical evidence tells us that this scenario has exceptionally occurred. The conclusion is that the adequate use of sophisticated supportive means (ventilators and drugs) can maintain a cadaver 'functional' for different purposes such as maturing a fetus or holding vital organs suitable for transplantation.

DR. ROPPER Agree – it does not tell us much. As Prof. Estol says, the skin,

kidneys, eyes, testicles, ovaries, etc. do not 'die' until and unless the ventilator is removed and we need to avoid operational or circular definitions of brain death. In the case of pregnancy, the uterus is still perfused [i.e. blood circulation is maintained].

DR. SHEWMON I also agree that, considered in isolation, this phenomenon does not answer the question whether the brain-dead mother's body is still an 'organism as a whole' (though a very sick and technologically dependent one) or an unintegrated collection of live organs and tissues. I do suspect that some pregnancy-related changes occur in other parts of, or diffusely throughout, the mother's body and not only in the uterus (e.g., changes in blood volume and distribution, chemical homeostasis adjusting to transplacental exchanges, endocrine interactions that maintain the pregnancy, etc.). I am no expert in the physiology of pregnancy, and there are probably many aspects of it that are still poorly understood even in healthy mothers, let alone brain-dead ones, but I do strongly suspect that more is going on in these bodies to sustain the pregnancy than merely keeping the uterus perfused with blood. The phenomenon of brain-dead pregnant women becomes of greater interest, *vis a vis* the theory of brain death, when considered not in isolation but in conjunction with other lines of evidence for non-brain-mediated somatic integration (Shewmon, *J. Med. Philos.* 26(5):457-478, 2001).

DR. TANDON This only indicates the survival of a part of the body, but not the individual as a whole.

DR. POSNER Evidence indicates that in some brain-dead pregnant women, somatic organs can be sustained over days or weeks until a viable infant can be delivered. How often this is possible is not known. However, this tells us nothing about brain death, except that in some instances other organs can survive the death of the brain.

DR. WIJDICKS They do not tell us much. In our experience of pregnant brain dead patients both mother and fetus had a cardiac arrest, the fetus first, and aborted spontaneously.

22. (BISH. SÁNCHEZ S. 10IX06) *In particular, do the children of such mothers have a standard of normality in line with children not so born or do they have mental and physical impairments derived from the condition of death of their mothers?*

DR. ROSSINI I do not believe we have sufficient data (newborns and long

enough follow-up) to answer this question. We can only argue that even if the pregnancy was maintained in the most proper way, all the interrelationship which links in an emotional and biochemical environment the mother/child assembly is completely lost due to the mother's brain death.

DR. SHEWMON I also am unaware of any long-term follow-up data on this. All we seem to know is that some of the published reports indicate that a healthy baby was delivered by Caesarean section.

DR. POSNER Most of the few children delivered from brain-dead mothers appear to be normal, at least when examined several months to a year after delivery. The numbers of such children are small and, to my knowledge, have not been evaluated in long-term follow-up. Thus it is difficult to tell if their development is entirely normal.

DR. WJIDICKS Long-term outcome is not available but they are all premature.

23. (BISH. SÁNCHEZ S. 10IX06) *And are children born to brain dead mothers the same as children born to alive mothers, and this in a society that has laid increasing stress on the particular importance of the intrauterine relationship between mother and child?*

DR. ROSSINI This is the problem!

DR. ESTOL Do not know the data.

DR. ROPPER But I believe these children are at risk for low Apgars [i.e. an index used to evaluate the condition of a newborn infant based on a rating of 0, 1, or 2 for each of the five characteristics of color, heart rate, response to stimulation of the sole of the foot, muscle tone, and respiration with 10 being a perfect score] etc. We should propose that this be studied formally.

DR. SHEWMON What Dr. Ropper says about Apgar scores makes intuitive sense, although I am not aware of any formal study of Apgars of babies born to brain-dead mothers. I suspect the same could be said of the distribution of Apgar scores of babies born by Caesarean section to mothers in coma from severe brain damage short of brain death, to mothers with high spinal cord injury, and to mothers with all sorts of non-neurologic diseases.

DR. DEECKE To mothers in coma, yes. To mothers in the so-called vegetative state, yes. Whether the child is damaged or not depends on the circumstances that led to these states of the mother (accidents?, other conditions?). The really brain-dead mother is an extreme situation. Obstetrics has the term: '*Sectio in mortua*'. So why not '*Sectio in mortua cerebialis*'?

DR. TANDON No information is available, but it will be interesting to study such children, if available.

DR. POSNER Do not know.

DR. WIJCKES Do not understand this question.

24. (BISH. SÁNCHEZ S. 10IX06) *Is it the case that the neurological discoveries and advances of recent decades, in particular in relation to the brain, require the development of a new discipline of 'neuroethics' as some experts in the field propose (Marcus, S.J., Neuroethics: Mapping the field, Dana Press, New York 2002; Illis, J. ed., Neuroethics in the 21st century. Defining the issue in theory, practice and policy, Oxford University Press, Oxford 2005)? Or is it the case that we need to develop an anthropology which, although it takes into account these new discoveries about the nature and the working of the brain, does not identify the brain with the mind, the soul, selfhood or personhood? That is to say, an anthropology which understands neuroethics as that part of traditional ethics which provides a framework for our new knowledge about the brain? Here, of course, if we were to accept this new discipline of neuroethics, it would be necessary to avoid two dangers: we must not ignore the new discoveries and opportunities offered by modern neurology, as though science was of no value, and we must not constantly change ethics according to new scientific discoveries, as though absolute ethical principles did not exist.*

DR. ROSSINI I agree entirely on all these statements.

DR. ESTOL The field of neuroethics should be developed as a 'tool' to insert new scenarios/discoveries of the neurosciences in the background of absolute/basic ethical principles.

DR. ROPPER Well said but I/we cannot conclude that there is not an equivalence with the brain and the mind and selfhood – self awareness is totally dependent on the brain and this is demonstrable by a number of clinical and radiological techniques.

On the issue of the soul residing in or depending on brain function, I can only conjecture. I do not feel that a new field is required for these issues

to be discussed.

DR. SHEWMON I like Msgr. Sánchez's formulation of 'neuroethics' not as a new field with its own fundamental assumptions, rules and principles, but as a subspecialization of traditional ethics, with particular focus on issues related to the nervous system.

DR. DEECKE We are living at a time when new terms are continuously introduced in particular with 'Neuro': I have heard and seen the term 'Neurophilosophy'. Some are even talking of 'Neurotheology'. So 'Neuroethics' has to be looked at. Ethics is something comprehensive that cannot be restricted to a certain organ (brain or nervous system). In my opinion the term 'Neuroethics' is not sharp, it is a matter of fashion. Do you think that we really need it? In order to make my standpoint clear: Ethics are morals, but would you talk of 'Neuromorals'?

In case of brain death the *human personality* is dead. He or she is dead with all his or her mind, soul, selfhood, personhood, etc. What is left is a 'preparation' of heart, blood circulation (except the one through the brain), and the other organs (except the brain). This is clear for the doctor, scientist, neurologist, life scientist, etc. As a religious person believing in an eternal (immortal) soul, the consequence is to say: in case of whole death the soul or anima has left the body. In case of brain death the soul or anima has left the body as well (e.g. the 'heart and circulation preparation' without a brain / central nervous system).

DR. TANDON I firmly believe that recent advances in neurosciences demand concerted efforts to develop the discipline of neuroethics, sooner than later, as a part of the overall discipline of Bioethics. Such a request has already been made to the International Bioethics Committee of UNESCO.

The relationship between brain, mind and consciousness remains unresolved (Tandon, *Proc. Indian Natn. Sci. Academy*, 1993, B 59, 1-30, in *Decade of the Brains* (eds.) Koslow, Murthy, Coelho 1995, 17-22, in *On Mind and Consciousness* (eds.) Chakravorti, Mandal and Chatterji 2003, 32-44, in Sadhana 2002, II, 175-182). To add to this issue, the question of soul, or spirit is so far beyond any scientific discussion.

DR. POSNER In my view, the issue of brain death is settled. However, there are many difficult issues concerning permanent vegetative state, death of pregnant women, the minimally conscious state that need to be addressed from an ethical point of view. As the technology evolves, new challenges and questions, some ethical, will arise.

DR. WJIDICKS There is no controversy with the clinical diagnosis of brain death. I do not see any reason for a new field to discuss this further. Neuroethics is an important field but has other priorities.



## PROGRAMME

MONDAY, 11 SEPTEMBER 2006

- 8:55      *Word of Welcome:* Prof. Nicola Cabibbo
- 9:00      Chairperson: Prof. Nicola Cabibbo  
            Speaker: Prof. Conrado J. Estol  
            *What is Not Brain Death: Vegetative States /*  
            *Posturing and Body Movements in Brain Death*  
            Discussion
- 10:00     Speaker: Prof. Stephen Davis  
            *The Minimally Conscious State: Neuroimaging and Regeneration*  
            Discussion
- 11:00     Break
- 11:15     Speaker: Prof. Eelco F.M. Wijdicks  
            *Brain Death Worldwide: Acceptance of Criteria*  
            *but Differences in Procedures*  
            Discussion
- 12:15     Speaker: Prof. Paolo M. Rossini  
            *Neurophysiological Signs of Brain Death: Are They Safe?*  
            Discussion
- 13:15     Lunch at the Casina Pio IV
- 15:00     Chairperson: Prof. Antonio M. Battro  
            Speaker: Prof. Marcus E. Raichle  
            *Human Brain Functional Organization, Altered States*  
            *of Consciousness and the Assessment of Brain Death*  
            Discussion
- 16:00     Speaker: Prof. Werner Hacke  
            *Brain Death: an Artifact Caused by Critical Care Medicine*  
            Discussion

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- 17:00 Break
- 17:30 Speaker: Prof. Michael G. Hennerici  
*Surviving Areas of Brain Tissue in Brain Death:  
is the Whole More than the Sum of its Parts?*  
Discussion
- 18:30 Speaker: Dr. Jerome B. Posner  
*Alleged Awakenings from Prolonged Coma and Brain Death  
and Delivery of Live Babies from Brain Dead Mothers  
do not Negate Brain Death*  
Discussion
- 19:30 Dinner at the Casina Pio IV

TUESDAY, 12 SEPTEMBER 2006

- 9:00 Chairperson: Prof. Rafael Vicuña  
Speaker: Prof. Robert Spaemann  
*Is Brain Death the Death of the Human Being?*  
*On the Current State of the Debate*  
Discussion
- 10:00 Speaker: Prof. James L. Bernat  
*How Do Physicians Prove Irreversibility  
in the Determination of Death?*  
Discussion
- 11:00 Break
- 11:15 Speaker: Prof. Lüder Deecke  
*The Neurologist's View on the Determination of Brain Death*  
Discussion
- 12:15 Speaker: Prof. Louis Puybasset  
*The Assessment of Coma Outcome by the Use of Multimodal MR  
and Proportionality of Care in Neuro-Injured Patients*  
Discussion
- 13:15 Lunch at the Casina Pio IV

- 14:30    Chairperson: H.E. Msgr. Prof. Marcelo Sánchez Sorondo  
            Speaker: Prof. Heinrich Mattle  
            *New Guidelines for Determination of Death in Switzerland*  
            Discussion
- 15:30    Speaker: Prof. Robert B. Daroff  
            *The Historical Evolution of Brain Death*  
            *from Former Definitions of Death. The Harvard and AAN Criteria*  
            Discussion
- 16:30    Break
- 17:00    Speaker: Prof. José C. Masdeu  
            *Neuroimaging: A Window into Total Brain Destruction*  
            *and the Vegetative States*  
            Discussion
- 18:00    Speaker: Prof. Allan H. Ropper  
            *Apnea Alone, Misinterpretations and Improper*  
            *Application of the Apnea Test / Why is Brain Death Still Alive?*  
            Discussion
- 19:00    General Discussion
- 20:00    Dinner at the Casina Pio IV

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#### Acronyms

Edin, Edinburgh  
FAAN, Fellow of the American Academy of Neurology  
FACNS, Fellow of the American Clinical Neurophysiology Society  
FACP, Fellow of the American College of Physicians  
FAES, Fellow of the American Epilepsy Society  
FAHA, Fellow of the American Heart Association  
FCNS, Fellow of the Child Neurology Society  
FESC, Fellow of the European Society of Cardiology  
FNA, Fellow of the Indian National Science Academy  
FNASc, Fellow of the Indian National Academy of Sciences  
FRACP, Fellow of the Royal Australasian College of Physicians  
FRCP, Fellow of the Royal College of Physicians  
FRCS, Fellow of the Royal College of Surgeons  
FRSM, Fellow of the Royal Society of Medicine  
FTWAS, Fellow of the Third World Academy of Sciences  
LLD, Doctor of Laws (Legum Doctor)  
MD, Doctor of Medicine (Medicinae Doctor)  
PAS, The Pontifical Academy of Sciences  
PASS, The Pontifical Academy of Social Sciences  
PAV, The Pontifical Academy for Life  
PhD, Doctor of Philosophy (Philosophiae Doctor)  
PHD, Doctor of Science (Physics, Chemistry and Neurology)  
STD, Doctor of Sacred Theology (Sacrae Theologiae Doctor)



## SCIENTIFIC PAPERS AND DISCUSSIONS

# WHAT IS NOT BRAIN DEATH: THE VEGETATIVE STATE and MOVEMENTS IN BRAIN DEATH\*

CONRADO J. ESTOL

The main objective of this meeting convened at the Pontifical Academy of Sciences is to discuss the topic of Brain Death. Although in general there is no debate within the scientific community, the concept of Brain Death has been questioned by lay people and in some cases by physicians. For this reason it seemed appropriate to begin this two-day conference discussing 'What is not Brain Death', referring to the loss of consciousness that occurs in coma and in the vegetative state, two neurological scenarios that in different medical and non medical circles are not infrequently confused or used interchangeably with brain death.

It is important to remind ourselves that the objectives defined for this Working Group on the Signs of Death at the request of Chancellor Bishop Monsignor Marcelo Sánchez Sorondo of the Pontifical Academy of Sciences following the instructions of the Holy Father Benedict XVI, is to 'study the signs of death in order to explore at a purely scientific level the application of the criterion of brain death'. Following this request, I am presenting two scientific subjects and will avoid most philosophical aspects of the discussion. The first presentation is entitled 'What is not Brain Death: The Vegetative State' and the second is 'Movements in Brain Death'.

## WHAT IS NOT BRAIN DEATH: THE VEGETATIVE STATE

### *Consciousness*

To discuss 'consciousness', we should go back as far as 1890 when William James described it as 'awareness of the self and the environment'. This implies that the state of consciousness entails being awake and aware, but not just one of them.

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

Cognitive functions allow a person to live every day with capacities that are particular to a human being. These functions were thought to be located precisely in certain parts of the brain (Figure 1, see page 415). Scientific advances over the last decade have shown that the brain interacts within itself in very sophisticated ways that make it impossible to localize the functions to one single area. It is also known that plasticity and other capacities of the nervous system permit the regeneration of certain functions lost with brain injury or disease. Following a schematic diagram for didactic purposes, it can be said that some of the functions integrated on the right hemisphere include visual and spatial orientation and music recognition among others and, on the left side (this localization works for most right as well as left handed people) there is language, calculation and, on both hemispheres, memory is localized in the temporal lobes. The frontal lobes integrate the executive function that allows a person to plan, organize and execute activities. A generalized dysfunction of these areas results in the syndromes known as dementias. Selective injuries cause syndromes manifested by the function lost (i.e. aphasia with language alterations, acalculia if calculations are impaired, and mnestic disorders when memory is affected).

These so-called 'high intellectual functions' are localized to various regions of the cerebral cortex although their function and the state of consciousness are dependent on the existence of the ascending reticular activating system (ARAS) (Figure 2, see page 415). The ARAS is a network of neuronal circuits that extends throughout the brainstem providing the neurotransmission to subcortical brain nuclei that in turn activate the cerebral cortex.

Only the dorsally located part of this reticular activating system in the brain stem receives afferent inputs from various loci with different neurotransmitters to finally exert the activity over cortical regions that maintain consciousness. These nuclei are the locus coeruleus with the neurotransmitter epinephrine, the raphe nucleus with serotonin, the basal nucleus of Meynert with acetylcholine mediated activity and the intramedian and medial thalamic nuclei, a group more recently recognized as an active station in the process of consciousness. These thalamic nuclei are the last post preceding stimulation to the different cortical regions that guarantee a state of consciousness. Their important role in consciousness has been underscored by the neuropathological findings in the Quinlan case [1]. When this system is altered as a cause of disease or trauma, a person may fall in a coma and then, according to different variables, may recover or progress to a vegetative state. Some characteristics of the latter include that it mani-

feels as sleep-wake like cycles with complete or partial preservation of hypothalamic and brainstem autonomic functions.

By definition, when somebody loses consciousness (i.e. wakefulness and awareness) for a few seconds or minutes this clinical phenomenon is called 'loss of consciousness or syncope'. When the loss of consciousness lasts for an hour or more, then the condition is defined as coma, and the state of coma can persist for a few days or weeks following an injury to the brain. A popular scale based on the assessment of eye movements and best verbal and motor responses was designed to rapidly and reliably indicate the severity and prognosis of patients in coma (Figure 3, see page 416). In most cases, patients that remain in a coma progress to have signs of 'waking-up' after a few days or weeks. However, many of these patients fail to respond and become fully alert because they fall in the so-called 'vegetative state'. Jennett and Plum defined this neurological state in 1972 as a condition in which coma has progressed to a state of wakefulness without detectable awareness [2]. The term 'vegetative' was used many years before Jennett and Plum, referring to basic functions of the body identified even before the autonomic nervous system was described.

#### *The Vegetative State: Diagnostic Criteria*

Patients in a vegetative state show no evidence of sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile or noxious stimuli. In addition they show no evidence of language comprehension or expression, all have bowel and bladder incontinence and variably preserved cranial nerve and spinal reflexes. These clinical criteria should be fulfilled for someone to be diagnosed as being in a vegetative state (Figure 4, see page 416).

To avoid differences in opinion and varying diagnoses, a Task Force was put together and published in 1994 in *The New England Journal of Medicine* as a two-part manuscript referring to the medical aspects of the vegetative state (Figure 5, see page 417) [3, 4]. This Task Force included the work of five medical societies and of several members from the medical, ethical and law fields to ensure the appropriate construction of the criteria. Facts that were emphasized included that patients should have irregular but cyclic sleeping and waking-like states. This implies that patients are actually not sleeping when they have their eyes closed and not awake when their eyes are open but they appear as if they were in these states. Also, they do not follow a regular pattern of closing and

opening their eyes as in normal wake-sleep cycles. Patients move spontaneously and turn in their beds or move their legs around and show head turning to one side or the other and specially become active when stimulated upon being bathed or touched by caregivers. They can also look as if they are smiling or crying, although these are not consciously integrated reactions of happy or sad emotions. Patients can also make noises such as high pitched screaming, moaning or grunting spontaneously or after stimulation. Although visual fixation or tracking of moving targets (human or other) do not occur, vegetative patients have primitive orienting reflexes with eye or head turning towards certain moving or auditory stimuli. Withdrawal to visual threatening does not occur.

Although it probably added to confusion, the vegetative state was subdivided into the 'persistent vegetative state', defined as a vegetative state lasting at least one month after an acute traumatic or non traumatic injury (Figure 6, see page 417). Whenever it is possible to confirm that a person will be in a vegetative state indefinitely, the appropriate diagnosis becomes 'permanent vegetative state'. The latter implies prognosis because it defines that the patient's status is irreversible whereas when the diagnosis is 'persistent' the patient could eventually recover from the vegetative state to improved degrees of consciousness. This terminology is somewhat confusing because it is very difficult to predict with certainty that somebody will never recover to reliably give the diagnosis of a permanent vegetative state. It is easier to give this diagnosis retrospectively, as for example in the renowned case of Karen Quinlan, when one knows that the patient died without ever recovering from the vegetative state. By convention, when a patient has been vegetative for more than three months after suffering a non-traumatic injury or for a period greater than 12 months after traumatic brain injury, then the likelihood of recovering consciousness is essentially non-existent and the term permanent vegetative is appropriate.

#### *Epidemiology, Etiology and Neuropathology*

In the US there are approximately 10,000 to 25,000 adults and 4,000 to 10,000 children in a vegetative state. If we extrapolate these figures, then in the world there must be approximately 500,000 adults and approximately 200,000 children in a vegetative state, which gives an idea of the significant magnitude of this problem.

One of the most common and deadly etiologies of a vegetative state is traumatic brain injury. Non-traumatic brain injury includes toxic effects of

drugs, overdose, and more commonly the hypoxic-ischemic injuries. The latter group encompasses people who suffer asphyxia, drowning, carbon monoxide poisoning and the different forms of stroke. Other etiologies include degenerative or metabolic brain disorders, such as end stage of, for example, Alzheimer's disease. Finally, severe congenital malformations of the central nervous system such as hydranencephaly can also result in a vegetative state.

The neuropathological features in the brain of affected patients at autopsy depend on the etiology of the vegetative state. In many traumatic cases 'diffuse axonal injury' is found. In this, neuronal axons suffer a sheer stress force, which damages the fiber network causing disconnection of neurons from other circuits and nuclei in the brain. This mechanism commonly operates in car or motorbike accidents in which patients do not have hemorrhages or any observable lesion by imaging of the brain, but fall in a coma or vegetative state after the accident. In non-traumatic injury, the neuropathology shows diffuse cortical laminar necrosis where the cortical layers of the brain, specially the third and fifth layers that are the most sensitive to oxygen deprivation, suffer necrosis with interruption of all neuronal activity.

#### *Recovery from the Vegetative State*

Recovery entails two different variables: consciousness and function. Recovery of consciousness may occur without any functional recovery, thus a person may remain completely paralyzed and regain consciousness. However, functional recovery cannot occur without recovery of consciousness. Approximately 1 to 14% of people that suffer traumatic coma develop a persistent vegetative state, and approximately 12% of those after non-traumatic coma will remain in a persistent vegetative state.

Figure 7 (see page 418) shows that 52% of adults and 62% of children with a diagnosis of persistent vegetative state after one month as a result of traumatic brain injury will recover consciousness at one year following trauma. The graphics on the right side show that recovery is unlikely for patients that have been one month in a vegetative state following non-traumatic brain injury. This poor prognosis affects both adults and children.

In a series of 434 adults with traumatic vegetative state reported by the American Academy of Neurology, the recovery of consciousness after 12 months was unlikely (Figure 8, see page 418) [5]. Good recovery between 6

and 12 months was seen in 0.5% of patients affected and none of the patients had good recovery beginning after 12 months. Most patients in this group recovered consciousness with moderate disability. Among 106 children with traumatic injury that survived 8 months, 54% persisted in a vegetative state, 32% had regained some consciousness and 14% were dead. At 3 months, among 169 adults with non-traumatic brain injury, 93% had died within one month or remained vegetative, 7% recovered consciousness, and only 1% recovered some function. Regarding the 45 children available in the non-traumatic series, among those surviving 6 months, 97% were in a vegetative state and 3% had regained consciousness with some degree of disability.

This series reflects that recovery after traumatic vegetative state can be expected to occur during the first 12 months, whereas in the case of non-traumatic vegetative state the limit is reduced to 3 months.

### *Survival*

Despite significant advances in neurointensive care, the average survival of patients in vegetative state is from 2 to 5 years, and exceptionally beyond 10 years. The probability of prolonged survival is 1/15,000 to 1/17,000. Among patients with traumatic persistent vegetative state, 33% are dead at one year and among those with non-traumatic persistent vegetative state 53% are dead at one year.

### *Vegetative State: A Case Report*

A video was presented of a patient followed for the last eight years, who suffered anoxia from seizures and an allergic reaction to a drug given during her fourth delivery. She has remained in a vegetative state since the complication occurred. In the video it is clearly seen that she is lying in her bed in a fetal position with her eyes closed; however, unexpectedly and without stimulus she opens her eyes, yawns, grimaces and moves her head. Then upon clapping she blinks as if showing a startle response that appears consistent when she repeats the blinking upon clapping again. No sign of awareness of the environment was ever demonstrated in her despite the presence of her relatives and children. This patient is a clear case of persistent vegetative state and because of her long evolution without change and non-traumatic etiology, she probably could accurately be called a 'permanent' vegetative patient.



*Recovery from the Vegetative State in the Media*

The cases of 'dramatic' recovery from vegetative state often reported in the media should be discussed carefully and in depth. In general these cases are not well documented and no medical records are available. Also, in most, the etiology of the neurological cause of the vegetative state is unclear. However, late recoveries do exist and have been reported in the scientific literature and the variables in these reports are not significantly different from those in the media. The major difference is that well reported recoveries always have severe sequelae, which is not clarified in the media reports. Considering the significant prevalence of vegetative state, the total number of recoveries is relatively small and, again, there are no well-documented cases that have recovered to a normal life after being vegetative for more than a month or two.

The most studied and publicized case of permanent vegetative state is that of Karen Ann Quinlan, a woman who, in April 1975, suffered brain anoxia from ingesting a combination of barbiturates, benzodiazepines and an excessive amount of alcohol. She entered a persistent vegetative state and was kept alive with artificial feeding and ventilation. Later that year her parents went to court requesting permission to disconnect the respirator and by January 1976 the New Jersey Supreme Court granted permission to suspend respiratory support. However, the patient continued to breathe on her own (the respiratory centers in the lower brainstem were intact) and died ten years later on June 15th 1986.

The Quinlan case is different from those reported about men and women who had 'fully recovered' to the point of 'talking' to their families after spending years in a vegetative state. In such patients, it is likely that even in the best scenario for recovery, language as well as the capacity for clear articulation of words would probably remain severely affected. Most importantly, patients who have indeed recovered significantly were probably in the 'minimally conscious state' – a condition which will be discussed by Professor Stephen Davis from Australia – and represent patients that should be strictly differentiated from individuals in a vegetative state, since they do have some degree of preserved consciousness that obviously carries major implications for care and prognosis.

A case that recently brought up a very delicate and different issue was that of Terry Schiavo, a woman who had been in a persistent vegetative state for more than a decade after she suffered brain hypoxia from a cardiac arrest and in whom her husband had decided to discontinue feeding

(Figure 9, see page 419). In contrast to the case of Karen Quinlan, where discontinuation of ventilatory support did not result in the death of the patient, withdrawal of feeding would inevitably result in death, thus raising a very sensitive ethical issue. The US Supreme Court refused the appeal by the Governor of the State of Florida (J. Bush) and allowed Terry Schiavo's husband to discontinue feeding. The patient died soon after this measure was implemented.

The American Academy of Neurology had published a consensus of opinion in 1989 regarding this type of decisions, stating that artificial nutrition and hydration are forms of medical treatment such as the indication of antibiotics or any other medication (Figure 10, see page 419) [6]. Secondly, there was agreement in that no medical or ethical distinctions should be made between withholding or withdrawing treatment. No doubt there is a major psychological difference for the caregiver, and for the physician or nurse, between deciding not to give an antibiotic (i.e. withholding a medication) and withdrawal (i.e. discontinuing) of the tube used to feed and hydrate a patient. In the latter case it is acknowledged that, although the physician knows that by discontinuing feeding the patient will die, this does not imply that the physician's intention is the death of the patient. The argument used to accept discontinuation of feeding is that, in properly evaluated cases, the physician can define whether feeding or other means of support are actually prolonging death and not life. Once medical treatment fails to sustain a patient's well being and proves to be of no benefit to the patient and the family, there is no longer an ethical obligation to provide it. When artificial nutrition is discontinued, death occurs approximately within two weeks as a result of dehydration and from alterations in potassium, sodium and other electrolytes, but not from malnutrition. It is important to emphasize that patients do not experience thirst or hunger since by definition they are vegetative and not aware of these feelings. When feeding is discontinued some patients that are in a vegetative state may progress into a coma before they die.

#### *Misdiagnosis of the Vegetative State*

It is difficult to imagine a more horrifying situation than having completely lost the capacity for expression and movement while retaining consciousness and awareness and not being able to transmit this to the surrounding world. The book *The Count of Montecristo* by Dumas describes a character, Monsieur de Noirtier, Count of Villefort, who suffered what Dr.

Jerome Posner – present at this conference – dubbed the ‘Locked-in State’. In this situation, patients have a lesion in the ventral pons – a section of the brainstem – where all motor fibers are localized together in a relatively small space and thus, when this area is injured, the result is complete paralysis of the body. Only blinking or partial eye movements can be preserved with full coexisting consciousness despite the severe degree of paralysis. An emotional description about the experience of living in a locked-in state is found in the book *The Diving Bell and the Butterfly* published by the editor of a French fashion magazine who died after dictating his experience with the use of a blinking-based alphabetic system.

Surprisingly and of concern, misdiagnosis is not unusual in the vegetative state. Andrews *et al.* reported in the *British Medical Journal* in 1996 that, from a total of 40 patients admitted to their specialized rehabilitation unit in England, 40% were misdiagnosed as being in the persistent vegetative state, when they were actually in a minimally conscious state and thus able to communicate [7]. The authors reported that patients were able to develop consistent means of communication using eye movements or a special touch-sensitive buzzer system in their rehabilitation unit. The most frequent reasons reported as why patients had been misdiagnosed in a vegetative state were 1) their severe physical disability, 2) presence of blindness, 3) confusion with the terminology used, 4) examination by inexperienced physicians (it should be emphasized that vegetative states are not commonly seen by the general physician) and, 5) an insufficient period of observation. The authors emphasized that experienced physicians should examine every patient in detail and repeatedly, that families, caregivers and nurses should be meticulously interviewed, and that the medical records should thoroughly read looking for anything that would suggest that the patient may be severely impaired but not vegetative.

When a patient is transitioning from a vegetative to a minimally conscious state (a usual pattern of improvement) the first function to be recovered is visual pursuit (i.e. following objects or people with the eyes purposefully). This function should not be confused with the random eye movements seen in a vegetative person. The caveat, however, is that since almost 50% of patients in the report by Andrews (and in a significant proportion of all vegetative cases) were blind or severely visually impaired, then visual pursuit will obviously not be a useful clinical marker to determine a state of minimal consciousness.

*Do Patients in a Vegetative State 'Feel'?*

Only a few hours before this meeting took place, Owen *et al.* published in *Science* a report directly relevant to the question of 'perception' and 'feeling' in vegetative patients (Figure 11, see page 420) [8]. They examined with functional MRI (magnetic resonance imaging) a woman who had been 5 months in a persistent vegetative state after suffering traumatic brain injury in a traffic accident. Normally, following an adequate stimulus, functional MRI reveals activation of specific brain regions. The authors told the patient to imagine herself playing tennis or walking in her house and to their surprise MRI lighting was noted in the pre-motor cortex, reflecting activity in that region with no differences when compared to normal controls. Moreover, the investigators told the patient an ambiguous sentence ('the creak came from a beam in the ceiling') and noticed that she had an additional response in accessory language regions, similar to that observed and registered in normal volunteers. This further supported the possibility of comprehension, since activity in these secondary language areas occurs when the semantic processing necessary for equivocal language understanding is initiated. A similar type of cortical activation as that reported by Owen *et al.* has also been shown in partially conscious patients, during sleep and under anesthesia, suggesting that the results do not necessarily implicate full consciousness. However, the brain activity elicited when the authors talked to the patient about playing tennis, or when they asked the patient to take a tour around her house, suggests some degree of conscious processing of those commands. Further research will be needed before fully understanding the meaning of these findings in one single case. Adding to the debate, Owen's patient showed some visual pursuit activity at eleven months of follow up, which suggests that at that moment she was in a minimally conscious state. It could thus be proposed that functional MRI may predict which patients in a vegetative state will recover to a minimally conscious state allowing for tailored rehabilitation techniques and pharmacological treatments.

The different motor (body movements), autonomic (sweating, tachycardia), and endocrinological phenomena observed in vegetative patients are reflex responses to stimuli or pain but are not a sign indicative of pain perception. These nociceptive mediated subcortical responses may elicit grimacing and crying-like behaviors similar to those seen in consciousness but in this scenario are mediated by thalamic and limbic system circuits,

which do not involve consciousness. Clinical experience supports that there is no behavioral indication suggesting that vegetative patients feel pain or suffer. Post-mortem neuropathology findings of extensive bilateral brain necrosis are inconsistent with the capacity of feeling, moving or making conscious gestures. Positron emission tomography (PET) images show a severe reduction in cortical glucose metabolism incompatible with the capacity to feel pain or any other emotions.

The question about whether patients in a vegetative state suffer or feel is valid due to the fact that these patients grimace, cry and have different types of facial reactions to various stimuli. The topic has been well studied and, excluding patients with a misdiagnosis, it can be defined that pain and suffering are conscious experiences, and therefore unconsciousness – which is a prerequisite in the vegetative state – precludes these feelings.

## MOVEMENTS IN BRAIN DEATH

For almost four decades the medical profession has expressed consensus regarding the diagnosis of brain death. This unanimous opinion accepts that the diagnosis of irreversible and complete loss of brain function (i.e. brain death), in a body with preserved circulatory function due to a ventilator or any other means of artificial support, is death. Misunderstanding and confusion may arise from the term 'brain death' since it may suggest that there are two types of death, that only the brain may be dead or that death is 'incomplete'. As Bernat has pointed out, to reduce the possibility of misinterpretations, it should be kept in mind that 'death' is a non-technical word, that it is irreversible, that it represents a biological phenomenon, that it is an event and not a process (there is a process in dying and another one of disintegration following death itself) and that death can be accurately determined by physicians [9].

The occurrence of movements in a dead person is no doubt a counter-intuitive phenomenon. A priori, a comment implicating movement in a dead body would only be acceptable as a headline in yellow journalism (Figure 12, see page 420). Naturally, the notion of death is associated with no movements and the purpose of describing the fact that movements can occur serves to emphasize a caveat in brain death diagnosis. It is generally easy for anyone who sees a picture of a dead soldier in a battlefield or a body at the site of an accident, to understand that the image shows a dead person (Figure 13, see page 421). However, if the image shows a brain dead

body awaiting organ harvesting for transplantation purposes, lying on an ICU bed connected to a ventilator and other machines with active nurses in that setting, it would be difficult for anyone – including medical personnel – to understand and accept that this is the image of a dead person (Figure 14, see page 421). So it is indeed reasonable that movements be perceived as a contradiction of death.

There are recollections as early as in the 16th century, describing a surprised Vesalius when he opened a thorax during an autopsy and noted that the heart was still beating as staggering evidence of an erroneous diagnosis of death. On the other hand, during some cardiac surgeries, for technical reasons the heart is paralyzed but this does not implicate that the patient has died (Figure 15, see page 422). It is a common experiment in medical school to kill a frog and take the heart from the body, put it on a dish with saline solution and watch, to the amazement of medical students, that the heart continues to beat for minutes or hours. In this example, the presence of movement does not mean the frog is alive but rather reveals ‘automatism’ as one of the heart muscle’s properties.

A controversy has been generated regarding the presence of movements in brain death and that this could question the diagnosis of death. There are well-known clinical observations of body movements that are compatible with a diagnosis of brain death. These include spinal cord reflexes that are present in approximately 80% of patients up to 200 hours from brain death diagnosis [10]. These movements include the cremasteric, abdominal or plantar reflexes as elicited by an examiner. Also complex movements of the limbs have been reported as representing spinal automatisms. These are movements integrated at the level of the spinal cord without any influence from the brainstem or brain. Martí-Fabregas reported 2 out of 400 patients who had a diagnosis of brain death and showed ventilator-synchronized decerebrate posturing-like movements [11]. Because the patients had a diagnosis of brain death, by definition they could not have ‘decerebrate’ movements that imply some degree of brain activity. The authors were reporting not only that patients had movements that resembled those seen in comatose (live) patients, but also the fact that these movements were coordinated with the ventilator rhythm. Ropper reported respiratory-like movements without clinically functional significance during the apnea testing for certification of brain death [12]. These movements may occur spontaneously and also with stimulation during tube and other device removal from the dead body usually within minutes from the determination of death. Urasaki *et al.* studied the origin of movements in brain death and reported preserved spinal dorsal horn potentials with an absent cortical response, confirming

the isolated origin of these movements in the spinal cord [13]. Other responses that can be integrated in the spinal cord in brain dead patients generating from spinally mediated vasoconstriction or even adrenal gland stimulation include sweating, flushing, hypertension, tachycardia and other cardiovascular phenomena. In another report, Saposnik *et al.* commented on spontaneous and reflex movements on brain death and found that, among 38 patients with this diagnosis, 39% had different movements including finger jerks, undulating toe flexion, plantar responses, facial myokimia, and, as the most impressive, the so-called 'Lazarus' sign' (Figure 16, see page 422) [14]. In the latter, the patient – usually provoked with stimulation by head or neck flexion – seems to incorporate in the bed, raises the arms crossing them in the midline and extends the fingers. It is important to keep in mind the possibility that these movements may occur while devices are being disconnected from the dead body to warn medical and paramedical personnel and, more importantly, the family. In some instances, it is appropriate to consider using the injection of neuromuscular blocking agents to prevent these movements. It is unusual to see movements beyond 24-48 hs after brain death diagnosis. Movements observed at the surgical table during organ harvesting have been used as the argument to question the reliability and validity of the concept of brain death.

From the aforementioned discussion one can conclude that, in this context, death is not necessarily a synonym of immobility and movements can be seen in certain patients with recent diagnosis of brain death. These movements do not question the accuracy of a brain death diagnosis.

In his book *Descartes' Errors*, Antonio Damasio states 'we are, and then we think, and we think only inasmuch as we are, since thinking is indeed caused by the structures and operations of being' [15]. This statement elegantly reflects with a neuroscientific as well as a philosophical view the concept of consciousness, lack of consciousness and losing personhood according to whether a person is in a healthy state, with an injured brain or at the extreme of brain death. Not only it is difficult for a family member or even medical staff to accept a movement in a dead body but it has also been difficult for society as a whole to accept the concept of brain death mainly because it is rather recent in world history.

If adaptation to new concepts is the problem, it is then appropriate to quote the former President of the United States, Thomas Jefferson, when he said that 'I am not an advocate for frequent changes in laws and constitutions, but these must go hand in hand with the progress of the human mind. As new discoveries are made, new truths discovered and



opinions change, institutions must advance also to keep pace with the times. We might as well require a man to wear still the coat which fitted him when a boy as civilized society to remain ever after the regimen of their barbarous ancestors'.

I would like to conclude using an analogy to once again lay emphasis on the purpose of this meeting at the Pontifical Academy of Sciences. It has been extensively discussed in different contexts that the fertilized ovum has no life and has no brain in the first minutes, days, or weeks from conception. However, the critical distinction to be made is that the fertilized ovum is a 'being' precisely because it has a future, as do all of us present here during this conference today. In the fertilized ovum exists a life with a future and, on the other hand, what we shall be discussing in this meeting is not life with a future but only that which in the past was a person and now is only a body with organs that are being kept functioning only due to the effectiveness of modern technology. A body that seems to host a person but no longer does and organs that in their artificial functioning only contribute to the loss of dignity of the whole body. This is exactly the point. If a diagnosis of brain death has been made, we should not stand for the artificial prolongation of the functions of a heart, liver, or a kidney, in a body that is already a corpse with absolutely no hope either in the present or in the future.

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## DISCUSSION ON DR. ESTOL'S PAPER

DR. ROPPER I was wondering, Conrado, do you have any inside thoughts on the meaning of the fact that the transition from severe brain damage and severe brain stem damage to brain death often includes a transition from a Babinski sign to the undulating toe sign or flexor toe sign, which used to be called, or Bechterew sign? Does that suggest to you anything about the level at which brain death transects the nervous system in distinction to all forms of overwhelming brain damage? It is partly rhetorical; obviously, I am trying to make a point that there is a transition. Do you find, for example, Babinski signs in a lot of brain dead patients?

DR. ESTOL The last question first. No, I do not and probably none of us have seen it. Here are the world experts on having seen critical care patients and brain death, and a Babinski sign is not something that anyone sees commonly, not even neurologists. Again, I have not commonly seen the possibility of eliciting a Babinski sign in a brain dead person. This is the answer to the second question. To the first question, I am sure that you, Allan, have a better response than I do, so maybe you can tell us about the transition and the level and I am sure it will be a more interesting answer.

DR. ROPPER I offer this as an observation to suggest that it is indicative of something anatomically unique about brain death, that is distinctive from all other forms of overwhelming brain damage. Sometimes it is possible to demonstrate breathing at one particular time and then subsequently demonstrate no breathing, that coincides quite often with the transition from an upgoing toe to either a downgoing or undulating toes, suggesting that there is something about a Babinski sign that requires an active participation of a very lower centre that is then eliminated in brain death. It is just another subtlety that really does drop a curtain, like apnea, between brain death and all other states of overwhelming brain damage. What that structure is, where it is exactly, I do not know. It must be low, maybe even upper cord.

DR. ESTOL I would like to add one thing to what Dr. Ropper is saying about the timing of these movements. In some non-conventional literature, you may find that these movements are reported to be prolonged in time for months, which does not seem to be the case – I do not know if any of you have seen that – that people could be maintained with functioning organs for a long period of time and movements would be seen. These movements disappear. It is true that in the first few hours they can begin from a point of not having been there but they soon disappear. There was a case of a physician who said, 'Even since this patient has been dead, she has been getting better', referring to the movements originating in the spinal cord and progressively increasing in number after death was determined. However, we should not expect to see these movements for a long period of time. In the report by Saposnik, they were noted up to forty-eight hours, others have seen it up to seven or eight days. I mentioned 200 hours, but we would not expect them at one month. In a brain dead body, kept on a ventilator you would not expect to see the movements so late.

DR. POSNER To support Dr. Ropper's point, there is a paper published (*J. Neurol.*, 2005;252,106-7) looking at a fair number of patients who were brain dead and pointing out that it was quite uncommon to have Babinski responses in brain dead patients and maybe those who had them were in the transition between some brain stem function and total brain death.

DR. BERNAT I am interested in the correlation of the presence of these motor signs with the etiology of brain death, that is, in the traumatic brain injury patient compared to the hypoxic-ischemic neuronal damage patient. The reason for that interest is to study the impact of the presence or absence of a functioning cervical spinal cord. Many patients with traumatic brain injury have normal cervical spinal cords whereas in hypoxic ischemic patients often there is hypoxic-ischemic damage to the cervical spinal cord neurons. I wonder if you have made any observations about the integrity of the cervical spinal cord neurons as a predictor of whether the brain dead patient has these motor signs.

DR. ESTOL In the paper by Saposnik, which has one of the largest series, the etiology distribution is pretty much even between traumatic and hypoxic. Age was different in distribution and patients were forty years old in average and there were, I think, three children below the age of ten, but in terms of etiology, this was similarly distributed between hypoxic-ischemic

and traumatic. I do not know if there was anything noticed in other series but what you are proposing is a very reasonable speculation.

DR. DEECKE Your presentation was very good and I enjoyed it very much. The clinical and everyday life also shows us that spinal movements can occur after the neurologists have already determined brain death and we had this several times, even that the nurse gives an injection or the cuff is laid on or the specimen is taken for compatibility. Then the dead patient can make withdrawing movements, even those that would give points in the Glasgow coma scale. I think this comes after a while. First the patient is in spinal shock but then spinal function can recover and this makes these problems then.

DR. ESTOL Yes, movements begin a little after brain death diagnosis in some cases. Even though the percentage of patients with movements in Saposnik's report was quite large, in the Spanish series only two out of four hundred patients were noted to have these movements. They are not that common. However, they are common enough and impressive and disturbing enough that there was an article in *Neurology*, describing the comments of the coroner about the death of the Wicked Witch of the East in the Wizard of Oz, including that she was: 'Sincerely, merely, entirely, morally, spiritually, physically, positively, absolutely, legally, and ethically dead'. The authors wanted to emphasize how difficult is for a physician to communicate death and described in detail the procedures that physicians should observe and transmit to the family when telling them that a loved one is brain dead. They included the notion that the family should be warned regarding the possibility of movements when the endotracheal and nasogastric tubes and IV lines are taken from the body, and the family is present. It is known that in many cases during transplantation, neuromuscular blocking agents – anaesthesia as well, but this is a different topic – have been used to prevent movements during harvesting, because of understandable psychological reasons.

DR. DAROFF Regarding the paper by Owen in *Science* on 'Traumatic Brain Injury', am I not correct that in traumatic brain injury you cannot call it 'persistent' until twelve months? Therefore the patient was not in a persistent vegetative state but simply in a vegetative state with a chance for improvement. I would predict that there will be improvement, given the brain activity that was demonstrated five months after the injury.

DR. ESTOL Exactly. Without going into the semantics, first I would say she was in a vegetative state. A neurological examination should be accurate and reliable to confirm that. However, one may speculate that had she been examined by the specialized British group by Andrews that detected a high percentage of misdiagnosis in vegetative patients, they may have found some kind of response at five months when the functional MRI was showing spikes of activity in her brain. If she indeed was vegetative, we now know, that at eleven months post trauma the patient is following mirrors with purposeful visual pursuit showing that she has changed and we are still before twelve months. Regarding the semantics, Dr. Daroff, yes, there are criteria saying that 'persistent vegetative' may be defined at twelve months, but other criteria – accepted by the American Academy of Neurology – states that the timing is one month. Somebody that went into a coma from an accident, and then appears to wake up but persists in a cyclic waking/sleeping-like activity, is in a vegetative state. When this state is present one month after traumatic coma it is called 'persistent vegetative state'. Confusion may arise because what statistics say is that after twelve months of a traumatic vegetative state it is very unlikely that somebody will ever recover. In some reports you will find that the criteria is that a patient should be twelve months in a vegetative state to be labelled as being in a persistent vegetative state. However, this is not correct.

DR. HUBER Thank you for the nice presentation. My question is, is there a gender difference in the recovery rate? We have the impression that the female patient has a higher capacity for regeneration after severe brain damage and we have also the impression this depends, after traumatic injury, on which phase of the menstrual cycle the traumatic event occurred. So I think regeneration and recovery depend on many, it is quite different between individuals and I have also the impression that there is a very strong gender difference. Can you share this opinion or have you some other experience?

DR. ESTOL I do not know of any gender differences in recovery. I have just mentioned that there are many variables, among which age and etiology are the most common and the ones that have been studied better. I do not know of any gender differences although I agree that, despite the unfortunate comments of the former President of Harvard University regarding women and their intellectual capacity, recent studies about the effectiveness of brain function have shown how good women are. I strongly believe

that and they may have an advantage for brain recovery too but I do not know of any evidence.

DR. WIDDICKS I would like to emphasise the terminology and I think that is really important because the media is unable to do that. The patient who clearly is not in a persistent vegetative state or even in a permanent vegetative state is presented as a persistent vegetative state in the media, therefore causing a lot of concern. I just want to reiterate that it is important that those definitions are very clear from the outset.

DR. ROPPER I know that this last *Science* case should not be belaboured here because we are not talking about it and Dr. Davis is going to talk about a relatively similar subject, but the idea that there are patients who look vegetative but are responsive is almost fifty years old and it has to do with observations that the EEG is responsive. In other words, the EEG rhythms change with pressure on a bony prominence or with noise and there has always been known to be a discrepancy between a small group of patients who are clinically unresponsive but electrophysiologically show some response. I think that the recent *Science* material is a parlour trick, it is just that it is very elegant and snazzy because it is functional MR and maybe it is a little deeper because there is some sense that there is meaning to what is going on in the imagery, but I would not assume too much and it is not new. It does mean we do have a group of patients who may look vegetative and have some degree of electrophysiologic brain response that, if not generated at the cortical level, at least projected to the cortical level and it has been known for a long time, I do not think we have grappled with that as neurologists.

DR. ESTOL I entirely agree and it has not been the most adequate way how the media presented the *Science* Journal's data because there must now be millions of people in the world thinking that their loved ones who were supposed to be vegetative actually listen and understand them but still cannot respond appropriately. So a potential misinterpretation is unfortunate, you are right.

DR. TANDON In such cases where you have doubts because of the variation of the electrical activity in a persistent vegetative state a test that we found was of great prognostic value was 8-hours sleep EEG record. No patient who had no electrographic evidence of sleep ever survived. In con-

trast to that, if there was evidence of even distorted sleep patterns there were chances of that person surviving.

DR. BERNAT I want to make a brief clarification of Dr. Daroff's question and Dr. Wijdicks' response regarding the difference between the terms 'persistent' and 'permanent' as adjectives for the vegetative state. In the original description, Drs. Plum and Jennett called the vegetative state 'persistent' if it continued longer than one month. The MultiSociety Task Force in 1994 coined the term 'permanent vegetative state' if the patient remained that way after three months following a hypoxic-ischemic injury or a year following traumatic brain injury. I think that both these terms have engendered confusion and it would be preferable to abandon the adjectives 'permanent' and 'persistent'. It is preferable to call the condition a 'vegetative state' as a diagnosis and then separately issue a prognosis based on a number of factors including the etiology, the age of the patient, and the length of time it has been present. But the terms 'persistent' and 'permanent' are confusing particularly to the public. Most scholars now writing about the subject use the term 'vegetative state' as a diagnosis and issue a prognosis separately.

DR. ESTOL I agree.



# THE MINIMALLY CONSCIOUS STATE: NEUROIMAGING AND REGENERATION\*

STEPHEN DAVIS

## *Background*

The minimally conscious state (MCS) is a clinical manifestation of severe brain injury. While there are no evidence-based criteria, diagnostic guidelines were reached in a series of consensus development workshops [1]. The differential diagnosis of the minimally conscious state is important and includes the vegetative state (transient, persistent and permanent), coma and the locked-in syndrome (Table 1). Although sometimes confused in the lay media, none of these states indicate brain death. In recent years, neuroimaging studies have shed light on the underlying pathogenesis of both minimally conscious state and vegetative state and providing insights into the basis of the neural network subserving consciousness. These investigations are likely to have an increasing diagnostic role in severe brain injury.

Like the vegetative state, the minimally conscious state may be a long-term disorder of consciousness, but it may also represent a transition phase between coma, followed by the vegetative state and eventually normal consciousness. Animal studies and more recent human research have indicated, contrary to earlier understanding, that late restoration of functioning can occur due to underlying axonal repair. These imaging studies, utilising positron emission tomography (PET scanning) and functional MRI (fMRI) have shed new light on this potential for neural recovery. These techniques may potentially provide a substrate for experimental interventional therapies, such as drugs and neurotrophic factors. Furthermore, a recent study has challenged the clinical criteria for the persistent vegetative state and underlined the importance of neuroimaging in assessment of disorders of consciousness [2].

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

*The Minimally Conscious State: Definition and Diagnostic Criteria*

To develop consensus criteria for the definition of minimally conscious state, a series of Aspen workshops were held between 1995 and 2000 representing specialists in neurology, neuropsychology, neurosurgery, bioethics, allied health and nursing. The criteria were published in 2002 and have been endorsed by many groups, including the American Academy of Neurology [1].

Core criteria for the definition of minimally conscious state include a severely altered conscious state with minimal but definite behavioural evidence of self or environmental awareness. Key to the diagnosis is evidence of reproducibility, to distinguish responses from reflexive behaviour. Indeed the key distinction between minimally conscious state and vegetative state is some objective evidence of behaviour reflecting conscious awareness.

In the assessment of the minimally conscious state, adequate stimulation for arousal must be present. Potential confounding influences include sedative drugs, seizures, environmental distractions and focal neurological deficits such as hemiplegia or aphasia. Hence, the physician eliciting motor or other responses needs to be aware of the neurological capacity of the patient. A variety of behavioural responses are tested on serial occasions, ideally by independent observers. These might include the ability to follow simple commands, reproducible verbal responses and purposeful behaviour. Behavioural responses might include appropriate emotional reactions to linguistic or visual content, vocalisation or gestures in direct response to the linguistic content of questions, reaching for objects in a meaningful manner, touching or holding objects relevant to the size and shape of the object, pursuit eye movements or sustained fixation in direct response to a relevant tracking stimulus. In the assessment of the minimally conscious state, input from professionals, family and caregivers is valuable.

Duration of the minimally conscious state is not used in the definition, unlike vegetative state, where the persistent vegetative state indicates a duration of 1 month or longer and permanent vegetative state has been used for more than 3 months duration in non-traumatic cases and more than 1 year in traumatic cases. However, these terms are often used in an interchangeable manner (PVS).

*Differential Diagnosis of Minimally Conscious State*

The differential diagnosis of the minimally conscious state includes coma, vegetative state and the locked-in syndrome [3]. Whereas in coma and

the vegetative state, consciousness is absent, there is partial consciousness in the minimally conscious state and full consciousness in the locked-in syndrome. Sleep/wake cycles are absent in coma, but present in the vegetative state, minimally conscious state and the locked-in syndrome. In the minimally conscious state, motor function is preserved to some extent, depend-

TABLE 1. DIFFERENTIAL DIAGNOSIS OF ALTERED CONSCIOUS STATE IN SEVERE BRAIN INJURY

Condition	Consciousness	Sleep/ Wake	Motor function	Auditory function	Visual function	Communication	Emotion
<b>Coma</b>	None	Absent	Reflex responses	None	None	None	None
<b>Vegetative state</b>	None	Present	Postures, withdraws to noxious stimuli	Startle	Startle	None	None
			Occasional nonpurposeful movement	Brief orienting to sound	Brief visual fixation	None	Reflexive responses
<b>Minimally conscious state</b>	Partial	Present	Localize noxious stimuli	Localizes sound	Sustained visual fixation	Contingent vocalization	Contingent responses
			Purposeful movements	May follow commands	Sustained visual pursuit	Inconsistent but intelligible verbalization or gesture	
<b>Locked-in syndrome</b>	Full	Present	Quadriplegic	Preserved	Preserved	Aphonic/ Anarthric	Preserved. May be labile
						Vertical eye movements, blinking intact	

Adapted from: Giacino J.T., Ashwal S., Childs N., Cranford R., Jennett B., Katz D.I., Kelly J.P., Rosenberg J.H., Whyte J., Zafonte R.D., Zasler N.D., The minimally conscious state: definition and diagnostic criteria, *Neurology*, 2002;58:349-53.

ing on neurological function. Hence, the patient may be able to exhibit purposeful reaching or touching of objects, depending on their motor ability. In contrast, patients in coma have only reflex responses and this is generally the case in the vegetative state, although there may be occasional non-purposeful movements. In patients with the locked-in syndrome (most commonly due to brainstem infarction at the level of the pons), there is motor paralysis due to quadriplegia. Because the midbrain is usually spared, vertical eye movements and blinking are typically preserved. Auditory and visual functioning may be partially preserved in minimally conscious state and patients may be able to localise sound and sustain visual fixation.

These functions are absent in coma, preserved in the locked-in syndrome, while only startle responses or very brief orientation to sound or vision are evident in the vegetative state. Some contingent vocalisation may

be evident in the minimally conscious state, while there is no vocalisation in coma or vegetative state. Patients with a locked-in syndrome have bulbar paralysis and are unable to speak. Emotional responses are absent in coma and the vegetative state, although in the latter, reflexive crying or smiling may be evident. Contingent smiling or crying may be present in the minimally conscious state, while emotional responses are preserved in the locked-in syndrome.

At a more fundamental level, key to the understanding of the distinction between the minimally conscious state and these other disorders involves assessment of the two key components of consciousness, namely arousal (wakefulness) and awareness (of the environment and self). These are both absent in coma, while in the vegetative state there is normal arousal but absent awareness. They are both normal in the locked-in syndrome. In the minimally conscious state arousal is preserved (as in vegetative state) and awareness is impaired, but not absent. In summary, demonstration of some level of awareness is key to the diagnosis of the minimally conscious state.

#### *Etiology and Pathogenesis of Minimally Conscious State*

The etiology of the minimally conscious state is varied and may include trauma, hypoxic encephalopathy, stroke, neurodegenerative and neurometabolic disorders. Following acute brain injury, patients may emerge from coma with a variety of neurological states. These may include the vegetative state, protracted or chronic coma, the locked-in syndrome or the minimally conscious state [3, 4]. The minimally conscious state may be transient or permanent. Many patients gradually emerge from the minimally conscious state with a confusional state and varying degrees of independence.

In assessing recovery or emergence from the minimally conscious state, reliable and consistent demonstration of functionally interactive communication and functional use of objects is required [1]. Positive testing may include accurate yes/no responses to a number of basic situational questions on two consecutive evaluations. There should be evidence of appropriate use of at least two objects on two consecutive evaluations. Neurological confounders need to be excluded, including aphasia, agnosia, apraxia and sensorimotor impairment.

The natural history of minimally conscious state is poorly understood. While the condition may be transient or permanent, generally outcomes are better than in the persistent vegetative state, particularly after traumatic brain injury.

### *Anatomical Basis of Vegetative State and Minimally Conscious State*

The vegetative state is typically due to lesions that diffusely damage cortical neurones, thalami or white matter tracts that connect the thalamus and cortex, sparing the brainstem and hypothalamus.[3] Minimally conscious state is associated with less severe pathological changes, with a lower grade of thalamic injury and less severe high-grade diffuse axonal injury. Traumatic causes of both minimally conscious state and vegetative states predominantly affect the white matter (diffuse axonal injury), whereas in non-traumatic causes (classically hypoxic encephalopathy), grey matter is chiefly affected.

### *Imaging in the Diagnosis of MCS and Vegetative State*

Global cerebral metabolism (Fig. 1, see page 423) is depressed in states associated with depressed consciousness, but to varying degrees [5]. Hence, cerebral metabolism is depressed in deep sleep and anaesthesia, as well as coma and the vegetative state. In the vegetative state, cerebral metabolism is more severely depressed than in the minimally conscious state. By definition, cerebral metabolism is absent in brain death. In the vegetative state, cortical metabolism is reduced to about 30-50%, with preserved brain stem functions. External auditory and noxious stimuli can induce neuronal activation, but this is limited to primary cortices [3, 5]. Dissociation from higher order associative cortices (prefrontal, Broca's region, parieto-temporal, posterior parietal, and precuneus) is thought to underlie the absence of conscious perception and awareness. In rare cases of recovery, PET scanning has shown functional improvements in these regions, presumed due to resumption in functional connectivity [5].

In the vegetative state, residual cerebral activity can be shown using a variety of modalities including PET scanning and fMRI [6]. In a study of 5 patients with vegetative states, severe reductions in global metabolic rates were found, but there were islands of relatively preserved function with metabolic and functional integrity.

In the minimally conscious state, there have been fewer functional imaging studies [5]. In contrast to the vegetative state, the medial parietal cortex (precuneus) and the adjacent cingulate cortex (the regions most metabolically active in normal consciousness) are relatively preserved, compared to the vegetative state. This region is considered a critical part of the neural network for consciousness. Compared with the vegetative state, auditory stimulation produces more widespread activation of both primary

and auditory association areas, indicating evidence of more cortical to cortical connectivity.

In summary, in healthy conscious individuals, the medial posterior cortex is the most active metabolic region of the brain and is the least active in those with the vegetative state who are awake. In the minimally conscious state, this region demonstrates an intermediate level of metabolism [5]. Recovery of consciousness in vegetative state has also been associated with partial recovery of glucose metabolism in this critical brain region and hence recovery of cortical/thalamic/cortical interactions [4].

In the minimally conscious state, large network activation has been shown using fMRI [7]. In these studies, personalised narratives elicited cortical activity in the superior and middle temporal gyri in patients and normal controls. The reversed signal, which was linguistically meaningless, produced markedly reduced responses in patients. In the minimally conscious state, patients may retain widely distributed cortical systems, despite an inability to reliably communicate or follow simple instructions. This may underlie rare cases of later recovery of verbal fluency.

#### *Diffusion Tensor Imaging in Brain Injury*

Diffusion tensor imaging (DTI) is an advanced MRI technique, evaluating direction of movement of water in the magnetic field. DTI uses 6 or more diffusion measures to characterise white matter structure. Because the brain has structure, movement of water is not free in all directions and is best represented as a diffusion ellipsoid. Motion is anisotropic. Reduced anisotropy, reflecting damage to myelinated axons, is typically seen in head injury or stroke, where barriers to translational motion of water are disrupted [8, 9]. In patients with even mild head injury, reduced diffusion anisotropy is evident within 24 hours. These signs of fibre pathway disruption have clinical prognostic value.

#### *Use of DTI to Demonstrate Late Axonal Regrowth in the MCS*

Recently, a remarkable patient has been reported with late neurological recovery from the minimally conscious state [10]. This 39-year-old male, with severe head injuries, developed reliable expressive language over a month, after 19 years of the minimally conscious state. At this late stage, he started to develop meaningful vocalisation. He was studied on two occasions, 18 months apart, using DTI techniques. During this interval, he

exhibited striking improvement in his speech and some meaningful motor improvement, although still remained severely neurologically disabled. His imaging results were compared with another patient who remained in a stable minimally conscious state for 6 years and 20 normal controls.

In his first study, increased right-left fractional anisotropy, reflecting the density of myelinated fibres, was demonstrated in the posteromedial cortices and these had reduced to normal levels on the second study. These changes correlated with increases in right-left fractional anisotropy in the midline cerebellum and clinically with gains in motor and speech performance. His PET findings were concordant, with increased glucose metabolism in these regions. The changes were postulated to reflect late axonal regrowth and improving connectivity between brain regions.

This clinical example of late axonal regrowth has been supported by experimental studies. Hence, axonal sprouting has been seen surrounding strokes in animal models [11] and after motor cortical ischemic injury [12].

Caution has to be exercised in extrapolating from a single case report. The patient was already conscious and improving at the time of the first study and the neuroimaging changes reflected predominantly white matter injury, with relative preservation of neurones. However, this case report is provocative and does suggest late brain rewiring. This has implications for further neuroimaging research and therapeutic trials [10].

### *Challenging the Clinical Criteria of Vegetative State*

A challenging case has been recently reported, with demonstration of presumed awareness in a patient with the presumed vegetative state [2]. A 25-year-old woman had been diagnosed with severe head injuries after a motor vehicle accident and fulfilled the clinical criteria for the diagnosis of the persistent vegetative state. Using fMRI, she was asked to imagine playing tennis and moving around her home. Neuroimaging studies indicated activation of cortical regions that were indistinguishable from normal controls. Again, it needs to be emphasised that this is only a single case report and that this patient may have been in a transition phase between the vegetative state and the minimally conscious state.

### *Future Research Direction*

Although these recent publications indicate the potential for axonal regrowth in the very late stage after severe brain injury and provide diagnostic insight into both the minimally conscious state and persistent vege-

tative state, it needs to be emphasised that the amount of data is sparse. However, neuroimaging research has the potential to allow better characterisation of the differences between the minimally conscious state and persistent vegetative state, using larger number of patients with careful clinical correlations and serial studies.

Importantly, these neuroimaging studies provide potential surrogate endpoints for therapeutic trials in relatively small numbers of patients, compared with purely clinical endpoints such as functional rating scales. Modalities such as fractional anisotropy, tractography, fMRI and PET could be used in patients treated with experimental neurotrophic drugs and other therapies to measure functional and structural changes in the brain. This opens up exciting research opportunities. Finally, these recent studies have challenged our reliance on purely clinical criteria for delineation between the minimally conscious state and persistent vegetative state and shown the potential of the brain for very late recovery.

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## DISCUSSION ON DR. DAVIS' PAPER

DR. ROPPER Thank you, Stephen, I have two disparate questions. The first is a query to the group, including Dr. Daroff. The following of oneself in a mirror is frequently used as indicative of various levels of alertness, awareness and even alluded to in one of these two articles, self-awareness. Do you have a view on that? Does it reflect self-awareness or is it just the optokinetic response? Could you do the same thing with a rag that had stripes? And I have another related question after that.

DR. DAVIS I think certainly in the second case that we have probably all read the paper from *Science*, there did seem to be a change which to me was of some significance. The neuroimaging findings induced by these mental imaging tasks, preceded by a few months some evidence, in my view, of more obvious awareness. Bob, do you think this is evidence of awareness?

DR. DAROFF I do not know. We neuro-ophthalmologists use it to distinguish functional psychogenic blindness, and in people who are malingering. If you can see and claim that you cannot see, a large mirror slowly tilting in front of the eyes is a compelling stimulus for eye movements. If the eyes move, vision is present. If the eyes do not move, there is no vision. If you can see, does that mean you are aware? That question is beyond this simple neuro-ophthalmologist's understanding.

DR. DAVIS What was part two?

DR. ROPPER Part two is, if this diffusion tensor imaging reflects myelination or alterations in myelin content around axons, why do they consistently fail to show Wallerian degeneration after an injury? And, could they be showing, not myelination, but just Wallerian change, which is what a lot of these traumatic brains show? The critical issue with diffuse axonal injury from a neuropathologic point of view, from my perspective, is that there are

frequently callosal lesions and as often, cortical lesions that, in a static snapshot of postmortem neuropathology. There is a considerable amount of Wallerian change, and that is rarely discussed. It is just assumed these lesions are primary and not an epiphenomenon.

DR. DAVIS I would assume that a lot of the abnormalities shown reflected a combination of axonal injury through demyelination, an element of Wallerian degeneration and additional neuronal damage. I do not think that one can be confident of these distinctions based on the neuroimaging findings, but I would be interested in other opinions, whether one can make absolutely these distinctions with diffusion tensor imaging.

DR. ROPPER What about the changes they show? Do you know that is not Wallerian? It is the opposite of what you are saying.

DR. DAVIS What is important is that the investigators were able to correlate the diffusion tensor MRI changes with metabolic change. I think that this is interesting, consistent with axonal regeneration and that they thought the regions of change were relevant to functional improvement.

DR. WIDDICKS I think it is also important again to emphasise, in the case from Cornell – and Dr. Posner may have additional information about this – that the improvement in that particular patient that was correlated with MRI and PET scan was not an improvement in consciousness but was a very minimal improvement in his verbal output that I would think most of our neurologists would not be able to detect, and there was very little improvement in his movements in a patient who had very severe contractures. It has been linked towards major improvement in his consciousness and major improvement in his speech but those MRI scans were done after his improvement and they do not have any MRI scans before, which the authors acknowledge, but it has been lost in the presentation of this case.

DR. DAVIS I absolutely agree.

DR. HENNERICI This is an extremely fascinating case, is it not? The question is exactly what was the hen and what was the egg. I mean, is the finding that they saw and observed associated with improved activities or is it really that the structural changes finally led to better functions? This is always the difficulty that we have. And in the paper which I also read, and

I used some of the slides as you did for my presentation tonight, this was not clear, I read it twice, I could not find it, and they did not offer any answer or speculate about what might have happened during 19 years without clinical changes observed. So it is likely that we really need a closer follow-up in these patients even if no clinical changes occur and probably more studies in other patients. In stroke patients where we are now using tensor imaging regularly the changes observed look completely different. Thus the type of long-waiting re-generation seems to be completely different from short-waiting conditions.

DR. DAVIS I agree with your comments, Michael. I think in stroke the particular interest is not the area of the infarct but the perilesional area where you may see reduction of fractional anisotropy but not to the severity of the actual infarct region. What strikes me is the paucity of the information in the literature concerning axonal repair, but these are very powerful techniques.

DR. BOUSSER Yes, you both insisted on the etiology and I think it is absolutely crucial to differentiate acute and chronic situations. For instance, at the end stage of subcortical vascular dementia, patients are also in a minimally conscious state, sometimes for years before they die and it has been shown by tensor MR diffusion imaging that indeed there is a progressive increase in water diffusion over time. Such situations are completely different from acute brain lesions and yet both can lead to minimally conscious states

DR. ROSSINI Just a technical comment that might have some practical implications for the data interpretations. Do we have any proof that the neurovascular coupling mechanism, which is linking the neuronal firing with the absorption of oxygen and the local metabolism, is more or less the same in these kinds of brains as in normal subjects?

DR. DAVIS Marcus? I think I might handball it to you as a PET expert, these values in an injured brain.

DR. RAICHLE I am not aware of a study that has examined a brain like this with that question in mind. It is a perfectly reasonable question and it is something worth looking at. There are some fascinating possibilities with regard to these techniques but understanding exactly the relationships

between what neurons are doing and the blood vessels becomes a critical issue here. I will say a little bit about that this afternoon because I think it is key to where this is going, but I am not aware of anybody looking at this particular population of people specifically.

DR. ROSSINI I am just referring to some studies in stroke in which a sort of dissociation was demonstrated between the presence of neuronal firing and the lack of the BOLD signal because of very poor extraction of oxygen in some brain areas. So I am just wondering whether the gain which is regulating the neuronal firing and the local metabolic response can change following a lesion and can obviously produce a different kind and different amount of response, and if we compare that with a normal condition we are probably interpreting in the wrong way, or partly in the wrong way, our data.

DR. RAICHLE It is entirely possible, so many variables get involved in this including the time after the injury so that acutely you might expect one thing that would be more akin to an acute stroke but many months or years later it could be an entirely different set of circumstances. I am just not aware of enough data to make any definitive statement about it, but I would have to say, for example, the data that appeared this week in *Science* (313:1402, 2006), they are clearly getting a BOLD signal, no question about it, and that is a very good group, they know what they are doing.

DR. POSNER A comment and two questions. One is, I talked to Dr. Shiff just before I left: this patient is continuing to improve, both with respect to verbal and motor function. He has some movement in his lower extremities now. He will continue to be studied, so we will hear more about this. The two questions are, one, would you expect the changes in anisotropy with neuronal degeneration to be the same as those that occur with axonal regrowth and the second is, in those patients who do emerge from the minimally conscious state to be severely disabled, as this patient clearly is, do we have any data on their quality of life?

DR. DAVIS I am struck by the lack of information in relation to the second question. Concerning the quality of life issue, I think that Eelco referred to this patient Terry Wallace as still being profoundly disabled and it is a very difficult issue. In relation to the clinical improvements in the minimally conscious state in this patient, there was a striking speech improvement. In contrast the motor improvement was relatively non func-

tional. As I understand it there was improvement in one limb but not of a significantly functional nature. Perhaps we should tackle the quality of life in people with minimally-conscious state. I am not aware of data but probably others are.

DR. WIDDICKS I can add a little bit to this and I know there is a problem with looking at videos of patients, particularly in the United States, but the Terry Wallace case has been aired on The Discovery Channel several times, so we all, as neurologists, have been able to look at Terry Wallace and also look at earlier videotapes of him in his room with his family and I think we all, without doubt, can conclude that he is not in a vegetative state but in a minimally conscious state, if you accept those criteria, and that he is very severely disabled and is unable to even have a normal functioning life.

DR. DAVIS I think the first part of the question, did that relate to the Wallerian regeneration versus axonal regrowth? And I think that these changes were suggested to be axonal, because there was directionality of the change, changes in diffusivity. This technique is predominantly measuring the directionality of water movement with anisotropic imaging. I think the information one is receiving is about the axons and their diffusivity. I think it is difficult to make a comment about Wallerian degeneration.

DR. POSNER The reason I asked is, I would have thought, and I do not know a great deal about this, that if there were Wallerian degeneration you would have an increase in isotropy rather than a decrease, which you would get with axonal degeneration. I do not know whether this is true. Another comment is, Giacino has described some patients who have emerged from the minimally-conscious state and yet remain severely disabled. One of those patients, at least, believes she has an acceptable quality of life, which I thought was very interesting.

DR. ESTOL The quality of life issue is very important, I think it is crucial. We have not mentioned *The Diving Bell and the Butterfly*, which is a book that describes not the case of minimal conscious state but rather of someone with a locked-in syndrome. A Paris editor of a popular fashion magazine spent a while in a locked-in state and managed to write a book through someone else by blinking. I am not sure the quality of life was acceptable.

DR. BOUSSER Just a comment about that book. The author died just after writing his book and I think this was not a mere coincidence. I do not know if you have read this absolutely fascinating book in which you can see that his brain was functioning really very well. The man even has humour, particularly when he describes the doctors coming to see him. It took him a year to write his book because one blink corresponded to a given letter of the alphabet, A, B, C. There was, sitting near the patient, a psychologist who tried to guess what could be the next letter and she started with E which is the most frequent letter in the French language. The patient would then indicate again by blinking yes or no, and if no, she would try another letter and so on. It thus sometimes took a whole day for one sentence. What I think is really fascinating is that the man died shortly after the book was published so in a way he stopped fighting after he had said everything he wanted to convey about this terrible locked-in state and then he died just afterwards. I think that his quality of life was acceptable as long as he was writing his book but became unacceptable afterwards

DR. RAICHLE Given the number of stroke experts here in the audience and the point you raised, I would just like to put a question on the floor for you. I too have had a big interest in this posterior cingulate precuneus which appears to be part of a very important system in the brain. It is the area that you pointed out that Steven Laureys said was important for the conscious awareness of the world. That area to me is very interesting. First off, we know very very little about it physiologically or functionally and one of the most striking features of it is that I am not aware of a single recorded stroke in this area. It is interesting that its metabolic rate is 30% higher than the average for the cortex, so it is truly unique, and it also has a dual arterial supply. When I was being trained as a neurologist by Jerry and Fred Plum, we always worried about things in the watershed zone of the brain. Here is an area in a watershed zone of the brain that survives through thick and thin, except in traumatic brain injury and hypoxia ischemia. It is something truly unique. So if anybody in this audience is aware of an isolated acute lesion of this area, I would appreciate knowing about it. As far as I know it has never been reported.

DR. DAVIS I do not have any information but there are a number of experts. Michael? An isolated lesion of this region?

DR. HENNERICI The question is interesting but the area, as shown in the paper, is really large. It is beyond the corpus callosum, I did not see the

thickness of the lesion but it looks quite large. I suppose the gyrus angularis area was involved too. We have seen lesions in this location mainly in patients with severe subcortical vascular encephalopathy but I agree, an acute lesion of that size is probably rare due to the excellent vascular collateral circulation reserve in critical territories of the brain.

DR. RAICHLE I will just reiterate my challenge. I would be delighted to see somebody with an isolated lesion in this area, I am simply not aware of it. Indeed, it is a good-sized area and from a neurobiological perspective there is no doubt whatsoever that it is highly complex. We know a lot about its connectational anatomy from higher primates in terms of what goes into it, what goes out of it, it talks to lateral parietal cortex, medial temporal cortex, medial frontal, a lot is known about it in this regard but its functionality as part of a very unique system is really underappreciated and I would still, despite your comment, reiterate my challenge that I would like to see evidence of an acute lesion involving this relatively large area to which we have some clinical material. It would be enormously valuable to have this and I am not aware of it and I have asked this question many times.

DR. HACKE There are two points to address here. First of all, this is a large region and there are a lot of eloquent areas next to it. So the question whether this is an isolated lesion is difficult to address. Secondly, we know many patients who have injury to this area, in addition to others, and that is in the setting of a complete MCA or hemispheric infarction. Interestingly, this is the only condition where you have onset of unconsciousness within a few hours after stroke onset. There are supratentorial lesions that can influence consciousness. Although more than half of the brain is unaffected, consciousness is influenced. However, pinning that down to a small affected area is difficult, simply because of what Prof. Estol eloquently demonstrated: we do not address one function to one region in the brain anymore. Everything is interconnected and there are so many parts of eloquent functions in this area that you cannot get consciousness isolated out of them, I assume.

DR. RAICHLE I think there is both the issue of the complexity of the area and the behavioural significance of that complexity and the simple plumbing fact that we have not infarcted it in isolation. And I come back to that point simply because what I am suggesting to you is that whoever designed and built this system thought highly of that area and saw to it that it was uniquely protected.



DR. DEECKE I just have a question: Is this the gyrus cinguli or is this a cingulate area?

DR. RAICHLE You saw pictures of it here, it stands out, it is uniquely susceptible in Alzheimer's, for example, the first metabolic changes in Alzheimer's, as the Michigan Group showed many years ago, are here. It involves Area 7, the posterior end of the cingulate. The retrosplenial cortex...

DR. DEECKE It is a limbic system then, is this correct?

DR. RAICHLE I hate to put names on it. When this first came up as an interesting observation in imaging, we noticed that when you engage in any kind of effortful cognitive task as a normal person, you not only observe increases in the areas that are task-relevant, but also decreases in activity in a complex system of areas among which is this one. I will illustrate this in my talk later today.

DR. DEECKE But in cortical systematics, this would be the retro-rolandic limbic system which is for perception, whereas the pre-rolandic part is for motor. You have a limbic system also for the initiation of voluntary movement, for instance close to the supplementary motor area (SMA), there is the cingulated motor area (CMA). But this system would then be a perception-related system and it would fit very nicely to have consciousness there.

DR. RAICHLE I wish I knew that for sure. I suspect it may be a bit more complicated.

DR. MATTLE It is a very interesting question you raised here but I have never seen a stroke in this area either, but tumours. If you would like to study this question, then you should look for patients with tumours, with gliomas. They can originate in isolation in the posterior cingulate area.

DR. ESTOL As Professor Raichle said, the cingulated gyrus not only has been recognised for a long time as related to Alzheimer's disease, neither with acute nor isolated lesions, but recent studies by Steve De Kosky in Pittsburgh and at UCLA using volumetric techniques with MRI have shown that this is the most significantly and earliest affected area in Alzheimer's disease.

## THE CLINICAL CRITERIA OF BRAIN DEATH THROUGHOUT THE WORLD\*

EELCO F.M. WIJDICKS

The use of neurological criteria of death rather than cardiorespiratory criteria of death is a fascinating chapter in the history of medicine and neurology [1]. This paradigm change came when patients with an acute brain injury could be resuscitated in emergency departments and intensive care units and survived. Apnea would not lead to asystole and the brain lesion could go on to further cause catastrophic damage while the rest of the body was artificially supported. In most cases this resulted in development of brain edema, shift, and eventually massive increase in intracranial pressure that would stop the blood flow at the entrance of the skull base. This would then result in total necrosis of the brain. In other situations, brain and brainstem would become destroyed directly (e.g., encephalitis, intoxications).

Pathologists noted a necrotic brain never seen before ('respirator brain') but there was no good clinical correlate, only fragmentary observations. Most likely, an isoelectric EEG was the first clinical observation that the brain has lost its function – 'Isoelectric EEG with a Heartbeat' [2]. The recognition of loss of all brainstem reflexes including apnea was first described in a comprehensive manuscript by Mollaret and Goulon [3]. This paper was hardly noticed at the time, but should now be considered a landmark paper. It was followed almost 10 years later by 'the Harvard Criteria' written by an Ad Hoc committee in 1968, consisting of representatives of several Harvard schools. Symposia were organized in Sweden, the United Kingdom, and Australia that tried to formulate brain death on the basis of neurologic criteria. Brain death examination became a prerequisite to allow organ donation and its concept has been fully accepted. However, until recently, it was largely unknown how brain death criteria had been codified in different parts of the world. In this paper, I will discuss the results of a recent survey [4].

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

*The Gold Standard*

The Harvard Committee, appointed by the Dean of the Harvard Medical School and chaired by anesthesiologist Henry Beecher included multiple specialties including a transplant surgeon and transplant immunologist [5]. Their presence has been criticized by some and conflict of interest has been suggested. The guideline was written mostly by the neurologists Schwab and Adams, who in only a few drafts within four months completed an important document that included neurologic evaluation of the patient with no brain function. There was a desire to produce a brief but succinct document but also to work swiftly because of a pressing need in the community to provide guidelines. The transplant physicians commented on this document but left the final say to the neurologists. The document was also important because for the first time it clearly mentioned the confounding effect of CNS depressants and hypothermia. The Harvard criteria remain an example of simplicity.

The criteria were as follows.

1. Unreceptivity and unresponsivity.
2. No movements or breathing.
3. No brainstem reflexes.
4. Flat electroencephalogram.
5. With all of tests repeated at least 24 hours with no change and exclusion of hyperthermia (below 90° degrees F or 32.2°C) or central nervous system depressants.

There have been modifications to the clinical examination of the brain dead patient. Undoubtedly, the influential paper by the Harvard Ad Hoc Committee has been the basis of many hospital policies throughout the United States of America.

A few years later, the conference of Medical Royal College in the United Kingdom further defined criteria by describing further details on brainstem examination and determined a target for PaCO<sub>2</sub> to assess breathing drive. This influential document also determined that the brainstem is the main part of the brain to be tested and lead to the term 'brainstem death'. It is noticeable that the somewhat subtle differences between the UK and the US criteria permeate throughout the world, particularly in those countries that were prior colonies of the UK (eg. India)[4]. Much of the work on brain stem death in the United Kingdom should be credited to Pallis [6].

*Brain Death Criteria throughout the World*

I had the opportunity to survey the brain death throughout the world. Through helpful neurologists and neurosurgeons and other physicians, I was able to obtain the original brain death documents of 80 countries throughout the world, representing all major continents (Table 1). There is global acceptance of the concept of brain death. There are no concerns with the validity of the concept and physicians all over the world recognize – without a scintilla of doubt – that when the clinical criteria of brain death are met, the patient has died. However there were major differences in the technical procedures used to arrive at the clinical diagnosis. No major differences were noted when the methods of examination of brainstem reflexes were compared with each other; but there were marked differences in how the apnea test was performed. The presence of apnea using a PaCO<sub>2</sub> target value was used in only 59% of all guidelines. In others, preoxygenation with 100% oxygen followed by 10 minutes disconnection was deemed sufficient. There was no evidence that the insufficient apnea testing was a result of failure to obtain timely arterial blood gasses or a general reluctance to do the test. In Central and South America countries, a large proportion of patients were either examined with disconnection from the ventilator only, or criteria or guidelines for the apnea test were not present. This is potentially concerning because apnea can only be determined after

TABLE 1.

<i>Surveyed Countries (No. of countries)</i>	
United States of America	
Canada	
Caribbean	(4)
Central and South America	(13)
Europe	(29)
Africa	(5)
Middle East	(9)
Asia	(16)
Oceania	(2)

introducing acute hypocarbia resulting in CSF acidosis that in turn maximally stimulates the respiratory centers. Ten minutes disconnection in a patient with a baseline hypocarbia (not uncommon after induced hyperventilation for increased ICP) could potentially show apnea with a  $\text{PaCO}_2$  not reaching a target value.

The number of physicians required to diagnose brain death varied significantly throughout the world. In 44%, one physician was required (including Canada); 34%, 2 physicians; and 16%, more than two physicians. In 6%, the number of physicians was not specified. Confirmatory tests were required in 40% of the 80 nations of the world. The complexity of criteria did not seem to be influenced by cultural differences. There was no difference between Eastern and Western civilizations, and the differences were largely already apparent in one single continent. In some countries, an academic grade was needed to perform the test (associate professor level).

The type of confirmatory tests and the need for confirmatory tests has been different throughout many countries. The choice of confirmatory tests seems to be very arbitrary, with Sweden as a notable exception. In this country, a cerebral angiogram has to be performed twice with an adequate period of observation in between documenting an absent of flow to the brain [4]. Surprisingly, in many countries stricter criteria (confirmatory test) were present when organ donation was considered. This is a common qualifier in guidelines throughout the world.

### *Remaining Concerns*

In at least half of the surveyed nations in the world and in several US States, confirmation of brain death requires examination by a second physician. This remains very reasonable, but there is no data to suggest criteria should go beyond two physicians. However having two physicians available in order to determine brain death may lead to logistic problems, but, in most modern neurological intensive care units, this could be done by a designated neurologist or neurointensivist, a neurosurgeon, or anesthesiologist. The documentation of absence of respiratory drive remains essential in the diagnosis of brain death. Although the outcome is likely similar, the apnea testing should not be deferred. Documentation of destroyed respiratory centers is the most important test of medulla oblongata destruction; however, it almost always coincides with marked hypotension. Loss of medulla oblongata function results in loss of vascular tone

that only temporarily can be supported with high and incremental doses of vasopressors and vasopressin.

It should be emphasized that in many civilized countries the cultural attitudes and religious attitudes are very supportive towards brain death and organ donation. There is no evidence to suggest that cultural values play a major role in further complicating the determination of brain death such as multiple observations, multiple confirmatory tests, with multiple physicians. It may simply be a consequence of collective decisions of task forces. Variability among hospital policies may also be present and was recently documented by Posner [7]. We can easily assume that similar differences can be found throughout the world when different hospital policies would have been surveyed. There also is a lingering concern on the accuracy brain death documentation. A study by Wang [8] from the University of California examined patients declared brain dead at Los Angeles County General Hospital and found there were major problems with chart documentation. Cornea reflex was not documented in 43% of the cases, and motor examination was not documented in 34% of the patients. It remains unclear whether this is truly a problem of documentation or a lapse in performing a clinical examination of brain death. The organ donation procurement organizations may play an important role in fact checking these examinations. The accuracy of documentation of brain death in countries outside the US is not known.

When reviewing the complex guidelines of brain death determination and preparation for organ donation, one can only conclude that consensus is needed. This would require a task force that reviews the data and provide evidentiary tables. Acceptance of uniform criteria of brain death would then lead to a more uniform policy for brain death determination. Many countries have come to their own judgment in how to solidify these criteria. Usually special committees have been formed but the members of the committee may not always have been most qualified, active practitioners or major specialties have been missing. Complicating the diagnosis with additional laboratory tests must have been driven by a concern that inaccurate assessment of these fatally injured patients may occur. However, more physicians and more confirmatory tests cannot solve that. What remains needed is appropriate education of staff, introduction of checklists in intensive care units, and brain death examination by designated neurologists who have documented proficiency in brain death examination. A qualifying examination should be considered.

### Conclusions

There is broad medical and legal acceptance of the concept of brain death throughout the world. The acceptance of brain death and organ donation permeates throughout countries with different religious values. All major religions have embraced this concept and it allows organ donation (the ultimate gift of life). There are procedural differences that could delay declaration of death and a consensus should be desirable.

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## DISCUSSION ON DR. WIJDICKS' PAPER

CARD. MARTINI Just a question for information. How old is this suspicion, this difficulty in accepting the signs of death? I add this because I now live near Arab countries and I see that when somebody is dead they hurry to make a funeral in four or five hours or as soon as possible. When is the date of this suspicion and this, I would think, precision in deciding the moment of death and the cause of death?

DR. WIJDICKS Well, I do not know how long the suspicion is there, I think we can go back even several centuries, in which they were suspicious that doctors were able even to be absolutely sure that someone was dead and I do not even want to go into Edgar Allan Poe to look at that suspicion. The point here is that if a patient, if there is an adequate neurological examination, you should be able to assess that, in a similar way as a cardiologist is able to document that the heart has stopped. The problem is that, after that has been done, there is a prolonged period of observation, there is a prolonged period of laboratory tests that may lead to more laboratory tests that may lead to even more laboratory tests that eventually would lead to making the decision that the person has died. And there is such a diversity that I do not understand. I do not understand why, for example in Europe, in several countries confirmatory tests are mandatory while in other countries they are not. It is not relative to certain continents, it is within a continent that there is such a significant diversity. In Arab countries, there are only a few countries in which there are brain death criteria as far as I know, but they are largely influenced by their Islamic religious objections. There are no religious objections but their burials are quick and should be quick, which is predicated on their Islamic beliefs.

DR. HENNERICI I have a very short question, probably. You did not talk about the criteria for brain death diagnosis in children. Is the disparity even worse?



DR. WIJDICKS No, the brain death criteria in children are exactly the same, except that an EEG is mandatory in children less than 18 years old. Even in neonates there is a prolonged observation plus two EEGs necessary. That is also currently reviewed. These are old criteria that have not been looked at for a long time and it is also uncertain whether these additional confirmatory tests are necessary.

DR. HENNERICI And is it more or less the same all over the world?

DR. WIJDICKS I do not know that. I think that most countries have accepted the American Academy of Paediatrics guidelines and have not changed them. I know that, with all due respect, the Japanese have made it even more complicated. There are brain death criteria for children in Japan that are, I think, fifty pages thick and made it far more complicated, also excluding brain death or donation of organs in children less than six years old who are brain dead.

DR. TANDON One of the areas which remains quite different from country to country is the use of the term 'brain stem death' equals death, 'whole brain death' equals brain death and is there any consensus because to declare a whole brain dead is not, in my opinion, and at least in our country, legally is not necessary, as long as one can demonstrate by clinical testing all the signs that you have mentioned here that the brain stem is irrevocably lost. So is there difference between various countries in this regard?

DR. WIJDICKS There are some differences. Many countries have used the British criteria for brain stem death examination although there are some differences. For example, Hong Kong is using the British criteria and it has to do with being a prior British colony. So those countries would use the British criteria for brain death and therefore also do not necessarily use any confirmatory test. But the vast majority of countries would look into it, would define this whole death as involvement of the cortex and not only brain stem death. Now, it is important to realise that pure brain stem death is a very uncommon situation. Patients who have had an infarct to the brain stem or a gunshot to the brain stem or traumatic brain injury, the vast majority still will have brain stem reflexes and there are very few in which all the reflexes are lost, very few. In my own experience I can even count how few I have seen in which there was primary brain stem injury and no injury to the rest of the brain.

DR. TANDON The question is, do we insist on whole brain death, because one has seen cases where the brain stem is irrevocably damaged and the patient has never survived fulfilling all the criteria, yet in these patients there is enough evidence of the rest of the brain having some functionality still in place. In contrast to that, one has seen the other way around, when the whole of the cortical mantle is gone yet brain stem reflexes are totally intact. So where is your emphasis?

DR. WIJDICKS Well, as practical neurologists our emphasis is on the brain stem, our clinical examination is exactly what we are doing, we are technically looking at the brain stem. We are not so much interested in whether there is a single nest of neurons still functioning, because that would require a confirmatory test and then the question is, is that confirmatory test as valid as you think it is? And we will be having a discussion on what the use of confirmatory tests is but we all know that one confirmatory test can lead to another confirmatory test and no closure. I think, practically speaking, what we are doing is looking at brain stem injury and loss of the brain stem.

DR. HACKE There are two points I would like to make. First of all, brain death is closely linked to availability of ICU capacities, so you will not find this discussion in Central Africa or other areas of the world where the medical system is by far not as developed as in other parts of the world. This is changing now, for example, in the Emirates and in the big metropolitan areas of some Arab countries, but still, and that comes back to the question of having dead bodies in the grave as quickly as possible, it does not constitute a real problem. Secondly, and some of us who also live in countries where we have an increasing number of Muslim people in our community, we have not had a single organ donor of Muslim confession in the past 15 years in our service and we had many such patients. So even if there is some ruling by some of the authorities in the Islamic religion, brain death is not accepted by the public, and they will essentially not allow organ donation, even discussing it is a major problem. I can say this regarding our Turkish population in Germany only, but I assume, in France and in England it is probably about the same. The third point is about the difference between prognosis and establishing the current status. Prognosis is something different from the question of, 'Is brain death present now?'. When it comes to transplantation you have to establish your diagnosis at this very time point. And that makes a big difference and leads over to isolated brain stem death

versus the death of the whole brain. Every one of us knows that, if you have a major injury to the brain stem, every brain stem function may be lost producing the full clinical picture of brain death. However, in the early phase cortical functions are preserved. You may see this in the EEG and I have seen patients with an Alpha-EEG and suppression reaction to light, and there is no brain stem reflex present any more. These patients will die in the next twelve hours if you do not put a ventricular catheter in. But there is the possibility that, with a ventricular drain, you can keep some function of the hemisphere alive. In PET studies you would see that there is perfusion and there is oxygen extraction still available. That means, despite the fact, that nothing can bring brain stem function back, there is no brain death right now, which would allow us to perform an explantation procedure. That is what I mean with the difference between prognosis on one hand now it is established on the other hand. Consequently, in our country, we ask for an EEG in a primary infratentorial lesion. If the EEG is not flat, brain death would not be established at that time point.

DR. WIJDICKS Thank you. That is one country's approach. One of your neighbouring countries would do something entirely different, and that, I think, is of interest. Whether there is a correlation between donation and brain death is obvious. I think that is absolutely true. I think the diagnosis of brain death is driven by whether there is a transplantation programme or whether there are transplantation surgeons. I do not think brain death examination now, in practice, would have much of any meaning if it were not for the sake of transplantation. We would be able to diagnose brain death but in many of those instances it would not necessarily matter whether there is still some function left, because the prognosis is not good and withdrawal of support will follow. So there is obviously a link between the determination of brain death and organ donation and the presence of a transplantation programme in that particular country. So, in countries in which there is not a transplantation programme, brain death criteria have not necessarily been developed, so I think that is absolutely true.

DR. MATTLE One of the problems in diagnosing brain death is ruling out intoxications and metabolic disorders: how is that dealt with in most countries?

DR. WIJDICKS The question is how is intoxication dealt with in the diagnosis of brain death. Most of the criteria would have preconditions and not

even go to determination of brain death if there is any evidence that there is sedation or any drugs that would depress the level of consciousness. Some countries, including Spain and I think Italy, would use a confirmatory test or a cerebral angiogram to document that there is absence of intracranial blood flow in a patient who still has sedative agents on board, if they can document absent blood flow. So there are at least two countries of which I am aware of that would allow brain death examination in a patient who has a confounding sedative agent on board, as long as they document that there is no blood flow to the brain. Most countries do not go there and would just simply say, 'We will not even examine the patient if we have not excluded a series of potential confounders'.

DR. DAVIS My points have really been covered by Werner, the isolated brain stem haemorrhage that we see where there is a devastating bleed which would really fulfil the criteria for brain stem death, other than the fact that some cortical activity may be present. So I think that issue has been covered. I guess the only other comment is that the diagnosis of brain death is obviously inextricably linked to organ donation, but is also very fixed in the public mind. This sometimes comes up in discussion with family, it is not just prognosis but, 'Is my relative brain dead?'

DR. WIJDICKS Yes, that is true. It is definitely true that a full brain death examination can be done when there is no organ donation because, in most practices, you would make a diagnosis first and then talk to the families about donation. That would be the most ideal situation. The unfortunate part is, I am not sure we should use the word 'unfortunate', but in practice it is often that families are already discussing organ donation when you do not even know in which direction the patient is going. And there is a drive coming from families, at least where I work, to think about that possibility. 'Yes, this is a catastrophic injury and we understand that the prognosis is hopeless, but please, it would be wonderful if organ donation could be given as a sort of a last gesture, it would give us so much better closure than just being told that our loved one has died'.

DR. ROSSINI I have a comment and a question. The comment is that probably the differences in the amount of hours and the number of people forming the team is coming from the awareness that the skillfulness in doing this job is not exactly at the maximum. In other words, we are speaking about something which is really not easy to do, both on clinical grounds

and as so-called ancillary tests. As an electroencephalographer I must confess that, I would say, the majority of people doing EEGs daily, if they have not a specific certificated skilfulness in interpreting a flat EEG cannot do that because they do not recognise the majority of artefacts which can appear in a so-called flat EEG. Something similar can probably be found on the clinical side when we explore patients with heavy face traumas, face traumas with facial edema where it is not easy to interpret papillary reactions, it is not easy to interpret facial muscle contractions and so on. This is a comment. The second point is the use of additional tests. I am not sure that Italy, probably in the next law but in the present law I do not think that we allow, in any case, to go on with the brain death definition when there is an intoxication. This I think is under discussion in the scientific community and the Parliament will filter that in the near future. But in this condition obviously we may use additional tests to help us make the definition of brain death. Do you think that, if we open a little bit more to these so-called additional tests, we can really enlarge this field?

DR. WIJDICKS Well, the criteria in Italy might be in flux. I know in Spain in the confirmatory tests a transcranial Doppler is used. In several papers that I reviewed in transplantation journals, not an EEG but a transcranial Doppler is used in patients who are heavily sedated to make the diagnosis of brain death followed by transplantation and they have argued against it in letters to the Editor but that is what their statute says, that a confirmatory test can override a clinical examination that is confounded. My personal view is that it is concerning. If there is a concern about skills, then the next question is, should you have some form of certification? Should the person who does the examination be certified? That is an appropriate question. The person who does that the exam, whom often are neurosurgeons, neurologists, anaesthesiologists, paediatricians, should they be taught and should they demonstrate their skills, is a separate discussion and I do not have a good answer to that yet. It will certainly make things more complicated and I am not sure how that would be organised and defined.

DR. DEECKE Since we are now in the middle of what can be called 'transcultural' determination of brain death I would like to add, after Werner Hacke, Germany and Heinrich Mattle, Switzerland, that in Austria we also very much rely on the EEG, the isoelectric EEG for the determination of brain death and we wait it again after 12 hours if there is some suspicion of barbiturate or other intoxication. And our doctors are travelling even to hos-

pitals outside the Vienna General Hospital with a portable EEG, which is no problem nowadays, and of course all the other clinical examination is done. My personal opinion is that a neurologist and only a neurologist should determine brain death because it must be a person who has no interest in transplantation. With us in Austria also the neurosurgeons want to be included and I am against it, they are an operative discipline and anaesthesiologists as well. I think it should be conservative neurologists who do it.

DR. WIJDICKS It is important to emphasise that the transplant surgeons should not be involved, I think that is present in many statutes. The practice is entirely the opposite, transplant surgeons in general, at least the ones I work with, it may be different in other places, would feel very uncomfortable to even go ahead if the person has some problems with his determination. I do not think there is much of any evidence that transplant surgeons drive the determination of brain death currently, in the current climate, and I doubt that that is the case, at least I have not seen any clear evidence that that is the case. They are really behind the scenes and when the diagnosis has been made, they become operative.

DR. BERNAT Thank you. I want to address the question that Dr. Wijdicks posed and on which Dr. Tandon commented regarding the difference between so-called 'brain stem death' and 'whole brain death', with particular emphasis on the functions of the brain stem that we measure at the bedside as part of the determination. The late Christopher Pallis of London was fond of pointing out to those of us who support whole brain death, that most of our examination was directed toward assessing brain stem function, and his claim is certainly true. But the significance of the loss of brain stem function extended beyond the brain stem itself. In most patients with large supratentorial lesions (such as massive intracranial haemorrhage, massive traumatic brain injury, or massive hypoxic ischemic brain injury), the resulting increased intracranial pressure produced transtentorial cerebral herniation, the evidence of which was a loss of brain stem functions. Thus tests measuring the loss of brain stem functions were not looking solely at the brain stem but more importantly viewing brain stem destruction as evidence that the cerebral hemispheres and thalamus also had been destroyed. The cases of brain death resulting from primary brain stem lesions (such as the brain stem haemorrhages or infarctions) are a completely different circumstance. Rarely in such cases, the cortex may be intact despite the fact that the brain stem has been destroyed. I feel strong-

ly (and most of the people who have looked at this issue agree) that it would be better to regard the loss of brain stem functions as evidence that all brain tissue in the supratentorial compartment has been destroyed.

DR. WIJDICKS I agree.

DR. PUYBASSET I am working in a neuro-intensive care facility. Nearly all of our patients developing brain death have been highly sedated before this fatal issue, in order to treat an increased intracranial pressure. This is the reason why in France we do the diagnosis of brain death based on arteriography in these patients, since EEG is no longer relevant because of sedation. Clinical symptoms cannot be evaluated because of sedation. In this case, the confirmatory test is mandatory. There are more and more patients with sedation before the occurrence of brain death, that is my point.

DR. WIJDICKS Well, yes. The question is that in many guidelines the determination of brain death is predicated on the use of preconditions. And one of the preconditions is, there should not be any sedative agents on board that would depress consciousness. So, if you would use that dogma, you would never examine a patient and come to the diagnosis of brain death because they have been sedated. That is the dogma. The clinical practice is that there are patients coming into an intensive care unit with massively increased ICP, with high dose of barbiturates and then something happens and the brain stem reflexes seem to be lost, and then there is an EEG done which shows a flat EEG and a transcranial Doppler is done which shows possibly no flow or reverberating flow and then, the question is, can we determine brain death in that particular patient. The answer is, I think, whether you would sign on to this dogma or not, or if you would say, well, if we can document that there is no flow to the brain with the laboratory tests that we do have available to us, and I believe that every cerebral angiogram documenting no flow to the brain is as reliable as can be, then that is one way to do it. But if you would argue that these preconditions are important, you would not go into that situation. There is also anything in between. Patients who have been on sedative agents that are not so potent as barbiturates or sedative agents that can be countered with antidotes, such as midazolam or even propofol that can be discontinued. In that particular case, confirmatory tests could potentially be useful, when there is uncertainty, but in general I think our principle remains that our precondition should be no sedative agents on board before you even go the

route of determining brain death. By that reason, you may lose patients that may be potentially organ donors or you have to wait for a period of time in which you can document that it is improbable that there are sedative agents onboard. With barbiturates it would take several days to document that barbiturate agents are below therapeutic levels.

DR. HACKE Just a short comment to that. First of all, brain death does rarely come as a surprise. It is usually a sequence of events that happen over a few days, maybe within 24 hours, that finally lead to this condition and there are, for example, diagnostic tests that you do while the patient is still alive, such as routine follow-up CTs that show that despite everything you do, the injury is growing and there is no way to reverse this. At this point in time we withdraw sedative drugs to start with. Secondly, I do not know of any guidelines that tell us that we have to use high dose barbiturates in those cases. When someone does this on a permanent basis, this interferes with the diagnosis of brain death but has no clinical validity to start with.

DR. WIJDICKS I think it is an important point. There are patients who come in with a catastrophic injury and very little brain function left and then are put on barbiturates as a last resort, worsen further which would lead to a loss of brain function but no organ donation is possible. That is unfortunate in many cases, I agree.



## NEUROPHYSIOLOGICAL SIGNS OF BRAIN DEATH (EEG & EVOKED POTENTIALS): ARE THEY SAFE & RELIABLE?\*

PAOLO M. ROSSINI

ElectroEncephaloGraphy (EEG) was introduced by Hans Berger in the 20s and 30s. This technique allowed for the first time to record from the scalp the electrical activity of a living brain. The signal picked-up via surface electrodes reflects the sum of the post-synaptic potentials of the underlying cortical neurons. In order to increase the signal-to-noise ratio (neurons produce very small electrical signals in the order of microVolts, that is a million times smaller than 1 Volt!) *differential* amplifiers were created – that is amplifiers which make an electronic subtraction of the signals entering grid 2 from those entering grid 1 at the same instant (if they are of the same polarity they go therefore to 0, while if they are of opposite polarity they double in amplitude) – with the need of having two different electrodes (one *exploring* and one *referential*) for each explored brain region which corresponds to one recording channel. In order to cover simultaneously the whole brain surface, multichannel EEG machines have been developed up to 250 channels of the modern ones utilized for research purposes. However, for clinical applications, 8 to 16 recording channels are routinely employed.

Since pioneering days, it was shown that the EEG signal is quite sensitive to the state of the neural cells producing it: moreover, it was shown that complete deprivation of blood flow provokes in a few minutes the rapid deterioration of the EEG signal, followed by electrical failure and cell death with complete electrical silence. In the 50s French researchers clearly demonstrated that in comatose patients with complete brain destruction the EEG was isoelectric or flat. When this EEG pattern was present for a sufficiently prolonged time, prognosis for survival was unfavourable.

In the following years the concept of *brain-death* clinical condition was progressively introduced and it was demonstrated that – when present – it is invariably associated to an isoelectric, flat EEG pattern.

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

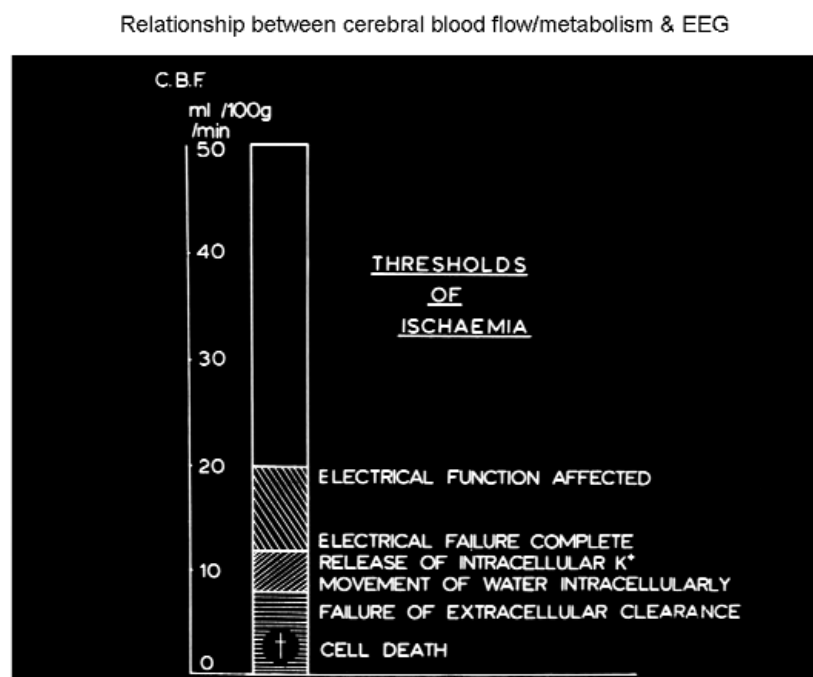


Fig. 1. Relationship between cerebral blood flow/metabolism and EEG. Notice that with a regional flow below 20 ml/100/min the electrical brain function is affected. Below 10ml/100 gr/min intracellular potassium is released and water enters intracellularly. This condition, if prolonged in time, provokes neuronal cell death.

One should remember that EEG records the spontaneous bioelectrical activity of the cerebral cortex to a depth of about 5 mm without information from the brain stem. Meanwhile, following about 8 min. of complete anoxia due to circulatory arrest – as it happens with the increasingly higher intracranial pressure of post-traumatic severe coma leading to brain death condition – EEG becomes irreversibly isoelectric and is a reliable test of brain death.

However, the clear identification of an isoelectric EEG is not an easy tool. Electromagnetic fields in the ICU can pose difficulties for artefact-free traces and the EEG is very sensitive to sedative drugs hypothermia and metabolic abnormalities; all these conditions can approach the isoelectric EEG pattern, despite a still vital brainstem. Blood levels of seda-

tive drugs and metabolic conditions must therefore be tested before the EEG examination can be interpreted safely.

Moreover, isoelectric EEG condition is reached progressively through different EEG stages in which the electric signal is deteriorating, finally becoming extremely low-volted, until it disappears completely. Therefore, in order to exclude any residual EEG activity, long-distance montages and amplifiers with a 'gain' of at least 2 microV/div. must be employed. Artefacts from environment (i.e. mains, ventilator shock and endotracheal tube vibrations, neon lights etc.) and from non-brain generated biological signals (i.e. EKG) can resemble spontaneous EEG activity and should be interpreted only by skilled and trained (possibly certified) personnel. EEG reactivity to external stimuli and to transient disconnection from the ventilator in monitored conditions (i.e. following standards for the apnea-test) should also be evaluated. However, even when the best skills are adopted, up to 20% of either false or positive pitfalls affect EEG recordings for brain-death diagnosis.

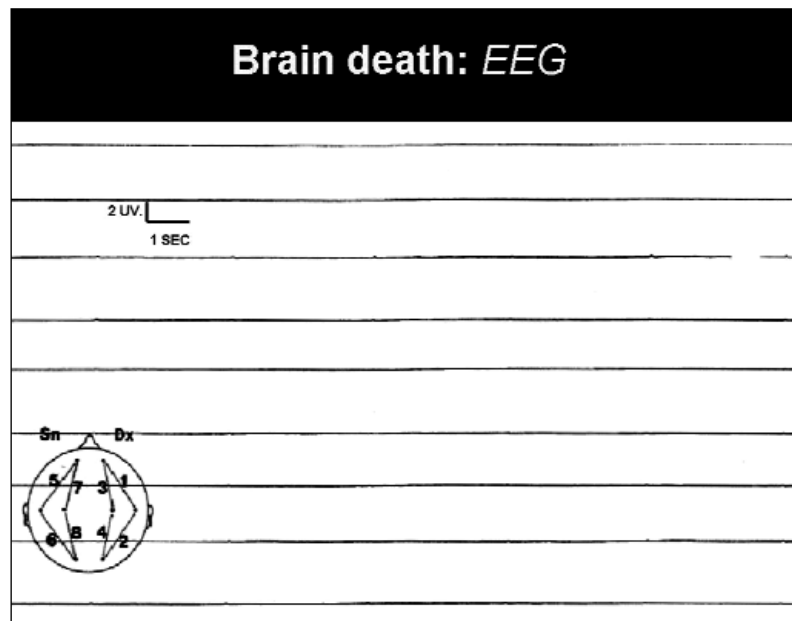


Fig. 2. Isoelectric or flat EEG in a brain-death condition. Notice the high sensitivity of amplifiers (2 uV) and the long distances of recording electrodes.

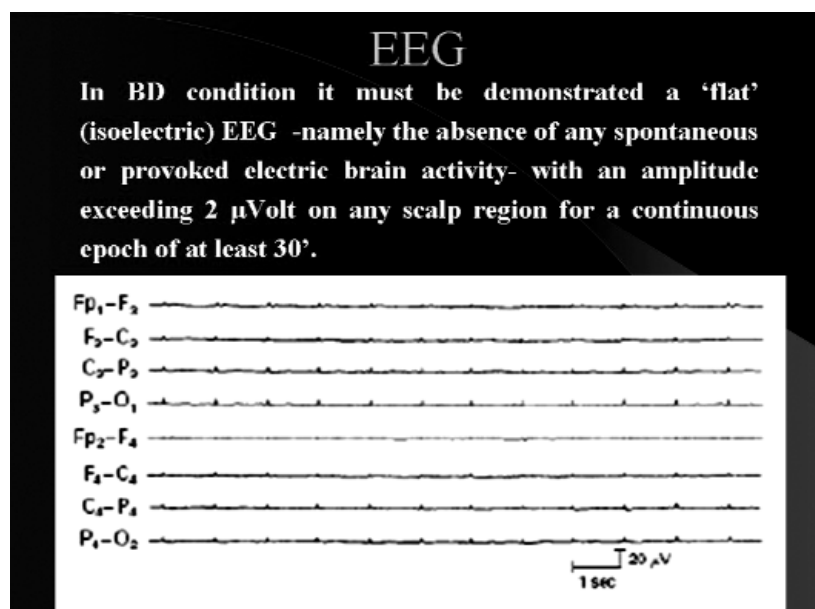


Fig. 3. Isoelectric EEG pattern due to brain-death condition notice the presence of rhythmic artefacts of biological origin due to EKG volume spread to the scalp recording electrodes.

#### MINIMAL TECHNICAL STANDARDS FOR EEG RECORDING IN SUSPECTED BRAIN DEATH (Daly and Pedley 1990)

1. Minimum of 8 scalp electrodes and 2 earlobe reference electrodes following an initial study using all 21 electrodes of the 10-20 system
2. Interelectrode impedances under 10 000 but over 100  $\Omega$
3. Tests in integrity of the entire recording system
4. Interelectrode distance of at least 10 cm
5. Instrumental sensitivities of 2  $\mu$ V/mm for at least 30 min
6. Low- and high-frequency cutoffs must be no higher than 1 Hz and no lower than 30 Hz, respectively
7. Monitoring of artifacts, especially the electrocardiogram, and elimination of EMG artifacts by neuromuscular blocking agents
8. Tests of EEG reactivity to intense noxious, auditory, and, whenever possible, photic stimuli
9. Performance of the record by a qualified technologist experienced in recording EEGs in intensive care units and working under the supervision of a qualified electroencephalographer
10. Repetition of the whole test after an interval (e.g. 6 h) whenever electrocerebral inactivity is doubtful

In the late 1960s and in the following two decades, the progressive introduction of computers for analog-to-digital conversion of biological signals allowed to record *stimulus-related Evoked Potentials*; they were mainly based on electronic devices performing mathematical averaging of brain responses triggered by external (i.e. visual, acoustic, somatosensory) stimuli and analog-to-digital transformed signals via appropriate sampling rates. After such and electronic averaging and a sufficient number of repetitions, all the EEG waves which had a precise chronology with the stimulus tended to 1, while all the EEG activities (both biological and artefactual in origin) randomly occurring, without any precise stimulus-related chronology tended to 0. This method allowed to improve the signal-to-noise ratio at a level that also peaks at submicrovolt amplitude could be disentangled from background noise of higher amplitude. Individual waves of stimulus-related Evoked Potentials were labelled either with letters indicating their polarity (P for positive, N for negative) followed by their modal latency in the control population (i.e. P14 for a wave of Positive polarity and a modal latency of 14 milliseconds) as it was for the Somatosensory Evoked Potentials (SSEPs) or with roman numbers (I to VII) as it was for Acoustic Brainstem Responses (ABR). A bulk of experimental evidences either in animal models or in humans following focal lesions, allowed for the anatomo-functional description of the generator source(s) for individual peaks.

As far as ABR is concerned it was clearly demonstrated that wave I and the early part of wave II are generated from the eighth nerve in its extracranial trajectory, while the latter part of wave II and the following waves are entirely generated within the brainstem acoustic pathways and relays from cochlear nuclei to lateral lemniscus, inferior colliculus and trapezoid body.

As far as SSEPs are concerned, it was found that – by using the appropriate reference electrode positioning on a non cephalic site or on the earlobe – both far-field waves (generated within the brachial plexus = P9, cervical dorsal roots and dorsal horn = P11, brainstem medial lemniscus, gracile and cuneate nuclei = P13-14) and near-field waves (generated in the thalamocortical projections i.e. = N18, and postcentral primary somatosensory cortex = N20) can be reliably recorded.

The diagnosis of brain death often uses median nerve somatosensory evoked potentials (SSEPs) or auditory brainstem responses (ABRs) which have been repeatedly and reliably shown to disappear when the clinical signs of this condition are evident. In fact, the progressive loss of the intracranially generated waves of ABR (namely waves II to V) in serially

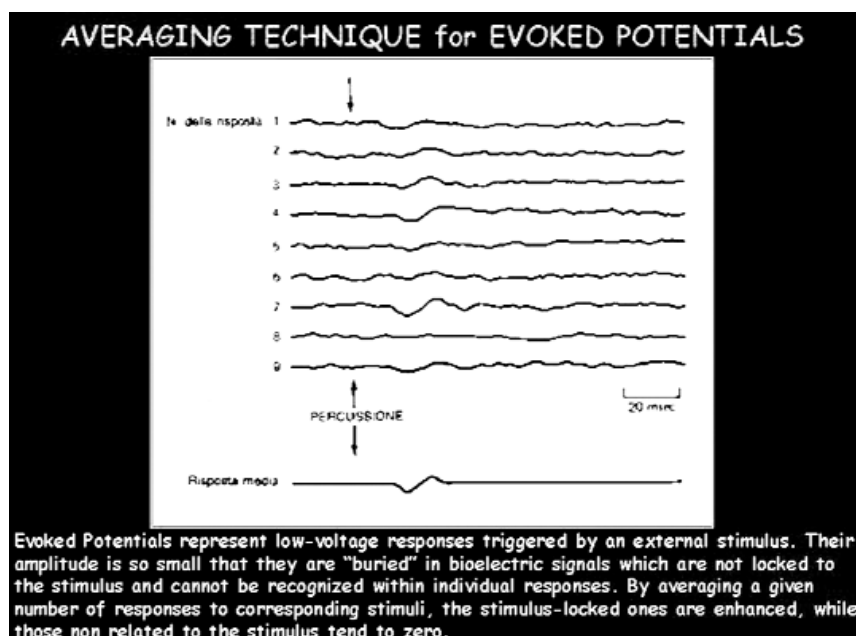


Fig. 4. From traces 1 to 9 we have individual EEG responses to individual external stimuli at the instant of the vertical arrows. Such traces contain both stimulus-related peaks and non-stimulus-related peaks which are randomly occurring. Following averaging procedures (bottom trace) only the stimulus-related response is clearly evident, while all the other trace deflections go to zero.

executed recordings, confirm the loss of function of the acoustic pathways in the brainstem. Similarly, in median nerve SSEPs the progressive loss of waves N20, N18, P13-14 are reflecting the rostro-caudal deterioration of the sensory relays and tracts from the primary somatosensory cortex to the brain stem. Such electrophysiological patterns fit well with the clinical signs of brain death.

Evoked-potential testing (like EEG recording) is non-invasive and not painful for patients and can be performed at bedside by specialized personnel. It is worth recalling that these types of brain responses – at great difference from EEG signals – are virtually independent from the effects of sedative medications.

ABR responses compatible with brain-death diagnosis are clearly showing only wave I and sometimes the early part of wave II.

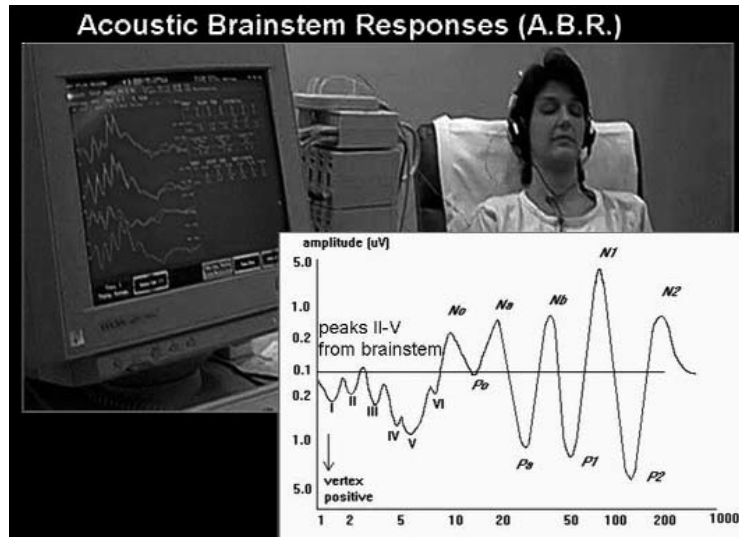


Fig. 5. ABR recordings during monaural acoustic stimuli with clicks delivered via headphones. The non-stimulated ear is masked with white noise. Note in the traces the peaks with Roman numbers from I to VI, which are all generated in the brain stem.

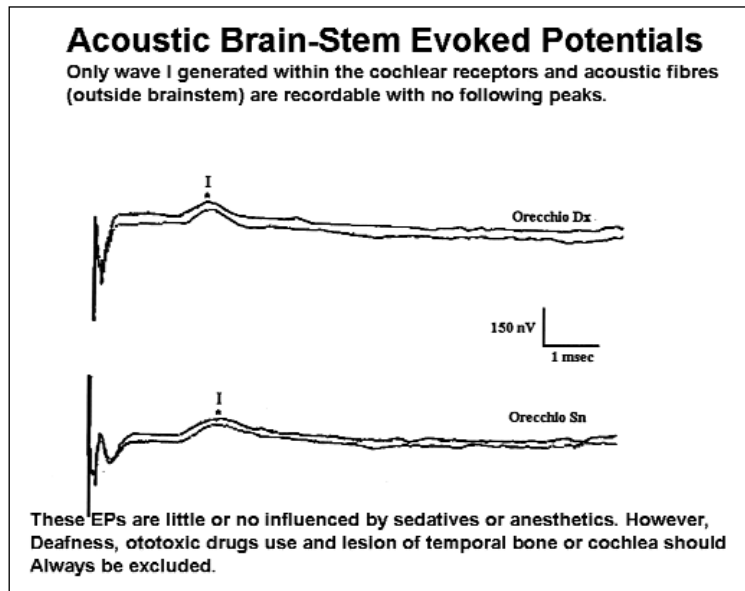


Fig. 6. ABR in brain-death condition. Notice that only wave I (generated within at the eighth nerve level) is elicited by the stimuli of either ear.

Median nerve SSEPs in brain-death conditions are typically limited to waves P9 and P11, while all the following waves are missing. When a P13-14 peak is still present, one can safely maintain that the brainstem is still functioning.

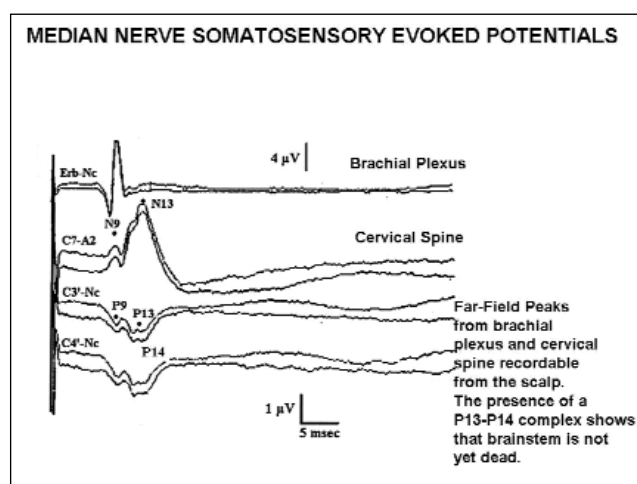


Fig. 7. Median nerve SSEPs in a comatose subject. On the top responses from the brachial plexus, 2nd from top cervical cord-roots responses, 3rd & 4th scalp responses. The presence of the P13-14 suggests that in this case the brain stem is still functioning.

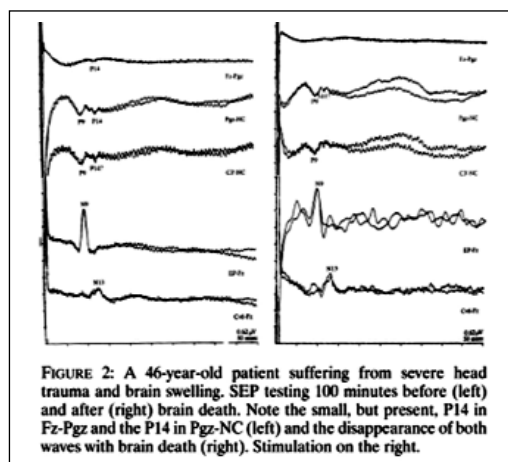


Fig. 8. Median nerve SSEPs in a comatose subject. Traces have been recorded before (left column) and after (right) brain death condition became clinically evident. Wave P14 disappears in the BD condition.



When matching EEG with Evoked Potentials for brain-death determination several main advantages of the latter with respect to the former can be clearly seen: their relative insensitivity to environmental noise with a higher signal-to-noise ratio (due to averaging procedures), a straightforward assessment of brainstem function, their relative insensitivity to sedatives and neuromuscular blockers. Meanwhile, two main limitations should be recognized: they only explore sensory pathways and remain entirely normal in the presence of selective motor pathways derangement (however, modern techniques for transcranial magnetic stimulation of corticospinal fibres and spinal roots can easily circumvent such a limitation), they can be – as already stated in the main text – severely affected or totally missing because of lesions outside the brainstem and CNS (i.e. cochlear damage, 8th nerve lesion within the temporal bone, spinal cord or brachial plexus or peripheral nerve traumatic avulsion).

In conclusion, the following points might be outlined:

- Neurophysiological methods should be considered an extension of the clinical examination
- They are safe, reliable, non-invasive and cheap
- They are not sensitive to muscle blockers and – when EEG is combined with Evoked Potentials recording – to sedatives and metabolic agents
- Instead of being considered redundant, they might actually increase diagnostic safety. A combination of EEG, short- and middle-latency EPs is probably conveying the most reliable bulk of information on cortex and brainstem conditions (>95% of abnormalities compatible with brain-death definition).

## DISCUSSION ON DR. ROSSINI'S PAPER

DR. HACKE Not a question, just a comment. First of all, thank you very much for this comprehensive overview. I can support everything you said fully. We started to discuss the elements of the SEP, asking whether they are generated in the medulla or the spinal cord. The discussion was about the P14A and the P14B, one originating just under the foramen magnum and the other just inside. There is one additional point I wanted to make regarding the brain stem acoustic evoked potentials. In brain death you find, in many patients, a very small wave II, which is about 1/3 of the amplitude of the regular wave II and which is probably the far field reflection of the exit of the acoustic nerve out of the canal.

DR. ROSSINI When they bend.

DR. HACKE Right, when the nerve enters the cerebral spinal fluid this, in a far field projection, generates a potential. This is sometimes confused with the proof of some remaining intrinsic brain activity, which it is not. Can you confirm that?

DR. ROSSINI Well, first of all, as you probably noticed, I stayed away, to be safe, from a P14A and P14B definition and from going in detail on the level of the generators, but I think that if we accept the idea of combining the two methods, we have in our hands an easy method to test the entire brain stem segment, without any discussion whether one wave comes two millimetres below or above a certain generator but still we have a number of waves and peaks that reliably come from there. This gives the answer to your question, yes, it is true that wave II sometimes is seen in brain death subjects, this is probably related to the particular anatomy of that particular subject. We know that wave II is mainly coming from the cochlear nuclei but these kinds of waves are not only generated in the relays but also are generated physically whenever you have an abrupt bending of the nerve fibres. So when you have an angulation of the nerve fibres, like in the

brachial plexus or at the axilla for the peripheral nerves, then you have a far field generator wave and wave II probably has a small component coming from there, which is still outside the cranium.

PROF. BATTRO Thank you Professor. This is a question for you, because I am ignorant of that. I see that most of the problem here is about the signal to noise relation, isn't it? And you dedicated part of your talk to that in a very nice manner. I wonder, do you have any evidence, in this kind of studies, instead of using electricity, of using optical devices, for instance systems like near-infrared light? We are using very often in normal subjects this technology of near-infrared light that goes through the cortex some 30 millimetres deep. Do you have any information on using that? Because it is non-invasive, portable and perhaps could be a supplement to electrical sensitive devices.

DR. ROSSINI The first part of your question was mentioning noise, and let me tell you only a few words more. We should remember that we are working and managing with signals of the amplitude of less than 2 microvolts. We are very close to the limit of our amplifiers, at the present time. Meanwhile, you have signals coming from all the electronic devices very close to your patient which propagate hundreds of volts around the environment so it is not really easy to discriminate, at your recording level, what is coming from the brain and what is coming from outside. Moreover, you have some biological noise, like from the heart or from the expansion of the thorax due to the ventilation, which is confounding. So it is not a trivial problem, the noise, and near infrared spectroscopy might certainly be useful. I have limited experience only in normal subjects and in some stroke patients and I must say that, in our hands at least, it is not an easy tool to be used, it is not as easy as the EEG in terms of having reliable recordings. But in theory, yes, you might add it because it is an indirect proof of some living neurons but still only gives you information on the cortex, because the depth of the exploring system is a couple of centimetres below the scalp, maybe three centimetres, so nothing to do with the brain stem. So it still has the same limitations as the EEG.

PROF. BATTRO Another question about transcranial magnetic stimulation, do you have any experience on that?

DR. ROSSINI Yes, the problem with magnetic transcranial stimulation is that in the real brain stem damaged, but even in the real comatose but even

in the light comatose under barbiturate sedatives magnetic stimulation is completely gone because it is trans-synaptically stimulating the corticospinal fibres and, as you know, the effect of conscious level and the effect of sedatives is very heavy at that level. You might use electrical transcranial stimulation, which is going directly into the corticospinal fibres, therefore bypassing the cortical mantle and that provides you with some hints on that. There are few reports because it is considered somewhat invasive.

DR. WIJICKS Thank you very much for this important talk. You talked about false positives and noise but could you elaborate about false negatives, that the EEG is isoelectric while the patient does not fulfil the criteria of brain death. We sometimes see trauma surgeons order an EEG and then almost forget to do the examination.

DR. ROSSINI Yes, for the EEG, false negative mainly comes from body temperature and sedatives. So you may see a flat or nearly flat condition not due to real damage but due to lack of function because of low temperature and so you have to warm up the body and very often you see some activity coming back. For SSEP and ABR, I suppose the two most important warning points are, for the acoustic, whenever you have a lesion of the temporal bone you might have a lesion of the eighth nerve, and therefore you have no more input, you are stimulating a system which is not arriving to the central nervous system, so you are wrong in terms that you are using the wrong channel. For the somatosensory you might have again either a traumatic avulsion – if you have a traumatic coma – of the cervical roots, but that chance is less because there are many roots if you stimulate that median nerve (you have at least three roots which are involved by the stimulus and you have both sides that you can use, so it is quite unusual to have bilateral avulsion of so many roots), or you might have a spinal cord lesion like the one I showed before. But in this case you still have some peripheral waves that help you. If you have a neuropathy you will see that the Erb's point response is much later and much slower, indicating that you have, for example, a diabetic neuropathy or somebody who has some immune mediated neuropathy or you have nothing because of the rupture and lesion of the peripheral nerve. So I think that if you can exclude, but again it is the same for the EEG, you need people with skill in this specific field, if you ask somebody who is doing only SSEPs in multiple sclerosis and propose to him to interpret something coming from a comatose patient, well, it is dangerous.

DR. WILDICKS Isn't it true that approximately a third of the patients who are comatose after anoxic ischemic injury have absent SSEP or cortical responses on their SSEPs while their brain stem is intact?

DR. ROSSINI For the cortical responses you might be right about, but if you make the correct montage you will see exactly the dissociation I showed you, you still see the far fields the peaks coming from the brain stem, and no cortical responses. Obviously if you use only one channel with the wrong montage you will see a flat trace, which does not provide you with any information on where the propagation of the impulse is getting blocked, which is exactly what you want to know, but if you use the proper montage you will still see the components coming from the periphery, from the brain stem, and nothing coming from the scalp.

DR. ESTOL Discussing also about false positives and false negatives, I would like to ask you about a positive-positive, or a different kind of false-positive that is not the result of artifacts. I am referring to at least one publication from the early 90s, which showed EEG waves in up to 20% of brain dead people up to five to eight days after the diagnosis of brain death.

DR. ROSSINI That opens a big question mark on the meaning of the electrical activity that is produced by those neuronal activities that we were speaking of before. You might have a situation in which you still have some isolated surviving neurons which are producing for some hours or days some electrical activity, completely disconnected from the brain stem centres, but again if you use only the EEG you will see this kind of activity and you will say: '*...no this is not an EEG compatible with a brain death definition ...*', but if you combine the EEG with the evoke potentials and you do not see any brain stem response you may say that you are in presence of a dissociation with some activity coming from surviving, isolated cortical cells but nothing is propagated through the brain stem anymore. And if this is compatible with your clinical condition, I think that you are in the safe condition of saying that you have a brain death in that condition.

DR. ESTOL You understand that I fully agree with you. It is just that this issue raises doubts in people who question the validity of brain death diagnosis when EEG waves are present and it is difficult to answer them.

DR. ROSSINI I understand perfectly. In my early experiences in brain death at least in Italy I have seen sometimes EEG tracings only full of envi-

ronmental artefact and the subject was still not declared brain dead but there was nothing biological in that EEG so I think that it is a complicated matter, we need some good skill and we need teams of people who are devoted to this kind of delicate problem as we have in many other places in medicine. What is astonishing to me is that for such a delicate problem medicine is really not investing new resources in education and also in organising things.

DR. TANDON Have you seen alpha EEG in any patient who has been declared clinically brain stem dead?

DR. ROSSINI No, not myself.

# HUMAN BRAIN, FUNCTIONAL ORGANISATION, ALTERED STATES OF CONSCIOUSNESS AND THE ASSESSMENT OF BRAIN DEATH\*

MARCUS E. RAICHLE

I appreciate very much the invitation to attend this interesting and important meeting but it was a somewhat challenging experience for me. Why, because 'signs of death' have not been a topic that my colleagues and I have specifically addressed in our research. At an evening meal preceding the conference those around the table including a delegation of bishops from Canada as well as conference participants, discussed the upcoming agenda. It was clear that most expected the topic would be restricted to brain death. As a result I became concerned that what I might have to offer would add little of substance to the deliberations of the meeting. Why was that so?

I am a neurologist and have spent most of my research career in the development and implementation of functional brain imaging techniques. These techniques emerged with the introduction of X-Ray computed tomography or CT in 1972, followed by positron emission tomography or PET in 1975. Magnetic resonance imaging or MRI had a somewhat more protracted germination period. The idea for MRI appeared in 1973 with the first anatomical images appearing in 1980 and the first functional images appearing in 1992. The latter work has become known as functional MRI or fMRI. These neuroimaging techniques have become a central element in cognitive neuroscience, a multidisciplinary research enterprise now being conducted world-wide to understand the relationship of brain and behaviour, especially in humans (for a more complete history of functional neuroimaging readers may wish to read Raichle, 2000).

It is critical to note, particularly in reference to this meeting that among these neuroimaging techniques PET is uniquely able to provide accurate, quantitative measurements of brain blood flow and metabolism. If cessa-

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

tion of blood flow and metabolism in the brain is a criterion for brain death then there is little doubt in my mind that PET could provide that information accurately and unequivocally.<sup>1</sup> However, I need not have journeyed to Rome in order to make such a declaration. Neuroscientists including most if not all of those present already know this.

But, as I thought about this a bit more deeply, it seemed to me that measurements of brain circulation and metabolism in an individual in whom the diagnosis of brain death was being considered could yield two possible outcomes. One, of course, would be that the circulation to the brain would be absent and no metabolic activity would be measured. This would certainly be consistent with the diagnosis of brain death. But suppose measurable circulation and metabolism were present. How should such information be interpreted? In considering this question I thought it useful to examine what functional neuroimaging has to offer. What follows is brief overview of functional brain imaging and how it might contribute to our assessment of brain death and altered states of consciousness. Many important scientific details are dealt with only briefly. Readers interested in a more detailed treatment may wish to consult (Raichle and Mintun, 2006).

It is of interest to note that an important scientific element of functional neuroimaging was discovered in Italy by the distinguished Italian physiologist Angelo Mosso. He was an enormously talented 19th century scientist who studied many different things among which was the relationship of brain blood flow to brain function. His book (*Über den Kreislauf des Blutes im Menschlichen Gehirn*, Mosso, 1881), describes a gentleman by the name of Bertino who had a permanent defect in his skull (covered of course by the soft tissue of the scalp) from a neurosurgical intervention. What interested many prominent scientists in those days including Mosso were the brain's pulsations and what they might mean. Through the use clever devices of his own design Mosso was able to measure simultaneously the blood pressure in the forearm and the pulsations of the brain through the defect in Bertino's skull (one can liken the pulsations that Mosso was studying to those observed by every parent who notices the pulsations in the soft spot [fontanelle] of their newborn infant's skull). As Mosso was recording Bertino's brain pulsations the church bells rang. It was noon. Mosso noted immediately that the pulsations over the brain went up briefly prompting

<sup>1</sup> It is fair to say that future developments in MRI likely will make quantitative measurements of brain blood flow a reality with this technique as well.



him to ask the Bertino if he should you have said a prayer? Surprisingly, the brain pulsations again went up briefly. What Mosso did next was clearly the mark of a great scientist. He seized the opportunity to ask Bertino to multiply 8 by 12. When asked to do this Bertino's brain pulsations once again went up briefly and again moments later when he provided his answer to the question. Throughout there was no change in Bertino's blood pressure. Mosso concluded that Bertino's mental activity had changed blood flow to the brain. The validity of Mosso's conclusion has been reaffirmed literally thousands of times in the 125 years since it was presented and now resides at the heart of our understanding of the functional neuroimaging signals (Figure 1, see page 424).

While the measurement of blood flow itself was critical to functional neuroimaging with PET, it took an unexpected finding on the relationship of blood flow to brain oxygen consumption to pave the way for fMRI. As researchers began to explore in more depth the nature of the blood flow and metabolism changes occurring in the brain as function varied it was discovered that blood flow changed much more than did brain oxygen consumption (Fox and Raichle, 1986; Fox, Raichle *et al.*, 1988) (Figure 1, see page 424). This discovery was at variance with the standard view that blood flow varies to keep pace with the need for oxygen. This novel observation, as discussed in detail elsewhere (Raichle and Mintun, 2006), became the key to fMRI, a technique that has been responsible for the vast majority of functional brain images appearing in scientific journals and the lay press for the past 15 years. A full discussion of the physics behind fMRI is beyond the scope of this presentation. Suffice to say the MRI signal is quite sensitive to the amount of oxygen in circulating blood. As this changes regionally within the brain so does the intensity of the MRI signal. This has come to be known as the blood oxygen level dependent or BOLD signal of fMRI after the work of Ogawa and colleagues (Ogawa, Lee *et al.*, 1990).

In the past 15 years literally thousands of functional neuroimaging studies have been performed with fMRI. Among these many studies one stands out in terms of its relevance to the concerns of this conference. This report (Owen, Coleman *et al.*, 2006) presented fMRI studies of a patient in a vegetate state following severe head trauma. A vegetative state has come to be recognized in the neurological community as a condition in which a patient appears to be awake but exhibits no awareness of his or her environment. Surprisingly, despite fulfilling the criteria for the diagnosis of vegetative state, this patient exhibited changes in brain activity measured with fMRI that appeared remarkably similar to a group of

normal control subjects when she was asked to imagine entering her house and walking from room to room.<sup>2</sup> While it remains to be determined whether these findings will generalize across patients currently receiving the diagnosis of vegetative state it is highly likely that such measurements will become increasingly important in the clinical management of these tragic patients. Future studies of this type will challenge scientists, theologians, ethicists and lay persons alike to understand more fully the relationship between brain function and behaviour and how this is being revealed by modern functional neuroimaging techniques.

With the exponentially increasing number of functional neuroimaging studies present in the scientific literature and often widely discussed in the lay press it is difficult to maintain a sense of perspective on just how much this information is telling us about how the brain works. Why is this so? It relates to the fact that the brain activity changes observed with functional neuroimaging represent very small changes in the overall activity of the brain (Raichle and Mintun, 2006). How do we know this?

Let us begin with a few simple facts about the human brain. It represents approximately 2% of the body's weight and yet it accounts for at least 20% of the body's energy consumption. This is 10 times the energy consumption predicted on the basis of its weight alone. Even more importantly between 60 and 80% of this energy consumption is related to the function of the brain. Yet, the changes reported in functional neuroimaging studies may be as little as 1% (see Raichle and Mintun, 2006 for a recent detailed summary of this literature).

Focusing in this manner on how the brain allocates its considerable energy resources for the functions it performs introduces a debate about the nature of brain function that has existed since the 18th century and possibly longer. This debate concerns two perspectives (Llinas, 2001).<sup>3</sup> One posits that the brain is primarily driven by external inputs; the other holds that the brain operates on its own, intrinsically, with sensory information interacting with rather than determining its operation. While today neither view is dominant, the former clearly has motivated the majority of research at all levels of neuroscience including almost all functional neuroimaging. This is not entirely surprising given the enormous success of experiments

<sup>2</sup> She also exhibited findings similar to normal controls when asked to imagine playing a game of tennis.

<sup>3</sup> Rodolfo Llinas provides a wonderful introduction to this interesting history in the first chapter of his book *I of the Vortex*.

measuring brain responses to controlled stimuli. From an energy, cost-based perspective, however, intrinsic activity may be far more significant than evoked activity in terms of overall brain function.

It is natural to inquire as to the nature of these costly intrinsic functions. In some ways it is similar to the questions surrounding 'dark energy' in astronomical terms (Raichle, 2006). The challenge we face is how to evaluate an aspect of brain functionality that is not directly related to the performance of an observable task. Fortunately, there are some important clues about how to proceed that will likely be relevant to discussions of altered states of consciousness in the future.

The first clue about the organization of the brain's intrinsic activity comes from the observation that when we engage in a task we observe not only task-relevant increases in brain activity but also highly organized activity decreases (Shulman, Fiez *et al.*, 1997; Raichle, MacLeod *et al.*, 2001) (Figure 2A, see page 425). The discovery of these activity decreases provided, we believe, the first glimpse of the nature of the brain's intrinsic activity and have increasingly suggested that this intrinsic activity exists in a highly organized manner at all times (Gusnard and Raichle, 2001; Raichle and Gusnard, 2005). This view has been reinforced by studies of what was initially viewed as 'noise' in the fMRI BOLD signal.

When conducting an fMRI functional neuroimaging study it has been customary to repeat studies many times in subjects in order to enhance signals of interest and suppress noise. This was standard operating procedure until it was discovered that the 'noise' in the fMRI BOLD signal (Figure 2B, see page 425) contained much valuable information on the organization of the brain's intrinsic activity. As demonstrated in Figure 2C (see page 425) large scale brain systems are revealed through patterns of spontaneous coherent activity emanating from the apparent 'noise' in the fMRI BOLD signal. While the images in Figure 2 (see page 425) depict one such system, and one likely important in the context of altered states of consciousness (Laureys, 2005), many other systems have been detected in the same manner (readers will find examples of interest in (Fox, Snyder *et al.*, 2005; Vincent, Snyder *et al.*, 2006) as well as reviews of this rapidly expanding literature).

What is important to note about the network of areas depicted in Figure 2 is that not only do these areas exhibit as a group activity decreases during the performance of a variety of tasks (Figure 2A) but at rest the areas within this network exhibit continuous, activity fluctuations (Figure 2B) that are coherent within the network (Figure 2C). This is also true of

networks that exhibit task-relevant increases in activity (for example see (Fox, Corbetta *et al.*, 2006; Vincent, Snyder *et al.*, 2006). They too can be found to exhibit continuous activity fluctuations that are coherent within the network. In an interesting way this ongoing, dynamic organization of the brain, exhibited here as spontaneous fluctuations of the fMRI BOLD signal, appears to anticipate relationships among areas used in the performance of a wide range of tasks.

What is this intrinsic activity? One possibility is that it simply represents unconstrained, spontaneous cognition – our daydreams or, more technically, stimulus-independent thoughts. But our daydreams are highly unlikely to account for more than that elicited by responding to controlled stimuli, which accounts for a very small fraction of total brain activity (Raichle and Mintun, 2006).

Another possibility is that the brain's enormous intrinsic functional activity facilitates responses to stimuli. Neurons continuously receive both excitatory and inhibitory inputs. The 'balance' of these stimuli determines the responsiveness (or gain) of neurons to correlated inputs and, in so doing, potentially sculpts communication pathways in the brain (Haider, Duque *et al.*, 2006). Balance also manifests at a large systems level. For example, neurologists know that strokes damaging cortical centers controlling eye movements lead to deviation of the eyes toward the side of the lesion implying the pre-existing presence of 'balance'. It may be that in the normal brain, a balance of opposing forces enhances the precision of a wide range of processes. Thus, 'balance' might be viewed as a necessary enabling, but costly, element of brain function.

A more expanded view is that intrinsic activity instantiates the maintenance of information for interpreting, responding to and even predicting environmental demands. In this regard, a useful conceptual framework from theoretical neuroscience posits that the brain operates as a Bayesian inference engine designed to generate predictions about the future (Olshausen, 2003). Beginning with a set of 'advance' predictions at birth, the brain is then sculpted by worldly experience to represent intrinsically a 'best guess' ('priors' in Bayesian parlance) about the environment and, in the case of humans at least, to make predictions about the future (Ingvar, 1985). William James, in his *Principles of Psychology* (1890) captured this perspective in another way when he said: 'Enough has now been said to prove the general law of perception, which is this, that *whilst part of what we perceive comes through our senses from the object before us, another part* (and it may be the larger part) *always comes ... out of our*

*own head'*. Finally, it has long been thought that the ability to reflect on the past or contemplate the future has facilitated the development of unique human attributes such as imagination and creativity (Hawkins and Blakeslee, 2004; Gilbert, 2006).

How might such information be useful in the evaluation of individuals with altered states of consciousness? Following a long tradition in neurology, clinical assessments of prognosis and decisions about treatment continue to be made on the basis of clinical examinations by competent physicians. However, that assessment has been increasingly augmented by sophisticated tests of every conceivable sort the most sophisticated being those that assess directly the integrity and function of the brain. In this category functional neuroimaging is rapidly taking its place. The recent report by Owens and colleagues (Owen, Coleman *et al.*, 2006) mentioned earlier is the latest and certainly the most provocative to date. Other studies of this sort are sure to follow and fuel discussions about the relationship of brain function to behaviour in patients with altered states of consciousness.

In addition to this more traditional use of functional neuroimaging (i.e., examining the brain's response to momentary demands of the environment); e.g., (Owen, Coleman *et al.*, 2006) there is now before us the prospect of obtaining an even deeper understanding of the functional organization of the brain based on its intrinsic activity which we presently posit to underlie our ability to maintain information for interpreting, responding to, and even predicting environmental demands. Because this type of information can be obtained with functional neuroimaging without the need for any response on the part of the subject it is particularly suitable for the evaluation of patients with altered states of consciousness. However, our use of such information must be based on a thorough understanding of the basic neurobiology as well as the prognostic value of such information. Coming to this understanding will be one of the great challenges for researchers and clinicians in the coming years.

As we seek an ever deeper understanding of brain function and its relationship to behaviour it is of paramount importance to keep in mind that the brain is not just another organ with *a* function. Rather, it is a modular *system* of immense complexity which must function as an integrated whole for there to emerge the behaviours we associate with sentient human beings. Critical to our assessment of prognosis in cases with severe brain damage will be information on the integrity of brain systems as a functioning whole. Information from functional neuroimaging will likely be of considerable utility in this regard.

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## DISCUSSION ON DR. RAICHLE'S PAPER

DR. HACKE Thank you very much, that was a wonderful presentation and I hesitate to discuss something that I have not even read yet. Obviously it is a science paper, and I would act like a politician, if I discuss something that I have no knowledge about. But what you presented was what I would expect if a patient in a locked-in syndrome were tested without sedation or anaesthesia. It is not what I would expect in a patient who has permanent vegetative state after diffuse brain trauma. So what I am missing right now is the information, what the patient's real physical condition was. What did the imaging look like, did we see the typical defects after a diffuse trauma or did we see something that is related mainly to the upper brain stem. If these findings were true for permanent vegetative state it would simply throw away our whole concept of what permanent vegetative state means to the cortex, means to the hemisphere and therefore, I feel that there is reasonable doubt about the correctness of the diagnosis permanent vegetative state.

DR. RAICHLE I have read the article but I would defer to the experts. All I can say, from my vantage point is that the researchers involved in this study were experts.

DR. POSNER She is 23 years old and is only five months out from a head injury so it is unlikely...

DR. RAICHLE She is now 11.5 months out and may have some responsiveness according to the article... she was studied at 5 months.

DR. POSNER Five months, so she is probably in a vegetative state that may very well recover and she is beginning to recover some function apparently.

DR. RAICHLE I do not know, I know these people fairly well and last night I tried to get hold of Adrian Owens by email because I had a number of



questions about it. For example, it would be very nice to know more about the anatomical imaging. I would also be very interested to know whether this woman exhibited the clear decreases in her system that I would expect when performing these tasks. And, I would love to know what her resting fMRI looked like. In other words, how well is this brain really organised. Are the systems that I have been talking about operational in there because in a normal person you could easily do that but I do not know whether that exists at the moment.

DR. HACKE And in addition, the tasks that they asked for are pretty complicated. It is a difficult thing to imagine how to play tennis.

DR. RAICHLE I agree, if you had a graduate student that came in and said the first thing they wanted to do was have somebody envision playing tennis you might say, wait a minute, this sounds pretty uncontrolled. On the other hand, when I read the paper, my reaction to it was, that the complexity of the task makes the results all the more compelling. If you had simply presented a visual stimulus or a painful stimulus, you could argue that she might not actually be aware.

DR. BERNAT That was a beautiful talk, Marc. The goal of people doing fMRI is to try to understand the brain processes that underlie various acts. I think you pointed out very correctly that it underestimates the brain's complexity merely to look at those areas in which that fMRI can measure an increase in activity. I do not want to use the word 'activation' after what you have said but that is the word that is usually used. To look at the areas are activated underestimates the complexity of the function because other areas also play a role. I have a technical question regarding the ability of this technology to identify the order of activation of the various elements. Again addressing the question of how is it done, does the technology exist to see which areas are activated first, second, and third?

DR. RAICHLE There is quite a history of this in terms of tasks, it has been called functional connectivity, so people engage in some kind of a task, you get an array of areas in the brain and then various mathematical approaches are attached to that, looking at the strength of the relationships and inferring the way information moves within these pathways but what is particularly interesting to us at the moment is what is going on without any task. In other words, what is the correlation structure

within a system, within the brain, while it is at rest, assuming that it is probably not just going up and down together, that things are happening here before they are happening there. The hints we have are that that is indeed true. This is mathematically very challenging and techniques such as what is called Granger causality are being applied with some success I might add. Another issue is whether the strength of the relationship among areas in a system change over time and also does it matter when you are doing a task where on this fluctuating background it occurs. Think of it as the tide going in and out, does it matter if you squeeze your hand at high tide or at low tide. So there are a host of questions beyond just laying out the architecture and I think timing within the systems is very important. I am certain that imaging will not carry the day entirely here, that we need, in addition to putting more and more electrodes in the one spot in a brain, that we need to be able to put electrodes in highly distributed, identifiable like the monkey ocular motor system and ask the question how information is being moved. I may have failed to tell you that these fluctuations are exceedingly slow, they are .1 Hz and people have generally not spent as much time looking at very low frequency, I know it has been looked at in the EEG, but we are very interested in knowing, in terms of the EEG itself, what is that relationship and one good guess is that the slow frequencies represent nested higher frequencies so we are looking at power envelopes in different frequencies which is very intriguing, in other words the brain is operating almost like an AM radio station in terms of the way it talks to one part or another.

DR. ROSSINI Yes, for the very low frequencies one piece of the story might be the recent studies by the group of Tononi in Wisconsin.

DR. RAICHLE I am actually a collaborator with Giulio Tononi.

DR. ROSSINI They believe this is an EEG sign of consolidation of synaptic activity collected during the wakefulness during sleep and this is going to consolidate your experience of the daytime for the rest of your life. So it seems to be a very localised EEG activity, which has a lot to do with consolidation of the synaptic experience in the previous hours.

DR. RAICHLE We are actually collaborating with him in order to provide the metabolic side of the story. While I did not elaborate, these fluctuations in our own imaging signals, as best we can tell it, are probably related to

ongoing glutamatergic transmission and the reason you can see them with fMRI is that glutamate is processed by glycolysis in the astrocyte. Why the brain was designed that way is not clear, but that is the fact so that causes the separation of oxygen consumption, blood flow and glucose utilization, opens what we call the glycolytic window and now you have BOLD and the question is, obviously, now you are talking about glutamate, you are talking about NMDA receptors and all of the things that have to do with learning and memory. And the question would be, would the ongoing fluctuating structure of this thing change with experience? And we are actually doing the same task as Giulio and Licci Vilardi and the group in New York were using and we are getting some hints that that is probably true and the next question is, does that reorganize? But you probably did not realise, and I was stunned to find out, that when you go to bed at night, your brain blood flow is 20% higher than when you wake up in the morning. That is published and is published by a very good group. And I do not believe the oxygen consumption is 20% higher, my guess is it is glycolysis because if we went to bed and our brain oxygen consumption was 20% higher I think we would be a little breathless. So, anyway, you are absolutely right, this is a fantastically interesting area, I am a big fan of what Giulio is doing.

BISH. SÁNCHEZ S. When the brain is dead is there evidence that we do not have flow or chemical...?

DR. RAICHLE I would assume that if the brain were truly dead, that all circulation had stopped for a sufficient period of time to destroy the cells in large measure in the brain that none of what I talked about would be evident, I would be quite surprised. At what level that occurs, and how much it takes to do that, I think is a very important question to ask. It is one way beyond... simply, people like myself say, yes, the brain is getting blood flow or not, I think we can do better than that and say more about the organisational structure and in concert with people who do EEG for example. I think the whole relationship there is very important to understand and I think we have some ways to think about it. So, if nothing else, coming to this meeting stimulates me to think about stuff like this. But if the blood flow is down and gone for long enough and we already know from isolated strokes brain dies and if it is for the whole brain the whole brain is not going to be there and I would not expect there to be any of this. Some people have occasionally said, well, are these respiratory signals or are they vascular? I did not get in to all the arguments that that is not the case. These

are neuronally-driven signals and if you do not have neurons in the astrocytes and the other cells that support them, if they are not alive, I would bet you will not have these signals but did the lady in *Science* have them? I would dearly like to know!

PROF. BATTRO Thank you. May I ask you a question that complicates perhaps the issue. Will you agree that we can make a difference between the neuronal death at the glial death?

DR. RAICHLE You know, maybe I would expand it further and say, can we even differentiate the neurons? You know, there is one big division here and that is the interneurons which are 20% of the population and the principal cells which are 80% but the interneurons are firing 10 to 20 times higher rates of firing, but you know you can get into all this way of thinking about this and I have been puzzling a good bit with Yuri Bessaki, we have been trying to write a review about this and we still have not quite agreed. That itself, the neuronal populations and how you might begin to understand the roles, the individual roles they are playing, is very important but from an imaging perspective it is a very difficult question. The astrocyte is a late-comer but a very important part of this story.

PROF. BATTRO There are more astrocytes than neurons.

DR. RAICHLE That is right, and they are metabolically active but in very special ways. This partitioning of glycolysis is quite unique. I do not want to get too far afield but there is a whole story, I mean, sodium potassium ATPase is a very important energy consumer in the brain and the glycolytic enzymes that support it are the same whether it is in a dendrite or in an astrocyte but at the moment it looks like it is the astrocyte that is giving us this signal and while we have known this fact about sodium potassium ATPase for heaven only knows how long, it has been largely overlooked so there are all these questions that are being driven by the data that we are trying to explain and I am very excited by the fact that a lot of good people are beginning to think about this.

# BRAIN DEATH – AN ARTIFACT CREATED BY CRITICAL CARE MEDICINE OR THE DEATH OF THE BRAIN HAS ALWAYS BEEN THE DEATH OF THE INDIVIDUUM\*

WERNER HACKE

In this presentation I will bring you back to a very basic level discussing the brain dead patient as an artefact of critical care medicine.

While preparing this talk I decided to include very basic information on how the human body and the brain die because I feel that some of our colleagues are not familiar with those physiological details. For my medical colleagues, on the other side, this information is probably very trivial and my excuses for being too superficial here.

## *A Couple of Introductory Theses*

The death of the brain was always part of the death of the human being. In former times it was not possible and not necessary to distinguish between the death of different body systems because once the heart stopped beating, after a couple of seconds, the patient became unconscious and, as we know from animal experiments, there is only a limited time that brain integrity can survive without oxygen, blood flow and glucose. So it made no difference whether one would talk about the death of the heart or the death of the brain. These conditions were intercorrelated. The cessation of heartbeat and ventilation led to coma and death within seconds or minutes and the damage to the brain happened within the same timeframe. In older days, breathing and heartbeat were easily accessible to physicians and to lay people while coma was the only thing that gave a hint about the functioning of the brain.

Times changed, however, when resuscitation became available. With resuscitation, we can probably interrupt the process when we interact quite early. However, some phylogenetically old parts of the brain are a little more resistant to oxygen depletion and may survive longer intervals of

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

anoxia while newer parts of the brain, specifically the hemispheres, are more susceptible to injury and die. This may result in a permanent vegetative state. If the resuscitation took too long or was unsuccessful, brain death occurred, followed by the interruption of reanimation leading to the death of the remaining body systems.

Brain death, therefore, is not a new concept. The brain died with the rest of the body and it simply did not make much of a difference whether it died because it was injured first or it was injured by the cessation of, for example, heart or pulmonary function.

The problem that we are facing, and this is why the topic of brain death became so interesting, is that we are not only able to perform short time resuscitation, but also are able to replace some of the basic functions of the body with modern medical technology. We can even replace organs. We can transplant hearts and lungs. We have patients surviving with artificial hearts, waiting for their transplant, for months. One essential part of the body is not functioning anymore, a situation that would have caused death in older days, but now it can be replaced. Here is where Critical Care Medicine comes into play.

I would like to discuss ‘natural death’ versus ‘brain death’. I will talk about the definitions and about misperceptions and misunderstandings among lay people and among physicians, which frequently are based on different terminologies. Most problems that we are facing today is based on wrong definitions and wrong terminology, for example confusing persistent vegetative state with brain death.

### *A Primer on Physiology*

The three central players in the whole game are the heart, the lung and the brain. All three are essential for the integrity and the survival of the human being. They have different characteristics.

The heart has very simple functions: it is a muscle, a machine that pumps blood into the body. It is autonomous in its action. The heart beat is automatic and may be modulated by the nervous system. This modulation, however is not needed for the heart’s survival. The heart is fully dependent on the lung, on oxygen and on the blood’s fuel, which is glucose. It needs energy and oxygen.

The lungs are also simple in their function. They are responsible for the gas exchange and oxygenation of blood. This mechanical process of breathing is generated by muscles. These muscles are activated by a tiny region in

the lower brain stem. Without the brain's signals, no breathing is possible. The respiratory drive is completely dependent upon this small area in the lower brain stem.

The brain is, as we all know, much more complicated. It has multiple functions and one of the very basic ones is the function that controls the ventilation process. The brain, this unbelievable organ, is completely dependent on blood flow from the heart carrying oxygen from the lung and glucose from other parts of the body.

In summary, there is the control of the lung by the brain stem, there is the interaction between oxygenation in the lung and blood flow that goes back and forth (without blood flow there is no oxygenation and, vice versa, without oxygen the heart will stop beating at one point in time), and finally there is the complete dependency of the brain from blood flow that is coming from the heart.

### *Natural Death*

So how does a person die? What happens in so-called 'natural death', for example in a fatal heart attack, is quite simple. The brain is the organ that suffers immediately after the heart stops beating. The brain does not get blood anymore, it is missing  $O_2$  and it is missing glucose. Coma will occur within seconds. This leads to a failure of the respiratory drive within and that adds to the full loss of oxygenation in the blood. All parts of the brain will quit their function irreversibly after five to eight minutes. Maybe some small areas of neurons or glial cells will survive for ten minutes. When we interfere at an earlier time point by resuscitation, then we will see some of remaining parts of the brain surviving with the well-known sequelae.

Another type of 'natural death' occurs when the lungs quit their functions, e.g. in massive pulmonary embolism. Again,  $O_2$  is missing, the brain does not receive enough oxygen, coma is the answer. Cardiac output is also affected and the failure of the respiratory drive coming from the brain after 30 to 300 seconds leads to brain death and heart arrest. Again, all three areas are interdependent.

Everybody has always accepted massive trauma to the brain as natural death, for example a shotgun wound, a massive haemorrhage, or a massive subarachnoid haemorrhage. These conditions lead to immediate coma, loss of respiratory drive, cessation of breathing. The heart may continue to beat for maybe five or ten, sometimes twenty minutes and then stops because of anoxia (if we do not interfere).

There is no death of a human being without death of the brain. Brain death, the irreversible loss of function of all parts of the brain, was always the decisive part of any individual's death. I will use the term 'brain death' as opposed to 'loss of function' for all the other organs, for some good reasons that I would like to discuss in a minute.

### *Some More Definitions*

Now we all agree that the death of the brain is the death of the human being and that the irreversible damage of the brain is the basis for brain death. Unlike in heart failure or pulmonary failure, a dead brain cannot be substituted by machines or transplants. Once this diagnosis is established the individual is dead and the patient is not a patient anymore. That is an important thing when it comes to psychology, like care for a brain dead body. It is, in my opinion, not care of a patient anymore and we will come back to that.

The term 'isolated brain stem death' is misleading because it does not cover the death of the whole brain. Therefore I propose to call it 'isolated loss of brain stem function'. Once the other parts of the brain are included, we may call it 'brain death' but we should not call it 'brain stem death'. The permanent vegetative state for some time can be identified with proper examination and good training, which is essential for those people who are dealing with those types of patients. Frankly it cannot be confused with brain death.

### *Critical Care Medicine*

The most important advances in medicine in the past fifty years are imaging and Critical Care Medicine. Critical Medicine started with the simple substitution of the excursions of the thorax, which the lung will follow passively – the 'iron lung' in the polio epidemics of the 40s and 50s of last century. Oxygenation of the blood became possible although the respiratory muscles were paralyzed. In the meantime, we have much more sophisticated interventions such as extracorporeal circulation, artificial heart techniques and advanced ventilation protocols to allow individuals to live with the function of a part of the body that previously was thought to be essential for life being replaced.

We can lose the function of the lung and survive, we can lose the function of the heart and we substitute it with a machine or a transplant, and the brain may remain unhurt.



But what if the brain is irreversibly damaged? The ventilatory support of a patient who has suffered major brain damage that would eventually lead to immediate death simply interrupts the cascade that I described previously by substituting nothing else than the mechanical excursion of the chest.

The loss of brain function is now compatible with the survival of the remaining body. The loss of the respiratory drive is substituted by a machine and does not lead to complete loss of function in the remaining parts of the body. The brain has died but the lung can continue to do its job. Anoxia will not occur and the heart will continue to beat with its endogenous rhythm and that leads to a situation like those famous or notorious cases where a brain dead pregnant woman can give birth to a healthy child eight months later or six months later.

Was this still a human being? Physiologically it is not a problem. Many parts of the body may function on, while the brain is dead. This is only achievable by Critical Care Medicine. Without Critical Care Medicine this problem does not exist at all. Even nowadays, when patients do not have access to Critical Care Medicine, brain death does not exist.

I do not believe that, in a time that we all will experience, there will be a replacement for a dead brain and if there will be, it would be a replacement of a body to a brain, in my opinion, and not of a brain to a body. But this is a discussion that we probably do not need to enter today because we all will not experience a situation like that.

When we have a respirator started on such a patient, it does not substitute the brain function.

Therefore I would like to submit that the death of the brain is the death of a human being and I know that there is probably no discussion about that among us. I would also submit, that this is only true if all functions of the brain are irreversibly damaged.

### *The Definitions of Brain Death*

The definitions of brain death are much more straightforward than the definitions of natural death. The fear that there may be wrongdoing in the diagnosis of brain death is probably less important than the fact that coroners always tell us of how many mistakes are being made when the natural death of a human being is assessed or the cause of the natural death.

Is it a problem, that there may be some cell groups not finally disintegrated? One argument regarding those potentially still viable cell groups is that we cannot assess it with other tests. Well, this is true for the death of the

body as well. All cultures have accepted for centuries and even longer, that after the death of an individual there is some growing of hair, there is some growing of fingernails. In fact, the old Nordic mythology describes that the end of the world will come when a ship built of the still-growing fingernails will arrive, with a sail woven from the still-growing hair. Do we have to care about a little group of cells in the brain that is still sending some electrical signals? Think of the fact that the semen of a recently dead man can still be used for artificial insemination. Obviously, some cells are viable but that will not hinder us to say this patient is dead. I would like to take this example and carry it forward to the clusters of nervous cells somewhere in the brain that may still be there for five or eight or twenty more minutes.

The German rules for brain death take care of the question of training. In Germany we need to have two independent and experienced investigators, who must have training in the critical care of nervous diseases. Neurologists and neurosurgeons take care of that, and that is part of the training. Training takes care of experience, there is no such thing that someone drops by and does not know the examination of a brain dead patient. This certainly makes the diagnosis even safer in our hands. We have different observation times for different causes of brain death. It is different when you have a primary injury to the central nervous system – the observation time is shorter – than if you have a secondary insult. Ancillary tests can be used and in some specific situations they are required for example in isolated brain stem functional loss, where an EEG is required. Of course, precautions including intoxication, hypothermia and so on exist like in others.

### *Brain Death: Concerns and Misperceptions*

Relatives of patients frequently do not accept that their loved one is going to die. When we start talking about transplantation, their idea is that you will let the patient die in order to harvest organs! There was very bad press about that when we had the discussion about the new transplantation law in Germany and people really stood up and described patients who were not brain dead that would be considered organ donors.

You may have noticed that, until now, I have not talked about transplantation, because I feel the concept of brain death is not exclusively linked to transplantation. For us it is an important area also for utilisation of resources on an ICU. We cannot go on to ventilate someone who is brain dead and is not a candidate for organ transplantation because of sepsis, because of HIV, because of metastatic cancer and so on. If they

have or developed a brain death syndrome the same rules apply and the same decisions are needed afterwards. Interestingly, the group of people who usually accuse critical care physicians of overuse of critical care facilities not allowing people to die now blame us of 'stopping critical care prematurely to harvest organs'.

How to deal with a brain dead patient actually, I submit, this is semantically wrong: It is not a 'brain dead patient' because it is not a patient anymore. It was a patient, it was a human being and now it is a dead body. And this dead corpse needs the same dignity and the same behaviour from our side that we would offer to every demised former person. There is also no specific need for nursing in this situation, unless we have organ-preserving therapy, if organ donorship is an option. But otherwise, this is not a patient anymore. If no transplantation is planned, organ support – it is not life support anymore – should be terminated after close counselling with the relatives who are now the ones who need our attention much more than the former patient.

## DISCUSSION ON DR. HACKE'S PAPER

DR. ROPPER Thank you. Well, I appreciate that you saved me enormous amounts of trouble for my talk tomorrow. While everything you have said is valid and you are speaking to people who have been brought along in this conceptual process of brain death which has evolved while our careers were in progress, we have had the opportunity of 20-30+ years to accommodate ourselves to this but the fact remains there is still a major public problem in its acceptance. In part this is because the body is warm, it looks like air is moving, there is a pulse, there is blood pressure. That is our next responsibility, I think. I also think it might be a little bit harsh to necessarily have the medical profession insist that just because this patient has fulfilled the criteria for brain death that nothing can be done medically, you cannot administer drugs, it creates a little bit of a problem. Now, I am in favour of it, that is not the problem, the problem is it is an extension of the problem. I am not being facetious but I think we need a name or a terminology or an identity for these transitional bodies. Something like, like neonates are newly born, these are *neomorts*, newly dead. I am told by Dr. Bernat that this term was proposed by Dr. Willard Gaylin. I do not mean it to be funny because, it is 2006 and we are still having this conversation, not just among ourselves, which is a particular type of medical sociologic problem but with the public and with the press and even if you cut out all the paranoids who think that you are trying to harvest organs, I think there is a big issue. So what is the sociologic solution? It is a little glib for us, having again had decades to come to an understanding of this, to project to the public. I just wonder where you would like to go with it now that we are here.

DR. HACKE I believe one point that you made is absolutely correct and we have to acknowledge it. Our societies have no idea about biology; even academicians have no idea about physiology. Brilliant people, outstanding scientists from other fields need to understand and to learn how those three basic organs work together, they do not know that! They have no idea that the heart beats by itself and that the lung needs a little place in the brain to

steer its function. This is where we have to start and when you talk in our educated way about some physiological basics, they do not understand that. They have no training in physiology or in biology whatsoever and this is why we have a big problem when we talk to a journalist who is similarly untrained and inexperienced and, in addition, has this endogenous fear that something wrong could be done to you. That is simply the reason why we failed in Germany to have the useful new law in which, for example, at the age of 18, when you get your driver's licence, you would simply tick 'I am willing to be an organ donor' or not. We did not get it in because it created an enormous discussion and there was fear and panic and paranoia of wrong diagnosis and premature 'organ harvesting' even in the highest level of academicians and politicians.

DR. TANDON Thank you very much. I think Professor Ropper has pointed out the real practical issues. Talking among us whatever you say may be acceptable. But it is not talking among us that matters in day to day professional work, it is talking to the family, it is talking to others not directly family as you say, the journalists for that matter, therefore we should be as precise in our statement as is unlikely to be misunderstood or misquoted. My worry is, again and again, with the use of term 'all functions of the brain', a legal expert can tear you to pieces by giving hundreds of examples from studies by scientists that say 'all functions are not lost' at the time when you are declaring the patient 'brain stem dead'. We are here to discuss scientific issues but a scientist cannot live in total isolation anyway, therefore I have a little reservation in using that word. Similarly when you say, isolated brain stem death is not death unless the whole brain dies and yet all the tests we do today, that most countries have legalised, do not require that qualification. So that is a little concern because as a practicing neurosurgeon there are many many occasions when we knew the patient had brain stem death we could not declare the patient dead, we could not ourselves have the conscience to switch off the ventilator till it was legalised in the country and the legal statement is very clear and unambiguous, stating that by the following criteria if this group of people declares a person brain stem dead, then the person is dead. All the treating team is fully authorised to switch off all the support system to maintain that, as you say, 'cadaver'. That is an unequivocal statement. But when you keep on arguing about whole brain and brain stem etc I think this is likely to be misunderstood. Now you used another word, when you said, the life support system must be terminated, I think that is

a little too harsh in clinical practice. You are critical care physician and I happen to be... you have to get your family to understand...

DR. ROPPER That is what I said.

DR. TANDON I will not argue. Lastly I would like to ask a question. A paper was published three years ago from a very good group of scientists who said they had isolated neuro stem cells from cadavers and cultured them and grown them and modified them into various... I have not been able to see if there is any follow up, because there are many papers that say that there are cells still surviving but I am not sure that that has been confirmed or not confirmed since you mentioned about some of the cells.

DR. HACKE Well, let me address first that we certainly disagree about brain stem death or complete loss of function in the brain stem. That may be because in your country it is accepted, in my country it is not. To come to a diagnosis of brain death you need to know what the underlying disease of a patient is. That is number one. There is, in reality, 90 to 95% of patients who develop a brain death syndrome, start with a supratentorial lesion and if you have that and they develop all the criteria of brain stem death then you can be pretty sure that yes, this syndrome of brain stem functional loss translates into brain death. This is not true if you have a massive haemorrhage into the brain stem, it is not true with complete basilar artery occlusion, it is not true with a massive cerebellar hemispheric infarction leading to compression of the aqueduct. They can fulfil all criteria of 'brain stem death' without fulfilling at that time the criteria of loss of hemispheric function. We agree upon that. Here I ask for that we have to have evidence that there is complete loss of function in the brain, that is what I am asking for, so this patient should not have an EEG like I mentioned before, and you asked 'Have you seen someone?' I have seen several patients at a very early time point of an infratentorial lesion with preserved EEG and preserved reactivity of the EEG and I frankly would not. In a scenario where I would be allowed to do so, as a physician, I would not declare this patient brain dead unless he loses, what I can assess, the function of the hemispheres. That is my point and here we may disagree and this is probably caused by different legal situations in our respective countries.

DR. TANDON The fact remains that for a few minutes or a few hours you may see electrical activity but if you fulfil all the clinical criteria of brain

stem death, that is, at least six hours repeated twice, then it does not remain, I have never seen such a patient.

DR. HACKE If you put in a ventricular drain, a six-hour observation period would not be sufficient. Some countries, like Dr. Wijdicks showed us, require 48 hours. Regarding stem cells: I am not aware of stem cells taken from the brain, I am aware of stem cells taken from bone marrow, which is like the semen that I mentioned earlier.

DR. TANDON I will give you the paper later.

DR. HUBER Thank you for this wonderful presentation. As an obstetrician, I agree, of course, that the brain cannot be substituted like other organs like the heart or the uterus but, especially in Italy, we have some serious groups working in the field of nanotechnology and nanobiology and they are also working very hard for simulating exactly the small areas of the brain stem. Of course, they cannot simulate the whole brain but they do their best to simulate these activities in the small areas of the brain stem. Of course I cannot imagine if this is science fiction or if it is reality but they are very serious working scientists and I think we are also in confrontation with a coalition, a coalition between nanobiology and nanotechnology, medicine and computer technology and of course, what you mentioned today, what you have said is okay for today, but I think we should remain open, nobody knows what this coalition will bring and you are a young man, so you can expect many other things. So my only message is, we do not know in the background of the scientific world what is really going on and of course you are right, for today, but we should remain open for tomorrow.

DR. HACKE I am more than willing to remain open minded and I am aware of the development of neuro-prosthesis for example in the retina or cochlear implants. However, they aim at replacing one function, not the whole system. Think of ALS patients with predominant bulbar and phrenical involvement, if you put in a phrenical stimulator in a situation like that, it is a completely different situation. We replace some neuronal function in the lower brain stem to do the oscillatory work of pumping the lungs. I am more than in favour of trying to do everything to replace singular functions wherever it is possible and maybe at one day in time we will even have patients who start seeing with their occipital lobes,

although they previously had no visual input whatsoever. This type of prosthesis would be a wonderful thing if it is developed, but it has very little to do with our problem right now. I do not see a brain prosthesis coming up.

PROF. BOUSSER Just a comment about the last slide and one of your last sentences when you said 'we must stop'. I disagree when you say 'we must stop because this is no longer a patient but a dead body'. I think this is not just for us to decide. Such decisions vary according to the socio-cultural environment and religious beliefs so that, in my opinion, it is one thing to define brain death – although we might disagree on the definition – and something else to define what to do when we think the patient is dead. I wonder if this is really the topic of this meeting? As a doctor, if you are in front of your patient, of course you will have to decide what to do but I am not sure this needs to be discussed here.

DR. HACKE Prof. Bousser, what you are now emphasising is some uncertainty that even a very experienced doctor has about brain death.

PROF. BOUSSER No, it is just the fact that you said, 'you must stop'.

DR. HACKE If you agree that this is a dead body, what is your argument to continue to ventilate him?

PROF. BOUSSER No, it is not at all that, it is just that you said 'you must' and I disagree with the 'must'.

DR. HACKE So what else?

PROF. BOUSSER I think it depends again on...

DR. HACKE If the heart has stopped, what do you do then?

PROF. BOUSSER That is not the question, I think. I do not know, maybe...

DR. HACKE You are probably still discussing two types of death.

PROF. BOUSSER No, I think we can discuss among scientists about the signs of death, whether it is the heart, whether it is the brain, whether it



is whole brain, whether it is the brain stem, okay? But in your last slide you said 'we must stop the care because they are no longer patients', there I disagree.

DR. HACKE What do they do after explantation? If the patient was an organ donor, and organ donation was performed, it is over, right?

PROF. BOUSSER Okay, it is you as head of department who decides but again, I disagree because for me it is still a patient, the family is still there.

DR. HACKE Is a dead patient still a patient? That is a question.

PROF. BOUSSER Yes, it is, yes I think it is. In a way it is, you have to deal with the family, you have to deal with the social surroundings...

DR. HACKE This is probably a more philosophical question, for me it is not a patient anymore.

PROF. BOUSSER Okay. We will stop our discussion there

PROF. BATTRO Perhaps we can continue that in the following sessions because it is important.

DR. WILDICKS I will not make any comments about the last discussion but I do agree that there is a territory where compassion is necessary and that there are complicated situations in which families... I have only one experience in which families do not want you to take off the ventilators even if it is legally... There are difficult situations in which some family members may tell you that you cannot take off the ventilator and there is a complex issue of compassion there if it does occur and I only have one experience with that and the corollary of my question is, and first I must compliment you on your talk to give a very good, stripped down neurocritical care lecture about the basic topics here, my major question is, if you make the clinical diagnosis of brain death, which we do agree is a separate definable entity of coma, do you believe that or do you think that that always will lead to cardiac arrest?

DR. HACKE I must tell you, I had the same problem as many of us, I did not follow entirely your arguments.

DR. WIJDICKS Let me explain it again. There are situations in which the family will tell you that they will not discontinue the ventilator and we have had situations in which we did not discontinue the ventilator despite the fact that the patient fulfilled all the criteria of brain death, despite the fact that it is legally justifiable to disconnect the ventilator, that you have no obligation to ventilate a 'dead body' if you believe that that is the way to say it and there is an area of compassion there in trying to understand the situation as best as possible, often ethical committees are involved, again I have only one experience, but if that does occur, if you have a patient that is on a ventilator and you continue ventilating the patient do you think that it always will lead to cardiac arrhythmias and cardiac arrest.

DR. HACKE At one point in time this artificial situation will be terminated but we are not talking about minutes or hours or even days. We can go on for six months, or longer, like in the case of pregnant brain dead women, and still preserve the physiological integrity of other parts of the body. I have no idea how long the maximum survival of a proven brain dead person was.

DR. WIJDICKS Do you have your own experience? I am just interested in experience, because I do not have that experience other than one, perhaps two patients, one that I personally took care of, another that I was involved in, in which we continued the ventilator and maintained and in that particular patient it was, you could see, a gradual increase of vasopressors, multiple cardiac arrhythmias that then eventually would lead to cardiac arrest after, I think, twelve or thirteen days, which I think is one of the examples that this is a different setting, not only the brain is dead but it also leads to disintegration of the rest of the organ systems.

DR. HACKE That may be possible. It depends upon the primary cause of brain death, primary insult to the brain or is it secondary? If it is secondary it is much easier to envision that at one point in time other parts of the body will also stop their functioning. Even being on a ventilator long term has an intrinsic risk itself. This will eventually lead to infections there in the critical care environment, so it is pretty tough to keep such a situation alive for the remaining months of a pregnancy, for example.

The whole discussion comes from one word, 'must'. I think that was the trigger. I just wanted to make clear a point, that there are no two classes of death. If an individual who has died from a heart attack is dead and the

family insists on giving him more infusions into the vein, you would say no, no way. In brain death, some argue for the contrary: keep the body on the ventilator. For those of you, who do not do this every day, taking someone off the ventilator seems a very big, emotionally challenging thing. In practice, we are not rude. In my slide I said, 'after counselling with the relatives who need it more now than the former patient', and that is exactly what I mean. And that counselling may take a couple of hours, of course. We have to do everything to try to help those poor relatives who just lost a loved one, usually very unexpectedly, to clear this situation, but thereafter, well, we have to stop, not 'must' but 'have to'.

DR. WILDICKS It is my understanding you have not been in the situation that the family asks you, 'Well, you can say whatever you want but I think this patient is as alive as can be and I want to continue the ventilator', and I am telling you this because this is my personal belief and it may not be based on a religious belief, in my opinion it is rarely based on a religious belief, the only exception that I know of is a subgroup of the Orthodox Jews in New York and New Jersey who feel that there is a religious exemption possible. I am just looking for more experience on how that was handled.

DR. HACKE In our practice we handle this differently, even if the relatives are fully aware of what is going on. The activity of disconnecting from a ventilator is brutal. Many relatives nowadays want to stay with their loved ones so immediate disconnection would be an incredibly aggressive act in their eyes. We would not disconnect immediately, but we start a procedure of dead space hypoventilation, and some time later, the heart will slow down and eventually stop beating. The heart stops beating. That is, for the relatives, a natural 'death' so it is a humanitarian act to do it this way. I described this approach this in my first neurocritical care textbook twenty years ago.

DR. DEECKE Werner Hacke, I would want to say it is allowed. I am with you that you do it, but you must not say it, especially if the press comes this could make problems.

DR. HACKE This is what we do on the ward and what our nurses know. For them it is also helpful. Did you notice, that we have not talked about the nurses who deal with brain dead people at all? For them it is also a very difficult thing and they know this procedure and again it is essentially...

DR. DEECKE It is playing theatre.

DR. HACKE Well, I would not call it 'playing'. I would call it, it is a very gentle misleading thing in very good intention for the sake of the relatives.

DR. DEECKE In German you would say, an act by mercy.

DR. HACKE Yes. It does not change the outcome.

DR. PUYBASSET Just a comment and a question. The comment is that I agree entirely with what you said and especially when you said that we can have some patients with the issue of brain death without the issue of organ transplantation, especially HIV patients or hepatitis C. I am still wondering if some of the issues we have in the public regarding brain death, do not come from the different definitions that we use. In some countries it is brain stem death, with still cortical activity, and in other countries, like in Spain, France or Germany, we need a flat EEG to be sure that we have a whole brain death. So, don't we have to be more precise on this concept of whole brain death versus brain stem death? Isn't this issue causing problems especially in the public?

DR. HACKE We heard today that the WFN is setting up a task force to work on this. As long as we depend on the legal system we are working in, we may have different approaches, and this does not give a very good impression to the public. And we have not even touched on the problem of non heart-beating donors. This just adds another level to the discussion.

PROF. CABIBBO Of course I speak as a physicist. I find very important your title, that brain death is an artificial construct of the ventilator, in a way. If you did not have intensive care units, these people would simply be dead. I think that is an important point that people should know.

DR. HACKE Yes, even in developed countries, if you live alone and you suffer from a disease that in a few days would lead to brain death and you are not found, you will never develop it, you will be dead. If you were living in Outer Mongolia or in the Sahara, nothing would bring anybody into the condition of brain death...

PROF. CABIBBO Before the ventilator was discovered, you would take care of these people until they died and now you put them on the ventilator and then you have this problem.

DR. HACKE Exactly. In some developed countries, where the access to intensive care medicine is easy, you get this problem more frequently. In our country, for example, some of the emergency physicians find someone 95 years old, demented with a heart attack. They go forward and intubate the patient and transfer him to an intensive care unit. Again, the discussion of resource use, the lowest hierarchical point, however, an important one, comes into play.

PROF. CABIBBO The whole point is how you manage people who die while in the intensive care unit, because if they become brain dead they are dead but with a ventilator this situation could be prolonged for many many days.

DR. HACKE If you do not think of the diagnosis of brain death, this may continue for many days. We see that in intensive care units in almost every hospital.

# SURVIVING AREAS OF BRAIN TISSUE IN BRAIN DEATH: IS THE WHOLE MORE THAN THE SUM OF ITS PARTS?\*

MICHAEL G. HENNERICI

## *Introduction*

In a recent review published in *Nature Neuroscience* (2005) Steven Laureys updated the conflict of death and diagnosis of brain death, which has evolved since the invention of the positive pressure mechanical ventilator by Bjorn Ibsen in the mid 1950s and its widespread use in intensive care units (ICU) in the 1960s: patients with severe primary or secondary brain damage who otherwise died within hours or a few days from failure of neuroendocrine and homeostatic regulation, circulation and respiration, could have their heart beat and systemic circulation provisionally sustained and with nowadays refined ICU technology, even deliver a mature child artificially. Until that time of technological progression such patients had died from

TABLE 1. MILESTONES IN DEATH AND DYING DEFINITIONS

1952 Bjorn Ibsen invented mechanical ventilation
1957 Pope Pius XII ruled that there is no obligation to use extraordinary means to prolong life in critically ill patients
1959 Mollaret & Goulon coined the term „coma dépassé“ and defined death on the basis of neurological criteria
1968 Harvard MedSchool AdHocCommittee defined irreversible coma as new criterion for death
1976 Conference of Medical Royal Colleges and their Facilities in the UK defined <i>Diagnosis of brain death</i>
1982 C. Pallis ABS of <i>Diagnosis of brain stem death</i>
1995 AAN Practice parameters for determining brain death in adults

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

apnea in line with the traditional and ancient cardio-respiratory-centric diagnosis, which has turned on to a neurocentric diagnosis of death.

Although the majority of people around the world, when asked, declared death by cardiopulmonary criteria (>86%), i.e. when cardiac functions cease, versus the concept of brain death (9%), the latter has been accepted and legally used in many countries since the mid seventies of the last century for specific conditions, based on strict definitions and standardised diagnostic formulations as proposed.

TABLE 2. A DEFINITION OF IRREVERSIBLE COMA

There are two reasons why there is a need for a definition:

- (1) Improvements in resuscitative measures have led to save those who are desperately injured. Sometimes these efforts have only partial success so that the result is an individual whose heart continues to beat but whose brain is irreversibly damaged. ...
- (2) Obsolete criteria for the definition of death can lead to controversy in obtaining organs for transplantation....

(Ad hoc Committee of the Harvard Medical School to examine the definition of brain death, JAMA 1968;205:pp. 85).

TABLE 3. CHARACTERISTICS OF IRREVERSIBLE COMA

1. unreceptivity and unresponsivity
2. no movements or breathing
3. no (cranial) reflexes
4. flat electroencephalogram

(Ad hoc Committee of the Harvard Medical School to examine the definition of brain death, JAMA 1968;205:pp. 85).

*Brain Death Formulations*

Roughly the human brain consists of two hemispheres, the dominant and the non-dominant one, the basal ganglia including the thalamus, the cranial nerves including the retina of the eyes, the pituitary gland, the brain stem and the cerebellum (Figure 1, see page 426).

The *whole-brain formulation* states that an individual who has sustained irreversible cessation of all functions of the entire brain, including the brain stem, is dead. This formulation is the most commonly applied worldwide and forms the foundation of legal qualification in many Western nations. It is characterised by irreversible loss of function of both supra- and infratentorial brain territories with the brain stem being integral to the preservation of most regulatory and homeostatic mechanisms, while in particular, thalamus and cerebral hemispheres play important roles in the preservation of consciousness. Global disruption of these structures forms the basis for the *whole-brain* formulation of death.

A notable exception from this definition exists in the United Kingdom, where the *brain stem death formulation* was originally promoted, because people thought that ‘irreversible loss of the capacity for consciousness combined with irreversible loss of the capacity to breathe’ was the more correct term of death irrespective of whether this condition was induced by intracranial events or by extracranial phenomena, and irrespective of a combined supra- and infratentorial or infratentorial lesion only, the latter invariably heralding asystole. Data, although sparse, showed convincingly that indeed asystole developed within days after the diagnosis of brain stem death.

Practically that means that clinical testing is identical for both *whole-brain death*, and *brain stem death* formulations of brain death. Both represent the same pathophysiology, e.g. irreversible cessation of brain stem function. However, as patients with a primary lesion affecting the brain stem *only* may have supratentorial parts of the brain still active, this condition requires – according to diagnostic regulations in many countries – additional technical studies to support the persistent absence of supratentorial *brain perfusion* and absence of *electrical activity during* EEG recordings.

Christopher Pallis anticipating criticism wrote in his early book, *ABC of Brain Stem Death, From Brain Death to Brain Stem Death* (1982), *British Medical Journal*:

Judicial hanging is another cause of lethal, primary brain stem injury. Death in such cases is widely believed to be due to a fracture-dislocation of the odontoid, with compression of the upper two segments of the spinal cord. Although such a lesion may be found in some cases,



Professor Simpson, Home Office Pathologist when capital punishment was still resorted to in the UK, has told me (Christopher Pallis) that a rupture of the brain stem (between pons and medulla) was more common.

In judicial hanging respiration stops immediately, because of the effect of the brain stem rupture on the respiratory centre. The carotid or vertebral arteries may remain patent. The heart may go on beating for 20 minutes. Circulation continues, and parts of the brain are probably irrigated with blood (or diminishing oxygen saturation) for several minutes. I would guess that an electroencephalogram might for a short while continue to show some activity, despite the mortal injury to the brain stem. *Is such an individual alive or dead?* The very posing of such a question forces one to focus attention on the reversibility or irreversibility of the brain stem lesion and away from extraneous considerations.

Some have continuously argued against using the brain stem formulation for other reasons, e.g. because of the possibility of 'a super-locked-in-syndrome', in which awareness might be retained in the absence of all other signs of brain stem activity. Laboratory evidence has also been used, suggesting that retained hypothalamic pituitary or isolated cellular activity, may reflect, despite absence of clinical signs of function, subtotal brain death (noting that perfusion of all these structures arises from extracranial vessels only). To understand this better I would like to briefly review the different states of condition after acute brain injury resulting in similar but not identical clinical presentation of comatose patients and to present an example from our department. Doing this I will try to avoid, inasmuch as possible, overlap with what has already been reviewed during this symposium.

The history of brain death definitions from former definitions of death was reviewed by Robert B. Daroff and the changes and modifications in procedures to determine brain death around the world were discussed by Eelco F.M. Wijdicks. In addition, Conrado J. Estol clearly strengthened the differences in diagnosis and prognosis of patients with unconsciousness and coma after acute brain injury, who suffered from (i) *locked-in syndrome* (a term coined by Fred Plum and Jerome Posner) (1966), (ii) *the vegetative state*, similarly introduced by Bryan Gennett and Fred Plum (1972) and (iii) *brain death*. This is essential in order not to misdiagnose and mix these entities with brain death for medical, philosophical, legal and ethical issues, and to avoid wrong definitions and formulations. The tragic death of Terri Schiavo illustrated the world's difficulties that surround death in the vegetative state, as many journalists and even authorities inaccurately referred to Schiavo's condition as 'brain death'.

Our patient was an 83-year-old man, admitted for progressive right sensorimotor hemiparesis, resulting from left paramedian pons infarction, due to moderate basilar artery stenosis (Figure 2).

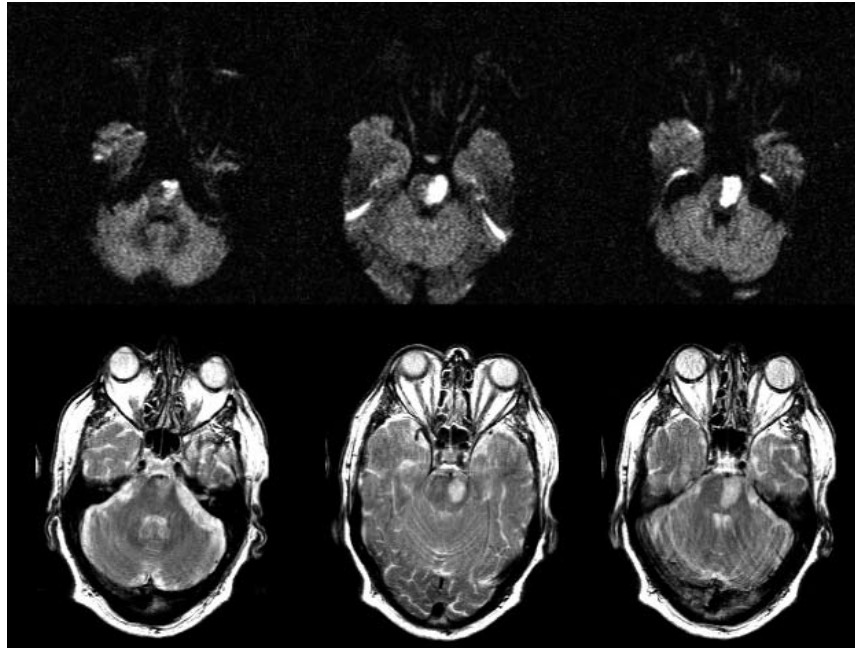


Figure 2. Patient (83 years, male) admitted for progressive right sensori-motor, hemiparesis due to a left paramedian pons infarction in presence of moderate basilar artery stenosis.

About two weeks later he suddenly deteriorated and suffered from quadriplegia, dysphagia, anarthria, and presented bradycardia during vagal stimulation on treatment and finally became comatose. This was caused by a second right acute pontine infarction and persisted for another two weeks. The patient was neither intubated nor artificially ventilated and died finally from renal failure and sepsis (Figure 3).

As you can see this patient, with a typical locked-in syndrome, did not develop, at any time of his illness, signs of *brain stem* or *whole-brain death*. However, had he been artificially ventilated and basilar artery thrombosis progressed, producing all signs requested for the diagnosis of brain stem death, this situation might have occurred, despite preservation of supra-

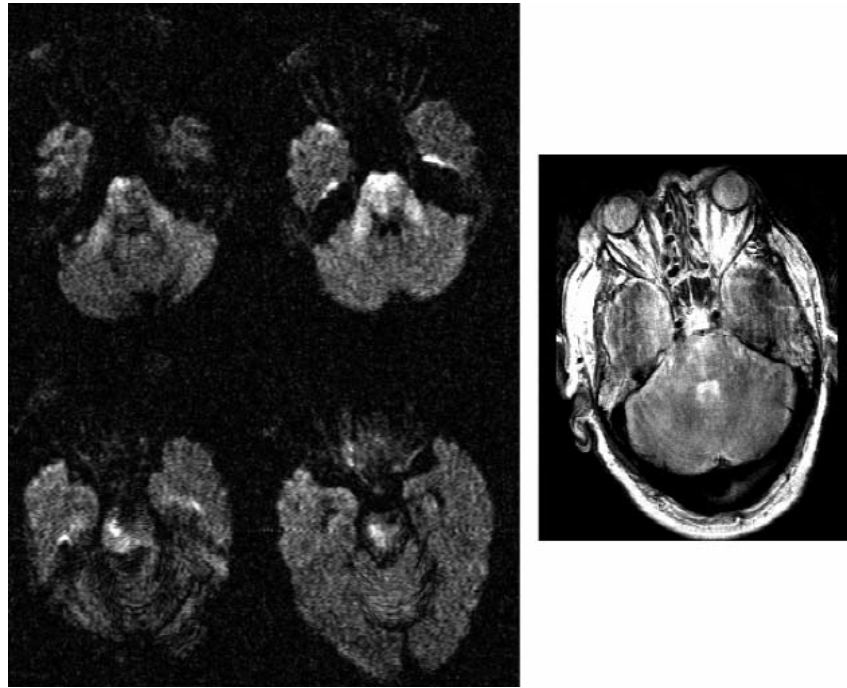


Figure 3. Same patient as in Figure 2, two weeks later, presenting tetra-paresis, reduced activity, dysphagia and anarthria, vagal stimulation during treatment causing bradycardia and coma due to a second, right acute pontine ischaemia demonstrated in a new MRI.

tentorial brain perfusion and cellular activity in both hemispheres. Thus a so-termed 'super-locked-in syndrome' might have occurred and only with additional demonstration of global loss of brain perfusion and absence of brain activity, the diagnosis of brain death might have been justified according to the rules in our country.

#### *Brain Death Syndromes vs. Mimics: Clinical and Technical Issues*

Clinico-pathological reports date back to the 19th century and many definitions of this syndrome have been proposed since 1876. In literature this syndrome is very well known, in Alexander Dumas' famous novel, *The Count of Monte Cristo*, where Monsieur Noirtier de Villefort is referred to as the corpse with 'vivid eyes' and Emile Zola introduced the mother of

Camille Raquin, who communicated only with her eyes. In a more recent very nice book Jean-Dominique Dobe recounts the locked-in syndrome from a former patient's view, *The Diving Bell and the Butterfly*.

This syndrome is to be separated from other conditions such as vegetative state, where consciousness is lost. However, once the reticular formation and connections with the thalamus and cerebral hemispheres are destroyed and completely disrupted, the condition changes into what is termed the *brain stem death formulation* if persistent over time.

In the following I will concentrate on other specific brain-centred definitions of death and in particular work on both medically accepted definitions of death as *whole brain death* and *brain stem death formulations* versus the not medically accepted *neo-cortical formulation*. According to the neo-cortical definition of death, Terri Schiavo's case would have been considered death emphasising a fundamentally different concept: the irreversible loss of the capacity of consciousness and social interaction. Terri Schiavo was never brain dead but suffered from coma and vegetative state with intact or only moderately affected brain stem functions. The same is true for a patient who was nursed in our hospital for more than ten years after global hypoxia and persistent vegetative state.

Post mortem examination showed extremely severe atrophy of major parts of both hemispheres, thalamus and basal ganglia, both atrophic but macroscopically intact brain stem and cerebellum (Figure 4, see page 427).

*Brain death* formulations such as whole-brain death and brain stem death are medically accepted at least in different countries and have been successfully and beneficially used for decades, however, the *neo-cortical formulation* is not.

This most controversial concept of death originally supported by Scottish neurologists Brierley and his colleagues in 1971 urged that death be defined by the permanent cessation of 'those higher functions of the nervous system that demarcate man from the lower primates'. It has been developed further by others, mainly philosophers and its conceptual basis rests on the premise that cognition and social interaction, not the bodily physiologic integrity, are the essential characteristics of human life – thus if functions of the neo-cortex but not the whole brain, or brain stem are permanently lost, neo-cortical death results according to the promoters of this concept. However, neither clinical nor confirmatory tests have ever been validated, nor can they be established in a scientific way that would be reliably adjusted to an anatomical and functional criteria of present brain research. Today it is impossible – in contrast to brain death, for which

neuro-anatomy and neurophysiology are well-established – to determine human consciousness and *even less reliably* higher brain function by clinical or surrogate parameters, nor are there any *behavioural parameters* available showing that consciousness has been irreversibly lost. Patients in the vegetative state unlike patients with brain death, following an acute injury or chronic degenerative disease and anencephalic infants are considered dead according to this neo-cortical formulation, although they are often not apallic as previously thought and may show preserved islands of functional brain cortex. Neuroimaging studies – as nicely reviewed by Stephen Davis during this symposium – have shown re-activation in patients in a vegetative state and even recovery cortical functions after 19 years in a patient with minimally conscious state (MCS) as recently published (Voss *et al.*, 2006). These authors studied diffusion tensor imaging in two patients with traumatic brain injury (Figure 5, see page 428).

This technology allows demonstration and display of fibre connections in the brain, which are responsible for multi-focal and systemic network activity, underlying basically human brain function such as consciousness, recognition, attention, awareness, spontaneity, thinking, reflecting, communicating, memorising, suffering, laughing, creativity, intellect, etc.

Their patient, a 39-year-old male, who at age 19 suffered a severe closed head injury in a motor-vehicle accident, spontaneously emerged from MCS 19 years after the initial injury and recovered spoken language. He initially remained in a coma 1-2 weeks followed by further recovery to a vegetative state and subsequently a level of function existed of MCS within several months of injury. Although gradual improvements in responsiveness were noted over an ensuing 19-year period, the patient was unable to communicate using gesture or verbal output. Limited head nodding and grunting were only inconsistently present. Eight months prior to the authors' first evaluation, he spoke his first word after his brain injury ('mum'), which was followed by a recovery over a period of several days of increasingly fluent, but dysarthric speech and reliable communication. He was oriented to person but did not know his age, misidentified his location and indicated that he did not know the current year, selecting '1984', the year he was injured, from a list of four alternatives. Eighteen months later, at the time of the second diffusion tensor imaging scan, several areas of neurological improvement were identified: reassessment of motor functions demonstrated recovery of both lower extremities, which were paretic on initial examination, showed improvements in strength to at least 4 + / 5 on volitional movement. Cognitively there was an overall increase in baseline arousal combined by

generalised improvements in attention and focus and response persistence. He was able to count from 1 to 25 without interruption, speech intelligibility improved, he remained oriented to person only and conversational speech remained free of paraphasic and dysnomic errors. At the time of the first scan there were well-confined regions of pronounced right-left anisotropy in the medial, parietal and occipital (MPO) areas of the brain (visible as the red occipital areas in B). These areas were also significantly larger than in normal controls but reduced in the second scan 18 months later (E) and were no longer significantly separated from controls. However, another striking region of right-left anisotropy had become evident in the inferior part of the cerebellar vermis (H), directly correlating with the patient's regaining of limited use of the lower extremities motor function recovery as well as improvement of dysarthric speech disturbances.

Increased metabolic activity in the MPO regions in a PET-CT scan was consistent with these findings.

In summary, the authors have taken the initiative to carefully check this individual's history and personally examined this 'miracle recovery from coma', which was widely discussed in the popular media. The MRI assessment of transiently increased fractional anisotropy and directionality in the posterior midline cortices, interpreted as increased myelinated fibre density and novel cortico-cortical sprouting paralleling the emergence of the patient from MCS is a most remarkable and unique finding in the literature. As this patient's brain also showed amplified metabolic activity measured by PET these structures seem to be of importance in consciousness of self and interaction with the environment and hence for future research a most challenging area: this is further supported by previous knowledge that this area is very active in conscious waking and in altered states of consciousness, such as pharmacological coma, sleep, dementia and post- and anoxic amnesia. It has been assumed that it is originally connected multimodal associate area in the neuron network subserving human awareness. However, this patient like others in less spectacular cases was *not considered brain dead in the term of whole brain death and brain stem death formulations* but was consistent with the concept of death in the neo-cortical formulation. This underlines the importance of a strict separation and differentiation of patients with chronic unconsciousness, or minimally conscious patients, where even painful stimuli do not elicit any cortical activity as seen on functional MRI scans.

To summarise, brain and brain stem death, vegetative state and locked-in syndrome are different entities, clinically as well as during technical

studies: if adequately and accurately diagnosed they can be separated, as well as consciousness and sleep versus anaesthesia can be separated, or the vegetative state and the minimally conscious state in chronic patients with severe brain lesions. Severe destruction of parts of the brain is more than the sum of its parts and may be consistent with brain death according to clinical and biomedical testing, however, survival of parts of the brain are also more than parts and may be consistent with a living brain.

More recently fMRI studies and PET testing became available as research tools and in addition to new molecular biological tests, these techniques may provide useful information to a better understanding and knowledge about this complex issue and the underlying physical and metaphysical changes in the process of dying, which to some extent and purpose are well known and useful in clinical medicine, however, to some extent they are still poorly understood and insufficiently termed.

#### *New vs. Old Concepts and Definitions*

At present the best accepted definition of death is the 'permanent cessation of the critical functions of the organisms as a whole' (Bernat, 1998). This traditional concept refers to functional integrity – not simply representing some of its parts but of course including important critical functions, such as control of respiration and circulation, neuroendocrine and homeostatic regulation without which the organism cannot work and hence they are all irreversibly lost. However, this concept also implies that when cardiac function ceases, the patient is dead: this rationale has *regained* interest once the discipline of transplantation surgery has matured and the number of patients with end-organ failure eligible for organ replacement surgery has increased. Despite the growing demand 'for organs' the number of potential 'brain-dead donors' remains limited and hence, a new group was declared dead by cardiopulmonary criteria: the *non-heart beating donors* (NHBD).

Essentially this group was already the major source of organs for transplantation prior to development and adaptation of brain death criteria and remained so in countries such as Japan, where the concept of brain death has only recently been a subject in legislation, but not widely accepted by the general population. Furthermore, the determination of death by cardiopulmonary criteria is by far better accepted in the general populations around the world and the pool of potential donors would include a larger group of patients, not only those patients dying from catastrophic brain injury. However, there are major ethical concerns with the use of NHBD, in

particular as questions about time, timing and the determination of death are crucial: e.g. is there a specified duration of absent cardiac activity and how long is it? Is this period not associated with spontaneous 'auto-resuscitation' and hence in the absence of activity should be considered reversible? Are 2-20 minutes of asystole reasonable estimates of this period and are they sufficient to avoid organ damage due to 'warm ischemia'? And, if it requires ten or more minutes without perfusion for the brain to die, how can its status be ignored after a shorter time? This raises the issue of a patient experiencing pain or worse, regaining consciousness when cardiopulmonary function and brain perfusion are restored by mechanical means, such as intermediate cardiopulmonary by-pass.

The term 'brain death' has become so familiar that it is not likely to be replaced by a more precise and less confusing term, as proposed in an editorial in *The New England Journal of Medicine*, e.g. 'brain-based determination of death'. Furthermore, death is as reflected by the issue of the concept of non-heart-beating donors, a complex issue itself not only from a biological and medical point of view but also from a philosophical and ethical point of view. With terms such as brain death used by doctors, it is difficult for families to understand on the basis of a diagnosis of death, when the respirator-supported body of their loved ones manifests many signs of life. Many decades after its introduction this term still causes confusion among the public and healthcare personnel alike. Despite good and sufficient reasons why the existing consensus about the determination of death has endured more than thirty years in the face of persistent criticism, reconsideration of terminology along new details of investigation of the biological transition from life to eternity or whatever people expect and believe after this final period, remains a matter and challenge for modern medicine. Whether or not a recent proposal (Zamparetti *et al.*, 2004) reverting the old term of 'irreversible coma' to 'irreversible apnoeic coma' is helpful and acceptable has to be seen. Such a term could abandon the presumption of diagnosing the death of all intracranial neurons and/or the patient's biological death.

Whether or not death is a process or an event can be discussed *ad infinitum*, remembering the longstanding growth of hairs, nails, skin and bone cells, days and months after death. Rather death may be regarded as an event that separates the continuous process of dying, from subsequent disintegration, which arrives at a certain borderline where irreversibility is reached and a point of no return can be identified. Traditionally, and prior to the invention of artificial mechanical ventilation in intensive care units, a circulatory relation of death was defined by the irreversible cessation of



circulation in this process: whether at home or in the hospitals, most of the people 'died and still die their own deaths', without machines or elaborate interventions being involved. The irreversible loss of the capacity to breathe spontaneously and hence to maintain a spontaneous heartbeat, thus defining death of the whole organism in traditional form. Both are essentially brain stem functions and both can be taken over by machines before a certain period until recovery of brain stem function or in the presence of functional integrity of the brain stem. However, if catastrophic brain stem lesions cause irreversible destruction of both critical brain stem capacities, life can no longer persist without mechanical support, exactly a situation that is described by 'permanent loss of the breath of life' and forms the implicit basis of the UK formulation in diagnosing brain stem death.

The whole brain formulation requires the bedside demonstration of irreversible cessation of all clinical functions of the brain and is the most widely accepted. The brain stem formulation regards irreversible cessation of clinical functions of the brain as not only necessary but also sufficient for the termination of the death. Brain death is classically caused by a brain lesion, resulting in an intracranial pressure higher than the mean arterial blood pressure. This causes intracranial circulation to cease and brain stem damage to herniation. However, the brain stem formulation of death may be applied to cases of catastrophic brain stem lesions (often of hemorrhagic origin) that spared the thalami and cerebral cortex and even leave intracranial circulation intact, which would be sufficient according to the brain stem formulation, even in the absence of raised intracranial pressure. Theoretically multiple brain stem lesions could selectively impair all brain stem function that can clinically be tested, while preserving residual (but clinically undetectable function) of the reticular activating system – in practice no such cases have ever been reported, if confirmatory examinations by two independent physicians experienced in intensive care unit medicine and neurology are requested. With repeat testing after strictly defined intervals and surrogate studies according to meticulously defined protocols and legal regulations are sufficient and widely used safe requisites.

Some people have criticised the brain-centre definition and advocated circulatory formulation of death only as we all know. In this view a living body possesses not only integrator but integration, a holistic property that derives from interaction among all parts. However, functions of circulation, respiration, homeostasis and neuroendocrine regulation are all regarded as critical functions, which, if irreversibly and permanently lost are inevitably followed by cardiac arrest: (no single case has been reported since their use

in 1959, where appropriate history taking diagnosis of circumstances and conditions and appropriate testing by experienced physicians were unreliable and caused misdiagnosis) hence the neurocentric criteria of death may be considered among the safest medicine which can be achieved.

### *Conclusions*

*In conclusion:* i) brain death is death, but an irreversible vegetative state is not; ii) the whole brain and brain stem formulations determine both death; iii) irreversible cessation of critical functions of the organism, which means neuroendocrine and haemostatic regulation, control of circulation and respiration as a whole are accepted and practiced criteria worldwide; iv) 'the whole brain formulation does not require confirmatory tests for brain death' but 'the brain stem formulation may'. Future technology might be useful to support this concept further. Julia Chan recently reviewed a framework of transnational research on brain stem death, that is based on systematically coordinated, clinical and laboratory efforts centred on this phenomenon. It begins with the identification of novel clinical markers from patients suggested to be related specifically to brain stem death. The author has voted the idea that 'life-and-death-signals' are related to functional integrity of the brain stem, expressing traces to the rostral and ventro-lateral medulla and having been applied to animal models of brain stem death to provide a notion of both 'pro-life' and 'pro-death' programmes, actively involved in the progression towards death. These programmes involve mitochondrial functions, nitric oxide, peroxynitrate, superoxide anion, coenzyme Q, e-shock proteins and ubiquitin-proteases. The authors propose that such programmes are involved in the neurosubstrate determining the final fate of the individual (being dead by definition). Parameters such as these are suggested by the authors to identify regulatory mechanisms becoming active at the life-death border and hence challenging our scientific knowledge about many questions in this crucial area which still remain open.

Whether or not future technologies may one day change our current ideas of irreversibility and cause revision of the definition of death remains to be seen.

## DISCUSSION ON DR. HENNERICI'S PAPER

DR. DAVIS Thank you Michael. I can agree with your conclusions. It is my sense of it, listening to your talk and Marc Raichle's and some of the others, that imaging is really going to give us more information about devastating brain injury and the correlations between what we observe clinically and what can be imaged metabolically and functionally, rather than being utilised to revisit brain death. I just wonder if you could comment.

DR. HENNERICI Yes, although I think if we consider the most recent reports, which we discussed this morning, and I have no doubts in believing the findings that were reported, that even for the definition of brain death or, more precisely, brainstem death there may be some more arguments to come which we do not know at the moment. So this is a little bit in the direction as Dr. Huber argued this afternoon to be open for future things. At the time where we have to make a decision, we can do it at the best of our knowledge, what we think is ethically and medically correct, but I was also impressed by the testing of the laboratory people who now look for genes that are promoting death in the brainstem while other genes are candidates for preventing or delaying death processes in cells. And we know that nearly never all the cells are dead, so this is something which was, I think, not discussed or could not be discussed because the technology was not available ten or twenty years ago.

BISH. SÁNCHEZ S. I am very impressed by the title of your paper: Is the whole more than the sum of its parts? What is your conclusion?

DR. HENNERICI The answer is yes, to be very short. Well, the original title or the original proposal which was given to me was mainly to discuss about the brain-stem issue and the issue of cells distributed like islands in the brain with some electrical activity and I think this is just a simplification of what I have tried to do with the three formulations. You could argue that really there are several parts of the brain that present with the same issue,

some people declaring neocortical formulation as brain death, some others purely nuclear fibre tracking systems such as the brain-stem and I think this may be reasonable for an operative procedure. It may be useful to say yes or no, to agree or disagree with that for an operating decision in the emergency unit but I do not think it is the final answer to this very difficult question. So it is an apologia against yes or no, and against the very simple idea that only if all the cells are dead this is the death of the person – we know that 'the whole' is more than the sum of all cells and that this can be seen in all kind of cardiovascular deaths, where many cells are not dead at the time when death declarations are signed.

PROF. BOUSSER Could you elaborate a little bit more on this neocortical definition because as a clinician, as a neurologist, I do not really understand that. OK, Alzheimer's disease is a neocortical condition but if you look at our patients with subcortical vascular dementia the lesions are subcortical and yet their cortex is still functioning. Could you elaborate on that a little bit?

DR. HENNERICI Well, I found this definition dating back thirty or forty years from now, and it had a philosophical approach. The definition says that permanent loss of consciousness or severe mental deterioration with reduction of consciousness is no longer consistent with a personality because communication and consciousness are lost and this means neocortical functions vanished. It has not much to do with a biological definition but rather it is a philosophical and psychological driven hypothesis and you can find it in the literature and more recently in discussions about life quality and what is life worth and what is the support we need to give these patients when faced with costs that we cannot tolerate any longer. And that is why the wording is also established, the neocortical correlation of death.

## ALLEGED AWAKENINGS FROM PROLONGED COMA AND BRAIN DEATH AND DELIVERY OF LIVE BABIES FROM BRAIN-DEAD MOTHERS DO NOT NEGATE BRAIN DEATH\*

JEROME B. POSNER

The topic assigned to me for this presentation is ‘alleged awakenings from prolonged coma and brain death and delivery of live babies from brain-dead mothers do not negate brain death’. I will divide that topic into three sections: 1. Awakening from brain death. 2. Awakening from prolonged coma. 3. Delivery of live babies from brain-dead mothers.

I start with the premise that there exists a clinically definable state in which formerly functioning individuals suffer irreversible destruction of cerebral hemispheres and brainstem (i.e., loss of all brainstem responses), such that they do not have, and can never achieve, awareness of self or environment. This state has been given several names: It has been called ‘irreversible coma’, ‘brain death’ or, as I will attempt to show in this presentation, just ‘death’. When such a state is identified, electrophysiologic and metabolic tests demonstrate no functioning intracranial activity. For example, a glucose PET scan shows no metabolic activity [1], an angiogram shows no blood flow.

The clinical criteria for the neurological determination of death are well-established [2]. These clinical criteria demand knowledge that the etiology of brain damage is irreversible (i.e., that there is no possible reversible condition capable of mimicking neurological death), that the body is totally unresponsive with bilateral absence of motor responses, (excluding spinal reflexes) and that all brainstem reflexes are absent including respiration, usually proved by an apnea test. Two examinations, usually several hours apart, assure irreversibility. In most but not all countries, meeting these *clinical* criteria is sufficient to pronounce death. In some countries confirmatory laboratory tests may be required. These include electrodiagnostic, metabolic or vascular tests. Dr. Wijdicks, in his 2001 book entitled *Brain Death*, has detailed the criteria for individual European countries [3].

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

The first question is does one ever awaken from 'brain death'? I believe the short answer is no. Interestingly, although there is to my knowledge no instance of a body meeting the clinical criteria for brain death ever awakening, there are several instances in the literature in which patients unexpectedly regain spontaneous circulation following a cardiac arrest after resuscitation has been discontinued and the patient pronounced dead (cardiac death). This recovery has been called the Lazarus phenomenon. At least 18 such cases were reported in a review in 1998; some of these patients actually recovered consciousness [3].

Although the recovery from correctly diagnosed brain death has never been reported, prolonged survival of organs other than the brain has been achieved using artificial respiration and pressor agents. In 1998, Dr. Shewmon [4] described 175 such instances; in 7 instances, peripheral organs survived longer than six months and in another instance 20 years [5]. This unique instance was a 4-year-old child who appeared to meet the criteria for brain death after an episode of bacterial meningitis. Twenty years later at autopsy 'no neural elements were recognizable at the light microscopic level on any of the stains or with immunohistochemical markers' [5]. Many experts believe that (perhaps most) of the patients reported by Dr. Shewmon may not have met the clinical criteria for brain death and even in the child there is some question. There are, however, other reports in the literature that indicate that with major efforts directed at maintaining respiration and hemodynamics, one can keep peripheral organs alive for several days [6, 7]. Nevertheless, none of these patients ever recovers.

Dr. Shewmon, who does not believe that a brain-dead body is actually dead [8, 4], chides neurologists who accept the concept for using language that often suggests they themselves are not certain. A cardiologist who pronounces a patient dead does not say that the individual is 'cardiac dead', but simply that he/she is dead. We should use the same language. Language such as that quoted by Dr. Shewmon in his written presentation to this meeting ('children who are brain-dead can be kept alive by artificial means for a long period of time', 'the bodies of two [brain-dead] lived on until the 10th and 16th day', 'all of the [brain-dead] patients died within 24 hours') must be avoided if we are to convince the public that a brain-dead body is dead.

For the first part of this presentation, I conclude that if the proper clinical criteria for brain death are applied, no patient recovers consciousness and although prolonged survival of somatic organs may be possible, it is rare.

The second question is do patients awaken from 'prolonged coma'? If one defines coma as eye-closed unconscious without sleep-wake cycles or periods

of eye opening, I know of no instance of a patient awakening from that state. Actually, prolonged coma is quite rare, almost all patients transitioning to a persistent vegetative state within a matter of a few weeks. For patients in the vegetative state and those minimally conscious the situation is different.

The Royal College of Physicians of the UK guidelines have defined the *vegetative state* as occurring in an individual who has no evidence of awareness of self or environment at any time, no response to visual, auditory or noxious stimuli of a kind that suggest volition or conscious purpose, no evidence of language comprehension or of meaningful expression, with cycles of eye closure and eye opening. Hypothalamic and brainstem functions may be sufficiently preserved to insure maintenance of respiration and circulation [9]. The *persistent vegetative state* is defined as a vegetative state lasting more than one month. The *permanent vegetative state* is defined as a vegetative state persisting for one year after a traumatic brain injury or three months after a nontraumatic brain injury. Using the three month and one year definitions, an occasional patient does recover from the so-called *permanent vegetative state* [10, 12]. Such patients may emerge from the vegetative state to the minimally conscious state (see below). Thus, patients believed to be vegetative require expert periodic re-evaluation. The re-evaluation may include not only the clinical examination, but also laboratory techniques such as functional MRI [13]. It may even include trials of drugs [14] and techniques [15, 16] that have been reported to awaken some minimally conscious patients.

The *minimally conscious state* [17] describes a patient with limited but clearly discernible evidence of self or environmental awareness on a reproducible or sustained basis. Such evidence includes one or more of the following behaviors: The following of simple commands; gestural or verbal yes or no responses (independent of accuracy); intelligible verbalization; purposeful behavior (contingent relationship to environmental stimuli). Patients may recover from the minimally conscious state after several years [17]. The mechanism of that recovery is uncertain, but could include axonal regrowth [15] or neurogenesis [19].

For the second part of this presentation, I conclude that patients do not awaken from prolonged coma but may recover from the vegetative or the minimally conscious state.

The third question addresses delivery of live babies from brain-dead mothers. Pregnant women suffering brain death are uncommon. In one series from a transplant center, of 252 brain-dead women of childbearing age, only seven were pregnant; another four were in the early postpartum

state [20]. However, there are several reports of brain-dead pregnant women whose fetus and organs were maintained for as long as 117 days resulting in delivery of a viable and apparently normal infant [21-23]. Whether all of these women actually met the clinical criteria for brain death is unclear, but it is likely that at least some of them did. Thus, for the third part of the presentation, I conclude that somatic survival in pregnant women who are either dead or vegetative is possible for some individuals in that viable babies who appear to be normal can be delivered. Maintaining the body of the mother is not easy and it is not clear if there are any long-term effects on the infant.

One fact that is important to recognize is that death is not an event, but a process. At the time a heart stops beating (cardiac death), the rest of the cells of the body are still living. Five to ten seconds after the heart stops the individual loses consciousness. However, at that point, neurons are still alive. After about four minutes, hippocampal neurons and Purkinje cells begin to die. Some evidence suggests that some neurons can be successfully cultured from the brain of individuals two to eight hours after death has been pronounced [24]. Other organs survive longer, often many hours. It is said that hair and nails grow for days after death. Thus, death does not occur at a moment in time, but only over hours or perhaps even days. The physician can be certain that death has occurred, but cannot define exactly when.

### *Addendum*

I have listened to the presentations of my colleagues with great interest. I do not consider myself an expert on the topic of brain death. I learned much from my colleagues and based on their presentations, as well as my own experience and reading, I have reached the following conclusions:

1. *All death is brain death.* If the brain dies, but other organs are preserved, that individual is dead. If the brain lives, but other organs have died, that individual is alive.

2. *Death is a process.* The process begins when the integrative functions of the entire brain and the brainstem fail. The process ends when every cell in the entire body is dead. The damage to the brain may be primary (for example, head injury or brain hemorrhage), or secondary (for example, loss of brain blood flow after cardiac arrest).

*Death is pronounced* during the process when irreversibility is established but not all cells are yet dead. If it is true that hair and nails grow for days after death, waiting for every cell to die would be excruciating and monstrous.



3. When the neurologist appropriately uses the clinical criteria to establish brain death, the diagnosis of death is certain. There have been no documented exceptions. When the cardiologist announces cardiac death, the diagnosis is less certain. Many documented cases of patients pronounced dead after failure of cardiac resuscitation have subsequently been discovered to be alive and a few have actually recovered consciousness (Lazarus phenomenon).

4. Technology can preserve the organs of the dead person (one appropriately pronounced dead by neurologic criteria) for a period of time, usually only hours to days, sometimes longer. Nevertheless, that individual is dead.

5. If the phenomenon of 'heart-beating death' defies our common sense perception and is counterintuitive, so is the fact that the Earth is not flat. The history of science and medicine contains many discoveries that are contrary to our perceptions and are counterintuitive. One of the tasks of physicians and scientists is to educate the public concerning these discoveries. With respect to the concept that all death is brain death, the task may be difficult, but we are obligated to pursue it.

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## DISCUSSION ON DR. POSNER'S PAPER

DR. DEECKE I have a question for both of you, Professor Posner and Professor Huber as our obstetrician. In case of delivery in a brain dead mother, it has to be a cesarian section in any case or can you think of a normal natural delivery?

DR. POSNER They are all sections, yes. And they are mostly premature, they are not carried to term. Mostly the organs begin to fail in the dead mother and they try to get the fetus to the point where it is going to be viable and then they do a caesarean section and within hours the heart stops.

DR. DEECKE So if you try to induce by hormones the birth, the delivery, it would not work? What would you say?

DR. HUBER The so-called feto-maternal unit is very important, it is the communication between the fetus and the mother and for this communication the fetus needs the placenta, the uterus from the mother, the adrenal gland and the liver but not the brain. So, the brain of the mother, especially the pituitary gland for example is not necessary, because this endocrine unit, placenta, adrenal gland and also the fetus produce everything and every hormone that are important for the pregnancy and therefore, perhaps, this part of the mother, without the brain, belongs to the fetus, it can be interpreted, but it is a philosophical question, as a part of the fetus.

DR. POSNER I do not disagree with you, in fact I do not, no, but it seems to me that we do not know all of the things the brain secretes or causes to be secreted which may affect a developing fetus. Now, it is clear that these fetuses who were delivered look normal and they look normal at 8 months and 1 year, and so certainly they are developmentally reasonably normal. I was just raising the question, maybe something is not quite the same as if the mother had lived to the point where the fetus was delivered as a viable infant.

PROF. SPAEMANN In some cases the mother produces also milk and it seems to me that it needs some very complex cooperation of functions to reach this result, this consequence and it seems to me against our way of speaking to say that someone is dead when she begins to produce milk, for example, but also other functions. It is a question of semantics, when do we say she is dead? Normally we do not speak so.

DR. POSNER The brain dead criteria however accepts the fact that the liver continues to produce bile and that there may be endocrine output by the peripheral endocrine organs. These organs are functioning even though the brain itself is dead. The same might be true for minutes following a cardiac arrest, there continues to be some function, these cells do not all die immediately. The fact that the mother may produce milk and there may even be output from the pituitary of prolactin does not suggest to me that the individual is not dead. I am trying to be very provocative about this because I think we need to address some of these questions.

DR. VICUÑA These women were maintained with the ventilator in order to give birth to their babies. How was that process actually conducted? Were they under ventilation during the caesarean section and thereafter disconnected? Is it conceivable that they could have been kept ventilated after delivery?

DR. POSNER In most instances if the organs were functioning at the time the infant was delivered, the respirator was then disconnected. There were a couple of instances where they maintained respiration for a while and then asystole occurred in a short period of time. None of them were kept with peripheral organs functioning for a long period of time after the delivery of the infant.

DR. ESTOL Briefly, regarding lactation, the external carotid artery feeds the anterior pituitary gland, prolactin is produced and the Schultz fascicle mediates a reflex from breast stimulation to the pituitary gland causing milk production and this is acceptable for brain death. But you also mentioned the report by Shewmon, about 'chronic' brain death. First, the cases are not described whatsoever in the article. He states that physicians' reports 'look' reliable but the cases are not described. Secondly, among a total of 150 patients or among the 57 more strictly accepted, there are only

three outliers: two babies, with a couple of years of artificially maintained organ function and the famous, man that 'survived' almost two decades whose autopsy has been reported. One word about this latter case: Shewmon showed a video of himself examining that boy, during a coma meeting in La Havana, Cuba, about eight years ago. If the case is useful for something it is because Dr. Plum, who was there at the podium shouted, and I have it here written by a journalist, 'This is anti-Darwinism!' and he went on to say a few more criticisms. I trust Dr. Plum as somebody knowledgeable on this topic. But besides that, none of us argue that there should not be brain circulation to define brain death and in the report of the autopsy they described that MRA, magnetic resonance angiography, showed intracranial filling of vessels, that is, this angiography showed blood flow at the clivus and at the anterior fossa. So I agree with you, Dr. Posner, that brain death occurred at some point in that child but we cannot tell whether it was one, eight or more months before he had heart arrest. In yet another point, movements are described in that autopsy report as occurring along the ten, fifteen or twenty years, although it is widely accepted that spontaneous movements would be unusual in brain death during such prolonged period of time

DR. POSNER I do not argue with that but I think that brain death must have occurred a fair period of time before the autopsy was performed, because first of all the head never grew after the four-year-old had the episode. He was basically microcephalic. The brain was basically calcified and the pathologist could not identify anatomic structures. The pathologist could not identify where the cerebellum or the brain stem were; he just cut at the foramen magnum and made sections. This is a brain which had undergone dissolution and calcification, almost ossification, and that must take a period of time, that could not have been, say, a week before he had his cardiac arrest. In my view, it does not make any difference, if your brain dies, it does not make any difference whether Dr. Hacke can keep that body functioning with respect to peripheral organs for one day or one month or one year; the patient died at the time he met the clinical criteria for death. I suspect that as our technology gets better we will be able to maintain peripheral organs for longer and longer periods of time and we are going to have to address this more and more.

DR. DAROFF Jerry, how old now is the oldest child that has been delivered from a brain dead mother?

DR. POSNER I do not know, the report is a year.

DR. DAROFF So we do not have any reported school-age children who were so delivered?

DR. POSNER There is one 8 months and one 1 year. Now, there may be some others...

DR. DEECKE He must be much older now.

DR. POSNER Oh, now, he is much older, yes. These are old reports, so one could go back and find them, I suppose.

DR. WIJDICKS It is also interesting to know how old the fetus should be to be able to maintain the mother as an incubator. My understanding is that you found a number of 46 days?

DR. POSNER 46 days was the median time they could maintain the fetus. None of these were younger than 15 weeks at the time.

DR. WIJDICKS There was one of the questions we had recently, how old does the fetus have to be to consider using the mother as an incubator?

DR. POSNER At least 15 weeks I think.

DR. WIJDICKS But 15 weeks seems to me... I think the oldest fetus was in the 20 to 23 weeks.

DR. POSNER The youngest was 15 weeks I think.

DR. WIJDICKS But that did not survive, there was a spontaneous abortion there.

DR. POSNER But the attempts were made. I cannot recall how long the viable fetus was.

DR. WIJDICKS I think it is an important question often asked when you are faced with a brain death mother that has a fetus, when do you consider, with the best available literature, that the fetus is not viable. We had an

example of a fetus that was 14 weeks when the mother was declared brain dead and we decided that the fetus was not viable and in fact two days later the fetus died. And the reason why the fetus died, and most of these died, I think, is because there is a rapid onset of diffuse intervascular coagulation caused by the thromboplastin that is released by a necrotic brain. So I am personally surprised to see that those children are doing well with placentas that must have had major infarctions.

DR. POSNER Remember we are talking about half a dozen cases, really.

DR. WIJICKS Yes, but I am surprised that nobody has looked at the placentas of these children. I think that would be of interest.

DR. HUBER The most important question is the maturity of the lung. The prolongation of pregnancy is a question of avoiding infection, a problem of nutrition and so on. point. I totally agree with you, we have not enough data and we have to look for more experience in this field. But beside them, there is also another interesting topic in connection with pregnancy – the impressive stimulation of neurodegeneration in the pregnant woman. We know that the bulbus olfactorius is enhanced by pregnancy and proliferates more than 30%. Of course, after brain death that is not possible, but perhaps for the future more alternatives are coming over and I personally believe that pregnancy can guide us also for regeneration of the brain and this scientific topic has a very great future in my opinion.

PROF. SPAEMANN Wenn ich Sie richtig verstanden habe, sagten Sie dass unter normalen Umständen 12 Stunden nach dem Hirntod der Organismus definitiv tot ist. Dazwischen scheint mir zu liegen die Phase, die man Sterben nennt. Im Augenblick sprechen wir immer über Leben oder Tod. Aber es gibt einen Prozess des Sterbens, der irreversibel ist von einem gewissen Moment an, aber das ist nicht der Tod. Jedenfalls, so erleben wir den Tod unserer Angehörigen, sie liegen im Sterben und ich frage mich sollten wir nicht den Begriff des Sterbens, der immer noch ein Teil des Lebens ist, beibehalten und von Tod erst sprechen, wenn der Prozess des Sterbens abgeschlossen ist.

[If I have understood properly, you said that, under normal circumstances, the definite death of the organism happens 12 hours after brain death. It seems to me that between them there is the phase called dying. At the moment we always speak about life or dead. However, there is a process of dying which is irreversible from a certain moment on, but which is not death. At least that is how we experience the death of our relatives, they are



on the point of dying, and I ask myself if we should keep the concept of dying, which is still a part of life, and speak about death just when the process of dying is finished.]

DR. POSNER The question has to do with the fact that dying is a process that goes on to death of all cells. There is no specific point where you can say all the cells in that patient have died. There is a point where you can say, either, asystole has occurred or you have examined the patient's brain and the brain is dead and at that point you can say that death has taken place. You can say when the process began, in the sense of when the illness began but you cannot reach a point in time where you can say, that moment is when the patient died because there are some cells that live longer and some cells that live shorter, hair and nails being a long time, I am told.

DR. DEECKE A very short question on the topic of the brain dead mother. If the mother is close to the term, I think everything applies that we have discussed. But could you think of maintaining pregnancy with artificial respiration over a period until at least a premature section can be done.

DR. POSNER 100 days.

DR. DEECKE 100 days? But then you should think of toxic substances that are in the blood due to the necrosis of the brain.

DR. POSNER I think it is not easy. And I do not think we have any denominator, we have a few individuals who have been carried to the point of being viable and the infants appear to be okay but we have no idea how many individuals. In fact, gynaecological societies could poll memberships and study this to see what the denominator might be. I just do not have any idea how common this is. Luckily it is rare, not common.

PROF. CABIBBO Just a physicist's comment. One could try to do some statistics from the number of women who die from brain death, probably in a given time there is a certain percentage of women who are pregnant so you could guess how many of them would be pregnant.

DR. POSNER They have to, of course, die in an intensive care unit, so that peripheral organs can be preserved for a period of time. They have to be known to be pregnant, so that that is why the data comes from a transplant centre, it must be very uncommon.

DR. DAVIS I think that there is a disconnect. I agree with your comment, Jerry, that these women are dead. They are not dying. The precise time of their death, when it occurred, as you pointed out, may be unclear but the period between brain death and the delivery of the fetus is not 'dying', they are dead.

DR. POSNER No, they are dead, I agree.

DR. DAVIS There are perfused organs and there is some organ function but they are dead. And I think this is the essential debate.

DR. POSNER There are all sorts of interesting problems. If the pregnant woman is unmarried, then the woman's surrogate of course is one of her parents but the baby's surrogate is the father and there may be legal disagreements as about what is to be done, so there are some interesting legal phenomena associated with this as well.

DR. HUBER A little provocation: the mother belongs to the fetus from the physiological point of view.

DR. DAVIS Who speaks for the fetus?

DR. POSNER In a married woman it is the husband, the father, in any event it is the father who is the next of kin, so the next of kin speaks for someone unable to speak for him or herself.

DR. WIJDICKS We had exactly a situation like this, a sixteen year old girl who was pregnant and was not married and the mother had made the decision not to carry it on in this fourteen week old fetus for more than a few days which resulted in spontaneous abortion of the fetus two days later, fortunately for us.

DR. POSNER But the father was unknown, I take it.

DR. WIJDICKS The father was known, he was there and he agreed, so there was no discord there, which is another fortunate thing, therefore we could resolve this but I can easily imagine there will be other situations in which it is far more difficult.

DR. POSNER A difficult problem.

## IS BRAIN DEATH THE DEATH OF THE HUMAN BEING? ON THE CURRENT STATE OF THE DEBATE \*

ROBERT SPAEMANN

1. Death and life are not primarily objects of science. Our primary access to the phenomenon of life is self-awareness and the perception of other humans and other living beings. Life is the being of the living. *'Vivere viventibus est esse'*, says Aristotle. For a living being, not to live means ceasing to exist. Being, however, is never an object of natural science. It is in fact the *'primum notum'* of reason and as such secondarily an object of metaphysical reflection. Because Life is the being of the living, it cannot be defined. According to the classical adage *'ens et unum convertuntur'*, it holds true for every living organism that it is alive precisely as long as it possesses internal unity. Unlike the unity of atom and molecule, the unity of the living organism is constituted by an anti-entropic process of integration. Death is the end of this integration. With death, the reign of entropy begins – hence, the reign of 'destructuring', of decay. Decomposition can be stopped by means of chemical mummification, but this way of preserving a corpse merely holds its parts together in a purely external, spatial sense. Supporting the process of integration with the help of technical appliances, however, is very different. The organism preserved in this way would in fact die on its own if left unsupported, but being kept from dying, it is kept alive and cannot be declared dead at the same time. In this sense Pope Pius XII declared that 'human life continues even when its vital functions manifest themselves with the help of artificial processes'.

2. We cannot define life and death, because we cannot define being and non-being. We can, however, discern life and death by means of their physical signs. Holy Scripture regards breath as the basic phenomenon of life, and for this reason it is often simply identified with life itself. The cessation of breathing and heartbeat, the 'dimming of the eyes', rigor mortis, etc. are the criteria by which since time immemorial humans have seen and felt that a fellow human being is dead. In European civilization it has been cus-

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

tomary and prescribed by the law for a long time to consult a physician at such times, who has to confirm the judgment of family members. This confirmation is not based on a different, scientific definition of death, but on more precise methods to identify the very phenomena noted already by family members. A physician may still be able to discern slight breathing, which escapes a layperson. Besides, the physician could nowadays point out the reversibility of certain phenomena, like e.g. the cessation of heart-beat. The heart which has stopped beating can very well still exist. Due to such sources of error in the perception of death, it is a reasonable traditional rule to let some time elapse between first noting these phenomena and the funeral or cremation of the deceased. Similarly, consulting a physician serves the purpose of making sure that a human being is not prematurely declared dead, i.e. non-existent.

3. The 1968 Harvard Medical School declaration fundamentally changed this correlation between medical science and normal interpersonal perception. Scrutinizing the existence of the symptoms of death as perceived by common sense, science no longer presupposes the 'normal' understanding of life and death. It in fact invalidates normal human perception by declaring human beings dead who are still perceived as living. Something quite similar happened once before, in the 17th century, when Cartesian science denied what anyone can see, namely, that animals are able to feel pain. These scientists conducted the most horrible experiments on animals and claimed that expressions of pain, obvious to anyone, were merely mechanical reactions. This incapacitation of perception fortunately did not last. It is returning in different shape, however: namely, by introducing a new definition of death, or rather, a definition of death in the first place, in order to be able to declare a human being dead sooner. That way, it would also be possible to define away pain by defining it in terms of the neurological processes which constitute its 'infrastructure', and consequently to define everyone as pain-free for whom these diagnostic findings cannot be confirmed. It is merely a matter of transforming the explanation of pain into a definition, in order to be rid of it as pain. Just like pain, its foundation, life, is equally undefinable. The hypothesis that the total loss of all brain functions immediately and instantaneously brings about the death of a human being frequently eludes discussion in scientific debates by being transformed into a definition: If the death of a human being and the loss of all brain functions are by definition equated, any criticism of this hypothesis is naturally bound to go nowhere. What remains to be asked is merely whether what was defined in this way is really what all human

beings have been used to call 'death', as when Thomas Aquinas, proving the existence of a Prime Mover, a non-contingent Being, etc., concludes his proof with the words: 'This is what they all mean when they say "God"'.

Is brain death what they all mean when they say 'death'? According to the Harvard Commission, not at all. The commission intended to provide a new definition, clearly expressing their main interest. It was no longer the interest of the dying to avoid being declared dead prematurely, but other people's interest in declaring a dying person dead as soon as possible. Two reasons are given for this third party interest: (1) guaranteeing legal immunity for discontinuing life-prolonging measures that would constitute a financial and personal burden for family members and society alike, and (2) collecting vital organs for the purpose of saving the lives of other human beings through transplantation. These two interests are not the patient's interests, since they aim at eliminating him as a subject of his own interests as soon as possible. Corpses are no such subjects any more. The first of the two interests mentioned is incidentally bound to an erroneous premise and a correspondingly problematic practice of the judiciary: It presupposes that for every human being not declared dead, life prolonging measures are indicated always and without exception. Where this premise is dropped, the interest in declaring death at an early point ceases to exist. What remains is the second interest. This interest is self-contradictory, insofar as it requires on the one hand to collect live organs, for which reason the dying person needs to be kept alive artificially, while on the other hand the dying person has to be declared dead, so that the collection of those organs does not have to be considered an act of killing.

4. The fact that a certain hypothesis regarding the death of a human being is based on the interest of other people who would benefit from the verification of this hypothesis, does not prove its falsity. It must alert us, however, to be extremely critical, and it requires setting the burden of proof for this hypothesis very high. This holds true more than ever when the hypothesis is immunized underhand by turning it into a definition. Precisely because nominal definitions are neither true nor false, the question of whose interests they serve gains relevance. The strategy of immunization thus has a counterproductive effect. The legislation of my country allows for a physician's conflict of interests, insofar as prior to a transplantation, death has to be determined by physicians who themselves are not involved in the transplantation. But unfortunately, transplantation physicians did have their share in drafting the criteria for the determination of death. Having as little to do with the formulation of the criteria for the

determination of death as with their application ought to be in the moral interest of transplantation physicians regarding their personal integrity – even if not in the professional interest of transplantation medicine, although the professional interest of transplantation medicine, considered as it is in itself, is a highly moral interest, the interest in saving the lives of human beings. It has to be ensured, however, that saving lives does not happen at the expense of the lives of other people. A transplantation physician professionally sides with the recipient, not the donor of organs.

It is a fact that since 1968, the consensus about the new definition of death has not been consolidated; to the contrary, objections against it have increased. Ralf Stoecker states in his 1999 habilitation thesis *'Der Hirntod'* [Brain Death] that the switch-over from cardiac death to brain death is more contended today than thirty years ago (p. 37). The arguments against brain death are brought forward not only by philosophers, and, especially in my country, by leading jurists, but also by medical scientists, e.g. the American neurologist Shewmon, prominent as a radical advocate of brain death still in 1985, until his own medical research convinced him of the opposite.

The observer of the discussion is bound to discover that it suffers from a marked asymmetry. The proponents of the new definition argue from a 'position of strength'. They feel that it is an unreasonable demand to waste more time with arguments, aware that they have the 'normative power of the factual' on their side, i.e. an established medical practice which meanwhile has already become routine, as well as, for believers, the blessing of the Church (which, however, was categorically called into question last year by a public statement of the Cardinal Archbishop of Cologne). They do not even distantly make the same effort dealing with the arguments of their critics as vice versa. Consequently, the weight of the arguments has shifted for every unbiased observer more and more in favor of the skeptics. I myself have to confess that their arguments have meanwhile convinced me. Life and Death are not the property of science, hence it is the duty of scientists to convince ordinary laypeople of their viewpoint, who are endowed with a certain degree of intelligence. Where scientists refuse to make this effort under the assumption that they can use arguments of authority instead, their case is indeed in a sorry state. In the following, I would in fact like to make my argument against the new definition of death. What it defines is not '*quod omnes dicunt mortem*'.

5. The proponents of the thesis that the loss of all brain functions is identical with the death of the human being divide into two separate sub-groups. The first group distinguishes between the life of the human being

and human life, i.e., the life of a person. According to them, the term 'human life' should only be used as long as mental processes of specifically human nature can be discerned. When the organic basis of such processes ceases to exist, the human being is no longer a person, hence his or her organism is at other people's disposal to use for their purposes. Consequently, a total loss of all brain functions is not even required at all. Sufficient is the failure of those brain areas that constitute the 'hardware' for these mental acts. People in persistent vegetative state are thus dead as persons. Not only is this position incompatible with the doctrines of most high religions, in particular of Judaism and Christianity; it also contradicts the tenets of today's medical orthodoxy. A well-known proponent of this position is Australian bioethicist Peter Singer. The second group starts from the assumption that we can only speak of the death of a human being when the human organism as whole has ceased to exist, i.e. when the integration process constituting the unity of the organism has come to an end. According to this second group's thesis, this process is terminated with the total loss of all brain functions, assuming the brain to be the organ responsible for integration. Hence, according to the views of this group, death of the brain is the death of the human being. If the underlying hypothesis is correct, so must be the conclusion, and even the Church would have no reason to defy this conclusion. But obviously, the hypothesis is not correct, and those who wish to adhere to the conclusion are consequently forced to draw closer to the unorthodox theory of the first group, i.e. the cortical death hypothesis.

6. The hypothesis of at least extensional identity of the total loss of brain functions and the death of the human being is incorrect for several reasons. First of all, it contradicts all appearance, i.e. normal perception, similar to the Cartesian denial of pain in animals. When a German anesthesiologist writes, 'Brain-dead people are not dead but dying', and that even after thirty years in the profession she could not convince herself of the opposite of what everybody can see, then her statement stands for many others. One of the most well-known German neurologists, Prof. Dichgans, head of the Neurologische Universitätsklinik in Tübingen, who had until then not followed the latest criticism of the brain death concept within the medical community, told me recently that he personally was not prepared to diagnose death based on standard neurological criteria, and therefore did not participate in the determination of death. German intensive care physician Peschke reports that according to his investigations, nurses in transplantation units are prepared neither to donate organs nor receive donated organs. What they see on a daily basis makes it impossible for them to become part

of this practice themselves. One of these nurses writes: 'When you stand right there, and an arm comes up and touches your body or reaches around your body – this is terrifying'. And the fact that the allegedly dead person is usually given anesthesia, so that the arm stays down, does not contribute to putting less trust in one's own senses. Does one anesthetize corpses? This is merely a suppression of vegetative responses, goes the argument. Yet a body capable of vegetative responses requiring complicated coordination of muscle activity is obviously not in that state of disintegration which would entitle us to say that it is not alive, i.e. does not exist any more.

7. Here the reasons of common sense converge with those advanced by medical science. Thus it was already pointed out by Dr. Paul Byrne in the *Journal of the American Medical Association* in 1979 that it is unjustified to equate the irreversible loss of all brain functions with 'brain death', i.e. with the end of the existence of the brain. Likewise, we do not equate the cessation of heartbeat with the destruction of the heart. We know today that in some cases this loss of function is reversible. But it is only reversible because the heart precisely does *not* cease to exist when it ceases to function. And only because the cessation of breathing was not equated with the 'death of the lung', it became possible to utilize mechanical ventilators which restarted those functions. Based on considerations of this kind, e.g. P. Safar and others began to work on the resuscitation of brain function in brains considered dead by standard criteria. The reply that the loss of function in resuscitated brains had just not been irreversible, makes for a circular argument. Irreversibility is obviously not an empirical criterion, since it can always be determined only retrospectively. Just because we assume that the brain still exists, we try to resuscitate its function.

Similarly circular is the reasoning in the question what constitutes 'total loss of brain function'. The proponents of brain death reject the substitution of this term by 'loss of all brain functions' on the grounds that this would also pertain to 'peripheral brain functions' which can survive the brain as a whole. What are such 'peripheral functions'? The Minnesota criteria for this are different from the British criteria, and some authors already declare brain stem activity peripheral when the cortex has ceased functioning. Anything can apparently be regarded as peripheral which is not identical with the integrative function of the brain for the organism as a whole. But the question had precisely been to prove just this integrative function! So Paul Byrne's words are arguably still valid: 'There is no limit to what real functions may be declared peripheral when the only nonperipheral function is imaginary'.



8. Is it justified to call the somatically integrative function of the brain 'imaginary'? Among the authors who claim this and give reasons for their views, maybe the most important one is Alan Shewmon. A summary of his empirical research and theoretical considerations can be found in his essay 'The Brain and Somatic Integration: Insights into the Standard Biological Rationale for Equating "Brain Death" with Death', published in the *Journal of Medicine and Philosophy* in 2001. Here I will only present the abstract of this essay, which of course contains neither empirical evidence nor theoretical arguments, but only the theses.

The mainstream rationale for equating 'brain death' (BD) with death is that the brain confers integrative unity upon the body, transforming it from a mere collection of organs and tissues to an 'organism as a whole'. In support of this conclusion, the impressive list of the brain's myriad integrative functions is often cited. Upon closer examination and after operational definition of terms, however, one discovers that most integrative functions of the brain are actually not somatically integrating, and, conversely, most integrative functions of the body are not brain-mediated. With respect to organism-level vitality, the brain's role is more modulatory than constitutive, enhancing the quality and survival potential of a supposedly living organism. Integrative unity of a complex organism is an inherently nonlocalizable, holistic feature involving the mutual interaction among all the parts, not a top-down coordination imposed by one part upon a passive multiplicity of other parts. Loss of somatic integrative unity is not a physiologically tenable rationale for equating BD with death of the organism as a whole.

From Dr. Shewmon's text I will only quote a short paragraph: *Integration* does not necessarily require an *integrator*, as plants and embryos clearly demonstrate. What is of the essence of integrative unity is neither localized nor replaceable – namely the anti-entropic mutual interaction of all the cells and tissues of the body, mediated in mammals by circulating oxygenated blood. To assert this non-encephalic essence of organismal life is far from a regression to the simplistic traditional cardio-pulmonary criterion or to an ancient cardiocentric notion of vitality. If anything, the idea that the non-brain body is a mere 'collection of organs' in a bag of skin seems to entail a throwback to a primitive atomism that should find no place in the dynamical-systems-enlightened biology of the 1990s and twenty-first century.

9. A nonmedical person, trained in the theory of science and wishing to form an objective opinion about the *status quaestionis*, must strive to evaluate the arguments brought forth in the debate. Where results of empirical research are concerned which he or she has no way of verifying independently, it is necessary to confront them with the counter-arguments. Insofar as these counter-arguments are of an empirical nature as well and challenge the accuracy of the presented research results, any judgement is to be abstained from until further empirical verification. As far as a theoretical interpretation of the results is concerned, he or she is qualified to verify and evaluate it.

Regarding the findings presented by Dr. Shewmon, I am not aware of any criticism targeting the core of his argumentation. I conclude from two facts that such criticism indeed does not exist:

- a) When Shewmon presented his research results at the Third International Symposium on Coma and Death, in Havana, Cuba, February 22-25, 2000, attended largely by neurologists and bioethicists, there was surprisingly broad acceptance. What ensued was a shift of the domain of the debate from the medical to the philosophical arena, with the defenders of brain death appealing exclusively to consciousness-based concepts of personhood rather than the previously standard medical rationale of bodily integrity.
- b) In fall 2002, the American *National Catholic Bioethics Quarterly* published an article by editor-in-chief Edward J. Furton, 'Brain Death, the Soul and Organic Life', which is dedicated exclusively to the debate with Alan Shewmon. In this article, Dr. Shewmon's empirical research results are not disputed, nor is any reference made to literature which would justify such doubts. From this I conclude that indeed there is no such literature.

10. All the more interesting is Furton's article itself, which defends the equation of brain death with death against Shewmon. I will conclude my own remarks with a critical report about this article, beginning with a summary: Furton's primarily philosophical arguments in favor of brain death convinced me more than anything else of the opposite. The reason is that Furton is only able to sustain his thesis of brain death as the death of the human being by distinguishing between the death of the human being as a person and the death of the human being as a living being. He writes:

Although the difference between the death of the person and the decay of the body had long been obvious, it is only in our time that the difference between the life of the person and the life of the body has become apparent.

This, now, is exactly the position of Peter Singer, and it is incompatible with the belief of most religions, and certainly with that of Christianity. If Church authorities cautiously accepted the premise of brain death, this was always done under the premise that the brain is responsible for somatic integration, the loss of the brain functions hence being identical with the death of the organism. It is beyond the scope of religious authority to judge the validity of this premise. Where the premise becomes doubtful, the conclusion ceases to apply.

Furton would like to hold on to the conclusion, even though he abandons the premise under the impression of Alan Shewmon's arguments. His appeal to papal authority is, therefore, not justified, and it is surprising that he makes such excessive use of the argument of authority in his debate with Shewmon. Just because the Pope bases his own equally hypothetical conclusion on it does not mean that a scientific hypothesis is thereby withdrawn from further scientific discourse. Otherwise the Ptolemaic world view would have been dogmatized forever, just because the Church drew conclusions with religious and practical relevance from it while it was generally accepted. At the same time Furton himself concedes in his essay that 'the determination of death does not fall under the expertise of the Church, but belongs to the physician who is trained in this field'. I would like to render this more precisely: The physician is qualified to determine the existence of pre-defined criteria for death. The discourse about these criteria themselves falls into the domain of philosophers and philosophizing theologians after they have received the necessary empirical information from the medical profession. Furton bases his argument on the Furton bases his argument on the existence of pre-defined criteria for death. The discourse about these criteria themselves falls into the domain of philosophers and philosophizing theologians after they have received the necessary empirical information about the medical profession. Furton bases his argument on the Aristotelian-Thomistic doctrine of the soul in connection with the teaching of the Church, dogmatized after the Council of Vienna 1311/12, according to which the human soul is only one, from which follows that the *anima intellectiva* is at the same time the *forma corporis*.

From this doctrine, however, Furton draws a conclusion which is diametrically opposed to the intention of St Thomas as well as the Council of Vienna. Thomas assumes that the human being initially possesses a vegetative and then an animal soul, and that the spiritual soul is created only on the 40th day of pregnancy, and not in parallel with the other two

souls but in their stead, so that it is now the spiritual soul that simultaneously fulfills the vegetative and the sensorimotor functions. This is drastically different from Aristotle, for whom *nous*, reason, is not part of the human soul, but *thyraten*, entering the human being from outside. St Thomas, by the way, excludes Jesus Christ explicitly from successive animation: The incarnation in the moment of his conception presupposes that Jesus' soul must have been a human soul in the full sense from the very beginning. The Church, herein following science, has given up the idea of successive animation long ago and regards not only Jesus, but any human being as a person from the moment of conception, with his or her soul being an *anima intellectiva* – even though the newborn infant is not yet capable of intellectual acts. This inability is due to the lack of sufficiently developed somatic 'infrastructure'. Similarly, a pianist 'cannot' play the piano when there is no piano available. Just as the pianist nonetheless remains a pianist, the soul of the human being is an *anima intellectiva* even when it is factually unable to think. The being of man is not thinking but living: *Vivere viventibus est esse*. Furton's way of thinking is radically nominalistic. For him, a personal soul exists only as long as an individual is capable of specifically personal acts. For him, the reality of the soul of the human being is not in allowing man to exist as a living being, it is not *forma corporis* but the form of the brain and only indirectly the form of the body. 'The soul is... what enlivens a material organ, namely the brain, and from there enlivens the rest of the human body'. (This view was rejected already in 1999 by the Würzburg-based neurologist Prof. Joachim Gerlach, for whom the error in the equation of brain death and the death of the individual consists in 'regarding the brain as the, seat of the soul'. Similarly, Paul Byrne wrote already in 1979: "Brain function" is so defined as to take the place of the immaterial principle or "soul" of man'). Furton identifies that which Thomas calls 'intellectus' with factual intellectual consciousness. He does not conclude from the obvious continued existence of a living human organism that the personal soul, which is the *forma* of the human body, is still alive, but contrariwise: because a human being is not capable of intellectual acts any more, the soul has left him and he is, as a person, dead. The fact that the organism as a whole is obviously still living does not play any role. Without actual brain function, the human organism is nothing other than a severed organ, which also still shows expression of life.

This position is consequent. It largely coincides with Peter Singer and Derek Parfit, for whom persons exist only as long as they are capable of

personal acts, hence sleeping people, e.g., are not persons. Under the weight of the arguments of Shewmon and others, the group of medically and theologically 'orthodox' defenders of brain death is apparently disintegrating. In the light of the untenability of the thesis of the integrative function of the brain, the identification of brain death and the death of the human being can only be held up if the personality of man is disconnected from being a human in the biological sense, which is what Singer, Parfit and Furton are doing. To do this under reference to the doctrine of St Thomas is absurd indeed. Furton avails himself of an equivocation in the term 'intellectus' when he claims that being a human consists in a connection of intellect and matter, seemingly as though Thomas understood 'intellect' in terms of actual thinking rather than the capacity to think. This capacity belongs to the human soul, and this soul is *forma corporis* as long as the disposition of the body's matter permits it. Instead of concluding: where there is no longer any thinking, the *forma corporis* of the human being has disappeared, we can thus only conclude: as long as the body of the human being is not dead, the personal soul is also still present. Only the second conclusion is compatible with Catholic doctrine as well as the tradition of European philosophy. Furton's adventurous conclusion to declare a human being dead when his or her specifically human attributes do not manifest themselves any more, is contrary to all immediate perception. Even Peter Singer and Derek Parfit are still closer to the phenomena when they do declare the person expired, but do not already for this reason consider the human being dead.

I conclude with the words of three German jurists who wrote after immersing themselves in the medical literature:

To be correct, the brain death criterion is only suited to prove the irreversibility of the process of dying and to thus set an end to the physician's duty of treatment as an attempt to delay death. In this sense of a treatment limitation, the brain death criterion is nowadays likely to find general agreement (Prof. Dr. Ralph Weber, Rostock).

The brain dead patient is a dying human being, still living in the sense of the Basic Constitutional Law [scil. of the Federal Republic of Germany, ESS] Art. 2, II, 1 99. There is no permissible way to justify under constitutional law why the failure of the brain would end human life in the sense of the Basic Constitutional Law. Accordingly, brain dead patients have to be correctly regarded as dying, hence living people in the state of irreversible brain failure. (Prof. Dr. Wolfram Höfling, Bonn).

It is impossible to adhere to the concept of brain death any further ... There is no dogmatic return to the days before the challenges to the concept of brain death (Dr. Stephan Rixen, Berlin).

11. After all that has been said, for anybody who is still doubtful, the principle applies, according to Hans Jonas: *In dubio pro vita*. Pius XII declared just that:

In case of insoluble doubt, one can resort to presumptions of law and of fact. In general, it will be necessary to presume that life remains.

## DISCUSSION ON PROF. SPAEMANN'S PAPER

CARD. COTTIER J'ai écouté avec grand intérêt la conférence du Prof. Spaemann qui a touché plusieurs arguments. Certains me font difficulté.

Le Prof. Spaemann affirme comme un constat que le consensus quant à la définition de la mort clinique est en train de s'effriter. Mais, en philosophie, le consensus est le plus faible des arguments. Il convient donc d'examiner pour eux-mêmes les arguments proposés et de juger de leur validité. Dans la conférence du Prof. Spaemann l'argument du consensus revient à la fin et semble être avancé comme une preuve de la fragilité de la position de la majorité des médecins et des scientifiques.

La deuxième observation est directement philosophique. Vous citez Aristote, que je reprends dans la traduction de saint Thomas: *vivere viventibus esse*, vivre pour les vivants c'est être. Et vous interprétez cette phrase comme si le vivre était l'équivalent de l'être, ou: l'être des vivants est le vivre. Vous interprétez cette phrase comme si le vivre était l'équivalent de l'être. La conséquence que vous en tirez est que, comme on ne peut pas définir l'être, de même le vivre est indéfinissable. L'être ne peut pas être défini parce qu'il est le premier concept, et que, pour le définir, on aurait besoin d'un autre concept qui lui serait donc antérieur. En réalité le *vivere* désigne une *modalité* de l'être. Et c'est pourquoi il est parfaitement définissable. Aristote a consacré un ouvrage à ce sujet: le *peri psyche*, où il définit le vivant à partir de ses propriétés et de ses activités qui sont la nutrition, la croissance et la reproduction.

On peut donc définir le vivant et la vie et par là également définir la mort.

Une conséquence de votre interprétation de l'adage aristotélicien, est que vous êtes conduit à définir la mort comme annihilation. Or la mort n'est pas annihilation. Elle ressortit au phénomène de corruption. Cessant d'être tenus ensemble, les composants de l'organisme sont transformés en autre chose, ils retournent à leur état d'éléments. Ils ne sont pas anéantis.

Troisième observation: Votre critique porte sur la définition de la mort qui est présupposée à la pratique clinique. Mais aucun scientifique conscient des limites de sa discipline, n'a prétendu donner une définition

exhaustive de la mort. La définition clinique laisse intact le mystère de la mort comme événement s'inscrivant dans la destinée de la personne. En ce sens, la mort est un problème qui nous concerne tous. Socrate disait que philosopher est apprendre à mourir. La philosophie est hantée par le problème de la mort. Pour le chrétien, la mort n'est pas une annihilation, elle est séparation du principe spirituel, que nous appelons l'âme, du corps qui, laissé à lui-même, perd du même coup sa vie organique.

Quatrième observation: Vous appliquez à la connaissance de la mort, la formule que saint Thomas emploie à propos de la connaissance de Dieu: "ce que tous entendent [par Dieu] Ce que tous appellent [Dieu]". Si saint Thomas parle ainsi, c'est parce que nous n'avons pas l'évidence de Dieu, mais il existe des preuves *a posteriori* (plus exactement des *voies*) qui nous conduisent à reconnaître, au-delà des choses que nous connaissons et qui n'ont pas en elles-mêmes leur raison d'être, un principe, une cause, qui les transcende et n'est pas à la portée directe de notre connaissance. Nous ne pouvons pas faire un jugement semblable à propos de la mort. Je dirais que celle-ci, plus précisément le mourir, fait partie de l'expérience humaine.

Une dernière observation. Je ne voudrais pas être injuste, mais il m'a semblé qu'il y avait dans votre exposé une sorte de procès de tendance concernant les transplantations d'organes. Vous insistez sur des motivations malpropres et sur des abus, qui existent et peuvent exister. Mais on ne peut absolument pas généraliser. Ces transplantations telles qu'elles se pratiquent dans nos hopitaux occidentaux sont entourées de précautions assurant le respect de la personne du donneur et de celle du receveur. On ne peut pas dire qu'il y a marchandage.

Il y aurait encore d'autres remarques à proposer, mais elles sont davantage de la compétence des scientifiques.

L'âme donne au vivant son organicité, c'est-à-dire son unité et l'interdépendance des organes et des fonctions. Admettre qu'il y ait un organe directeur, ne fait pas difficulté. Que la mort clinique constatée ne signifie pas la cessation de fonctionnement simultanée de tous les organes, *a fortiori* quand ils sont maintenus en fonction artificiellement, ne fait pas problème non plus et ne constitue pas un obstacle pour reconnaître la mort sur la base de la mort clinique.

Si l'Eglise tient à être exactement informée sur le moment de la mort clinique, c'est parce qu'elle se préoccupe de la mort comme événement décisif dans l'existence de la personne appelée à la vie éternelle. Les critères objectifs permettant de fixer le moment de la mort se sont perfectionnés avec le progrès de nos connaissances scientifiques. Il y a des points



sûrs: peut-être demain en saurons-nous davantage, sans que cela remette en cause ce qui est acquis.

Merci encore pour votre riche exposé.

PROF. SPAEMANN Sie sagen, Eminenz, man könne Leben definieren. Kann man das wirklich? Wir können empirische Kriterien entwickeln, um das Vorhandensein von Leben zu testen. Aber was Leben heißt, haben wir damit nicht definiert. Wir erfahren Leben primär, wenn wir uns dessen bewusst werden, dass wir *s i n d*. Und zwar dass wir "jemand" sind, der als Individuum identifizierbar ist. *Ens et unum convertuntur*. Die Frage, ob jemand noch lebt, ist gleichbedeutend mit der Frage, ob sein Organismus noch als Einheit existiert, oder ob der Desintegrationsprozess bereits begonnen hat.

„Quod omnes dicunt mortem“ – die Frage ist doch die: will jemand eine neue Sache einführen, die verschieden ist von dem, was man bisher Tod nannte. In diesem Fall sollte man ehrlicherweise ein neues Wort einführen. Oder aber jemand will die Kriterien für das präzisieren, „quod omnes dicunt mortem“, also für etwas, was schon vor der neuzeitlichen Wissenschaft allen Menschen bekannt war.

Schließlich muss ich ein Missverständnis korrigieren. Ich halte das Motiv der Transplantationsärzte für ein nobles, humanes Motiv. Mit diesem Motiv konkurriert ein anderes, ebenfalls nobles und humanes Motiv, nämlich zu verhindern, dass ein lebendiger Mensch, der begonnen hat zu sterben, durch Organentnahme getötet wird. Die Hirntodthese kommt dem Interesse der Transplantationsmedizin entgegen. Ich sage nicht, dass diese These deshalb falsch sein muss. Ich sage nur, dass mit Bezug auf sie größte Vorsicht geboten ist und dass der „burden of proof“ deshalb besonders groß ist.

Erlauben Sie noch eine Bemerkung zu Kardinal Cottier: Der Tod des Menschen ist in gewisser Hinsicht tatsächlich eine Annihilation. Der heilige Thomas schreibt, dass der Mensch, die menschliche Person mit dem Tod aufhört zu existieren. Was den Tod überdauert ist die Seele. Aber Thomas sagt, die Seele ist nicht der Mensch und nicht die Person. Sie wird erst bei der Auferstehung der Toten zur „forma“ eines neuen Leibes und damit wiederum eines Menschen werden.

[You say, Eminence, life could be defined. Can that really be done? We can develop empirical criteria in order to test the presence of life. But there-with we have not defined the meaning of life. We experience life primarily when we become conscious that we 'are'. And that we are namely 'some-body' who is identifiable as an individual. *Ens unum convertuntur*.

The question whether somebody is still alive is equivalent to the question whether his organism still exists as a unity, or whether the process of disintegration has already begun.

'*Quod omnes dicunt mortem*' – That is the question: somebody wants to introduce a new fact that is different from what had been called dead up to that moment. To be honest, a new word should be introduced. Otherwise somebody wants to define the criteria for '*quod omnes dicunt mortem*', hence for something that was already known to all people before modern science.

Finally, I have to correct a misunderstanding. I consider the transplantation specialists' motivation a noble, human motive. With that motivation another motivation competes, which is also noble and human. That is to prevent that a living human person, who has begun to die, is killed by removing an organ. The thesis of brain death comes to meet the interests of transplantation medicine. I do not want to say that, for this reason, this thesis must be wrong. I just say that relating to it one has to proceed with caution and that because of it the 'burden of proof' is extremely important.

Please let me comment on Cardinal Cottier. In a certain sense, the death of a person is, in fact, annihilation. St Thomas writes that the human being, the human person with death ceases to exist. What survives death is the soul. But Thomas says the soul is neither the human being nor the person. Only with the resurrection of the dead it will become '*forma*' of a new body and therefore of a new person.]

DR. MASDEU Regarding the appearance argument, certainly appearance is important, it is probably more important to know what is behind the appearances, and appearances can be interpreted in different ways. You rightly mention one historical situation. We currently have a situation where the appearance of an unborn child, who is not seen, is thought to be part of the mother. Going deeper, with the tools that we have in medicine nowadays, we know that it is a different human being. The appearance is deceitful there.

I think that, in the case of brain death, exactly the same thing happens. The person has died. The integrative portion of the human body is lost, disintegration is already occurring and the problem is the appearance. Thanks to medical technology, just as the Egyptians embalmed their bodies, we are able to keep part of that corpse working. That is why appearance is a critical part of this argument.

Secondly, Dr. Shewmon bases much of his arguments on answers from medical people who are not necessarily trained philosophers. Dr. Plum is a

superb neurologist who has taught many of us but when he says, 'I'll grant you that the brain dead body is a living human organism, but is it a human person?', he is using 'living human organism' to refer to a clump of human cells. It would seem to us outrageous to say that, if we amputate someone's finger and put it in a flask and perfuse it and can keep it there for twenty years, as we can do now, that finger is Mr Jones. That is absurd. Well, that is what Dr. Plum is referring to, he is referring to a piece of the body that he is calling a human organism but most of us would not call it that, I would call it a corpse. It has lost the entity of a human being, so it is not a human being anymore, it is a different thing, it is now a corpse that we are keeping apparently in the same way that it was before, as we can keep that finger.

So, from the medical point of view, we see so clearly how difficult it is to keep those different organs that are not anymore a human being, that have no life but are simply his corpse, and therefore the integration argument has not been stressed enough in my opinion. I think that it is very obvious that, without respirators, without all the technology that goes into keeping those parts of what used to be a human body functioning, those parts would continue to disintegrate in a few minutes. Unfortunately, the argument for integration has not been made strongly enough.

PROF. SPAEMANN Mir scheint die Analogie: hirnloser Körper-Finger zu schwach. Die Beispiele von Alan Shewmon und das Repetinger-Beispiel weisen hin auf Menschen, die wachsen, pupertieren und altern, also hochkomplexe systemische Prozesse durchmachen. Davon kann bei Fingern nicht die Rede sein.

Dr. Masdieu zitiert Dr. Plum: „The brain dead body is a living human organism. But is it a human person?“ Dr. Masdieu nennt das, was Dr. Plum einen „living human organism“ nennt, einen clump of human cells. Aber einen clump of cells wird niemenad einen living organism nennen. Pater Cottier sagte: „l'âme donne au vivant son organicité, c.a.d. son unité et interdépendence des organes“. Genau darum geht es: hat der hirntote Körper noch seine Einheit und seine Organizität?

Dr. Masdieu spricht vom Leichnam. Aber der Hirntote ist nicht das, was alle einen Leichnam nennen. Ein atmender Mensch, dessen Herz schlägt, der die Reaktion zeigt, die ein Hirntoter zeigt und der noch sterben kann, wenn man die Apparate abstellt, wird von niemandem als Leichnam wahrgenommen. Ein Leichnam kann nicht mehr sterben. Die Wissenschaft kann unsere elementaren Wahrnehmungen zu erklären versuchen. Sie kann sie nicht außer Kraft setzen.

[The analogy brainless body-finger seems too weak to me. Alan Shewmon's examples and the Repertinger case allude to human beings who grow, go through puberty and grow old, which means that they pass through highly complex systematic processes. That is certainly not the case with fingers.

Dr. Masdieu quotes Dr. Plum: 'The brain dead body is a living human organism. But is it a human person?' Dr. Masdieu calls what Dr. Plum calls a 'living human organism' a 'clump of human cells'. But nobody would call a clump of human cells a living organism. Father Cottier said: 'l'âme donne au vivant son organicité, *i.e.* son unité et l'interdépendance des organes'. That is the point: does the brain dead body still have its unity and its organicism?

Dr. Masdieu speaks of a corpse. But the brain dead person is not what everybody would call a corpse. Nobody would perceive as a corpse a breathing human person whose heart is beating and who shows the same reaction shown by a brain dead person who can still die when the ventilators are shut down. A corpse cannot die anymore. Science may try to explain our basic perceptions. It cannot annul them.]

DR. ROPPER The briefest thing I could say is that I think there are factual issues that physicians can address, both in regard to Dr. Shewmon's work and the comments that have just been made. In the interest of brevity, I will say that it is not the case that Shewmon's research has not been disputed or is not disputed. In particular, I point to two outstanding aspects of his claim. The first is that brain death, as currently defined, does not lead to cardiovascular collapse, or that it is relatively easy to maintain a body that has a dead brain for an indefinite period of time. He does point out a few instances in which prolonged somatic survival has been shown and that is interesting, but it is highly exceptional. Number two, the case that he forwarded most recently, the Repertinger case, in which the brain was necrotic from the top of the spinal cord rostrally or upward, simply proves the point that it is possible to keep a corpse going for a long period of time. I do think that each of Shewmon's points deserves, on an intellectually honest basis, a response and that it has been perhaps a weakness of the proponents of the idea of brain death that they have not been met head on. Furthermore, I think my esteemed colleague Spaemann continues to mix up persistent vegetative state with brain death when he talks about mental processes and personhood, and that the distinction between these processes that neurologists have drawn for us is safe and we should stay on one side of it. In addition, the idea that physicians only have a role in society in

applying definitions of death that have been established on a religious or philosophical basis is a little bit frightening for us, so I would dispute that. Finally, I would just say that if one started with a clean slate of defining death, if we did not have five thousand years of religious view, this would be the place to start, brain death, not the appearance of the warm body that common sense currently brings to us.

Furthermore, the Cartesian argument that we see the dog suffer no matter what the scientist tells us, is in itself the point I am trying to make, because it is modern brain science that is the only manner in which we can reverse this incorrect sense perception. It is modern science that allows an evolutionary view of death, not just a clinical view of death, and speaking for myself as a neurologist, it is a matter of attending to what we now know, from our study of the brain. The testimonials of heartfelt persons who respond to the appearance of a warm body whose chest is moving does not help. Once we get into the soul, I do not think neurologists have anything definitive to say. So my summary would be what Mark Twain said, 'Reports of my death are greatly exaggerated', that reports of brain death are exaggerated by a large number of spurious clinical arguments, most of which I would dispute but in the interest of time I am not going to enumerate them all until there has been further discussion.

PROF. SPAEMANN Dr. Ropper sagt, dass das über den Hirntod hinaus verlängerte körperliche Überleben, das die Beispiele von Dr. Shewmon zeigen, sehr selten, „highly exceptional“ sind. Aber darauf kommt es nicht an. Dr. Ropper verwechselt, so scheint mir, eine Kausaltheorie, nach welcher der Ausfall des Gehirns den Tod des Menschen in der Regel zur unmittelbaren Folge hat, mit einer Definition, die beide Ereignisse miteinander identifiziert. Eine Kausaltheorie ist widerleglich, kann aber aufrechterhalten und in ihrer Gültigkeit eingeschränkt werden. Eine Definition kann kein einziges Gegenbeispiel zulassen, ohne dadurch aufgehoben zu werden. Dr. Ropper möchte die natürliche Weltsicht durch die Wissenschaft ablösen und ersetzen. Aber auch der Wissenschaftler braucht als Ausgangspunkt immer die natürliche Weltsicht. Wenn die Wissenschaft etwas, was jeder „Wasser“ nennt, untersucht und eine andere chemische Verbindung als  $H_2O$  findet, handelt es sich dann um Wasser oder nicht? Wenn es aussieht wie Wasser, wenn es schmeckt wie Wasser und wenn es reagiert wie Wasser, dann i s t es Wasser, auch wenn die chemische Definition von Wasser als  $H_2O$  hier nicht erfüllt ist. Und wenn wir eine dickflüssige braune, übelriechende und Übelkeit verursachende Flüssigkeit vor uns hätten, die als rei-

nes H<sub>2</sub>O analysiert würde, dann wäre es zwar für den Chemiker reines Wasser, aber niemand würde diesen Sprachgebrauch akzeptieren.

[Dr. Ropper says that physical survival prolonged beyond brain death, shown by Dr. Shewmon's examples, is very rare – 'highly exceptional'. But that is not the point. It seems to me that Dr. Ropper confounds a causal theory, which says that the loss of the brain normally has as an immediate result the death of the person, with a definition that identifies together both events. A causal theory is refutable, but it can be maintained and limited in its validity, too. A definition must not admit only one example which demonstrates the opposite if not being revoked by that. Dr. Ropper wants to replace and substitute the natural world-outlook by science.]

But also the scientist always needs to have the natural world-outlook as a starting point. If science analyses something which is called 'water' by everybody and if it finds a chemical combination different from H<sub>2</sub>O, is it water or not? If it looks like water, tastes like water and if it reacts like water then it 'is' water, even if the chemical definition of water as H<sub>2</sub>O is not fulfilled here. And if we have in front of us a viscid brown, evil-smelling fluid that causes nausea, it might be pure water for the chemist, but nobody would accept that linguistic usage.]

DR. ESTOL Allow me a few simple remarks. Because I cannot discuss about philosophy. I am concerned about the concept you have expressed that 'physicians are qualified to determine the existence of predefined criteria of death, and that the discussion about these criteria themselves falls within the domain of philosophers'. If I did not misunderstand you, then there was a statement about no monopoly of life/death to science, and in another point, that it was beyond the scope of religious authorities to judge these topics, so it is not clear to me where the discussion or the authority for the discussion falls. But let me limit myself to a few simple remarks.

You mentioned there was no unanimity of opinions in medicine, 'as in the time of Galileo'. However, most medical societies and physicians around the world actually do agree on this topic. Dr. Wijdicks showed us that there is slight disagreement maybe on the criteria for determining brain death, but there is unanimity about the concept.

Perception, as Dr. Masdeu said, is important. These people – these bodies – are perceived as living, but 'perceived by whom?' is the question. The answer is a question of time. For thousands of years we perceived as dead, people whose heart had stopped; brain death, on the other hand, is a forty-year-old story, which is nothing in human history. However, perception has

significantly changed and, many of us here walk into an ICU room, and I can tell you that before examining a patient, we can perceive whether the patient is brain dead to then have that perception confirmed by the examination.

As Cardinal Cottier has already emphasized, I would also disagree with the statement that organ transplantation is the main focus in the topic of brain death. I worked in the same hospital with Thomas Starzl, one of the most recognized transplant surgeons in the world, and he himself had a high sensitivity for this topic. As a matter of fact, I have read critical statements by Dr. Starzl regarding the notion that brain death was a concept created as a driving force for transplantation.

Regarding the movements in brain death, of course they are impressive to nurses, but, contrary to what you said, anaesthesia is exceptionally used. It is neuromuscular blocking agents that are used to prevent movements.

At the 'coma' conference in Havana you described there was 'surprisingly broad acceptance' about the presentation by Dr. Shewmon, but, again, as mentioned earlier, Dr. Fred Plum who is a very prestigious world leader of opinion in neurology, and well respected by all of us, was furious at what he heard in Havana and spoke out loud his disagreement during the meeting. Therefore, I would not say that there was 'surprisingly broad acceptance' at that meeting.

Finally, a word about the Harvard criteria. You mentioned that we should do what is in the best interest of the patient but what was done or promoted at the Harvard meeting was not in the patient's interest. So the question then is, whether keeping brain dead patients on a ventilator, for months or years as has been described in some reports or in Dr. Shewmon's report, is in the best interest of the patients.

Quoting Thomas Jefferson, he said that we should not force an old man to wear the coat that fitted him as a child, as civilized society should not remain under the regimen of their ancestors... but rather we should proceed and adapt to the advances in society.

PROF. SPAEMANN Ich stimme Dr. Estol zu: die Lebensverlängerung eines Hirntoten durch Ventilatoren liegt *nicht* im Interesse des Patienten. Man soll ihn sterben lassen. Aber diese Verlängerung geschieht oft im Interesse einer Transplantation, also eines anderen Patienten. Der Termin der Transplantation entscheidet über den Todetermin. Aber wenn Dr. Estol sagt, es liege nicht im Interesse des Patienten, endlos beatmet zu werden, so setzt er voraus, dass es überhaupt ein Interesse des Hirntoten gibt. Er setzt voraus, dass der Hirntote ein Patient ist. Das heißt, dass er tatsächlich

noch lebt. Ein Leichnam hat weder das Interesse, beatmet zu werden noch nicht beatmet zu werden. Er hat überhaupt kein Interesse. Auch Dr. Estol kann sich nicht konsequent der natürlichen Sicht der Dinge entziehen.

[I agree with Dr. Estol. Prolongation of a brain dead person's life by means of a ventilator does 'not' lie in the patient's interest. One should let him die. But such a prolongation often happens in the interest of transplantation, therefore in another patient's interest. The term of the transplantation decides the term of death. But if Dr. Estol says that it does not lie in the patient's interest to have endless artificial respiration, he presumes that there is actually an interest of the brain dead person. He presumes that the brain dead person is a patient. That means that he is actually still alive. A corpse has neither the interest to have artificial respiration nor not to have it. It has no interest at all. Even Dr. Estol cannot escape from the natural view of things.]

PROF. SCHAMBECK Ich möchte auf den letzten Satz des Referats von Prof. Spaemann eingehen. Er sprach von den rechtlichen Konsequenzen. Dazu möchte ich zwei Feststellungen treffen. In Österreich dominiert die so genannte Widerspruchslösung im Gegensatz zur deutschen Rechtslage, d. h. Organe können für Zwecke der Transplantation zur Rettung des Lebens oder Wiederherstellung der Gesundheit eines anderen Menschen auch gegen den expliziten Wunsch der Angehörigen entnommen werden, solange keine explizite Widerspruchserklärung des Verstorbenen vorliegt. Voraussetzung hierfür ist u. a. die Feststellung des Todes durch einen zur selbstständigen Berufsausführung berechtigten Arzt, der an der angestrebten Transplantation in keiner Weise beteiligt ist, sie also weder durchführt, noch auf Grund irgendeiner persönlichen Beziehung durch sie betroffen ist.

Die zweite und die letzte Feststellung, die ich treffen will als Jurist - ich bin Ordinarius des öffentlichen Rechts, habe aber Beziehung zum Fach von Prof. Spaemann, weil ich auch für Rechtsphilosophie zuständig bin. Die österreichische Rechtsordnung geht von einem einheitlichen Todesbegriff aus, an den verschiedene Folgen des Strafrechts, des bürgerlichen Rechts und des Verfassungsrechts gebunden sind.

Während früher - nicht zuletzt in Abhängigkeit von den jeweils zur Verfügung stehenden medizinischen und forensischen Möglichkeiten - überwiegend angenommen wurde, dass der Tod mit dem Ende der natürlichen Herztätigkeit und Atmung eintritt, wird in Österreich heute ganz herrschend nicht auf den Eintritt des „klinischen Todes“, sondern ausschließlich auf den Zeitpunkt des „Hirntodes“ abgestellt, d. h. die Hirnströme müssen endgültig-



tig solange versiegt sein, dass die irreparablen Schäden eingetreten sind und somit das Absterben des ganzen Körpers nicht mehr verhindert werden kann. Dass Atmung und Kreislauf mit Hilfe medizinisch – technischer Geräte noch fortgesetzt werden können, spielt keine Rolle!

Zum Abschluss kommend, möchte ich Exzellenz Sánchez Sorondo für die ehrende Einladung zu dieser Konferenz danken. Ich werde diese Konferenz bis zum Ende meines eigenen Lebens nie vergessen. Ich möchte Ihnen auch sagen, von meinen mehr als 600 Publikationen, vor allem aus dem öffentlichen Recht, den politischen Wissenschaften und der Rechtsphilosophie begleitet mich meine erste Publikation, die ich mit 19 Jahren geschrieben habe, nämlich über das Werk von Gabriel Marcel *Le Mystère de l'Être* – über das Geheimnis des Seins am nachhaltigsten. Wenn es einen Untertitel zu Ihrer großartigen Tagung gäbe, die Exzellenz Sánchez Sorondo wie ein „Karajan“ eines medizinischen Konzerts vorbereitet hat, dann wäre dies: *Le Mystère de l'Être*.

Ich wünsche Ihnen, dass Sie mit Gottes Segen und dem Wunsch unseres Heiligen Vaters Benedetto eine Antwort auf die Frage nach dem Sein und seinem Ende geben. In allen Erdteilen werden Ihnen die Menschen dankbar sein und ich selber auch.

[I would like to deal with the last sentence of Dr. Spaemann's paper. He talked about the legal consequences. On this point I would like to make two statements. In Austria there dominates the so-called solution of contradiction, in contrast to the German legal approach, i.e. organs may be removed for the purpose of a transplantation in order to save another person's life or to restore a person's health, even against the family's explicit request as long as no explicit contradictory statement of the deceased has been submitted.

The precondition for this, among other things, is a declaration of death by a doctor who is entitled to the independent practice of the medical profession and who in no way aspires to the envisaged transplantation, and therefore neither carries it out nor is affected by it because of a personal relationship.

The second and last statement I want to make as a lawyer – I am a Full Professor of Public Law, but I have a connection with Prof. Spaemann's field because I am also competent in the philosophy of law: Austrian legislation has a standardised conception of death, with different consequences for criminal law, civil law and public law.

Whereas in the past – not at least because of the medical and forensic possibilities available in each case – it was mostly supposed that death comes with the end of natural heart-action and respiration, today in Austria

it is predominantly not the moment of 'clinical death' but exclusively the moment of 'brain death' that is considered, i. e. the brain streams must have definitely dried up, irreparable defects must have occurred and consequently the dying of the whole body can no longer be prevented. It makes no difference whether breathing and blood circulation by means of medical-technical instruments can still be maintained!

In conclusion, I want to thank His Excellency Sánchez Sorondo for the honour of being invited to this conference. I will remember this conference for the rest of my life. I also want to tell you, after my more than 600 publications, mainly about public law, political science and the philosophy of law, that my first publication that I wrote when I was 19 years old still accompanies me in a most effective way – it was on Gabriel Marcel's work *Le Mystère de l'Être* and was about the secret of being. If there were a subtitle for this very important conference that His Excellency Sánchez Sorondo has organised, like a 'Karajan' conducting a concert, it would be *Le Mystère de l'Être*.

I hope that with God's blessings, and Pope Benedict XVI's blessing, you provide an answer to the question of being and its end. In all continents people will be grateful to you and so will I.]

PROF. SPAEMANN Nach Professor Schambeck gilt in Österreich als Todeszeitpunkt der Zeitpunkt, an dem „irreparable Schäden eingetreten sind und das Absterben des ganzen Körpers nicht mehr verhindert werden kann“. Aber dieser Zeitpunkt ist nicht der Todeszeitpunkt, sondern der Zeitpunkt, wo das Sterben begonnen hat. Der Todeszeitpunkt ist der, an dem das Sterben beendet ist. Ich muss immer wieder auf diesen Punkt zurückkommen: Sterben ist ein Teil des Lebens. Der Tod ist das Ende des Sterbens. Wir müssen die Würde des Sterbens verteidigen und das Sterben nicht durch eine neue Definition des Todes abschaffen.

Ich glaube, in unserem Gespräch wird oft der Prozess des Sterbens mit dem Prozess der Verwesung gleichgesetzt. Das ist ein Fehler. Die Verwesung beginnt, wo das Sterben endet. Wenn die Verwesung beginnt, ist der Kampf zwischen Leben und Tod beendet. Das Prinzip der Einheit des Organismus ist verschwunden, die chemischen Elemente beginnen ihre Eigengesetzlichkeit zu entfalten. Die Entropie hat die Oberhand gewonnen. Im Sterben findet das allmähliche Schwinden des systemischen Prinzips statt. Aber erst wenn es verschwunden ist, kann der Zerfall beginnen, also vom Augenblick des Todes an. Der Sterbende verwest ja nicht, sondern der Organismus kämpft gegen den Zerfall. Erst der Tod ist das Ende dieses Kampfes. Auch die künstlichen Formen der Lebensverlängerung verhin-

dern das Sterben solange, bis das Abstellen des Ventilators den raschen Tod herbeiführt. Auch das ist nicht menschenwürdig

[According to Prof. Schambeck, in Austria the moment of a person's death is the moment when 'irreparable harm becomes evident and when the extinction of the whole body cannot be avoided anymore'. But that moment is not the moment of death but the moment of the beginning of dying. The moment of death is the moment when dying has finished. I always have to turn back to that point: dying is a part of life. Death is the end of dying. We have to defend the dignity of dying and not abolish dying by a new definition of death.

I think in our discussion the process of dying is often put on the same level as the process of decay. That is a mistake. Decay begins when dying ends. When decaying begins, the struggle between life and death has ended. The principle of unity of the organism has disappeared; the chemical elements start to unfold their autonomy. Entropy gets the upper hand. In dying there is the gradual disappearance of the systemic principle. Only when it has disappeared decay can begin, thus from the moment of death. The dying person does not putrefy but his organism struggles against disintegration. Only death is the end of that struggle. Also the artificial forms of life prolongation prevent dying until the removal of the ventilator induces a rapid death. That is not human either.]

DR. HUBER Kardinal Cottier hat Aristoteles zitiert, nämlich dass es einen Unterschied gibt zwischen Leben und Sein und er hat richtigerweise gesagt, dass wann Leben endet und letzten Endes auch wie Leben interpretiert wird, eine Frage der Medizin ist, Kardinal Cottier, soweit ich ihn richtig verstanden habe. Das Gleiche gilt natürlich auch für das Sein, für den anderen Teil von Aristoteles, und ich darf darauf aufmerksam machen, dass die Quantenphysik nicht nur viele neurologische Prozesse beginnt zu erklären, sondern dass die Quantenphysik auch eine Neuinterpretation des Seins präsentiert. Wir wissen, dass jene Prozesse, die unsere Gehirnaktivität ausmachen nicht nur elektrisch sind, sondern quantenmechanisch ablaufen, und diese Quantenmechanik bleibt. Sie bleibt in unterschiedlicher Form. Es ist eine Form des Seins, das kontinuierlich und permanent, möglicherweise ewig bleibt. Hier glaube ich, dass sich eine neue Form der Interpretation zwischen Sein und Leben anbahnt am Horizont. Und ich glaube, dass gerade in dieser berühmten Stätte man unter Umständen auch darüber einmal diskutieren soll, weil die Definitionen sich verändern und die Quantenmechanik nicht nur die Quantenphysik, nicht nur die Medizin verändern wird, sondern auch unsere medizinische, möglicherweise auch unsere philosophische

Interpretation von Sein und einen starken Support gibt für das, was wir von theologischer Seite interpretierend in der Wirklichkeit sind.

DR. TANDON Thank you, I will just be very brief. What, as a physician, is one worried about when dealing with such a situation? There are two primary concerns. He is not making a mistake in diagnosing something that is reversible calling it irreversible. The answer to that is, years have shown us that none of the patients whom we declared under very strict conditions as irreversibly brain dead ever revived, even though we continued the supportive treatment because of the family's request. Number two, we are also concerned that we are not harming our patient. I would like to say something that nobody has mentioned. Keeping a brain dead patient on an artificial support system itself progressively destroys the brain and therefore you are harming that body if not the living being. Thank you very much.

DR. DAVIS I would just like to say two things. First, I am concerned about the confusion between persistent vegetative state and brain death that has been promoted by some authors on this subject. I think this is an absolutely fundamental issue that has been mentioned by Professor Ropper. We do not regard persistent vegetative state as brain death and this is a confusion that has been introduced that is not consistent with the concept of brain death. The second issue is the issue of perfusion of an individual who has died and the concept of masking of death. This has been alluded to but I wonder whether Professor Spaemann can comment on his view of whether death can be masked. He spent quite some time talking about appearances but, as Werner Hacke pointed out yesterday, this masking is an artefact of the intensive care environment, it is a masking of the death that has occurred and I think the third point that was made very eloquently by Jerry Posner, yesterday, is that there is no recorded instance, ever, of a person who is brain dead, of having revived.

PROF. SPAEMANN Was verstehen Sie, Dr. Davis, unter „Maskierung des Todes“? [What do you mean, Dr. Davis, by 'masking of death'?]

DR. DAVIS What does this appearance mean? It is perfusing organs, it is artificially ventilating organs, and produces pink skin and there is a heartbeat for a period of time that will unequivocally cease if the artificial control is removed, so this is an appearance that is not life and by that I think the term of masking is used. It is an artificial appearance when death has occurred.

PROF. SPAEMANN Ich würde nicht von Maskierung sondern von Verhinderung des Todes sprechen. Die Tatsache, dass jemand ein künstliches Herz hat, bedeutet nicht, dass sein Tod maskiert wird sondern dass er mit künstlichem Herzen lebt. Dadurch wird sein Leben nicht künstlich. Es gibt kein künstliches Leben.

[I would not talk about masking of death but about avoiding death. The fact that somebody has an artificial heart does not mean that his death is masked, but that he lives with an artificial heart. His life does not become artificial because of that. There is no artificial life.]

CARD. MARTINI I am not competent on these subjects neither in neurology nor philosophy but, as an incompetent, I would like to say three things. First of all, I was most impressed and convinced by what I heard yesterday and by the reading of the famous article of Professor Shewmon, although I could not really understand the value of his reasoning. Secondly, I would like to mention the many meanings of death, starting just from the Scripture. In the Scripture death may mean that *nefesh*, that is the breathing, is going out of the body, is taken by God or has disappeared, or it may also mean sociological death, that is, that one is separated from a community, or historical death, one is separated from history, has become nothing in history, or theological death, one is separated from God. Therefore, thirdly, I think I will briefly comment on a sentence that I find in the very interesting speech of Professor Spaemann, at number six, when he says, quoting a German anaesthesiologist, 'brain dead people are not dead but dying'. I could accept this statement if it meant that there is the beginning of an irreversible process which is not capable of integrating the person, and this process can go on and on up to complete disappearance of the body, but in fact when we speak of brain death we speak of the signs of this no longer existence of the principle of unity and of unifying the entire body and the life of the person. Therefore, I think that, although I would not equate verbally brain death with death as such, brain death is a real sign of death being there at work and therefore it is no longer to be considered a living person. That is my remark.

PROF. SPAEMANN Es gibt kein Kontinuum von Sterben und Verwesung. Der Sterbende verwest nicht, und der Verwesende ist tot. Sterben ist ein kurzer Abschnitt des Lebens. Der Sterbende ist „jemand“, der stirbt. Verwesung hat kein Subjekt. Verwesung beginnt, wenn das Subjekt nicht mehr existiert. Die Würde des Sterbens wird ebenso verletzt durch den the-

rapeutischen Fanatismus der künstlichen Lebensverlängerung wie durch die Tötung des Sterbenden.

[There is no continuum of dying and decay. The dying person does not decay and the decaying person is not dead. Dying is a short part of life. The dying person is 'somebody' who dies. Decay has no subject. Decay starts when the subject does not exist anymore. The dignity of dying is hurt by the therapeutic fanaticism of artificial life prolongation in the same way as by killing the dying person.]

CARD. MARTINI *Sterben* is a process but it is also a moment. There is a moment when the process is irreversible and from this moment you can say that a person is dead. Also, dying will continue with corruption of the body, therefore I think it is possible to distinguish between dying as process and death as the moment of beginning of the irreversible process, which, from inside the person, is no longer capable to keep united all the faculties of the person himself.

DR. RAICHLE Just a short comment. As I have been listening to this immensely interesting discussion, two words emerge in this that seem to me to demand some further discussion, not at this moment, but as we go forward. One word is perception. I think this is a deeply important issue to discuss, because what we perceive is necessarily what we conceive as a mental process of our own. We judge other people on the basis of appearances, but that is not necessarily the true reflection of what we are perceiving. It has been referred to in scientific terms as theory of mind, many different definitions of this, but, as I think we deal with our own, dealing with other people it is an inherently valuable human trait to be able to perceive the mental state of other people, but when that is not backed up by a living, viable brain, that perception can be deceiving in the extreme. And I think not only as we deal with our own perception of patients as others, but as we try to explain what is taking place, to family and the public, it is deeply important that they understand that their brain, if you will, is perceiving the events that they see and that this is not something that can be factually appreciated, because a lot of it is non conscious. I judge many of you in this room not by some intellectual process that I can think about, but by the movement of your eyes, the smile on your face, the scowl, the body language and all of this is integrated in a non conscious way, but it results in the actions that I subsequently take. In the

Terry Schiavo case I never once heard a discussion of the issue of how this perceptual process interferes with the manner in which we judge.

The second word that keeps coming up over and over again, and Cardinal Martini I think responded a moment ago in a way that I thought was right on, is the word 'integration'. And we talk repeatedly, or have, in the last hour and a half, about the word 'integration' as if it were something that is confined to the body of a single person. We live in a world in which integration is a social concept as much as a biological concept, and the human being is part of an integrated social structure and when that is destroyed a great deal of what we mean by humanity no longer exists.

DR. HENNERICI I just have a very short comment. I think we must remind ourselves in this discussion that the brain death definition came up in a very unique situation. It is still not the normal process of dying in the majority of people but it is an artificial situation, it is something where time plays an important role. When, Dr. Spaemann, you talked about the dying process and the dying is going lost, this is, just for this group of patients, a different sort of dying, it is a dying in unconsciousness of an artificially ventilated person after fatal deterioration of a disease for which ventilation was initiated. So the process of the disease leading to the dying, and the dying leading to the death and the death to the final solution of the body in years is different from the majority of dying people, and I think this is something that we have to remind and probably also to communicate in the future, because this is something that, even amongst physicians is not always kept in mind. You cited Prof. Dichgans from Tübingen whom I know very well, he is not an intensive care unit neurologist but he is an eminent general neurologist, so you see that there is still a difference between the ones who have the expertise in making the differential diagnosis and in brain death and persistent vegetative state. I repeat yesterday's discussion; several people said it is a very delicate diagnosis even for the experts. They consider that one day this patient has the diagnosis while the next day they say he probably has not. So expertise in a very small group of patients is needed and better communication to people about someone who is dying is needed.

## HOW DO PHYSICIANS PROVE IRREVERSIBILITY IN THE DETERMINATION OF DEATH?\*

JAMES L. BERNAT

From the beginning of recorded time, physicians have sought reliable signs of death to prove that the vital functions of newly deceased patients had ceased. In the pre-technological era (prior to the 20th century), physicians developed numerous creative bedside tests and procedures to prove that patients were dead.<sup>1</sup> Nevertheless, there remained widespread public fear that physicians would incorrectly pronounce death and that patients would be buried alive as a result.<sup>2</sup> Some 18th and 19th century commentators even suggested that the signs of death physicians used were so unreliable that before pronouncing death, physicians should await the development of rigor mortis to be completely certain the patient was dead.

In our contemporary technological era, in which resuscitation and organ support is possible, the principal issue in death determination has evolved from how physicians can accurately detect the cessation of vital organ functions to how physicians can confidently determine that vital organ functions have ceased irreversibly. This question is relevant in both 'brain death' and 'circulatory death' pronouncements.<sup>3</sup> Physicians declaring brain death must prove that the demonstrated loss of cerebral hemispheric, diencephalic, and brain stem functions is irreversible. Similarly, physi-

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

<sup>1</sup> Powner D.J., Ackerman B.M., Grenvik A., Medical diagnosis of death in adults: historical contributions to current controversies. *Lancet* 1996;348:1219-1223.

<sup>2</sup> Pernick M.S., Back from the grave: Recurring controversies over defining and diagnosing death in history. In: Zaner R.M. (ed): *Death: Beyond Whole-Brain Criteria*. Dordrecht: Kluwer Academic Publishers, 1988:17-74.

<sup>3</sup> Herein I use the slogans 'brain death' and 'circulatory death' simply to denote the two separate tests for physicians to determine death. It does not intend to suggest that there is more than one type of death. There is only one type of death that may be determined two ways. 'Brain death' and 'circulatory death' both are equivalent to 'death'.



cians declaring circulatory death must prove that the loss of cardiac, respiratory, and circulatory functions is irreversible. But the proof of the irreversibility of relevant organ functions in both circumstances remains far from obvious and has subtleties requiring explanation, justification, and verification. In this article I analyze the concept of irreversibility of organ functions in brain death and circulatory death, and explain how physicians can reasonably prove that the loss of these vital functions is irreversible.

### *Two Tests of Death*

Physicians can test for death in two ways: 1) in the patient not receiving mechanical ventilatory support, by showing the permanent or irreversible cessation of circulation and respiration; or 2) in the patient receiving mechanical ventilatory support, by showing the irreversible cessation of all clinical functions of the brain.<sup>4</sup> In the United States, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research proposed a model a statute of death called the Uniform Determination of Death Act (UDDA) incorporating these two alternative determinations that subsequently was enacted in nearly all American jurisdictions. In its relevant portion, the UDDA provides:

An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead. A determination of death must be made in accordance with accepted medical standards.<sup>5</sup>

My Dartmouth colleagues and I gently criticized the framers of the UDDA for not asserting a single brain standard of death (as the President's Commission itself had argued in *Defining Death*)<sup>6</sup> that could be tested by physicians in two ways depending on the presence of ventilatory support, because it was clear that the tests showing the irreversible cessation of circulatory and respiratory functions were adequate tests of death only because they inevitably led to the irreversible cessation of all brain func-

<sup>4</sup> This section is adapted in part from Bernat J.L., Are organ donors after cardiac death really dead? *Journal of Clinical Ethics* 2006;17:122-132.

<sup>5</sup> President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Defining Death: Medical, Legal and Ethical Issues in the Determination of Death*. Washington, DC: U.S. Government Printing Office, 1981:72-84.

<sup>6</sup> President's Commission, 1981:31-43.

tions.<sup>7</sup> Because patients who were successfully resuscitated prior to the complete loss of brain functions were not dead, the loss of all brain functions was the unitary criterion of death. Thus, the bifurcated so-called 'criteria' of the UDDA are not independent, and are not truly criteria, but simply are separate tests of death to prove the unitary brain criterion.

### *The Meaning of 'Irreversible' Loss of Vital Functions*

The concept of death requires irreversibility by its intrinsic nature because if a patient could be resuscitated successfully back to life, the patient was never dead in the first place. Thus, by definition, death is irreversible.<sup>8</sup> Moreover, the requirement for irreversibility is enshrined in many statutes of death (including the UDDA) that require physicians to demonstrate that the cessation of vital functions is irreversible. But what does *irreversible* actually mean and is it the same as *permanent*? The term *irreversible* was not defined in the UDDA or other statutes.

The *Oxford English Dictionary*, second edition, defines *irreversible* as 'that cannot be undone, repealed, or annulled; irrevocable'.<sup>9</sup> Thus, a loss of a function can be said to be irreversible if that function cannot possibly be regained spontaneously or restored through intervention. *Irreversible* is an absolute and univocal statement that reflects the physical reality of immutability, a condition that exists independently of our intent or action.<sup>10</sup>

The philosopher David Cole pointed out that the term *irreversible* is inherently ambiguous because it belongs to a class of modal terms in the philosophy of language that resists consensus analysis.<sup>11</sup> Cole identified two principal construals of *irreversible* functions. The strong construal of the term means that the function cannot be restored by anyone under any circumstance at any time, now or in the future. The weak construal means that the function cannot be restored by anyone now using available con-

<sup>7</sup> Bernat J.L., Culver C.M., Gert B., Defining death in theory and practice. *Hastings Center Report* 1982; 12(1): 5-9.

<sup>8</sup> I have defended this assertion in Bernat J.L., The biophilosophical basis of whole-brain death. *Social Philosophy & Policy* 2002;19(2): 324-342.

<sup>9</sup> *Oxford English Dictionary*, 2nd ed. Oxford: Oxford University Press, 2006.

<sup>10</sup> This section is adapted in part from Bernat J.L., Are organ donors after cardiac death really dead? *Journal of Clinical Ethics* 2006;17:122-132.

<sup>11</sup> Cole D., Statutory definitions of death and the management of terminally ill patients who may become organ donors after death. *Kennedy Institute of Ethics Journal* 1993;3:145-155; and Cole D.J., The reversibility of death. *Journal of Medical Ethics* 1992;18:26-30.

temporary technology but possibly may be able to be restored elsewhere now where emerging technologies are available or in the future with the development of new technologies. Thereafter, David Lamb pointed out that Cole's strong construal of irreversible (essentially, a return of functions that is logically impossible) fails the test of plausibility and should be rejected when applied to the definition of death.<sup>12</sup>

For three reasons I agree with Lamb that the weak construal of *irreversibility* of vital functions is our intended usage when applied to determining death. First, it is difficult to predict the capabilities and effects of future technologies even to assess biological possibility. Second, the availability of unanticipated future technologies may alter the concepts in question requiring a reanalysis at that time. For example, we may need to redefine human death if future technologies permit brain synthesis or brain transplantation. But, most importantly, the issue of death determination, governed by a statute of death, concerns the current possibility of the reversal of ceased vital functions. And I agree with John Lizza when he pointed out that our use of irreversibility in a definition of death implicitly refers to practical and not logical factors about the physical state of the person.<sup>13</sup>

### *The Meaning of 'Permanent' Loss of Vital Functions*

Some scholars have used the term *permanent* synonymously with *irreversible* but there is an important distinction between the two terms when describing loss of vital functions in determining death.<sup>14</sup> Although on first impression, *permanent* and *irreversible* seem synonymous, they have an important distinction. The *Oxford English Dictionary*, second edition defines *permanent* as 'continuing or designed to continue indefinitely without change; abiding, lasting, enduring, persistent (opposed to *temporary*)'. Thus, a loss of function can be said to be permanent if that function will not become restored either spontaneously or through intervention. *Permanent* is an equivocal and contingent condition that permits possibi-

<sup>12</sup> Lamb D., Reversibility and death: a reply to David J. Cole. *Journal of Medical Ethics* 1992;18:31-33.

<sup>13</sup> Lizza J., Potentiality, irreversibility, and death. *Journal of Medicine and Philosophy* 2005;30:45-64.

<sup>14</sup> This section is adapted in part from Bernat J.L., Are organ donors after cardiac death really dead? *Journal of Clinical Ethics* 2006;17:122-132.

ty. It may rely on our intent and action to be realized, and does not refer directly to a possibility of reversal.

Despite their distinct definitions, a spatial and temporal relationship exists between the sets of permanently and irreversibly lost functions. The set of permanently lost functions encompasses the set of irreversibly lost functions. Thus, all functions that are irreversibly lost also are permanently lost but not all functions that are permanently lost are necessarily irreversibly lost, at least at the moment that permanence is first established. And all functions that are irreversibly lost are first permanently lost, that is, once a function becomes permanently lost it quickly evolves to also being irreversibly lost. The important issue I discuss here is whether physicians declaring death can confidently rely on the permanent cessation of vital organ function or whether they must seek proof of irreversible cessation of function.

#### *An Analysis of 'Brain Death'*

*Brain death* is the common and colloquial (but misleading) term that refers to the determination of human death by showing the irreversible cessation of all clinical brain functions.<sup>15</sup> Determining human death by a brain criterion is based on the concept that death is best defined as the cessation of functioning of the organism as a whole and that irreversible cessation of clinical brain functions is the criterion fulfilling the definition because the brain provides the critical functions of the organism as a whole and therefore its destruction is both a necessary and sufficient condition for death.<sup>16</sup> My Dartmouth colleagues and I have offered a rigorous analysis of why brain death and human death are equivalent based on these concepts.<sup>17</sup> Our analysis was accepted by the U.S. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research in their influential book *Defining Death*,<sup>18</sup> and is regarded by many scholars as the standard paradigm of

<sup>15</sup> This section is adapted, in part, from Bernat J.L., The whole-brain concept of death remains optimum public policy. *Journal of Law, Medicine & Ethics* 2006;34:35-43.

<sup>16</sup> Bernat J.L., The biophilosophical basis of whole-brain death. *Social Philosophy & Policy* 2002;19(2):324-342.

<sup>17</sup> Bernat J.L., Culver C.M., Gert B., On the definition and criterion of death. *Annals of Internal Medicine* 1981;94:389-394.

<sup>18</sup> President's Commission, 1981:35-36.

brain death.<sup>19</sup> In response to critics, I have refined this account several times over the past quarter-century.<sup>20</sup>

Brain death as a determination of human death currently is accepted by physicians, medical organizations, legislators, and societies through the Western developed world and much of the non-Western undeveloped world.<sup>21</sup> Indeed, brain death generally is regarded as a formerly controversial bioethical and biophilosophical issue for which the greatest consensus has developed, permitting the development of more or less uniform standards for determining death around the world.<sup>22</sup> Importantly, despite the continued publication of scholarly articles arguing that brain death is not the equivalent of human death and that it is illogical, unnecessary, or an anachronism, these authors have failed to convince medical societies or lawmakers in any country to abandon brain death determinations. In fact, the opposite is the case. Over the past generation, more countries than ever before are practicing brain death.<sup>23</sup>

Brain death advocates can be divided into one major and two minor camps based on the amount of brain destruction that constitutes the criterion of death. These camps are often informally known as the 'whole-brain', 'brain stem', and 'higher brain' formulations.<sup>24</sup> Those who advocate the

<sup>19</sup> This claim was made recently, for example, by Shewmon D.A., Shewmon E.S., The semiotics of death and its medical implications. *Advances in Experimental Medicine and Biology*, 2004;550:89-114; and Chiong W., Brain death without definitions. *Hastings Center Report* 2005;35(6):20-30.

<sup>20</sup> See Bernat J.L., The definition, criterion, and statute of death. *Seminars in Neurology* 1984;4:45-52; Bernat J.L., How much of the brain must die in brain death? *Journal of Clinical Ethics* 1992;3:21-26; Bernat J.L., A defense of the whole-brain concept of death. *Hastings Center Report* 1998;28(2):14-23; Bernat J.L., The biophilosophical basis of whole-brain death. *Social Philosophy & Policy* 2002;19(2): 324-342; and Bernat J.L., The concept and practice of brain death. *Progress in Brain Research* 2005;150:369-379.

<sup>21</sup> Wijdicks E.F.M., Brain death worldwide: accepted fact but no global consensus in diagnostic criteria. *Neurology* 2002;58:20-25.

<sup>22</sup> Capron A.M., Brain death – well settled yet still unresolved. *New England Journal of Medicine* 2001;344: 1244-1246.

<sup>23</sup> I have summarized many of the arguments against brain death in: Bernat J.L., A defense of the whole-brain concept of death. *Hastings Center Report* 1998;28(2):14-23; Bernat J.L. The biophilosophical basis of whole-brain death. *Social Philosophy & Policy* 2002;19(2):324-342; and Bernat J.L., The concept and practice of brain death. *Progress in Brain Research* 2005;150:369-379. For data on the international acceptance of brain death, see Wijdicks E.F.M., Brain death worldwide: accepted fact but no global consensus in diagnostic criteria. *Neurology* 2002;58:20-25.

<sup>24</sup> Bernat J.L., How much of the brain must die in brain death? *Journal of Clinical Ethics* 1992;3:21-26.

whole-brain criterion of death comprise the large majority and represent nearly all laws and practices outside of the UK and a few other countries where the brain stem formulation is used. The higher-brain formulation has been advocated by a small group of philosophers and a few others but has never achieved acceptance in any jurisdiction and is accepted and practiced nowhere in the world.

The whole-brain criterion requires cessation of all brain clinical functions including those of the cerebral hemispheres, diencephalon (thalamus and hypothalamus), and brain stem. Whole-brain advocates require global cessation of neuronal functions because each part of the brain serves some of the critical functions of the organism as a whole. The brain stem initiates and controls breathing, regulates circulation, and serves as the generator of wakefulness through the reticular system that is a physiological prerequisite for conscious awareness. The diencephalon provides the center for bodily homeostasis, regulating and coordinating numerous neuroendocrine control systems such as those regulating body temperature, salt and water regulation, feeding behavior, and memory. The cerebral hemispheres have an indispensable role in awareness that provides the conditions for all conscious behavior that serves the health and survival of the organism.

Clinical functions are those that are measurable at the bedside. The distinction between the brain's clinical functions and brain activities, recordable electrically, chemically, or through other laboratory means, was made by the President's Commission in *Defining Death*.<sup>25</sup> All clinical brain functions measurable at the bedside must be lost and their cessation must be shown to be irreversible. But the whole-brain criterion does not require the loss of all neuronal activities. Some neurons may survive individually or in small clusters that may contribute to recordable brain activities (by an electroencephalogram, for example) but not to clinical functions.<sup>26</sup> The precise minimum number, location, and configuration of neurons necessary and sufficient for death remains unknown.

Despite the fact that the whole-brain criterion does not require the cessation of functioning of every brain neuron, it does rely on a pathophysiological process known as brain herniation to assure widespread destruction

<sup>25</sup> President's Commission, 1981:28-29.

<sup>26</sup> See description of residual E.E.G. activity in some brain dead patients in Grigg M.M., Kelly M.A., Celesia C.G., Ghobrial M.W., Ross E.R., Electroencephalographic activity after brain death. *Archives of Neurology* 1987;44:948-954.

of the neuron systems responsible for the brain's clinical functions.<sup>27</sup> When the brain is injured diffusely by trauma, hypoxic-ischemic damage during cardiorespiratory arrest or asphyxia, meningoencephalitis, or enlarging intracranial mass lesions such as neoplasms,<sup>28</sup> resulting brain edema causes intracranial pressure to rise to levels exceeding mean arterial blood pressure. At this point, intracranial circulation ceases and nearly all brain neurons that were not destroyed by the initial brain injury are secondarily destroyed by the cessation of intracranial circulation. Thus the whole-brain formulation provides a fail-safe mechanism to eliminate false-positive brain death determinations and assure the loss of the critical functions of the organism as a whole. Showing the absence of all intracranial circulation is sufficient to prove widespread destruction of all critical neuronal systems.

#### *An Analysis of 'Circulatory Death'*

*Circulatory death* is the basis for determining death by showing the irreversible absence of heartbeat, circulation, and breathing. It is a common means for physicians to determine death in patients for whom mechanical ventilatory support is neither provided nor planned. It produces the criterion of death once the brain has become completely destroyed by hypoxic-ischemic infarction. It is the means of death determination in essentially all non-hospitalized patients and in about 99% of hospitalized patients. Until recently, there was no controversy in determining circulatory death. However, the introduction of hospital programs of organ donation after cardiac death (formerly called 'non-heart-beating organ donation') have highlighted the issue of how long circulation must cease before death can be declared, and created a controversy that has been only partially resolved.<sup>29</sup>

Organ donation after cardiac death (DCD) has become a widespread practice in the United States over the past decade. In the early 1990s, in response to the growing demand for organs to transplant and to the desires

<sup>27</sup> Plum F, Posner J.B., *The Diagnosis of Stupor and Coma*, 3rd ed. Philadelphia: FA Davis Co, 1980:88-101.

<sup>28</sup> These are the most common causes of brain death. See Staworn D., Lewison L., Marks J., Turner G., Levin D., Brain death in pediatric intensive care unit patients: incidence, primary diagnosis, and the clinical occurrence of Turner's triad. *Critical Care Medicine* 1994;22:1301-1305.

<sup>29</sup> This section is adapted in part from Bernat J.L., Are organ donors after cardiac death really dead? *Journal of Clinical Ethics* 2006;17:122-132.

of the families of brain-damaged but non-brain-dead patients being removed from life-sustaining therapy in ICUs to have their loved ones serve as organ donors, the University of Pittsburgh Medical Center established the first modern DCD program.<sup>30</sup> Since then, greater numbers of American organ procurement organizations (OPOs) have encouraged DCD programs so that approximately half the OPOs in the United States now permit DCD.<sup>31</sup> The growth and acceptance of DCD programs was spurred by two influential reports from the Institute of Medicine in 1997 and 2000 that concluded that DCD was legitimate and desirable, and hospitals should be encouraged to implement DCD protocols.<sup>32</sup>

DCD protocols permit a hopelessly dying, ventilator-dependent patient (or, more commonly, her legally-authorized surrogate) to consent for organ donation after death once further life-sustaining therapy has been refused and discontinued. In the most common case, the patient has sustained profound brain damage from trauma, stroke, or cardiac arrest that creates ventilator-dependency and offers no hope for meaningful neurological recovery. Such a patient does not meet brain death criteria but is hopelessly ill because of profound brain damage with a very poor prognosis. Based upon the patient's prior wishes for stopping treatment in light of the poor prognosis, the family then refuses further life-sustaining therapy on behalf of the patient to permit her to die. They also request or consent to her organ donation after death.

DCD protocols coordinate the planning and timing of withdrawing the ventilator with the organ procurement team's readiness to procure organs. Once withdrawn from the ventilator, patients usually cannot breathe at all or breathe insufficiently to maintain life.<sup>33</sup> As the patient's

<sup>30</sup> University of Pittsburgh Medical Center Policy and Procedure Manual. Management of terminally ill patients who may become organ donors after death. *Kennedy Institute of Ethics Journal* 1993;3:A1-A15.

<sup>31</sup> The most current American DCD data were reported in Bernat J.L., D'Alessandro A.M., Port F.K., et al., Report of a national conference on donation after cardiac death. *American Journal of Transplantation* 2006;6:281-291.

<sup>32</sup> Institute of Medicine. *Non-Heart-Beating Organ Transplantation: Medical and Ethical Issues in Procurement*. Washington DC: National Academy Press, 1997; and Institute of Medicine. *Non-Heart-Beating Organ Transplantation: Practice and Protocols*. Washington DC: National Academy Press, 2000.

<sup>33</sup> Approximately 25% of patients in DCD protocols, following ventilator removal, continue to breathe and have heartbeat for greater than one hour before they die, rendering them unsuitable for DCD for logistical reasons. See Delmonico F.L., Sheehy E., Marks W.H., Baliga P., McGowan J.J., and Magee J.C., Organ donation and utilization in the United States, 2004. *American Journal of Transplantation* 2005;5(Part 2):862-873.



oxygenation rapidly declines, her heartbeat then stops from lack of oxygen. After five minutes of absent heartbeat, the patient is declared dead and rushed to the operating room where organ procurement is rapidly performed, usually yielding transplantable kidneys, liver, and occasionally other organs.

An important unresolved controversy over the conceptual foundation of DCD is whether the organ donors are truly dead at the moment they are declared dead according to most DCD protocols, namely after five minutes<sup>34</sup> of asystole<sup>35</sup>. Several scholars have argued that a DCD patient may not be dead after five minutes of asystole<sup>36</sup> because if the patient's heart could be restarted at a point before the brain was totally destroyed by ischemic infarction from lack of circulation, the patient would not be dead. I have argued recently that the answer to this important question turns on the distinction between the *permanent* and *irreversible* loss of circulatory and respiratory functions as a test of death. I concluded that the organ donors are dead at the point that their circulation permanently ceased.<sup>37</sup>

<sup>34</sup> American organ procurement organization DCD protocols vary on the stipulated length of time of asystole required to declare death. Most have adopted the Institute of Medicine's recommendation of five minutes but two use two minutes. In the Netherlands they wait ten minutes.

<sup>35</sup> DCD protocols usually use the term 'asystole' not meaning an absence of recordable electrocardiographic activity, but meaning an absence of mechanical cardiac activity sufficient to generate a pulse or blood flow. When the heart stops after apnea, the cardiac rhythm usually diminishes gradually before stopping, but the resultant weak cardiac electrical signal is insufficient to produce a cardiac contraction necessary to create a pulse or blood flow. This condition of absent pumping despite a present cardiac rhythm, known as pulseless electrical activity, precedes the total absence of cardiac electrical activity. But it is simpler merely to say 'asystole' because heartbeat and circulation stops even if an ineffectual cardiac signal persists temporarily. This phenomenon has been studied in a series of patients. See Wijdicks E.F.M. and Diringner M.N., Electrocardiographic activity after terminal cardiac arrest in neurocatastrophes. *Neurology* 2004;62:673-674.

<sup>36</sup> See, for example, Lynn J., Are the patients who become organ donors under the Pittsburgh protocol for 'non-heart-beating donors' really dead? *Kennedy Institute of Ethics Journal* 1993;3:167-78; Truog R.D., Is it time to abandon brain death? *Hastings Center Report* 1997;27(1):29-37; and Youngner S.J., Arnold R.M., DeVita M.A., When is 'dead'? *Hastings Center Report* 1999;29(6):14-21.

<sup>37</sup> Bernat J.L., Are organ donors after cardiac death really dead? *Journal of Clinical Ethics* 2006;17:122-132.

*Proving Irreversibility in Brain Death*

Every set of brain death tests requires that the measured loss of clinical functions be the result of an irreversible pathological process.<sup>38</sup> Thus, preconditions for all brain death tests require the absence of depressant drug intoxications, severe hypothermia, and neuromuscular blockade, each of which could mimic the signs of brain death but be potentially reversible by intensive medical treatment. Most set of brain death tests (notably those recommended by the U.S. President's Commission and the American Academy of Neurology<sup>39</sup>) require a demonstrable structural brain lesion that is sufficient to produce the clinical signs, to minimize the chances of a metabolic or toxic cause that might be reversible. Clinical irreversibility is demonstrated by: 1) demonstrating a structural lesion adequate to cause the signs of loss of brain functions; 2) excluding reversible causes; and 3) conducting serial examinations separated by an interval of hours to show no recovery. Although this plausible clinical claim for irreversibility is usually accepted, it is not self-evidently true and its empirical basis is limited to a few studies.<sup>40</sup>

We know that some examiners declaring brain death are careless in performing, interpreting, or recording the clinical tests, particularly the apnea test.<sup>41</sup> Despite the presence of standardized, widely accepted, and highly publicized guidelines for brain death determination,<sup>42</sup> physicians perform

<sup>38</sup> This section is adapted in part from: Bernat J.L., On irreversibility as a prerequisite for brain death determination. *Advances in Experimental Medicine and Biology* 2004;550: 161-167.

<sup>39</sup> President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Defining Death: Medical, Legal and Ethical Issues in the Determination of Death*. Washington, DC: U.S. Government Printing Office, 1981:Appendix F; and The Quality Standards Subcommittee of the American Academy of Neurology. Practice parameters for determining brain death in adults [summary statement]. *Neurology* 1995;45:1012-1014.

<sup>40</sup> For example, see NIH Collaborative Study of Cerebral Survival. An appraisal of the criteria of cerebral death. *JAMA* 1977;237:982-986.

<sup>41</sup> See Earnest M.P., Beresford H.R., McIntyre H.B., Testing for apnea in brain death: methods used by 129 clinicians. *Neurology* 1986;36:542-544; and Mejia R.E., Pollack M.M., Variability in brain death determination practices in children. *JAMA* 1995;274:550-553.

<sup>42</sup> See Wijdicks E.F.M., Determining brain death in adults. *Neurology* 1995;45:1003-1011, The Quality Standards Subcommittee of the American Academy of Neurology. Practice parameters for determining brain death in adults [summary statement]. *Neurology* 1995;45:1012-1014; and Wijdicks E.F.M., The diagnosis of brain death. *New England Journal of Medicine* 2001;344:1215-1221.

it incorrectly in many settings. It is not solely unskilled examiners at fault. A recent study from a prestigious medical center demonstrated the inadequacies of the methods and recordings of routine brain death determinations.<sup>43</sup> Therefore, I believe it is probable that some of the reported cases of 'chronic brain death' by Alan Shewmon, in which the heartbeat and systemic circulation of diagnosed brain dead patients had been technologically maintained for many months or longer, represented cases of profound brain damage who had been improperly declared brain dead.<sup>44</sup>

The surest method to demonstrate that the global loss of clinical brain functions is irreversible is to show the complete absence of intracranial blood flow. Brain neurons are damaged after just a few minutes of lack of blood flow and are globally destroyed when blood flow completely ceases for more than 20-30 minutes.<sup>45</sup> Thus, showing a total absence of intracranial blood flow that has persisted for more than 30 minutes proves the irreversibility as well as the totality of the loss of clinical brain functions. Blood flow to the brain is tightly regulated by the homeostatic system of cerebral autoregulation that operates over a wide range of systemic blood pressures to assure adequate cerebral perfusion pressures. Normal cerebral autoregulatory mechanisms can be disturbed when systemic blood pressures become excessively high or low, or when intracranial pressure rises to very high levels.

Traumatic and vascular global brain lesions leading to brain death produce diffuse cerebral edema. The cerebral edema results in an increase in intracranial contents but intracranial volume remains fixed by the rigid skull. Consequently, intracranial pressure (ICP) rises. In most brain death cases, intracranial pressure rises until it exceeds mean arterial blood pressure. In many instances of massive head trauma and massive subarachnoid hemorrhage, ICP exceeds systolic blood pressure. When ICP exceeds systolic blood pressure, no blood can enter the cranial vault and the brain loses all circulation. When ICP is lower than systolic blood pressure but higher than diastolic pressure but exceeds mean arterial pressure, blood enters the cranium and brain during systole but is pushed back an equal amount during diastole. This phenomenon of so-called 'reverberating' or 'oscillating'

<sup>43</sup> Wang M.Y., Wallace P., Gruen J.B., Brain death documentation: analysis and issues. *Neurosurgery* 2002;51:731-735.

<sup>44</sup> Shewmon D.A., Chronic 'brain death': meta-analysis and conceptual consequences. *Neurology* 1998;51:1538-1545.

<sup>45</sup> Miyamoto O., Auer R.N., Hypoxia, hyperoxia, ischemia, and brain necrosis. *Neurology* 2000;54:362-371.

flow cannot result in perfusion of the brain because it produces no net forward circulation. Thus, whether there is no intracranial systolic blood flow or there is no net blood flow because of reverberating flow, the brain becomes diffusely and irreversibly destroyed within minutes.

The clinical examination evidence of absent intracranial blood flow is the presence of one of the syndromes of cerebral transtentorial herniation, as shown by Fred Plum and Jerome Posner (1980).<sup>46</sup> Central and uncatal transtentorial herniation of the midbrain, results from intracranial tissue shifts caused by the development of lateralized intracranial pressure cones from an expanding mass lesion. The lateralized pressure cones induce a caudal shift of brain tissue that secondarily destroys brain stem neurons through a progressive pressure gradient-induced ischemia. All neurology residents are taught to seek the clinical evidence of these herniation syndromes because once the brain stem has been infarcted during transtentorial herniation, the loss of brain clinical functions has become irreversible.

An important added significance of requiring herniation syndromes resulting from raised ICP is that it provides proof that the destruction of brain neurons is widespread. The whole-brain criterion of death requires that all clinical functions of the brain cease irreversibly. Once full herniation has been completed and all intracranial blood flow has stopped, examiners declaring brain death can be confident that neuronal damage is widespread and that the herniation has eliminated all clinical functions of the brain. Thus, requiring a demonstration of absence of intracranial blood flow at once confirms both irreversibility and totality of the cessation of neuronal function. But it is essential that a total absence of intracranial blood flow not be confused with only a reduction of intracranial blood flow. In studies of the ischemic penumbra surrounding lesions in purportedly brain dead patients, Cicero Coimbra showed the importance of distinguishing between these two situations and emphasized the serious errors that can occur if they are confused.<sup>47</sup>

Tests showing absent intracranial circulation have confirmed brain death for over three decades.<sup>48</sup> Contrast arteriography was first used in

<sup>46</sup> Plum F., Posner J.B., *The Diagnosis of Stupor and Coma*, 3rd ed. Philadelphia: FA Davis Co, 1980:88-101.

<sup>47</sup> Coimbra C.G., Implications of ischemic penumbra for the diagnosis of brain death. *Brazilian Journal of Medical and Biological Research* 1999;32:1479-1487.

<sup>48</sup> These tests have been reviewed in: Young B., Lee D., A critique of ancillary tests of brain death. *Neurocritical Care* 2004;1:499-508.

the 1970s to show absence of intracranial circulation distal to the intracranial portions of the internal carotid and vertebral arteries. It continues to be used by physicians in some settings that lack access to simpler alternative techniques. Its principal drawbacks are its invasiveness, the fact that high injection pressures can force transient intracranial blood flow that would not occur otherwise, and that the patient must be transported to the radiology suite.<sup>49</sup>

Intravenous radionuclide angiography was first used in the 1980 to prove absent intracranial circulation. An intravenous infusion of the radioisotope pertechnetate is infused intravenously. The patient undergoes static and dynamic radionuclide brain scanning to measure entry of the radioisotope into the brain. Dynamic images show the isotope stopping as the internal carotid and vertebral arteries enter the dura mater. Static images show only the presence of isotope in the scalp and face because of the patency of the external carotid artery and its branches.<sup>50</sup> A radiologist or nuclear medicine expert who is experienced in this technique can confidently interpret absence of blood flow in the brain. Shortcomings of intravenous radionuclide angiography are the difficulty in distinguishing slight vs. absent blood flow in the posterior circulation and that the patient must be transported to the nuclear medicine suite.

Transcranial Doppler (TCD) ultrasound was perfected in the 1990s and now is the test used in many medical centers to document cessation of intracranial circulation in brain death.<sup>51</sup> TCD ultrasound can be performed in the patient's bed in the ICU. Current standards require three separate insonation sites.<sup>52</sup> Reproducible images of intracranial pulses usually can be obtained if they are present. Two principal patterns of TCD ultrasound abnormalities have been documented in brain death: absent systolic spikes

<sup>49</sup> Bradac G.B., Simon R.S., Angiography in brain death. *Neuroradiology* 1974;7:25-28.

<sup>50</sup> Goodman J.M., Heck L.L., Moore B., Confirmation of brain death with portable isotope angiography: a review of 204 consecutive cases. *Neurosurgery* 1985;16:492-497; and Newberg A., Alavi A., van Rhijn S., Cotter A., Reilly P., Radiologic diagnosis of brain death. *JAMA* 2002;288:2121-2122.

<sup>51</sup> Petty G.W., Mohr J.P., Pedley T.A., *et al.*, The role of transcranial Doppler in confirming brain death: sensitivity, specificity, and suggestions for performance and interpretation. *Neurology* 1990;40:300-303.

<sup>52</sup> Ducrocq X., Braun M., Debouverie M., Junges C., Hummer M., Vespignani H., Brain death and transcranial Doppler: experience in 130 cases of brain dead patients. *Journal of Neurological Sciences* 1998;160:41-46.

and reverberating flow. Systolic spikes are absent when ICP exceeds systolic blood pressure because no measurable systolic flow can be conducted to the intracranial arteries. When ICP exceeds mean arterial blood pressure but is lower than systolic blood pressure, reverberating flow is seen. Blood advances during systole but is pushed back an equal amount during diastole because intracranial pressure exceeds diastolic blood pressure. Both patterns confirm the complete absence of intracranial circulation.<sup>53</sup> The principal limitation to TCD ultrasound is that the results are operator-dependent.

More recently, emerging imaging techniques have been applied to this problem. There are several studies using single photon emission computed tomography (SPECT) scintigraphy with the radioisotope Tc-99m HMPAO that validate the complete absence of intracranial blood flow in brain death by this relatively simple technique.<sup>54</sup> Several case reports have been published demonstrating absent intracranial blood flow by magnetic resonance angiography (MRA), magnetic resonance (MRI) diffusion-weighted and perfusion-weighted imaging, and computed tomography angiography (CTA).<sup>55</sup> These newer techniques may replace the older ones once they have been more completely validated.

In a recent article, I suggested that a confirmatory test showing cessation of intracranial blood flow should become customary for a brain death declaration, at least if there is any difficulty in performing or interpreting the clinical testing.<sup>56</sup> However, the tests showing absent intracranial blood flow are useful only acutely when intracranial pressure is at its highest. If cardiopulmonary support of the brain dead patient is continued, cerebral edema subsides thereafter and ICP begins to fall within hours to days. Once ICP has fallen to a level lower than mean arterial pressure, intracranial cir-

<sup>53</sup> Ducrocq X., Hassler W., Moritake K., *et al.*, Consensus opinion on diagnosis of circulatory arrest using Doppler-sonography. *Journal of Neurological Sciences* 1998;159:145-150.

<sup>54</sup> Wilson K., Gordon L., Selby J.B. Jr., The diagnosis of brain death with Tc-99m HMPAO. *Clinics in Nuclear Medicine* 1993;18:428-434; Donohoe K.J., Frey K.A., Gerbaudo V.H., Mariani G., Nagel J.S., Shulkin B., Procedural guidelines for brain death scintigraphy. *Journal of Nuclear Medicine* 2003;44:846-851; and Munari M., Zucchetta P., Carollo C., *et al.*, Confirmatory tests in the diagnosis of brain death: comparison between SPECT and contrast angiography. *Critical Care Medicine* 2005;33:2068-2073.

<sup>55</sup> Lovblad K.O., Bassetti C., Diffusion-weighted magnetic resonance imaging in brain death. *Stroke* 2000;31:539-42; Qureshi A.I., Kirmani J.F., Xavier A.R., Siddiqui A.M., Computed tomographic angiography for diagnosis of brain death. *Neurology* 2004;62:652-653.

<sup>56</sup> Bernat J.L., On irreversibility as a prerequisite for brain death determination. *Advances in Experimental Medicine and Biology* 2004;550:161-167.

circulation restarts ('reflow') at least to a limited degree in the necrotic brain.<sup>57</sup> The so-called 'respirator brain', described by Earl Walker and colleagues in the 1970s, is a result of neuronal and glial liquifactive necrosis in the setting of intracranial reflow once ICP has dropped.<sup>58</sup> Once ICP has fallen, physicians should instead use tests to confirm absent brain electrical signals (the battery of electroencephalography, brain stem auditory evoked responses, and somatosensory evoked responses) because blood flow testing may show a false negative confirmation of brain death because of renewed blood flow to the necrotic brain.<sup>59</sup>

### *Proving Irreversibility in Circulatory Death*

In most circulatory death determinations in the hospital, merely detecting the loss of breathing, heartbeat, and circulation is sufficient to declare death. Physicians can determine that the loss of these functions is permanent because they know that once breathing and heartbeat cease for several minutes, they will not automatically restart ('auto-resuscitation'), and that no artificial resuscitation is planned. In the large majority of hospital circulatory death determinations, a long time elapses during the interval between the time the loss of vital functions is detected and the time a physician is summoned to declare death and completes an examination. This elapsed time usually is sufficient to allow a permanent loss of vital functions to progress to becoming irreversibly lost by the time death is declared.

For example, consider a dying patient with widely metastatic cancer who is admitted to the hospital for palliative care and who is expected to die in hours to days. The patient has a Do-Not-Resuscitate order and is receiving intravenous morphine. When the patient later is noted on nursing rounds to be without pulse or breathing and a house physician is called to declare death, the physician pronounces death once she demonstrates the absence of breathing and heartbeat. The physician does not need to prove

<sup>57</sup> Schroder R., Later changes in brain death: signs of partial recirculation. *Acta Neuropathologica* (Berlin) 1983;62:15-23.

<sup>58</sup> Walker A.E., Diamond E.L., Moseley J., The neuropathological findings in irreversible coma: a critique of the 'respirator brain'. *Journal of Neuropathology and Experimental Neurology* 1975;34:295-323.

<sup>59</sup> EEG and evoked potential tests to confirm brain death have been reviewed in: Wijdicks E.F.M., The diagnosis of brain death. *New England Journal of Medicine* 2001;344:1215-1221; and Young B., Lee D., A critique of ancillary tests of brain death. *Neurocritical Care* 2004;1:499-508.

that the loss of these vital functions is irreversible to declare death. That they are permanently lost is sufficient grounds for death determination. Thus, despite the fact that statutes of death generally include the requirement of an irreversible cessation of vital functions, the prevailing medical standard for employing the circulatory criterion of death always has been to determine that the cessation of these functions is permanent. Permanence always has been sufficient clinical grounds for determining irreversibility.

In a recent paper, I argued that vital function permanence should be sufficient to establish their irreversibility because circulatory death determinations in DCD should require a medical practice standard that is no higher than that employed when it is used in other hospitalized patients.<sup>60</sup> But this social question is a matter for medical societies, hospital policies, and public laws to decide.

### *The Time of Death*

In an article analyzing the precise timing of death, Joanne Lynn and the late Ronald Cranford asserted four possible choices for stating the time of death based on the loss of functions critical to life: 'T1' when the critical function is lost; 'T2' when the critical function is observed to be lost; 'T3' when the critical function is irreversibly lost; and 'T4' when the critical function is demonstrated to be irreversibly lost.<sup>61</sup> I have argued elsewhere that T4 is the most defensible time because death determination customarily is made in retrospect.<sup>62</sup> This practice is applicable to both brain death and circulatory death determinations.

### *Future Directions*

The doctrines of brain death and circulatory death are well-established and function successfully throughout the world without significant problems. One future goal in brain death determination is to refine with greater

<sup>60</sup> Bernat J.L., Are organ donors after cardiac death really dead? *Journal of Clinical Ethics* 2006;17:122-132.

<sup>61</sup> Lynn J., Cranford R.E., The persisting perplexities in the determination of death. in Youngner S.J., Arnold R.M., Schapiro R. (eds), *The Definition of Death: Contemporary Controversies*. Baltimore: Johns Hopkins University Press, 1999:101-114.

<sup>62</sup> Bernat J.L., The biophilosophical basis of whole-brain death. *Social Philosophy & Policy* 2002;19(2):324-342.



precision the exact physiological criterion of death: that precise array of neurons whose irreversible functional loss is both necessary and sufficient for death. This array probably will be a critical subset of the neurons generating the clinical functions of the cerebral hemispheres, diencephalon, and brain stem. A second goal is to work toward an international consensus on the clinical tests for brain death to achieve uniformity of testing throughout the world. A third goal is the gain consensus on the role of confirmatory testing in brain death, which I believe should be used more routinely than is presently practiced in many countries. Finally, it would desirable to resolve the conceptual debate over the coherence of the brain death doctrine but this goal seems improbable.

For circulatory death, an important future goal is to achieve consensus that demonstrating the permanent loss of respiratory and circulatory functions is sufficient to determine that their loss also is irreversible. More medical centers need to systematically record data on the occurrence and timing of 'auto-resuscitation' in patients who suffer cardiac arrest after they are removed from ventilatory support at their wish. These data will answer the empirical question of the minimum time of asystole required to prove that circulatory function has permanently ceased.

These advances will contribute to a better scientific understanding of the moment of death and an enhanced precision of its determination. They also will reassure the public that physicians can confidently and correctly determine death and that multi-organ procurement will occur only after the patient has been declared dead.

## DISCUSSION ON DR. BERNAT'S PAPER

DR. ROPPER Just a small technical thought or query. With regard to supplementary tests of angiographic blood flow, I have encountered two circumstances which make me hesitant to accept this completely. The first problem is that, after many days, if the organism is allowed to be perfused and the brain liquefies, an angiogram that showed no cerebral blood flow can later show some cerebral blood flow, so the timing I think is very important.

The other problem is that there is a little bit of arbitrariness, in my view. I have been shown by angiographers that, if you are willing to blast the dye into the cervical vessels under high enough pressure, you can often get it into the cranium. Just to be more specific, I think you are talking about angiography at physiological injection pressures, if I am not mistaken, I do not want to put words in your mouth.

DR. BERNAT I agree entirely with Dr. Ropper's points. It is certainly the case that raised intracranial pressure is produced in most instances of brain death. When that pressure falls there will be recirculation, so that testing for intracranial circulation is most useful in the acute determination and not in the more chronic determination. The acute determination is usually the time that we neurologists see the patient, not three or four days, or a week later. However, sometimes our examination is later. Thus, I accept Dr. Ropper's modification of my comments to add that, if brain death determination is performed during the acute period, showing a loss of intracranial blood flow would be most useful. Later, when intracranial pressure falls, and there may be recirculation to a necrotic brain, then the electrical tests would be more useful for confirmatory testing. I also agree that, if one performs contrast arteriography, and if the radiologist pushes radio-opaque contrast dye under high pressure, some apparent circulation may be seen. We have not used that technique to confirm brain death in many years, and I am sure you do not either, but there may be places in the world where that is still being done. But there are so many less invasive techniques that can

accomplish the same thing more easily that I do not even think about that problem. But you are absolutely correct.

DR. MATTLE I have got a pathophysiological question. Do you really think, or is it established, that raised intracranial pressure is needed in order that cerebral blood flow ceases? I have seen many patients after cardiac arrest with complete anoxic brain damage. On imaging they did not have any swelling, mass effect or any signs of herniation. Is it not possible that when all the neurons die, they do not need blood supply anymore and blood flow stops? I think this might be another possibility why cerebral blood flow arrests without having raised intracranial pressure, who knows it?

DR. BERNAT I do not know the answer to your question. My own experience is that, even in the patients with hypoxic-ischemic neuronal damage suffered during cardiac arrest who become brain dead, most of them have developed raised intracranial pressure and consequent loss of intracranial blood flow. But I will defer to other colleagues around the world who have seen cases such as those that you have described, where there is no cerebral edema despite diffuse destruction of all neurons, I have just not seen such a case myself.

DR. WIJDICKS Which I think is true. I think, in general, the ones that would fulfil all the clinical criteria of brain death in anoxic ischemic injury are those that have sufficient brain swelling to do that. The overwhelmingly vast majority of patients with anoxic ischemic injury do not fulfil the clinical criteria of brain death, but go on to develop a vegetative state. So, brain death determination in anoxic ischemic injury or asphyxia is unusual. The problem I have with cerebral blood flow is obviously that our experience with cerebral blood flow is still limited with insufficient validation. The only country that has major experience is Sweden, in which a cerebral angiogram is necessary as a confirmatory test. In every single patient in which an angiogram is done, thirty minutes is waited while the catheter is still inside and then a second angiogram is done documenting thirty minutes of no flow. As far as I know, there is not much data published on that experience. The problem I have with the cerebral angiogram is that I think radiologists do not entirely know how to define an intracranial flow: would you accept a little bit of trickle flow in the siphon or not, where would the flow exactly stop and indeed is it perhaps possible that with different pressures you could get contrast there where you do not really want it to be and

therefore make things far more complicated. In other words, the radiologists have difficulties, in some instances, in determining whether there is absence of intracranial flow.

DR. ESTOL It is interesting that you brought up the concept of cardiopulmonary death and the concept of 'donation after cardiac death', to make a parallel with brain death, because now, as you said, there is a need for uniform criteria about the timing for organ harvesting. Two centres in the USA use two minutes, which some people may want to question. Two minutes imply that the person becomes a donor after that time and you can harvest the organs. Discussion will ensue because there is one report of 'autoresuscitation' after seven minutes. I agree with you but we would not like to foresee that, once uniform criteria is settled for donation after cardiac death, someone may start with theoretical analogies arguing now with the more accepted concept of cardiocirculatory death. We can anticipate, as it happened with brain death, that people will start arguing, that two minutes is too short and that there was a case with resuscitation after seven minutes. We would not like to see this happen again – and for this reason the concepts you just presented are very important.

DR. PUYBASSET I wanted you to elaborate a bit regarding the ethical issue of the so-called class three of Maastricht, meaning patients in the ICU in whom you decide to withdraw support and in whom then, after cardiac death, you harvest the kidneys and sometimes the liver. Have you been confronted with that situation yourself and how do you deal with that, with the families and the nurses, because I have no experience right now with that.

DR. BERNAT Our medical centre has a protocol permitting organ donation after cardiac death that follows the basic outline of the criteria I described in my talk, and that follows the United States National Academy of Sciences Institute of Medicine recommendations for such protocols. These protocols are not without controversy. They require scrupulous adherence to the terms of the protocol. We all know that physicians tend to be rather autonomous persons and do not often like to be bound by protocols. So, in our institution, the Bioethics Committee that I chair, is charged with overseeing the operation of the protocol. Every case must be reviewed by me or a colleague, so I have had the opportunity to look the cases. I have had a few that I am a little concerned about. After review, we try to correct any variation from our protocol. But at our medical center, we permit only the Maastricht III donors, not the I or II. Class III donors are patients who

are severely brain damaged, but not brain dead, who are on ventilators in intensive care units, whose brain damage is irreversible, and whose prognosis is hopeless. This prognosis must be determined by neurologists. Secondly, there must be a decision by family members based on what they know about what the patient would have wanted for his own treatment. This preference may be to discontinue further life-sustaining treatment, which is a common occurrence in American intensive care units. Over half of the patients in American intensive care units die as a direct result of lessening or stopping life-sustaining treatment. Thus, this practice is not rare, and goes on every day. These patients would have had their therapy withdrawn whether or not they were organ donors, and it would be done in the same way by the same personnel. The only thing that changes if they are organ donors, is to coordinate the timing of the withdrawal of treatment to the readiness of the surgical team to rapidly procure their organs. Usually the donor's kidneys and liver can be recovered successfully. This entire practice is at the wish of the family that their loved one who will die also serve as an organ donor. Consenting to or requesting organ donation is largely driven by the desire of families to make some good of an otherwise tragic, meaningless death. In my experience in dozens of these cases, I feel that the presence of the organ donation provided a transcendent meaning to family members to think that parts of their loved ones live on and can help others survive. It made the death seem more meaningful. So, my long answer to your short question is that we do strive to rigorously adhere to the protocol and use only Maastricht III donor patients.

DR. RAICHLE Just a brief comment on the discussion about whether blood flow measurements would be adequate, and what happens if you see a bit of blood flow, which is something I mentioned yesterday. I would just say that, with the rapid progress in imaging in general, and the sophistication of things that can be gleaned from imaging not available widely today that I would suspect over the next five to ten years the information you could gather from imaging data would be far more sophisticated and helpful. I would hope as the deliberations of this meeting are made public, as with the recent case in science, researchers and clinicians will be provoked to apply sophisticated imaging strategies to this problem, and I would hope that will be the case.

DR. BERNAT Dr. Raichle's point is well taken (and Dr. Ropper had made it earlier) that there may be instances of recirculation where, depending on

the timing of the event, we can see some evidence of intracranial blood flow despite brain death. I think the decision to perform a confirmatory test should be left up to the discretion of the neurologist doing the determination. I tend to advocate doing it for the reasons I stated earlier. The choice of which test may turn on the time the patient is determined brain dead. Perhaps the electrical tests should be chosen if testing is being done later rather than earlier, because it may be that, because of the sophistication of our imaging tests, the imaging will show some degree of blood flow. Transcranial Doppler ultrasound in many cases shows 'reverberating flow', that is, during systole, blood is advanced but during diastole it goes back, to yield no net forward flow. It may be that a new technique could register that flow as perfusion rather than reverberation.

DR. RAICHLE One might add to that the fact that we are inferring, from the presence or lack of circulation, a causal effect on the brain and what I would add to your comment is that imaging should more directly address the causal consequences of that. In other words, the brain is either working or it is not as a result in the change of blood flow, and I would propose that imaging and, possibly, electrical techniques would answer that directly in the future.

DR. BERNAT Thank you. It may be that a multimodal approach assessing electrical activity, intracranial blood flow, and cerebral metabolism would be the ideal confirmatory test.

PROF. VICUÑA I have a question. You mentioned that reversible intoxication has to be ruled out prior to declaring brain death. I imagine that there are standard protocols for analysing that possibility and the question is, would it be possible that there may be some unknown substances that lead to brain intoxication that you would not detect, that would lead to a reversible intoxication of the brain but, since they are not known, there would be no way to diagnose that?

DR. BERNAT The fear of a potentially reversible toxicity providing the clinical signs of brain death is an important issue if someone is found unconscious outside the hospital with no known medical history. On the other hand, if a patient has had a massive traumatic brain injury or a massive intracranial haemorrhage, often the toxicity issue is not a big problem. So we need clinical discretion to choose among whom to worry about in intoxica-

tion and to exclude it. Standard toxicological analysis looks for barbiturates, opioids, etc., that could depress nervous system function to the point of interference with the clinical determination. Further, neuromuscular blocking agents administered during a resuscitation or surgery or some other time, in the hospital could interfere also. So the presence of those drugs must be considered and excluded. I do not know the nature of the mysterious substance you are referring to that would not be measurable as a barbiturate, an opioid, a neuromuscular blocking agent, or a benzodiazepine. There may be other drugs relevant to brain death determination that are not part of our routine screen that would produce a reversible toxicity.

PROF. VICUÑA There may be some but nobody knows. We do not know so many things.

PROF. BOUSSER Just a comment about such unknown toxics. I think it is usually possible to highly suspect that a coma is due to a toxic even though the toxic is not known. There are a number of clinical signs, which, together with a normal neuroimaging, point to a toxic coma and allow the differentiation with neurological causes of coma, such as stroke.

DR. BERNAT Thank you, I agree.

DR. HENNERICI I do not remember exactly the case, but I remember a patient with a baclofen intoxication had asystole, flat EEG, but recovered. But this baclofen is not in the normal programme of toxicology analysis.

DR. BERNAT Fair enough, there are other depressant drugs such as baclofen or tricyclic antidepressants that should be considered. I mentioned yesterday that, even in the presence of drug intoxication, demonstrating the absence of intracranial blood flow will still prove brain death irrespective of the presence of the toxicity, because once there is no perfusion there can be no surviving neurons.

## THE NEUROLOGIST'S VIEW ON THE DETERMINATION OF BRAIN DEATH\*

LÜDER DEECKE

It is a great honour to be invited again to a Study Workshop of the Pontifical Academy of Sciences in the beautiful Casina Pio IV in the Vatican gardens. The first time I was here was in October 1988, participating in the Study Week on the 'Principles of Design and Operation of the Brain', organized by the late Sir John Eccles, Nobel laureate (cf. Eccles & Creutzfeldt (eds.), *Scripta Varia* No. 78). We were dealing with the miracles of the living human brain in particular regarding movement, action and will (Deecke & Lang, 1990), while the topic is now the dying and dead human brain with all the consequences. Above all: is brain death the death of the whole person.

What is the most common clinical situation that leads to brain death? It is circulatory arrest. This has a very wide range extending from syncope to brain death.

### *From Syncope to Brain Death*

Transient circulatory arrest may lead to global cerebral ischemia and thus to syncope. Sometimes syncope is preceded by non-specific premonitory symptoms such as:

- paraesthesiae
- light-headedness
- palpitations, and
- greying-out of vision.

Syncope is associated with pallor and loss of muscle tone, but with prolonged ischemia, *tonic posturing* occurs (see Fig. 1), sometimes accompanied by irregular jerking movements that resemble seizures.

If postictal confusion occurs, it clears within 1 minute. In elderly patients, syncope may present simply as unexplained falls.

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.



Syncope may be related to:

- cardiac pathology,
- dysautonomia,
- postural hypotension,
- endocrinopathies, and
- metabolic disorders.

‘Neurocardiogenic’ (vasovagal) syncope is the most common variety. Depending on its duration, ventricular fibrillation or asystole may cause irreversible anoxic-ischemic brain damage.

The prognosis varies with

- the patient’s *age*
- the *duration* of circulatory arrest, and
- the *interval* before cardiopulmonary resuscitation and defibrillating procedures were undertaken.

Circulatory arrest from ventricular fibrillation has a better prognosis than that from asystole.

The neurologic consequences of the arrest may relate to the accumulation of intracellular calcium, increased extracellular concentrations of glutamate and aspartate, and increased levels of free radicals.



Figure 1. Decerebration with Extension Seizures. *Tonic posturing*.

In the mature nervous system, *grey matter* is generally *more* vulnerable to ischemia than white matter. The cerebral *cortex* is *more* sensitive than the brain stem. So-called *watershed areas* bordering the zones supplied by major arteries are especially vulnerable.

*Circulatory Arrest Under 5 Minutes' Duration*

Circulation arrest shorter than 5 minutes leads to

- transient confusion or
- temporary loss of consciousness and
- impaired cognitive function.

Complete recovery is usual.

In rare instances, circulatory arrest is followed after 7-10 days by a demyelinating encephalopathy, with increasing cognitive dysfunction and pyramidal or extrapyramidal deficits that may have a fatal outcome. In such rare cases (under 5 min.), patients regain consciousness several hours after the circulatory arrest but then develop progressive neurologic deficits, such as:

- intellectual deterioration
- personality changes
- seizures
- cortical blindness
- amnesic syndromes or rarely
- locked-in syndrome (characterized by quadriplegia and mutism)
- extrapyramidal syndromes
- bibrachial paresis, or
- intention (action) myoclonus

*Circulatory Arrest Over 5 Minutes' Duration*

Circulatory arrest that lasts longer than 5 minutes may cause widespread and irreversible brain damage, resulting in prolonged coma. Prognosis for survival or useful recovery is poor, especially when brain stem reflexes (most notably the pupillary responses to light) are lost. In particular, loss of pupillary reactivity for more than 24 hours or persistence of coma for more than 4 days indicates a poor prognosis.

In a study, comatose survivors of cardiac arrest who continued to have non-reactive pupils, failed to open their eyes in response to pain, or had absent or reflex motor responses 3 days after onset of coma, generally failed to survive or to regain useful independent function. In this study, the most accurate single predictor of poor outcome immediately after restoration of spontaneous circulation was the absence of pupillary responses, 73 had a poor outcome (i.e., death or persistent vegetative state). Even if consciousness is regained, focal or multifocal neurologic signs may lead to significant

disability from focal motor deficits, extrapyramidal disturbances (e.g. parkinsonism), sensory loss, seizures, myoclonus, and disturbances of higher cortical function from which recovery is usually delayed and incomplete.

TABLE 1. Clinical Evaluation of Prognosis in Comatose Survivors of Cardiac Arrest.

Sign	Patients with poor outcome %		
	Immediate	Day 3	Day 7
Lack of response to pain:			
No opening of the eyes	69	100	100
No motor response	75	100	100
Lack of response to verbal stimuli	67	94	100
Lack of pupillary response	83	100	100

Intention (action) myoclonus is particularly characteristic in such circumstances; it is often activated by startle or various sensory stimuli and is responsive only occasionally to clonazepam, valproate, piracetam, or 5-hydroxytryptophan.

Some patients never fully regain consciousness after circulatory arrest, remaining in a persistent vegetative state or showing evidence of brain death. The persistent vegetative state is characterized by the return of sleep-wake cycles and of various reflex activities, but wakefulness is without awareness.

### *Brain Death*

In the conditions discussed above the brain may be severely injured, but these patients are not all in the state of brain death. Brain death is defined as loss of *all* cerebral activity, including activity of the cerebral cortex, cerebellum and brainstem, for at least 6 hours, if confirmed by electroencephalographic evidence of electrocerebral inactivity or for 24 hours without a confirmatory (isoelectric) EEG.

### *Apnea Test*

In patients with suspected brain death the apnea test may be employed (*and is safe because oxygen is supplied*). This test involves evaluation of the respiratory response of the brain stem by allowing the carbon dioxide tension

( $P_{CO_2}$ ) to rise to 60 mmHg while 100% oxygen is given through the endotracheal tube. Brain dead patients have no ventilatory response to the apnea test.

### *Simulation of Brain Death*

Brain death may be simulated clinically by

- deep hypothermia
- sedative overdose, and
- neuromuscular blockade.

Such conditions must always be excluded, especially when no clear history of circulatory arrest can be obtained. Besides hypothermia (for example if drowned in winter under the ice) also children can look like being brain dead and are not. A list of some of the drugs that have to be excluded is given in Table II.

TABLE II. Drugs that may confound neurological examination in brain death.

<i>Lorazepam</i>	<i>Primidone</i>
<i>Clonazepam</i>	<i>Morphine</i>
<i>Midazolam</i>	<i>Fentanyl</i>
<i>Flurazepam</i>	<i>Ketamine</i>
<i>Diazepam</i>	<i>Amitryptiline</i>
<i>Phenytoin</i>	<i>Pancuronium</i>
<i>Chlordiazepoxide</i>	<i>Vecuronium</i>
<i>Carbamazepine</i>	<i>Pipecuronium</i>
<i>Valproic acid</i>	<i>Alcohol</i>
<i>Phenobarbital</i>	<i>Cocaine</i>
<i>Thiopental</i>	<i>Codeine</i>
<i>Pentobarbital</i>	

### *Cardiac Procedures*

In present day medicine, diagnostic and therapeutic procedures on the heart are very advanced, but embolism into the brain remains a certain risk. Cardiac catheterisation or percutaneous transluminal coronary angioplasty sometimes causes cerebral emboli that may lead to focal neurologic deficits or an encephalopathy manifested by a behavioural disturbance. Encephalopathy, seizures, and cerebral infarction after cardiac surgery usually result from hypoxia or emboli.

Postoperative encephalopathies may also relate to metabolic disturbances, medication, infection (especially in immunosuppressed patients), or multiple organ dysfunction syndrome (MODS).

Postoperative seizures may result from focal or generalized cerebral ischemia, electrolyte or metabolic disturbances, or MODS (multi organ failure). Recognition of the precise cause of encephalopathy in such cases can be difficult. After cardiopulmonary bypass is performed, intracranial haemorrhage may result because of diminished platelet adhesiveness and reduced levels of coagulation factors. Coronary angioplasty leads to cerebral emboli in app. 1% of cases. But when undertaken after acute myocardial infarction, it is associated with a higher risk of stroke and anoxic encephalopathy.

An encephalopathy may occur soon after cardiac transplantation as a side effect of an immunosuppressive agent or as the result of an infection, for example: meningitis, meningoencephalitis, or cerebral abscess related to immunosuppressive therapy. Infecting organisms include *Aspergillus*, *Toxoplasma*, *Cryptococcus*, *Candida*, *Nocardia*, and viruses (Fig. 2, page 429).

After *coronary bypass surgery* the occurrence of an encephalopathy may be caused by stroke, which develops in about 5% of bypass patients and is either embolic or, less commonly, the result of watershed infarction from hypoperfusion. A carotid bruit or radiologic evidence of atherosclerosis of the carotid artery does not clearly increase the risk of stroke, and carotid endarterectomy before cardiac surgery is of questionable utility. In rare cases, patients do not recover consciousness after surgery, and no specific metabolic cause can be identified. This encephalopathy is probably the result of diffuse cerebral ischemia or hypoxia. Hemispheric or multifocal infarction is sometimes responsible.

In Fig. 2, the possibilities of cardiogenic embolism in general are depicted.

### *Brain Death in Other Settings*

The cerebrovascular/post cardiac arrest scenario has been given more space here, because it is cause No. 1 for brain death. However, cerebral death may also result from severe *head trauma* (cause No. 2) and its complications in the form of delayed haematomas. Space-occupying lesions (brain tumours) in their final states may end in brain death (cause No. 3). Finally, inflammation has to be mentioned as cause No. 4 but is not to be discussed in the context of transplantation.

*The Lethal Final Pathomechanism: Brain Swelling and Herniation*

The fatal pathomechanism in all 4 causes is the same: it is *brain swelling*, which is the sum of brain oedema and hyperaemia. The problem arises when brain swelling gets out of control, i.e. when all possible therapies have failed. These consist of sedation (with morphine), muscular relaxation, ventricular drainage if necessary, mannitol, hyperventilation and – *ultima ratio* – ‘barbiturate coma’ (Pentobarbital narcosis). If all these therapeutic measures fail, the brain gets under pressure, i.e. the intra cranial pressure rises. It continues rising, and when the intracranial pressure overrules the systolic blood pressure, the heart is no longer capable of pumping blood into the skull / through the brain. In other words, the brain compresses itself within its hard shell – the absolutely rigid skull. The incarcerated brain herniates through openings. Upper herniation (upper red arrows in Fig. 3) occurs through the *tentorium* slit causing decortication clinically. Further in the process a lower herniation develops as well (lower red arrows in Fig. 3), in which portions of cerebellum and brain stem herniate through the *foramen magnum*. Clinically, this leads to a loss of all brain stem reflexes and finally to the cessation of breathing (Fig. 3, page 430).

If a four vessel Angiography is employed, it shows exactly the complete stasis of blood circulation: on the pictures the contrast medium suddenly breaks off exactly where the arteries enter the skull, i.e. the two internal carotid arteries at the upper siphon, and the two vertebral arteries at the *foramen magnum*. The four vessel angiography is a proof of brain death, however critics argue that the relatively large amounts of contrast medium could have negative effects on the brain, which is already pre-injured and compromised anyhow.

*Examination and Documentation of Brain Death*

Examining patients with regard to brain death should be done by neurologists, i.e. a conservative non-operative field of medicine with no interest in transplantation medicine. This is the ethical reason why operative disciplines including neurosurgery should not be involved in brain death diagnosis, nor should anaesthesiology. At our hospital two specialists in Neurology independently establish the diagnosis of brain death. The diagnosis of brain death has the following prerequisites:

1. Deep coma (3 points only in GCS [Glasgow Coma Scale])
2. Loss of all brain stem reflexes – ‘brain stem areflexia’
3. Apnea (documented by the ‘Apnea Test’)

The brain stem reflexes are as follows:

Pupillary reaction	→ dilated pupils, no reaction to light
Oculocephalic reflex	→ doll head phenomenon, no counterrolling of the eyes
Corneal reflex	→ no twinkling upon tactile stimuli to cornea
Trigeminal pain reaction in the face	→ no reaction to painful stimuli e.g. to the nose
Gag reflex	→ no reaction to manipulating the tracheal tube

(No vestibulo-ocular reflex [VOR] or nystagmus upon the caloric test with ice water irrigation of the ear canal as an option).

#### *Examination and Documentation of Brain Death Through 'Supplementary' Means*

The EEG (isoelectric EEG, zero line EEG, electrocerebral inactivity) is now in Austria a supplementary means only. We regret this. We still use it. It is a functional test. We are looking at *neuronal* function, at cortical function (EEG picks up activity from the cerebral cortex only, not from the brain stem). The EEG speeds up the process of brain death diagnostics: the waiting period is only 6 hours with confirmatory EEG, and as long as 24 hours without.

In case an EEG cannot be recorded e.g. in patients with head trauma and open wounds on the head, transcranial Doppler sonography (TCD) and colour-coded Doppler sonography can be used.

The classical angiography (digital subtraction angiography, DSA) should be performed only *after* brain death has been assessed. In the setting of transplantation it might still be useful, since 'on retreat', so to say, with the catheter other organs may be examined radiologically.

#### *The 'All or Nothing-Situation' of Brain Death*

It is important to realize that we have this all or nothing situation in the setting of brain death. Either our therapies against brain oedema (see above) are successful and brain death can be avoided or they are not successful. Then brain death is the inevitable result. If the galloping brain oedema cannot be stopped we have this mechanistic outcome that the brain compresses itself and in the end is totally destroyed. The galloping brain oedema is the result of a vicious circle: the normal brain has a blood flow of 55 ml/100g tissue/min. If blood flow goes down to 40 ml/100g tis-

sue/min, functional metabolism already begins to suffer, if it goes below 15 ml/100g tissue/min, structural brain metabolism is jeopardized. Poor blood flow results in lack of oxygen ( $O_2$ ) and a rise in carbon dioxide ( $CO_2$ ) that leads to acidosis of the brain. Brain acidosis leads to brain oedema, which leads to an increase in intracranial pressure and this leads to further lowering of cerebral blood flow. This is the vicious circle. Vicious circles are feedback cycles with *positive* feedback, i.e. they build up. Thus, the system is bound to take this disastrous course.

I think it can now be understood why neurologists are so certain about brain death, if this diagnosis is *lege artis* established. It is the inevitable end point of an inevitable cascade of fatal mechanisms resulting in the total destruction of the brain. The PET (positron emission tomography) is a functional method for measuring brain metabolism. Laureys S. *et al.* of the Cyclotron Research Centre, University of Liège, Belgium have investigated different states of consciousness in the PET looking at the glucose metabolism (see Fig. 4). They were recording the regional cerebral metabolic rates for glucose (rCMRGlu) using  $^{18}F$  fluorodeoxyglucose ( $t_2 \pm 2$  hours), neural activity of  $\pm 30$  min in the awake state (upper left image in Fig. 4), in deep sleep during anaesthesia in the unconscious state (permanent vegetative state, apallic syndrome) and in the state of brain death. In the latter the rCMRGlu was zero (lower right image in Fig. 4, see page 430).

The hypophysis (pituitary gland, some call it 'neurohypophysis') has a special status. If we look at Fig. 5 (see page 431), we see the hypophysis under the brain in the *sella turcica* and see that it may be somewhat protected from elevated intracranial pressures, a protection made efficient by the *diaphragma sellae* separating the pituitary gland from the intracranial space. Furthermore, the pituitary has its own blood supply directly from the carotid artery. Thus, a remaining basic hormonal secretion may be maintained after brain death has occurred. The posterior lobe even produces antidiuretic hormone, ADH or vasopressin, a lack of which causes *diabetes insipidus*, which is common in the brain dead state. Lack of *diabetes insipidus*, though, cannot be taken as evidence against the concept of brain death (Renner, 1995).

A basic hormonal secretion of the anterior lobe of the neurohypophysis is also of interest, in particular in the case of brain dead mothers. This was an issue at the study workshop, and in the pre-conference correspondence, H.E. Msgr. Prof. Marcelo Sánchez Sorondo had asked: 'Do the children of brain dead mothers have a standard of normality in line with children not so born or do they have mental and physical impairments derived from the



condition of death of their mothers? And are children born to brain dead mothers the same as children born to alive mothers, and this in a society that has laid increasing stress on the particular importance of the intrauterine relationship between mother and child?’

L. Deecke had replied: to mothers in coma, yes. (i.e. they can have normal children). To mothers in the permanent vegetative state, also yes. Regarding brain dead mothers: whether the child has a damage or not depends on the circumstances that led to the state of the mother (accidents? other conditions?). The really brain-dead mother is an extreme situation. There is not really an intrauterine interaction between mother and child. These conditions are, in a sense, emergency conditions. For a long time obstetricians have had this emergency situation in which the mother is dying (cardiac death) and they are trying to rescue the child. This is called: ‘*Sectio in mortua*’. If it is not cardiac death but brain death it should be analogous: ‘*Sectio in mortua cerebialis*’.

Prof. DDr. Johannes Huber Vienna (theology and gynaecology & obstetrics) declared in the workshop that pregnancy seems to be stable even in the absence of brain function. Prof. Huber asked the question: ‘Shall the delivery of the child by caesarean section be the only removal? Or do we allow at the same time that the brain dead mother also gives her organs?’

L. Deecke replied: ‘*Sectio in mortua cerebialis in pietate!*’ No other organs. Only the child!

Prof. Posner was of a different opinion.

So this point remains open and subject to individual taste and own decision.

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## DISCUSSION ON DR. DEECKE'S PAPER

DR. POSNER Why not the other organs, why only the child? In the brain dead mother, if you are going to take the child by caesarean section, as you do, and the other organs are still viable, why not take them for transplantation?

DR. DEECKE I think it is a reason of piety. I think it has to be this only topic, the birth of the child, with reverence and nothing else. We can discuss it, but I think the child has absolute priority. The operation has this name – caesarean section monothematically. The operation is done in special operation theatres specialized on this.

DR. POSNER It has been repeatedly discussed that the donation of organs is of enormous value to the family in the post-death period. I have had the experience myself, with relatives where, years after the donation was made, the relatives comment on how grateful they are that the donation was made and allowed other persons to live. So I do not see why the relatives of a pregnant woman should not be approached with the question of organ donation as well as delivery of the child. I agree that delivery of a viable child is obviously the first priority, but if the organs are still there and available I do not see why they cannot be harvested if the family agrees.

DR. DEECKE In your recollection, have there been cases in which this has been done?

DR. POSNER Not in my experience, and I do not recall from my reading, I just do not remember.

DR. DEECKE Maybe this is everybody's personal opinion, but coming closer to Dr. Posner's opinion: if the family has to be asked anyhow, it can be made their decision whether they allow for organ transplantation as well.

# THE ASSESSMENT OF COMA OUTCOME BY THE USE OF MULTIMODAL MR AND PROPORTIONALITY OF CARE IN NEURO-INJURED PATIENTS\*

LOUIS PUYBASSET

Thank you for giving me the opportunity to be here and to discuss this topic with you. For myself there are not that many ethical issues regarding brain death, it is pretty clear as soon as the diagnosis is perfectly made. We have more ethical issues regarding the way we deal with families, and this is where we should concentrate our work. However, as science goes on I will try to show you that we are confronted more with ethical issues regarding the treatment that we provide to patients in a coma and we have seen with Dr. Bernat that this might be related also to organ donation through the programme of non-heart beating donors, and I will try to discuss with you these issues.

As intensivists, what we have to deal with is to try to find out tests that give us the possibility of tailoring the intensity of care that we provide to each individual patient after major traumatic or non traumatic brain injury. We have to do that to avoid disproportionate care in patients that will end up in permanent vegetative state or minimally conscious state at one year but the opposite is also true, i.e. to provide major intensive care in patients for whom we expect a good recovery, even though it is two or three months later. So it is our duty to develop tools in order to assess prognosis and to proportionate care accordingly. There are many ways to do that and I will try to show you what we do in Paris in my hospital and what we have developed there.

The first thing is to look at the anatomical pathways of consciousness that rely on, let us say, a very basic appreciation of two systems. First of all, it has been called by Parvizi and Damasio the *protoself*, and it is based on the ascending reticular activating system in the upper pons, the midbrain, the intralaminar nuclei and the reticular nucleus of the thalamus, the hypo-

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

thalamus and the basal forebrain. All this is connected to the cortex and some areas of the cortex are more important than others, especially the cingulate areas (Figure 1, see page 432).

One hypothesis is to say that poor outcome regarding recovery of consciousness is linked to specific alterations of the protoself network or to diffuse alteration of both hemispheres. What is so complicated is that we have to consider the symmetry of a lesion and this complicates the picture a lot, especially when we think of a bilateral lesion. We have to take that into account, whether bilateral lesions are symmetrical or asymmetrical.

We made different attempts to try to assess recovery of coma in those patients with severe head trauma and I will show you some of these attempts. Here we studied with morphological sequences 73 patients with MRI and we distinguished two groups of patients, those who will die or stay in a permanent vegetative or minimally conscious state at one year and those who will have a good recovery. In this series we had 32 patients with a good recovery and 41 patients with a bad recovery, so to say.

### Weiss et al, submitted – n = 73 TBI patients

**Table 1. Baseline Characteristics of the Patients.**

	<b>All patients n = 73</b>	<b>GOS 1-3 n = 41</b>	<b>GOS 4-5 n = 32</b>	<b>P</b>
Age (years)	36 ± 14	40 ± 15	31 ± 13	<0.02
Sex (M/F)	58 / 15	37 / 4	21 / 11	NS
Mydriasis at scene	31 (42%)	22 (54%)	9 (28%)	NS
GCS at admission	6.1 ± 3.0	5 ± 3	7 ± 3	<0.01
Subdural hematoma	20 (27%)	17 (41%)	3 (9%)	<0.003
Epidural hematoma	12 (16%)	8 (20%)	4 (13%)	NS
Hypertonic saline use	36 (49%)	21 (51%)	15 (47%)	NS
Norepinephrine use	65 (89%)	37 (90%)	28 (88%)	NS

Figure 2.

We determined cluster analyses just to show you that it is possible, analysing the FLAIR images, to ponder each lesion and in doing that to have a prognosis likeliness regarding the outcome of the patient. Nowadays we have some tools that will provide us with more and more information regarding recovery.

### Weiss et al, submitted – n = 73 TBI patients

**Table 4. Independent risk factor for poor outcome – logistic regression analysis**

	Odds Ratio	[95% CI]	P
<b><u>MRI approach</u></b>			
Right upper pons and right lower midbrain	5.1	1.8-14.5	<0.003
Hypothalamus and basal forebrain	2.3	1.2-4.3	<0.02
Left parietal, left temporal, left occipital lobes and left insula	3.3	1.4-7.9	<0.009
<b><u>Combined clinical to MRI approach</u></b>			
Right upper pons and right lower midbrain	4.7	1.2-18.1	<0.03
Hypothalamus and basal forebrain	2.6	1.2-5.7	<0.03
Left parietal, left temporal, left occipital lobes and left insula	4.0	1.3-11.8	<0.02
Grasping	21.2	1.7-271.2	<0.02
Chewing	26.9	3.7-197.5	<0.002

OR are given per one lesion increase for the different clusters.

Figure 3.

And these are the results regarding the assessment of outcome with the MRI plus the clinical symptoms that the patient presented, such as grasping or chewing.

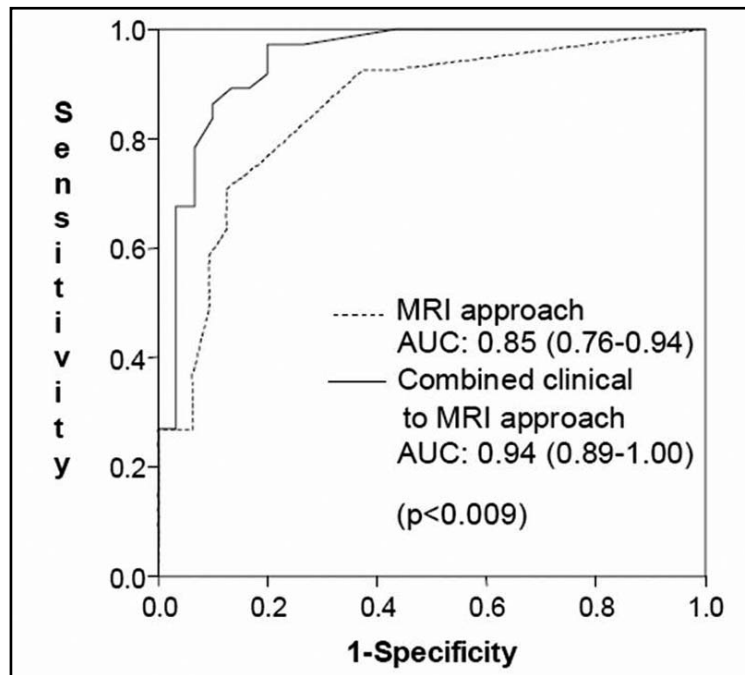


Figure 4.

The picture has changed a lot with the use of spectro-MR and diffusion tensor and I will now show you this type of analyses. Here we go from a purely morphological approach to a biochemical approach of the function of a pons. This is the normal aspect of a pons and the normal spectra with a first peak that is choline, a second that is creatine and a third that is n-acetyl-aspartate. The normal ratio for NAA/Cr is 2.33.

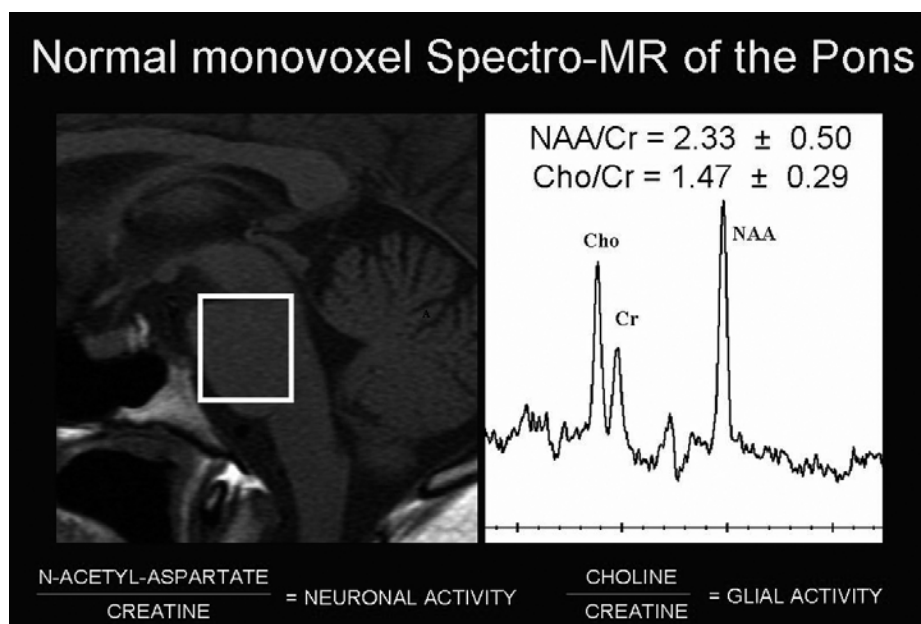


Figure 5.



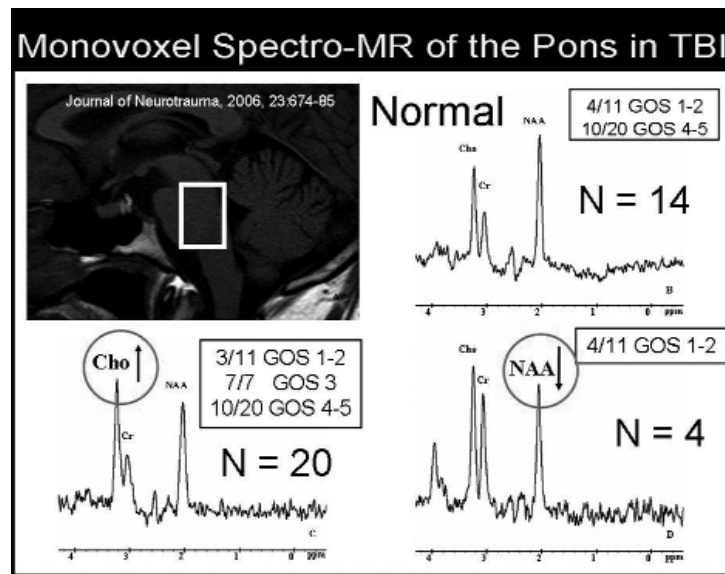


Figure 6.

This is a first study that we published in the *Journal of Neurotrauma*, showing the different aspect that we observed in the pons of traumatic patients and, as you see, 14 of these 48 patients had a normal aspect. Most of the patients had a cholinergic reaction, which does not mean that they will not end up in a bad clinical state, but all of the patients that presented a profound decrease in n-acetyl-aspartate over creatine ratio ended either in PVS or dead.

There are clear correlations between the number of lesions in FLAIR in traumatic brain injury and the disability rating scale at 18 months, so that we can somehow predict the outcome (Figure 7, see page 430).

Figure 8 (see page 433), shows a 4D Principal Component Analysis that we did. We analysed the FLAIR lesions in the hemispheres and combined that with the spectro-MR analysis of the pons. You can see that, in doing so, we were able to distinguish very clearly the group of patients that would have a good recovery, the group of patients that would stay in MCS and the group of patients that would either die or stay in PVS. That is another example of predictability of outcome. I have to specify that all these MRI were performed after the second to third week of insult. It is not done early because it is impossible to transport these patients to the MRI early, due of the increased intracranial pressure.

Another major issue is the use of diffusion tensor. For those who are not aware of this technique, Figure 9 (see page 433) shows a typical FLAIR image and a typical corresponding diffusion tensor. These techniques give you the major axonal routes in the brain.

Figure 10 (see page 434) shows the 3D images of a brain with diffusion tensor and this is now a sequence that we use in every comatose patient to see exactly where the white fibres insult is located. So here you have the typical brain stem with the four spinothalamic and the pyramidal signals, then we have the peduncles, and then we have all the hemispheric white fibres, and this is the normal assessment of the brain with diffusion tensor.

Another thing that we do on a systematic basis is the analysis of spectrometry on a section that goes through the basal ganglia. Figure 11 shows the normal aspects of the lenticular nuclei, of the insula, of the posterior thalamus, the parieto-occipital white matter, and the occipital cortex. With this technique you can put the voxel wherever you want and have an analysis of the biochemistry of the brain. As you see, usually the NAA is twice the creatine peak.

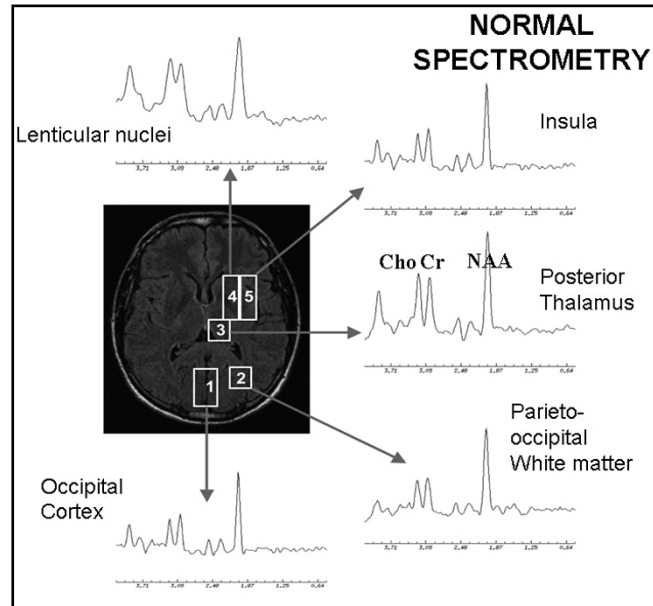


Figure 11.

Figure 12 (see page 434) is just to show you how efficient this imaging really is. This is what a totally destroyed brain stem looks like. This is not a brain death patient, these are patients who will end up either in permanent vegetative state, or in minimally conscious state. This destruction can be seen without any lesions on the FLAIR sequences. Here you have the destruction of all the white descending fibres in the pons and look also at the peduncles, at the mid brain, which is totally atrophic. And we see more and more of these diffusion tensor imaging abnormalities although FLAIR images might be normal.

Very interestingly, the usefulness of MRI goes in both directions, meaning that we can have patients with a very severe clinical state and good MRI and, therefore, good prognosis. The patient in figure 13 (see page 435) was a real cornerstone in our practice, he was 36 years old, he shocked us a lot. He had an initial Glasgow of 3 and was referred with a bilateral decerebration. I examined him myself so I know this is true. He had no increased ICP so we were able to reduce sedation very quickly and to have a real neurological examination. He stayed in decerebration for 15 days. He also had a neurovegetative crisis; we were very aware of this very poor clinical condition and went to the MRI quickly. We were surprised to see a normal MRI. This is a normal spectra for the pons and this is a normal aspect of the diffusion tensor in the pons.

These were the aspects of the diffusion tensor in the hemispheres, while figure 14 (see page 435) shows a spectro for the posterior thalamus on the right side. In fact, this patient recovered completely, even though we had to wait a long period of time, meaning that, with these types of techniques, we can clearly distinguish patients that have very severe clinical conditions and in whom we should continue care for weeks or months if necessary, because at the end they will wake up since they have a normal brain on the MRI. This could be apperanted to a kind of stunned brain.

Another thing that we use a lot is what we call 'Cognitive EEG' (figure 15, see page 436). I will not go into detail here but it is the assessment of the response to two different auditory stimuli. It is a summation of the EEG answers to the stimuli. This is a normal aspect, with this well-known mismatched negativity operating between 200 and 300 milliseconds. The P3A indicates a preconscious state and the P3B indicates a conscious state. In this patient, we had a delayed mismatched negativity and a P3A, meaning that he was in a preconscious state. We usually combine this MRI approach with this electrophysiological approach to further determine the prognosis.

I will just show you some other images. You see, for example (figure 16, see page 436), in this patient who has a severe head trauma patient, he had

a subdural hematoma on the right side here and a subsequent extradural hematoma on the left side, he was operated twice. You see the profound discrepancy that we observed in the FLAIR image, it looks pretty normal on the left side compared to the total destruction of the white fibres using diffusion tensor. In this case the right side seems to be more diseased than the left side but, in fact, regarding the diffusion tensor imaging and the axons themselves, it is exactly similar.

Figure 17 is another example. This is an SAH patient, 60 years old, she was found a long time after the SAH, she had a major increase in ICP. This patient finally died and, when we look at the FLAIR, we see these hyper intense signals on the basal ganglia.

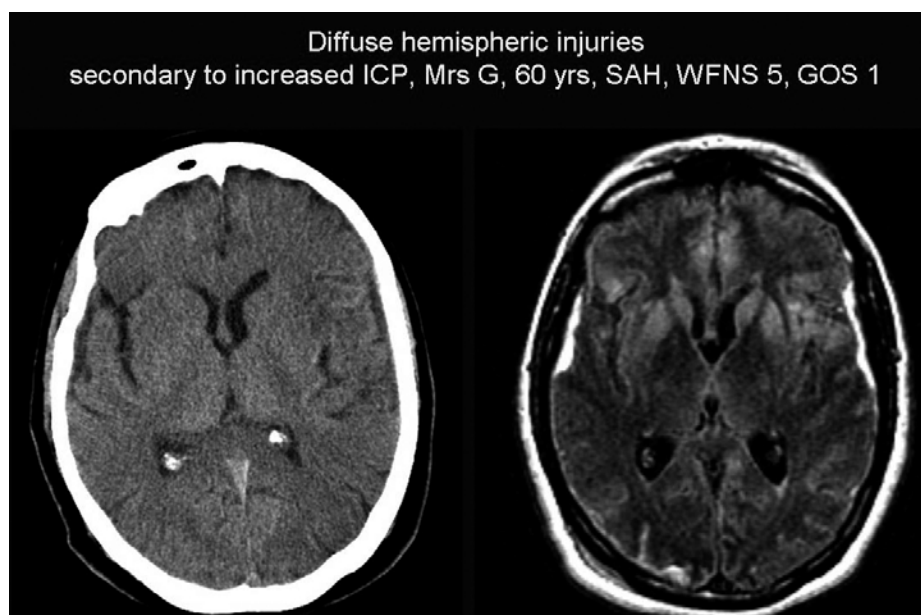


Figure 17.

However, when we look at the diffusion tensor (figure 18, see page 437), it is clear that there are no more white fibres in this brain and that ICU is helpless here.

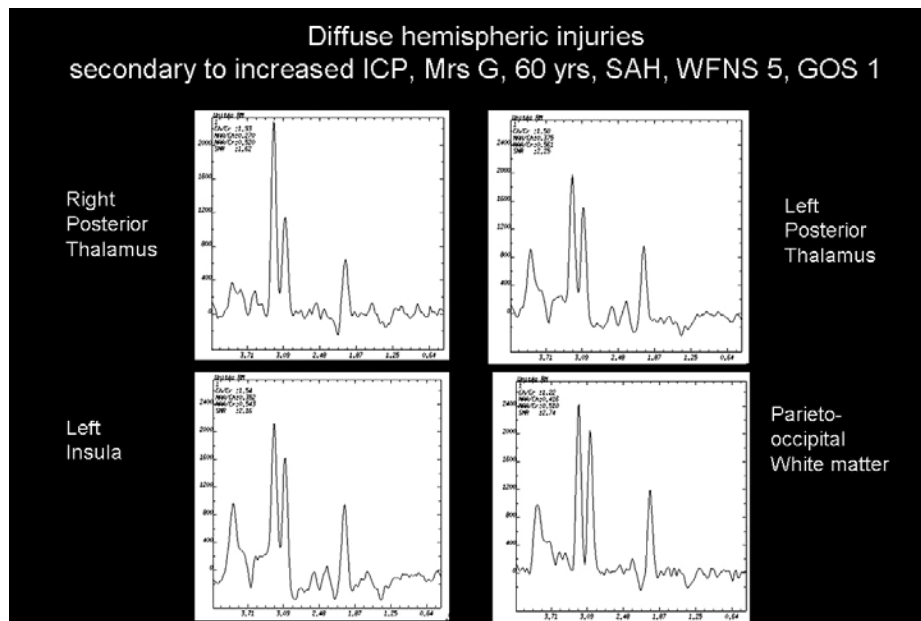


Figure 19.

This was confirmed by the spectro analysis of these different parts of basal ganglia (figure 19), showing a total destruction as assessed by the major reduction in the NAA / creatine ratio of about 0.5.

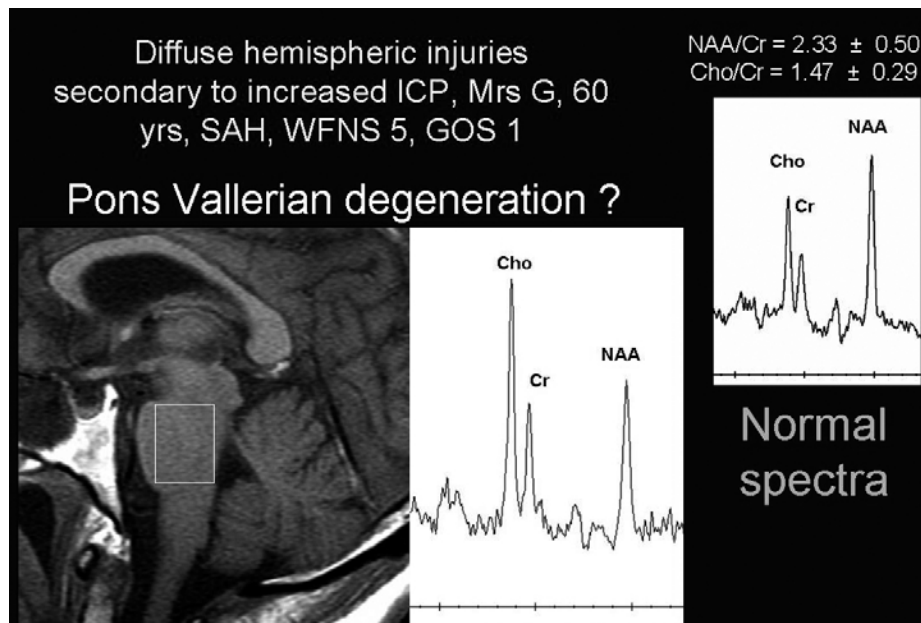


Figure 20.

One of the things that we discussed yesterday is the Wallerian degeneration of the pons. For example, in the patient I showed you before, who had a SAH, there was no primary insult to the pons, but when we look at the spectra of the pons (figure 20), we see a tremendous decrease in NAA / creatine ratio, meaning that we probably had a descending degeneration.

And when we look at the cognitive EEG (figure 21, see page 437), we see no answer; there is no mismatch, no P3A. All that is concordant to inform us that this patient will never wake up and will never recover consciousness, so maybe it is better if we stop the ICU care and let her die. We should go in this case from a curative logic to a palliative one.

We know today that quantitative assessment of spectrometry on the basal ganglia slice combined with fractional anisotropy measure allow a very good prediction of coma outcome.

Right now we are designing a study in France – I am the principal investigator – that will look at 400 severe TBI patients in 10 French centres and will do all these MRI analyses in a statistical blinded way and in a multi-centre trial, to make sure that this is a relevant matter. But our goal is obviously to provide a hard scientific basis for withholding or withdrawing care in neurotrauma patients and to help in the decision-making process.

On a final note, I would like to go back to the issue of organ donation. As I told you, I have no ethical concern with brain death. I often, unfortunately, have this discussion with families and I think that ethics lies in the way we deal with families, but I have no ethical problem or issue with the diagnosis of brain death because brain death is diagnosed in France only by EEG or DSA, it is not based solely on clinical examination. So diagnosis is not a concern to me. My concern is much more the issue of the Class III Maastricht patients, and I wanted to take a few minutes to present that.

You know that, because of a shortage of organs, there are a lot of programmes coming now from the US, and especially from England and from the Netherlands, that try to harvest kidneys from people who are dead. We have three classes here. Class I are patients that are brought in dead, so you take the tissue in these patients; Class II are brought in dead, cardiac resuscitation is a failure, the patient does not recover cardiac rate, so we turn on extracorporeal circulation and then speak to the families. If they accept, there can be a kidney donation. For me, the major problem is with Class III patients.

I would say that we are going to have a major problem because the more we develop diagnostic tools to predict the outcome of a patient, the more often these questions will arise. Because of the family or because of a patient's previous wish or because of the pressure of a surgeon, we might be asked to harvest the kidneys of such patients. This question is particularly relevant to neuro ICU, because it is in these neurological patients that death occurs without any major organ dysfunction.

Thank you for your attention.

## DISCUSSION ON DR. PUYBASSET'S PAPER

DR. DEECKE On what time window are you looking at for transplantation after cardiac arrest, within how many hours has transplantation got to be done?

DR. PUYBASSET I do not do that in my practice. It depends on the Maastricht class and on the centres. In class III in Pittsburgh, for example, if I understood correctly, they do a procedure of organ retrieval after two minutes of cardiac arrest so this occurs in the OR, but for class II patients, for patients who are recovered on the street without any cardiac activity, this time is much longer. What we have decided in our institution is to have an ineffective massage for thirty minutes and then to stop the massage for five minutes – it has to be ineffective, if the heart recovers there is no discussion – we then sign the death certificate and put on an extracorporeal circulation with a Fogarty on the abdominal aorta just to perfuse the kidneys and the liver, and then we will ask the family, under extracorporeal circulation. We have major difficulties with class III donors so that today we will only deal with class II, the opposite of what you do. However I recognize that I have no answer to this ethical question because on the other hand, patients need kidneys, so that this is a type of justice. I have never been confronted by a family asking for organ donation or with a patient having asked before for organ donation because we deal with young patients, with head trauma patients, SAH patients and usually they have not spoken about that before the accident. But if I were to be confronted with this case it would be very difficult, because death does not occur like that, I mean, even extubated, even after two or three weeks in the ICU, it takes a long time to have a stopping heart when you have a neuroinjured patient, unless you are with a major increase in the intracranial pressure but then you go into brain death quickly. So I have a problem here, I have no answer, that is why I was interested in your experience. We have to think from an ethical point of view on the one hand, the need for kidneys and on the other hand the conflict of interest that we may have regarding the treatment of these patients.



DR. TANDON Thank you for this elegant presentation of new diagnostic techniques where you use all sophistication. My question still remains: if a person has been clinically diagnosed to be brain dead, have any of these techniques added to our certainty of diagnosis?

DR. PUYBASSET Maybe not, but in psychological terms, and when we speak with the nurses and with the families the fact that we have a flat EEG makes things more simple, and you know that in France we need two flat EEGs at four hours intervals. However EEG is possible only if there is no sedation and no hypothermia. If there is sedation, and all of our patients have been sedated because before being brain dead patients they were patients that we tried to save with most often an increased ICP (intracranial pressure), it is not barbiturates, it is high dose midazolam and propofol EEG is not possible anymore. We know it takes days in these patients to get rid of these molecules after cessation so we perform a DSA (digital subtraction angiography) in these patients and it is true that, from time to time, there is a small perfusion. What we do nowadays is that we perform DSA only after a transcranial Doppler showing a small systolic peak and a large backflow. In this case, the DSA is always negative. Doing these confirmatory tests simplifies a lot, since there is no more room for doubt in the discussion with the families and with the nurses. I am afraid that a lot of the discussion that we have has arisen because of doubts regarding the brain death diagnosis, because for every layperson it has to be clear that the diagnosis is 100% certain. When you get rid of the ventilatory tube the patient dies within the next three minutes, there is no discussion, you cannot breathe with a dead brain. You told us about cases where you were a little bit uneasy with the clinical diagnosis of brain death and so that was why you were in favour of complementary exams.

DR. BERNAT Sometimes the clinical determination cannot be performed, particularly in patients with traumatic brain injuries who also had facial injuries that involved the eyes. In such patients, we may not be able to measure papillary reflexes, vestibular ocular reflexes, or corneal reflexes. Therefore we cannot perform the clinical assessment. Similarly, we see older patients with carbon dioxide retaining chronic obstructive lung disease, who are breathing by a hypoxemic respiratory drive rather than the usual hypercapnic respiratory drive. In those people we cannot perform apnea testing safely. Similarly, some patients may have neurogenic pulmonary edema such that we cannot get their PaO<sub>2</sub> high enough to safely

perform an apnea test. So there are cases in which we cannot complete the clinical assessment of brain death. In those people it is recommended to do a confirmatory test.

DR. TANDON There is no discussion that, whenever in doubt, you should do ancillary tests. My question was slightly different, that when clinical assessment is possible and fulfils all the criteria, at that stage, where is the need for doing this. Of course, the question of family, the nurses, we all have faced that position working in the wards, that is very important, that must be taken into consideration, but scientifically...

DR. PUYBASSET The case where you have a primary brain stem lesion is a small part of the patients, but still we have some haemorrhage of the posterior fossa. In this case there might be cortical activity even with no brain-stem reflexes, so again in this case EEG should be performed likely. I am so used to these tests I will not even discuss them, because we have never harvested the organs of someone on a clinical basis only, in France, it is not the law, so I cannot really answer your question.

DR. ROPPER On just a slightly different part of your talk, I really want to encourage and commend you to continue these investigations into more elaborate prognostic testing for patients who are not brain dead. I just wanted to ask you a question about your study: did you have preplanned criteria for this prospective study? Are there primary outcomes or is it another continuation and extension of an observational trial? I think that is one of the problems in neurologic intensive care, there is a little bit too much data collection and a little bit too little scrutiny of, let us call it, evidence-based medicine.

DR. PUYBASSET What we have decided is the following: regarding this MRI analysis with diffusion transfer and spectro-MR we have decided to enrol patients that will not respond to orders five days after stopping sedation and at least 15 days after trauma. Secondly, the ICU physician will be blinded not to the entire MRI, because it is too complicated, because these patients are ventilated, you know, so they will have only the morphological part of the MRI, knowing that no decision can be made on the morphological part. The diffusion transfer and the spectro-MR will be blinded to the doctor in charge. There is a central reading of all that, and there is a clinical systematic assessment at six months and one year. That is the way

regarding TBI patients. For the other causes of coma, it is an open basis, because we also need that the physician in charge learn how to deal with DTI and spectro-MR. So in the closed base it is blinded and a clinical assessment is scheduled at six months and one year, and for other causes of coma it is not blinded, it is an open base.

DR. ROPPER What is the hypothesis?

DR. PUYBASSET The hypothesis is that between the second week and the third week, MRI can predict outcome with a good certainty at one year.

DR. ROPPER But do you have predefined criteria which you say will predict outcome or are you still looking for the algorithm?

DR. PUYBASSET The idea is to look for the best statistical analyses of all these areas in the brain that will give a better answer to predict... It is a kind of expert system that we want to do.

DR. ROPPER Then you will have to have a validation set.

DR. PUYBASSET Yes, it will be separated. Theoretically, 200 patients will be analysed to build up the system and the next 200 patients will be analysed, to validate the system.

PROF. CABIBBO We open this afternoon session. Before we start with Professor Mattle I would like to thank Cardinal López Trujillo who brought us copies of the Lexicon produced by the Pontifical Council for the Family, and in fact he was so kind as to give us a few copies both in English and Spanish. Perhaps you would like to say a few words? Thank you, Eminence.

CARD. LÓPEZ TRUJILLO C'est un honneur pour moi, M. le Président, d'offrir comme humble cadeau un livre préparé par nous, qui s'appelle Lexicon and was recently translated in English. It is a first edition. It is a very great effort for us and it is an honour to bring it to you. Also we have some in Spanish translation, two editions, we have it in French, le Léxique, trois éditions, three editions, and it is being prepared in German, in Arab and in Portuguese. It is a book with a very good collaboration among almost one hundred experts in different matters and disciplines, giving the opportunity for a dialogue between theology, philosophy, theology, science, demogra-

phy, law etc. and I hope that it will be of interest for all of you. I am very happy to participate today and to hear you with your science, with your preparation. I hope in the future sometime to try this kind of very important dialogue. Thank you very much, Mr President.

PROF. CABIBBO We are really honoured by the fact that you gave your full day to be with us and for us this is a great honour and we are happy that you are enjoying the proceedings of this meeting. Thank you, it is a beautiful gift, we are very grateful.

Let us continue with Professor Mattle's paper.

## DETERMINATION OF DEATH. NEW GUIDELINES IN SWITZERLAND\*

HEINRICH P. MATTLE

The introduction of mechanical ventilators in medicine made it feasible to maintain vital functions in severely brain damaged individuals for a prolonged period. Ventilators interrupted the natural process of dying and lead to situations where the brain was irreversibly damaged while circulation and blood oxygenation were still maintained. Mollaret and Goulon called this 'coma dépassé' in their 1959 landmark report of 23 patients. The coma dépassé patients had lost all brainstem reflexes, their electroencephalograms were flat, and the coma was irreversible in all of them. In 1968 an ad hoc committee at Harvard Medical School in Boston defined the criteria of 'brain death': Unresponsiveness, absence of movements and breathing and absence of brainstem reflexes in a patient whose cause of coma was known. These criteria became widely known as the 'Harvard Criteria'. In Switzerland guidelines to define death were introduced by the Swiss Academy of Medical Sciences (SAMS) in 1969 and revised in 1983, 1996 and 2005. Organ transplantation made the diagnosis of death of potential organ donors a delicate matter, and this was the main reason that such guidelines were needed.

According to the Swiss guidelines death is defined as 'complete and irreversible cessation of all brain functions, including brain stem function'. Unlike in some other countries, irreversible loss of brain stem function is not considered as death. Dying is a natural process in the transitional zone from life to death. Death is a condition. It can result from primary injury or disease of the brain that causes irreversible loss of brain function, or from persistent failure of blood circulation or oxygenation long enough to cause irreversible damage to the brain and cessation of all brain function.

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The diagnosis of death by physicians relies on four points:

- the history
- results of ancillary investigations
- clinical findings
- and the proof that cessation of brain function is irreversible

Death is present when history and ancillary findings indicate a severe organic brain damage, clinical findings show absence of pupillary light reflexes, brainstem reflexes, and apnea in a deeply comatose patient, and when the physicians involved to determine death have proved that absence of brain function is irreversible. For this, the patient can be observed for a defined period, or ancillary tests can be used to show absence of cerebral blood flow.

Additional requirements to make the diagnosis of death are normothermia (body temperature  $>35^{\circ}$ ), absence of metabolic disorders or intoxication, absence of drugs interfering with neuromuscular transmission and absence of polyradiculitis.

According to the SAMS 1996 guidelines the proof that brain function had ceased irreversibly in a patient with known cause of coma and adequate circulation and blood pressure was made by observing the patient for 6 hours. In a child younger than 5 years this observation period had to be prolonged to 24 hours and in patients with unknown or uncertain cause of coma or suspected intoxication to 48 hours. Absence of respiration had to be documented by an apnea test and a doctor qualified as a neurologist, neurosurgeon or a pediatric neurologist who was not part of a transplantation team had to participate in the determination of death. Ancillary investigations were to be used only in situations when clinical signs were equivocal or could not be tested. Examples are facial trauma where cranial nerve function cannot be examined, or polyradiculitis, where facial muscles can be paralyzed because of nerve conduction failure. After cranial trauma, arteriography can show absence of cerebral blood flow and prove death, in polyradiculitis involving the cranial nerves, electroencephalography can show cerebral activity and prove existence of life.

In patients with cardiac arrest irreversibility of cessation of brain function was considered proved when cardiac function and circulation did not recover after 30 minutes of uninterrupted resuscitation. Such patients are potential organ donors, so-called 'non heart beating donors'.

The rationale behind the SAMS 1996 guidelines, i.e. the use of an observation period instead of ancillary tests to proof the irreversibility of cessation of brain function was its easy and wide applicability. Such

guidelines could be used in all hospitals, both in hospitals with advanced technical equipment and in small, regional hospitals with limited diagnostic technology.

In 1996 the legal time of death was at the beginning of the observation period (T1). After T1 medical measures to prepare organ donation and transplantation were legally permitted while the dying patient was awaiting confirmation of the diagnosis 'death' until the end of the observation period (T2).

Probably in 2007 a new law relating to transplantation of organs, tissues and cells will become effective in Switzerland. The SAMS guidelines for determination of death will be part of it. This law says that 'medical measures that serve only the conservation of organs, tissues or cells, must not be performed before the death of the donor, except the donor has been informed and has given his or her consent'. The lawyers drawing up this new law felt and determined that the time of death will be at the end of the observation period (T2). Only then medical measures to prepare organ donation and transplantation must be started. Such a change compared to 1996 would make transplantation of organs difficult and many organs and lives would be lost. Therefore, the only way out of this impractical situation was a revision of the 1996 SAMS guidelines and the use of ancillary tests to prove irreversibility of cessation of brain function, similar to guidelines in other countries. With the use of ancillary tests T2 can be moved closer to T1 and death can be diagnosed already shortly after the first observation of absence of brain function.

According to the 2005 SAMS guidelines the proof of irreversible cessation of brain function in a patient with adequate circulation and blood pressure can be made in two ways, either by observing the patient or with the help of ancillary tests. Observation periods are equal to the 1996 guidelines. One minor change relates to the age of a child requiring a 24 hours instead of an 8 hours observation period. It was lowered from 5 to 2 years. Ancillary tests have to prove the intracranial arrest of circulation. For this purpose appropriate are transcranial Doppler sonography, spiral computed tomography,  $^{99m}\text{Tc}$ -HMPAO-Scintigraphy, or intraarterial digital subtraction arteriography. Electrophysiological tests were considered inadequate because of potential false positive results. When cerebral blood flow falls from physiological levels of 40 to 60 ml/100 g white and grey tissue/min below 20 ml/100 g tissue/min electrical function of nerve cells may cease while there is still enough flow to preserve the structures of the brain cells. Therefore, methods demonstrating absence of cerebral blood flow are less

likely than electrophysiological tests and extremely unlikely to yield false positive results, provided that ancillary testing is performed by someone with the appropriate skills. Quality requirements are specialty certifications for the particular test for physicians performing it.

Another change from the 1996 to the 2005 SAMS guidelines concerns 'non heart beating donors'. In patients with persistent cardiac arrest irreversibility of cessation of brain function is proved when uninterrupted resuscitation during at least 20 minutes does not result in recovery of cardiac activity and circulation does not recur after an additional period of 10 minutes observation. If no resuscitation is attempted, an observation period of 10 minutes has to be respected as well.

New to the 2005 guidelines is a section on information and assistance to the patient's family and the therapeutic team. The patient's family, in particular, is faced with unusually severe stress and grief, especially if the death is unexpected. It is essential to inform the patient's family thoroughly, with empathy, in a suitable and calm environment and without time pressure. After an appropriate period of time the family can be asked about possible organ donation. Assistance must be offered to the patient's family not only before death and organ donation. Assistance is needed during and after death and organ donation even more. Special attention has to be paid to the emotional stress of the therapeutic team as well and, if needed, psychological support should be available to team members.

The Swiss guidelines and model protocols for 'The determination of death in the context of organ transplantation' are available at [www.samw.ch](http://www.samw.ch) in German, French, Italian and English.\*

\* This text is also printed in the Annex (see page 335).



## DISCUSSION ON DR. MATTLE'S PAPER

DR. WIJDICKS Thank you very much. A quick question: I noticed there were no neurosurgeons in your team and I wonder whether there was a reason why there was no neurosurgeon involved in the guidelines, is that correct?

DR. MATTLE Yes, that is correct, there was no neurosurgeon in the committee drawing up the guidelines, but the committee was put together by the Swiss Academy of Medical Sciences, we had nothing to say.

DR. WIJDICKS But I presume these guidelines were endorsed by the Swiss neurosurgeons?

DR. MATTLE Yes. Usually when the Swiss Academy of Medical Sciences makes new guidelines they are published in the *Swiss Medical Journal*, *Schweizerische Ärztezeitung*, corresponding to your *JAMA*, and then everybody can send in remarks. It is a written form of finding a consensus.

# THE HISTORICAL EVOLUTION OF BRAIN DEATH FROM FORMER DEFINITIONS OF DEATH: THE HARVARD CRITERIA TO THE PRESENT\*

ROBERT B. DAROFF

Throughout the ages, *death* occurred when breathing ceased, but with the invention of the stethoscope in the early 1800s, loss of the heartbeat became the defining event (Jennett, 2001). The Fourth Edition of Black's Law Dictionary, the definitive treatise of the law in the United States, published in 1951, defined death as the 'cessation of life, defined by physicians as a total stoppage of the circulation of the blood...'. End of life determination was simple, as there were no reliable techniques for resuscitating a non-beating heart and ventilating a breathless patient. Then, in the 1950s and 60s, came resuscitation and ventilation. A heart that stopped could be restarted, and machines could breathe for the patient, which created a situation where patients with no cerebral function were sustained artificially, often for long periods of time. The concept of brain death was thus created by medical progress or, as eloquently stated by Jennett, was 'an artifact of nature resulting from the capacity of medical technology to prolong and distort the process of dying'.

In 1968, the Ad Hoc Committee of the Harvard Medical School, a group of distinguished clinicians and neuroscientists set out to define 'irreversible coma as a new criteria for death'. They aimed to establish criteria, whereby irreversible coma indicated brain death, and therefore, somatic death, and provided two reasons for their efforts. The major one was the burden on patients, their families, and hospitals, whose beds were being occupied by patients with no chance of recovery. The second was the need for a new definition of death, given the advances in organ transplantation. The Harvard Criteria is summarized in Table 1.

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TABLE 1.

<u>Harvard Criteria, 1968</u>	
1.	<u>Deep</u> coma/no withdrawal to painful stimuli
2.	Arreflexia (cranial and spinal)
3.	Apnea (disconnect from ventilator for 3 minutes)
4.	Flat Electroencephalogram (EEG)
5.	Exclusion of hypothermia and drugs
6.	Repeat above evaluation in 24 hours

The patient had to be in 'deep coma'. Coma is 'unarousable unresponsiveness', from which the patient cannot be awakened, and 'deep coma' is when a comatose patient is without spontaneous breathing, doesn't withdraw reflexively from painful stimuli, has no cranial reflexes, and a flat EEG. The 'Apnea Test' (defined in detail at this meeting by Professor Ropper) required disconnection from the ventilator for three minutes without the start of spontaneous breathing. In 24 hours, if the above criteria remained, and hypothermia and sedating drugs were ruled out, brain death was established.

In 1971, two neurosurgeons (Mohandas and Chou) published the 'Minnesota Criteria'. It was similar to the Harvard Criteria, except that the EEG was omitted, the repeat examination was at 12 rather than 24 hours, and the ventilator discontinuation was 4, rather than 3 minutes. But, the most important difference from the Harvard Criteria was the necessity for the patient to have an 'irrefutable intracranial lesion', in addition to the signs of brain death.

In 1976, the United Kingdom Code (Conference 1976a; 1976b) eliminated the need for a repeat exam, and required a specific level of CO<sub>2</sub>, rather than simply time, to determine that the Apnea Test failed to re-establish respirations.

The U.S. Collaborative Study (1997) criteria reintroduced a flat EEG and the repeat exam (this time at 30-60 minutes), but dropped the Apnea Test. For the first time, absent cerebral circulation was added as an optional test.

The U.S. President's Commission (1981) brought back the Apnea Test and required a repeat exam, with cerebral blood flow again added only if needed to make the determination.

TABLE 2.

<u>Pediatric Ad Hoc Task Force, 1987</u>	
Same as adult, EXCEPT:	
1.	EEG and blood flow study recommended in infants less than 1 year of age
2.	Repeat exam dependent upon age:
	<b>7 days–2 months:</b> Two exams and two EEGs, 48 hours apart
	<b>2 months–1 year:</b> As above, but 24 hours apart, OR no repeat exam or EEG in absence of initial blood flow
	<b>1 year and above:</b> Two exams, 12–24 hours apart; EEG and blood flow optional

All the above tests dealt with adults. The pediatric criteria (Guidelines, 1987) had repeat exams depending upon the patient's age, and the first exam could not be done before the seventh day. These are summarized in Table 2.

The highly influential American Academy of Neurology Criteria (1995) provided very strict testing details for the Apnea Test, including delivery of 100% oxygen to prevent the test itself from causing further harm to the brain. EEG and blood flow were, again, not mandatory. The Canadian Neurocritical Care Group (2000) essentially endorsed the American Academy of Neurology Criteria.

Eighty countries share the same criteria used for establishing the loss of cranial reflexes (Wijdicks, 2006). The major differences are in the performance of the Apnea Test, the number of physicians required to confirm the diagnosis, and the need for, and type of, confirmatory tests (electroencephalography, cerebral blood flow, and evoked potentials). The basic criteria are graphically depicted in Wijdicks' pyramid (Figure 1), published in 2004, which also includes the pediatric criteria.

I cannot overemphasize, however, that we *must* adhere to the applicable governing laws wherever the brain death determination is made. As mentioned, these vary somewhat, and despite the guidelines and criteria from commissions and specialty societies, our actions must always conform to the applicable law.

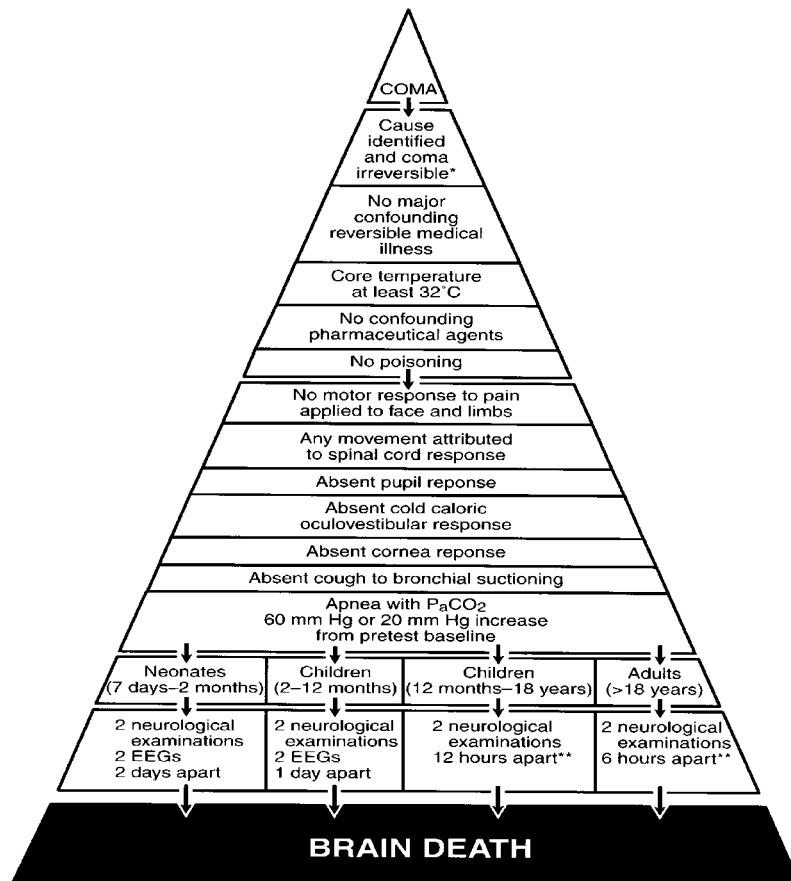


Figure 1. (From Wijdevicks, 2004).

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## NEUROIMAGING: A WINDOW INTO TOTAL BRAIN DESTRUCTION AND THE UNRESPONSIVE STATES\*

JOSÉ C. MASDEU

*Neuroimaging* is the study of the structure and function of the nervous system with techniques that provide anatomical renditions, both static and dynamic, of the nervous system and related structures, information on the physiology of the cerebral circulation, or information on the anatomic distribution over time of biological compounds in the nervous system and related structures. Neuroimaging techniques currently include mainly x-ray angiography, computed tomography (CT), nuclear magnetic resonance – the modality used for magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), magnetic resonance spectroscopy (MRS), diffusion-weighted imaging (DWI), diffusion tensor imaging (DTI) or tractography, functional MRI (fMRI), and perfusion MRI (PWI) – neurosonography, positron emission tomography (PET), single photon emission computed tomography (SPECT) and near infra-red spectroscopy. For the correct interpretation of neuroimaging studies, it is important the correlation of the clinical data with information derived from the various methods used to image the nervous system and related structures.

### *Neuroimaging in the Neurological Diagnosis of Death*

Neuroimaging is not needed for the determination of death by neurological criteria. I prefer not to speak about ‘brain death’ because the issue is not whether the brain is dead, but whether a human being has died. Additionally, speaking about ‘brain death’ often confuses the families of the so-called ‘brain dead’ individual, who end up by asking their physicians whether their loved one – forget about his or her brain – is dead or not [1]. And, to conclude a few considerations on terminology, the terms ‘persistent vegetative state’ and ‘minimally conscious’ state are not felicitous. Bernat

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has pointed out how it would be more appropriate to speak simply about a vegetative state, as a neurological diagnosis, and to enter into the prognostic considerations as a separate step [2]. Furthermore, the diagnosis of a vegetative state is not easy to make. Unresponsive patients may have a degree of cognitive activity unsuspected from their motor manifestations. This has been known to be the case in patients with the 'locked-in-syndrome' (a helpful term), but the tools of neuroimaging are now showing that occasional patients fulfilling criteria for the diagnosis of a vegetative state may not be as vegetative after all [3, 4]. Both the terms vegetative and minimally conscious assume that the examiner knows what is going on inside the patient's brain. It would be much better to use terms that denote both the observed phenomenon and its medical cause. For instance, instead of 'minimally conscious', Bernat has proposed the much more sensible term 'minimally responsive'. After all, what we observe is the patient's response. Leaving aside the issue of whether someone can be minimally conscious from a neurobiological viewpoint, the term minimally responsive has the advantage of assuming less about something difficult to measure [5]. The term 'vegetative state' has been consecrated by use, but an alternative, such as 'chronic neurological unresponsiveness' is much more phenomenological and conveys fewer assumptions. It is also more respectful with the patient in this situation.

Although neuroimaging is not usually needed for the determination of death [6], instances where neuroimaging is helpful include:

- When the clinical diagnosis is uncertain
- In cases with important metabolic derangements that cannot be corrected
- When the brainstem is selectively damaged
- When the brainstem function cannot be adequately assessed clinically, such as in cases with massive facial trauma that render it impossible to evaluate adequately the function of the oculomotor and facial muscles
- In very young children
- Some cultures or countries require the use of ancillary tests as a matter of principle and it is legislated that they be used

The ideal confirmatory test of death by neurological criteria should have no false positives, that is, when positive should be incompatible with the recovery of brain function, should not be influenced by drugs or metabolic disturbances (both of which affect the electroencephalogram) and should be easy to apply. Some neuroimaging tests fulfill these criteria, as indicated in a thorough review of the literature from 1966-2005 [7]. Current Canadian standards for the diagnosis of death accept cerebral angiography and



nuclear medicine perfusion studies for this purpose [7]. Perfusion studies with computed tomography or magnetic resonance could also prove to be suitable, but at present they are more cumbersome to perform than nuclear medicine perfusion studies [7].

An important consideration regarding the use of neuroimaging as an ancillary means for the diagnosis of death is how realistically applicable are each of the neuroimaging techniques in the complex intensive care situation surrounding the diagnosis of death by neurological criteria. For instance, the required respiratory and cardiovascular support may not be available at the radiology department where some of these procedures are usually performed. In a study of patients with a recent cardiac arrest and anoxic brain damage, 17 of 27 (63%) patients could not be safely transported to the radiology suite to undergo MRI [8]. If accurate, more mobile techniques that can be used in the ICU would be preferable.

### *Computed Tomography*

CT is used mainly to rule out potentially treatable lesions in patients suspected of brain death. For instance, after head trauma a massive subdural hematoma may be a treatable cause of unresponsiveness. When the process has caused irreparable brain damage, the findings on CT are diffuse cerebral edema with loss of gray-white matter differentiation and transtentorial herniation in about 80% of patients [9]. These findings are not specific for the total destruction of the brain and therefore CT alone helps little in the diagnosis of death. Perfusion CT techniques could prove helpful. For instance in a patient with very severe head trauma arriving intubated to a hospital, CT with perfusion could be used to diagnose both the lack of treatable pathology and the irreversible cessation of brain activity by the lack of perfusion in the entire brain [10]. The absence of internal cerebral vein opacification coupled with the lack of bilateral enhancement of cortical MCA branches have been proposed as characteristic findings of brain death on contrast enhanced spiral CT [11]. Perfusion CT will be greatly facilitated by the new 64-slice multidetector-row CT technology. A 64-slice CT scanner provides high-resolution 3D reconstructions and is capable of acquiring images from the aortic arch to the vertex in 11 to 16 seconds [12]. Thus, once the patient is positioned in the scanner, with the appropriate respiratory and cardiovascular support, diagnostic images can be obtained in minutes. There is yet little experience with this technique.

### *Magnetic Resonance Imaging*

As CT, MRI can be used to diagnose treatable pathology in patients with severe brain damage. Even when there is no treatable pathology, MRI renders a clear picture of the status of the brain. For instance, in a man with no brain stem responses after a road traffic accident, on MRI there was diffuse swelling of the cerebral gyri and cerebellar cortex, which showed prolongation of both the T1 and T2 signal with a decrease in apparent diffusion coefficient indicating hypoxic ischemic brain injury, Duret hemorrhages in the midbrain, and downward displacement of the diencephalon and the brain stem, indicating both central and tonsillar herniation [13]. As ominous as these findings are, their specificity is not high enough to define irreversible brain damage. In small series, lack of filling of the major intracranial arteries has been seen on MR angiography [13, 14]. Perfusion MR still lacks specificity defining irreversible tissue damage [15, 16].

### *Conventional Angiography*

An effect of many of the causes of irreversible brain damage, such as trauma or ischemia, is massive brain edema [17]. The molecular mechanisms are still poorly understood, but they involve all cellular components of the brain, including neurons and astrocytes [18]. Neuronal death is accompanied by a cessation of the membrane function consisting of extruding sodium from the neuron. As a result, sodium pours into the neuron and, following the sodium, water. The dead neuron swells, giving rise to what is known as *cytotoxic edema*. Massive brain edema leads to a greatly increased intracranial pressure [17]. When the intracranial pressure rises above the mean perfusion pressure of the proximal cranial arteries, blood perfusion through the brain ceases (*'brain tamponade'*) and quick ischemic destruction of the entire brain ensues. The lack of arterial perfusion of the brain can be imaged by conventional angiography. This procedure requires the injection of a non-ionic contrast media into the intracranial arteries. Each of the two carotid and vertebral arteries are injected through femoral catheterization. Once the patient is in the radiology suite, angiography takes about 20 minutes to perform [19]. This procedure is still required for the neurological diagnosis of death in some countries (e.g., Greece) and it is generally performed once the clinical diagnosis has been made, including the apnea test. The characteristic finding is absent filling of the intracranial arteries at the entry into the skull, although minimal intracranial arterial opacification is

compatible with the diagnosis of death. There should be absent flow in the parenchymal and venous phases of angiography.

Conventional angiography is not without risks, or ambiguities at the time of interpretation of the findings. The procedure is usually performed in the department of radiology, where critical care support may not be sufficient [8]. There is a concern about possible added vasospasm caused by the contrast medium in the intracranial vessels, thus causing cessation of blood flow in vessels that before the procedure remained patent. If the procedure has to be repeated, a local hematoma at the femoral puncture site may prevent repetition. Although unlikely, the contrast medium may cause damage to transplantable organs, particularly the kidneys, of dead donors. Finally, contrast agents could be artifactually introduced into the intracranial circulation with pressure injection or a dependent head, causing the impression of intracranial circulation where there is none [13].

#### *Neurosonography*

Circulation in the proximal intracranial vessels can be assessed by means of transcranial Doppler ultrasonography (TCD) and transcranial color-coded sonography (TCCS). An American Academy of Neurology practice guideline about the use of this technique concludes that TCD and TCCS provide important information and may have value for the detection of cerebral circulatory arrest/brain death (Type A, Class II) [20]. On TCD, the normal pattern observed from the flow in the proximal intracranial vessels is of higher systolic peaks and lower diastolic valleys, each peak following the arterial wave caused by the contraction of the heart. Even the diastolic valleys show flow in the arterial direction, of a smaller velocity than during the systolic phase. By contrast, in someone with arrested intracranial circulation, there are brief systolic peaks or spikes followed by an absent or even inverted diastolic flow. Systolic spikes are sharp unidirectional velocity signals in early systole of less than 200 ms duration, less than 50 cm/s peak systolic velocity, and without a flow signal during the remaining cardiac cycle [21]. Transcranial color-coded sonography (TCCS) may show in a vessel the forward arterial flow during the brief systolic peak, coded in red, and, in the same arterial segment, a diastolic reflow, coded in blue (*oscillating flow*). The pulsating flashing pattern is akin to that of a beacon, the *beacon sign* of intracranial circulatory arrest [19]. The Neurosonology Research Group of the World Federation of Neurology has published TCD criteria for the diagnosis of

death [21]. Once the clinical diagnosis of brain death has been established, cerebral circulatory arrest can be confirmed if the following extra- and intracranial Doppler sonographic findings have been recorded and documented both intra- and extracranially and bilaterally on two examinations at an interval of at least 30 min.

Systolic spikes or oscillating flow in any cerebral artery which can be recorded by bilateral transcranial insonation of the internal carotid and middle cerebral arteries, respectively any branch or other artery which can be recorded (anterior and posterior circulation). This pattern has to be recorded in at least two different arteries – the vertebrobasilar system counting as one artery.

No signal in the remaining arteries. Transitory patterns between oscillating flow and systolic spikes may be seen.

The diagnosis established by the intracranial examination must be confirmed by the extracranial bilateral recording of the common carotid artery, internal carotid artery and vertebral artery.

The lack of a signal during transcranial insonation of the basal cerebral arteries is not a reliable finding because this can be due to transmission problems. But the disappearance of previously recorded intracranial flow signals in conjunction with typical extracranial signals can be accepted as proof of circulatory arrest.

Ventricular drains or large openings of the skull like in decompressive craniectomy possibly interfering with the development of the ICP are not present.

These are the strictest criteria. Other diagnostic criteria for cerebral circulatory arrest/brain death by TCD have been published, with sensitivity and specificity of 91 to 100% and 97 to 100%, respectively [20]. In a meta-analysis of 280 cases with angiographic confirmation, there were no false positives following the criteria indicated above [19, 21]. However, in some of these studies, angiography was performed first, such that the neurosonographer was not blinded to the angiographic findings [19].

TCD is especially helpful in patients with suspected brain death who have loss of brainstem function due to isolated brainstem lesions or who received sedative or paralytic agents that render clinical examination or interpretation of EEG difficult. Because in some patients ultrasound does not penetrate well the skull (lack of a '*bone window*') and other technical factors, TCD cannot be performed in all patients. At an institution with experience in neurosonography, TCD may not technically feasible in approximately 10% of clinically brain-dead patients [19].

### *Radionuclide Angiography*

Radionuclide angiography is performed by injecting a radionuclide that remains in the circulatory system of the patient. A gamma camera is used to record the photons emitted by the radionuclide as it flows through the arteries, capillaries and veins of the brain. This intracranial flow is absent when someone has died because of brain destruction. Neuropathologically, six patients without intracranial flow for 20 hours had diffuse brain necrosis and autolysis, whereas six patients with residual flow at the time of radionuclide study had on autopsy less extensive necrosis and evidence of active tissue response [22, 23]. One problem with this technique is that it does not allow a good visualization of the perfusion of posterior fossa structures. For this reason, its sensitivity and specificity have been reported to be 0,97 and 0,67 respectively [24].

### *SPECT*

Single photon emission computed tomography is performed injecting intravenously an isotope, such as technetium, bound to a substance, as HMPAO or ECD, which is highly lipophilic and therefore crosses the blood-brain barrier and binds preferentially to brain. After an injection of one of these substances ( $^{99}\text{Tc}$ -HMPAO or  $^{99}\text{Tc}$ -ECD), the isotope binds to the brain, but clears from the tissues surrounding the brain in less than 30 minutes. Thus, the activity from those tissues does not obscure true brain activity, as happens with conventional radionuclide angiography. As the half life of  $^{99}\text{Tc}$  is 6.01 hours, the patient can be scanned several hours after injection, obtaining a snap shot of brain perfusion as it was a few minutes after injection. The patient can be injected in the ICU and images can later be recorded in the Nuclear Medicine Department. There is no need to do tomography: anterior and lateral planar views are sufficient, requiring only about 10 minutes to perform. With a portable gamma camera, images can be obtained even at the ICU.

SPECT depicts regional cerebral perfusion. As there is no perfusion after '*brain tamponade*', a characteristic pattern appears, called the '*empty skull*' pattern [25]. Activity in the skull and tissues at the base of the brain outline a space, normally occupied by the brain, that in this case is empty. The finding is so striking that it has also been called '*functional decapitation*'. The study of brain perfusion with SPECT agents is more accurate than with radionuclide angiography, because the posterior fossa can be well visualized. In 10 small series, the largest one comprised of 50 patients, there was

not a single false positive in the 193 patients studied [9, 25-33]. SPECT was independently compared to angiography in only 20 patients. In a study without angiographic control, two patients had a flat EEG, but SPECT showed evidence of brain perfusion, ruling out the diagnosis of death.

### *PET*

The findings with metabolic positron emission tomography ( $^{18}\text{F}$ -fluorodeoxyglucose [FDG] PET) mirror the findings with SPECT. Metabolic activity in the tissues surrounding the ametabolic brain gives the impression of an empty skull [34]. Also with this technique can be clearly shown the functional decapitation that results from total brain destruction. PET is more cumbersome than SPECT for the diagnosis of brain death and it is not generally used for this purpose.

### *Neuroimaging in the Unresponsive States*

Whereas the diagnosis of death based on neurological criteria can be made with a high degree of certainty, based on clinical criteria and, in some cases, with the use of ancillary means such as neuroimaging, the same cannot be said about the so-called vegetative state, which I prefer to call chronic neurological unresponsiveness (CNU). Unresponsiveness or poor responsiveness, as in the minimally responsive state (also called 'minimally conscious state'), usually results from severe brain damage, but there are instances when a surprising amount of brain activity remains in someone who is unable to let others know about it. Almost by definition, a situation such as this would be referred to in the neurological literature as the 'locked-in state'. However, the differentiation of these states requires determining which anatomical structures have been damaged. This determination is carried out with neuroimaging. Neuroimaging provides also a window into some of the mechanisms underlying brain plasticity and recovery, in patients who evolve from chronic neurological unresponsiveness to a minimally responsive state or even to wakefulness.

### *Chronic Neurological Unresponsiveness (Vegetative State)*

Structural brain imaging, such as CT or MRI, is particularly helpful in the acute stage leading to CNU, in order to rule out treatable lesions, such as a subdural hematoma after head trauma. They also provide an image of brain structures in the chronic evolution after severe brain damage. However, CT

or MRI images do not provide information on the activity of the residual brain structures. Regional metabolic activity can be sampled with FDG-PET, typically greatly reduced in CNU [35]. Responsiveness to external stimuli can be better studied with techniques that show transient increases in regional cerebral blood flow, such as water-PET ( $^{15}\text{O}$   $\text{H}_2$ -PET) or the study of the BOLD signal with functional magnetic resonance imaging. Several authors have made the observation that in CNU only the primary cortices become activated with sensory stimulation, whereas in the minimally responsive state also some areas of the association cortex can become active [34, 36].

Using FDG-PET, Schiff *et al.* were able to show a correspondence between metabolically active areas of the brain and the remaining activity observable in each patient. For instance, a 52-year-old man with postoperative asphyxia after cosmetic surgery had been in a vegetative state for 6-months. During wakefulness, he had spontaneous non-directed choreiform movements of the head, trunk and extremities. The authors described this behavioral pattern as a hyperkinetic vegetative state. Structures known to become activated with motor activity, such as the cerebellar vermis, central tegmental region, medial thalamus and the medial aspect of the frontal lobe, had a relatively spared metabolism in this patient. A 49-year-old woman with hemorrhages from a right hemispheric arteriovenous malformation, who had been unresponsive for 25 years, uttered single words in small clusters. This behavioral fragment corresponded to a less-damaged left perisylvian region. Metabolic studies can also show the critical importance of some brain regions for the organization of cortical activity and, therefore, for normal wakefulness. For instance, a 26-year-old male who had been unresponsive for 6 years after a motor vehicle accident had only targetless roving eye movements and posturing (without baseline spasticity) to exogenous stimuli. However, he had near-normal cortical metabolism but damaged medial thalamus and mesencephalon, illustrating the important contribution of these structures to organized behavior [36].

More striking is the recent finding of a normal brain response, detected by functional neuroimaging, in a young woman with CNU [3]. After a traumatic brain injury from a traffic accident occurred eleven months earlier, she remained unresponsive with preserved sleep-wake cycles, in a situation that met criteria for the vegetative state [37]. In an untrained situation, she was given spoken instructions to perform two mental imagery tasks: (1) to imagine that she was playing tennis, and (2) to imagine visiting all of the rooms of her house, starting from the front door. On fMRI, she generated the same BOLD response patterns as the controls, widely different for either task. (3)

Extensive areas of activation, approaching in some cases normal patterns, have been observed in patients in the minimally responsive ('minimally conscious') state [38, 39].

*Brain Mechanisms of Recovery: From Unresponsiveness to Responsiveness*

Finally, neuroimaging has also been used to try to understand the neurobiological mechanisms that underlie recovery from states of unresponsiveness. Such knowledge could have important implications for the design of more effective rehabilitation strategies. Looking at the entire brain metabolism of a 40-year-old woman in coma after CO poisoning, Laureys studied which parts of the brain were critical for the coordinated behavior of normal wakefulness [40]. Normalization of activity in the superior parietal lobule, including the precuneus, signaled the change from a cyclical unresponsive awakening by day 14 to regaining consciousness by day 19. FDG-PET studies were performed on days 15 and 37. Global glucose utilization remained the same in both scans and it was diminished by 38% compared to 48 normal controls. Laureys attributed recovery to the normalization of activity in the medial occipito-parietal region (MOP) [40]. This area has shown the most consistent impairment in PET studies of the postanoxic syndrome [41].

A recent study shows a neuroimaging pattern that suggests axonal reorganization during recovery [42]. This 19-year-old man had been involved in a motor vehicle accident with closed head injury. After a period of 2 weeks in coma, he was in a vegetative state for several months and had improved to a minimally responsive state in which he had been for 19 years. He was unable to communicate, either by gestures or by words. He made inconsistent head nodding or grunting. Then, 19 years after the accident, he said his first word: 'Mom'. In a few days he had dysarthric but fluent, logorrheic, speech. He was then studied for the first time. He had impaired phonemic and semantic fluency. On MR tractography (diffusion tensor imaging) there were abnormal fibers in the left medial-parieto-occipital region. These fibers were not present in controls. When studied in a similar manner 18 months later, these fibers had disappeared and there was a reorganization toward normalcy of cerebellar vermis fibers [42]. In this period of time, there had been an improvement in logorrhea and in motor function, including cerebellar function. Anosognosia remained [42]. Although this was a carefully designed and interpreted study, more experience with tractography is needed to determine its usefulness in evaluating brain changes in the recovery from the unresponsive states.



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## DISCUSSION ON DR. MASDEU'S PAPER

DR. DEECKE In Austria there was a case of waking up from vegetative state (apallic syndrome) after six years, I think there are examples also in other countries, and I believe the reason is that the reticular formation reconnects. Would you also say this?

DR. MASDEU The recovery may originate in the brain stem reticular formation or in a very complex network of structures that may include mesial frontal lobe, and mesial parietal lobe. In some patients with brain stem damage exclusively, like the man we saw in the paper, or the person with the damage primarily in the upper brain stem and thalamus, sure, the recovery will depend on the recovery of the brain stem circuits. In some other patients I think it could be much more complex. Your question is extremely interesting because it precisely highlights how, without neuroimaging, it is very difficult behaviourally to define the structures responsible for the vegetative state. You do not know why they are waking up. But with neuroimaging you can tell someone with a brain stem awakening from someone with a cortical awakening.

DR. DEECKE Another question is whether you have experience with electrical stimulation. In France, as you know, they have been able to wake up coma patients by electrical stimulation of the thalamus. I think this was done in Prof. Benabid's group.

DR. MASDEU I am familiar with some of the work but not specifically with this case that you mentioned. That would be extremely interesting. One of the things that neuroimaging allows us to do, as you point out, is to use transcranial magnetic stimulation to be able to see what happens with different parts of the brain when we excite or depress them.

DR. DEECKE Thalamic electro-stimulation is done through indwelling electrodes, like deep brain stimulation in parkinsonian patients.

DR. MASDEU Yes, I was not aware of that.

DR. PUYBASSET Can we look back at the tennis playing girl, the Owen case, just to look at the MRI. When you look at that, it looks like there is no brain atrophy or brain lesion.

DR. MASDEU It is interesting that you bring it, up because one of the things that makes this case rather credible is the rather obvious traumatic lesion on the MRI of the patient. Look at the skull of the normal control (pointing to the screen). By contrast, follow the skull of the patient, in the frontal region. There is a fracture there, this is unquestionably very different from the normal people. The fracture can also be seen here (pointing to the screen). This woman had two subdural hematomas evacuated. The other thing that strikes me is, look at the midline structures, how neatly they can be seen in the normal control. In this woman there is some degree of atrophy, the midline is not normal, this is not a normal MRI of an individual, so this woman has a considerable amount of structural abnormality and yet the functional study is remarkably neat. There is less damage laterally, but there is still damage. Fortunately, I think that the temporal lobe did not suffer a lot, although it is abnormal compared with the normal medial temporal region, which is nice and taut. Here (pointing to the control brain), you do not see either the perimesencephalic cistern or the temporal horn of the lateral ventricle. Here (pointing to the patient's brain) you see it quite well, suggesting that there is some atrophy in this region. This is a very young woman, she should not have all this space in here. So, in terms of the MRI, I am fairly convinced that this woman sustained a fair amount of damage.

DR. PUYBASSET Did she have a craniectomy? She had a major edema and they did not put the bone back. Yes, that is why we see that here.

DR. MASDEU Yes, you can see it. Compare this (pointing to normal skull) to that (pointing to the patient's skull).

## THE APNEA TEST AND RATIONALE FOR BRAIN DEATH AS DEATH\*

ALLAN H. ROPPER

I have been asked to address two subjects that are importantly related. One is a technical one on apnea, and because of this knowledgeable audience and the fact that it is essentially a technical issue, I am going to move through it fairly quickly. There are a few open questions in the apnea test, but they are essential to address. It is the last step in defining death and therefore requires the careful attention of clinicians. The second part of my paper is broader and addresses the medical and neurological reasons to consider brain death as death. It is largely a recapitulation of our talks over the past two days on this subject and I would hope to emphasize the central points and develop one or two particular themes.

### *The Special Significance of Apnea*

Apnea has special significance in all discussions about death because it indicates that the medulla, the most rudimentary part of the brain, is damaged and implies that other vital functions that require a degree of central nervous system control will be likewise damaged. In the proper context, apnea is the last technical step in the diagnosis of brain death. Apnea is further essential to the medical argument for the equivalence of brain death and death, because ultimate cardiopulmonary collapse is driven by the notion that the bodily systems cannot sustain themselves indefinitely without a form of gas exchange and that, with the withdrawal of the artifice of a ventilator, the rest of the corpus will dissolve. This argument is based on 'ventilation' as the last step in death, not on 'respiration', a point I to which I will return. Neurologists, from their own observations, can emphatically state that removing the ventilator, if the apnea test has been performed properly, inevitably leads to cardiovascular collapse. For this reason, the loss of ventilation leads to the loss of cellular respiration, and then to death of the entire organism.

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the general discussion are those of the participants and not necessarily those of the Academy.

*Context of the Apnea Test*

The test is performed only after all other features of complete unresponsivity (the inability to perceive environmental change) and unresponsivity (the inability to volitionally alter the environment) have been established and all other brain stem reflexes have been demonstrated to be abolished. As it is a technically demanding, and not a casual test, individuals who are highly familiar with brain death, not surrogates, should perform it, a point emphasized further on.

*Conduct of the Apnea Test*

There are a few technical issues in apnea testing but they have given rise to considerable study and some controversy. The first is that the current recommendations of the American Academy of Neurology suggest that there be apneic oxygenation to denitrogenate the alveoli, and thus create a pool of high concentration alveolar oxygen that causes passive diffusion of oxygen into the blood. I was a little bit disappointed to hear that an inspired fraction of 100% oxygen was recommended. The concern is that this kind of extreme denitrogenation rapidly leads to alveolar collapse and a degree of atelectasis that may itself lead to hypoxemia and cause the test to be shortened. I will not argue with this component of the technique since it is usually possible to get away with it if the test goes no longer than several minutes. I do, however, encourage some clinical investigation on the 100% preoxygenation approach and would expect that the patient's pulmonary status, length of time on a ventilator, recent inspired oxygen fraction and ventilator tidal volumes, and degree of humidification, would all contribute to the rapidity of atelectasis.

Another option in the apnea test is to determine the initial carbon dioxide tension in the blood. The ventilator is then removed for a period that is anticipated to produce a partial pressure of carbon dioxide that is high enough to drive the medulla and at the conclusion of the test. The end level of carbon dioxide is measured in order to demonstrate that it has exceeded a threshold that is believed to stimulate spontaneous breathing, even in a sick brain, but not in a brain that is dead. A third option relates to accelerating the test by insufflating carbon dioxide at the outset so that the starting level is closer to the desired end level. Both of these approaches would benefit from more investigation but they are in common use at this time and do not alter the larger perspective on

whether brain death and death are equivalent. Leaving the patient on continuous positive airway pressure or on a very low ventilator rate seem reasonable, rather than entirely disconnecting from the machine, but these techniques could benefit from further study. While there have been series of patients that suggest otherwise, I am concerned about the delivery of oxygen by a T-piece since there is potential for a Venturi-effect to pull oxygen out of the endotracheal tube and cause desaturation. Perhaps this concern is excessive. The potential for pneumothorax caused by a tracheal cannula should also be mentioned here.

I think that most physicians would agree that there is no conventional way to make the diagnosis of brain death until after this test is done and after some pre-specified threshold of arterial carbon dioxide has been exceeded. Therefore, the patient should be reconnected to the ventilator while the clinician waits for the result of the ending arterial carbon dioxide tension. It is a little bit paradoxical to carry out the test in this way but it is mainly for reasons of certainty that an adequate stimulus has been reached.

One could imagine circumstances in which the patient's prior wishes, the family or the clinician have determined that no transplantation will take place and that continuing ventilation is futile in view of brain death. In this case the ventilator could simply be left off to observe the absence of spontaneous breathing until cardiovascular function fails. While not strictly a technical issue relating to apnea, this latter scenario speaks to the essential equivalence of death and brain death since, had the ventilator not been initiated in the first place, there would be little need to go through the intermediate step of documenting the extreme degree of brain damage that characterizes brain death; the patient would simply die in what would have been considered a more conventional cardiovascular manner.

To address concerns of risk from apnea testing, and in part to balance what have been disingenuous arguments against brain death, there is general agreement that the test should be stopped if there is profound blood oxygen desaturation or if the blood pressure drops. There is always, of course, an intent to prevent inadvertent harm to what still might be a living patient, until it is clear that the medulla is damaged as reflected by apnea. Finally, one of the most curious things that I have observed is a lack of visual and tactile attention to the patient's thorax and abdomen during the test. Causal inspection of movement of the ventilator needle is not enough to determine if the patient is breathing. These are self-evident but perhaps need to be said.



*Additional Concerns Expressed About the Apnea Test*

The singular significance of the apnea test makes it desirable that it not be fallible, in other words that it not give a false positive result. The best protection against this is to emphasize to all physicians who might be participating in determining brain death that there are guidelines for the conduct of the test and they should be followed. Moreover, the proper personnel should perform the test after all of the usual exclusions have been addressed. Preferably, these are neurologists, neurosurgeons or intensivists who have experience with the test. Whether individual hospitals, local medical societies or other official entities should identify or certify such individuals is uncertain.

There should however be no ambiguity about the result of the test; the patient either breathes or does not breath. The result is binary. There are numerous potential misinterpretations and false negatives. The most common of these, and the one I think has created a degree of public fear, is the peculiar and stunning movements of the thorax, shoulders, arms that are known to occur minutes after the ventilator has terminally removed but may rarely occur at the end of the apnea test, most often associated with a degree of hypoxemia or hypotension. The intercostal muscles appear not to be involved because we have put EMG electrodes into them and do not find activity. These bizarre movements, which I coined in a 1984 Archives of Neurology paper as 'Lazarus phenomena', do not represent breathing. They do not provide ventilation and are not medullary in origin since they are seen in spinal man.

The second concern that has been expressed is that somehow the test could lead to death, or is risky or cruel. Again, this is ostensibly avoided by attending to details and to guidelines. After thirty-five years of studying the apnea test and refining the guidelines, they by and large prevent harm to somebody who may not yet have a totally destroyed brain.

The third misconception that is worth brief comment has been that apnea is itself death. This would be an extension, or an extreme, of the brain stem definitions of death as opposed to the whole brain definition of death. This view accords roughly with a classical view that loss of breath is loss of life. Virtually all clinicians, with some exceptions, have a larger context of brain death. The significance of the apnea test in this larger context, however, is limited to indicating that there is overwhelming medullary damage and the absence of self-sustainable breathing.

*Adequate Threshold of PaCO<sub>2</sub> to Stimulate Breathing*

This technical aspect of the apnea test has a long history but scant data. Dr. Plum's early work on post-hyperventilation apnea in brain damaged patients set the bar at 60 mm Hg as an adequate stimulus. As best I am able to determine, this is where the number 60 originated. In his work, patients with very large strokes who were hyperventilated, and then had the ventilator stopped, in a few cases did not breathe again until the arterial CO<sub>2</sub> tension exceeded 60 (actually, it was 65). I would point out that this model of medullary stimulation by CO<sub>2</sub> has little to do with brain death. The patients he studied had intact medullas and cerebrums, both structures participating in the control of breathing.

In the case of brain death we have some systematic experience with the CO<sub>2</sub> threshold, the biggest one being Rudolf's study that showed no advantage to going above 60 in the apnea test. Our own paper in the 1980s studied four patients with overwhelming brain damage but who were not brain dead solely because they had residual signs of medullary function. They had deep unresponsive coma, unreactive pupils, and no caloric-induced eye movements. For these reasons, we considered them to be as close as possible to brain death but they clearly breathed. It seemed that it was this ideal configuration to determine the CO<sub>2</sub> threshold that separated brain dead patients from those who 'almost' qualified for brain death and the group to study in order to prevent false positive apnea tests that would misclassify a patient as brain dead. We posed the question: What does it take to make a very damaged brain breathe? The result was that they all breathed in the range of PaCO<sub>2</sub> in the mid-30s mm Hg. Dr. Wijdicks has given his own experience in a previous lecture here. The patients he studied breathed at levels below 40 or into the low 40s. Based in these observations, and acknowledging perhaps 3 exceptional published cases in which a stimulus of 65 was apparently required, I think 60 is a safe target. We can perhaps have a discussion about that.

An associated question is when to stop the test and draw an arterial blood sample. What is the appropriate time to leave the patient off the ventilator? I have no particular recommendation, but my practice has been to calculate an endpoint based on the starting PaCO<sub>2</sub> (which requires that an initial gas be drawn) and use the formula that carbon dioxide goes up 2.5 mm Hg, on average, per minute in a euthermic patient. The rate needs to be adjusted for hypo- or hyperthermic patients. This model allows a reasonable estimation of the duration of the test, and determines when to check the CO<sub>2</sub>, return the patient to the ventilator, and establish that the preselected adequate thresh-

old has been met. If the arterial  $p\text{CO}_2$  is found to be too low at the end of the test, it allows new calculation based on the rate of change observed in that individual and the test must be repeated.

A final technical question is what to do in patients with COPD (chronic obstructive pulmonary disease). This is an issue that relates to the fact that these people chronically require or are accommodated to high  $\text{CO}_2$  and therefore need a hypoxic drive and a higher  $\text{CO}_2$  drive to stimulate breathing. We have studied several such patients and if they had been on a ventilator for 12 hours, their pH returned to normal and it no longer appeared that an excessive respiratory drive was necessary. If an apnea test is required before about twelve hours on the ventilator with normal  $\text{PaCO}_2$ , then there may be a problem and a target above 65 mm Hg should be chosen.

#### *Potential Serious Complications of Apnea Testing*

Hypotension is the most common complication and it is probably the result of hypoxia, and generally relates to inadequate preoxygenation. This can be eliminated for the most part by careful preparation as I have already discussed. Goudreau, Wijdicks and Emery from the Mayo Clinic indicated said that there was some degree of hypotension in 24% of patients overall and 15% had inadequate preparation. Twelve percent in Saposnik's series had hypotension and 1 had a cardiac arrest during the apnea test in 129 cases. Hypotension was said not occur if the pH was kept above 7.2 in a study from the Canadian Journal of Anaesthesiology. Hypercarbia and acidosis do not, however, seem to reach a severity that they become physiologic problems. I mention them because there is a paper that suggests them as theoretical problems.

#### *Why Brain Death?*

The reason we are here, is why brain death? And why death? I am not presumptuous enough to give an answer but maybe to guide one with the group. If we take the perspective that medicine has nothing, or little, to say about death, then there is not much point to further discourse. However, there is and always has been a medical perspective on death and it is sensible to attend to the medical perspective from a personal, societal, and technical point of view. Furthermore, brain death, being a contrivance brought about entirely by modern medicine, demands that a perspective be given by from physicians, even if this is only to be integrated with a philo-

sophical and theological perspective. Medicine is in a position to give an opinion on whether brain death is *equal* to death and whether brain death is *equivalent* to death. These are, of course, subtly different, and the differences in these phrases has led to terminological or semantic confusion that continues in part because there is a difference between being brain dead, as an event, and being on the way to dying. I do not know if medicine will be able to get at the precise moment of death as discussed below but medicine is a practical science and society needs medicine to be practical. Medicine, however, is not meant to be expedient; in other words care must be taken not to frame brain death as driven by transplantation.

### *Medical Meaning of Death*

The definition of death has continuously changed as has been elaborated by previous speakers. Someone whose heart stopped before 1947 was dead because external defibrillation had not yet been applied. In fact, many people, right up to 1969, when defibrillation was widely available, were dead. Someone with overwhelming brain injury prior to 1948, when Drinker introduced the negative pressure ventilator, or 1953 when Ibsen's mechanical positive pressure ventilator was applied, was essentially dead. An individual with overwhelming brain injury in the future might theoretically be resuscitated by some extraordinary scientific discovery but medicine has not evolved to that point. In fact these inceptions are not gradual, but stepwise change the definition of death by necessity. Medicine has done what it must adapt to by the changing of technology that is able to sustain bodily function.

### *The Time of Death*

It may be difficult to accept that the time of death has an element of arbitrariness. One hopes for a definition of death that is not arbitrary. We are adapting to our ability to measure survival of components of the organism that we deem are necessary for persistent life, the opposite of persistent death. John Paul II in 2000, in fact, said the exact moment cannot be precisely determined but there are biological signs that a person has indeed died. This is the practical medical view and is a reasonable starting point. I would repeat that the 'problem' of brain death has been created solely as the result of artificial ventilation and associated intensive care technology, as Dr. Hacke and other speakers have indicated. It is a given that artificial ventilation and other supportive techniques, including fluid and hormone

replacement and pressors, the medications that support blood pressure, are interposed elements between life and death, without which there would quickly be a complete cessation of ventilation and then very quickly, thereafter, complete loss of cellular respiration and the dissolution of the corpus.

So there is a dual medical rationale for brain death as death. The first is the idea that technology, and in particular the ventilator, of which apnea is the measure, 'masks' the cardiovascular collapse of the body, which is an inevitable, inexorable first step towards the loss of all cellular metabolism and all life. The second and perhaps more important rationale, and the one that needs to be articulated, is that this is irreversible AND inevitable. It is more than just permanent. Permanent means indefinite for now; until some extraordinary advance comes along brain death is inevitably and inexorably equivalent to death. With regard to the exact time of this event, I do not find appealing the idea that it occurs when a physician walks over and writes a note in the chart that the patient is brain dead, but I have no better way of defining the timing of death.

The medical-philosophical backdrop to this is deeper. It does indeed have to do with unity and integration of the organism and to the personhood and consciousness that goes along with the functioning of the brain. The brain must define, in some way, this personhood, and it must embody it. If it does not, then medicine has no starting point in the discussion of brain death and all further polemic is non-medical. Therefore, there are two durable, technical, current, temporal reasons to think of brain death as death and there is a larger philosophical backdrop.

I would make note also of the 1989 address by Pope John Paul II, to the Pontifical Academy of Sciences that '(Death) occurs when the spiritual principle, which ensures the unity of the individual, can no longer exercise its functions in and upon the organism, whose elements, left to themselves, disintegrate'. To me there are two elemental phrases here: 'the unity of the individual' and 'cannot exercise its functions whose elements, left to themselves, disintegrate'. That is indeed the medical view. You cannot say it any better. It is a disintegration predicated on this interposed technology.

### *Brain Death is Unique*

Brain death, of course, is unique, as we have heard repeatedly. The brain dead body in a medical view is just a collection of artificially supported organs and cardiorespiratory collapse occurs in almost most cases in some fixed period, that is, even without removing the ventilator. Dr.

Wijdicks expressed the opinion in our conversation the night before last that it happens in *every* patient. Without getting into this uncertainty, and acknowledging that it is very difficult to sustain a brain dead body for any length of time, if the artifice of the ventilator is removed, death is inexorable. I would remind everyone that we have arrived at a point where the differentiation between withholding (initiating) and withdrawing care in a critically ill patient has no distinction, morally, ethically and medically. Socially, it is harder to persuade lay people of the equivalence. Since the collapse is inevitable, arguing about the interval, the precise moment, is really not practical for the physician, because the goal posts of the football game are just moved and moved and moved, based on current technology.

#### *Technical Issues and Misdirection*

Dr. Shewmon has made some excellent points but I believe that there is misdirection and in two slides I would like to summarise why, but again I cannot speak for the group, so I am just going to create the theme. Let me address some of the arguments that have been made against brain death as death.

If one argues that people are constantly making mistakes in the application of brain death criteria and in the apnea test, that is a problem. Does it negate brain death? Of course not; it is a competency and professional issue. We have to educate our colleagues and insist on the highest standards. The risk of the apnea test as a refutation of brain death similarly makes no sense. Posturing and bodily movements have been pointed out as part of the common sense evidence that brain death is not death. How could a dead body move? I think we have had that discussion. You can cut the head off and the body can move; the brain is not required. The necessity for the entire brain to be necrotic has been raised as an objection to brain death. The example that is given is the retention of the antidiuretic hormone made in the posterior hypothalamus and elaborated in the back of the pituitary and so on and so forth. This would indicate that the entire brain, every cell, is not dead. Again, in medicine we make practical distinctions that are useful and valid and we acknowledge that it is not possible to know if every cell is dead. If every cell in the brain is not dead now, it surely will be very soon, but in any case, the brain is not working as the organ is meant to, in a unitary way. This issue of every cell not being dead is not valid as an objection to brain death. If one brings this argument to the reductionist level of every cell being dead, then we are similarly obliged to

await the cessation of all bodily cellular respiration before declaring death has occurred and this is a practical impossibility. We would be sitting in the mortuary with patients for a day or two. And if you put them in a cooler, for maybe longer.

There has been an argument that different definitions or criteria for brain death in different jurisdictions point to the fact that we are in disarray and the definitions are arbitrary. The differences are subtleties; they are not about brain death as death. They have instead to do with minor criteria and perhaps the pride of medical societies that need to have their say in the matter.

The purported 'awakenings' from brain death I think we can all dismiss. These are reported in the press by persons ill equipped and ill informed about the criteria for brain death. At the risk of sounding glib, I would say it is nonsense. I will dwell for a moment on the lack of validity of published statements that cardiovascular collapse is easy to prevent. I can attest to the fact that these claims are not correct as presented by one of our colleagues in his writings. One virtually has to live at the bedside of these patients to keep them going. Sustainability is contrary to the experience of neurologic intensivists. I will return to the meningitis case in a moment. Are there instances where younger patients with very healthy myocardial tissue can have cellular survival, can have a heart beat that goes on, on a ventilator for a long period of time (days, weeks)? The record I alluded to in my own intensive care unit is 45 days. Yes, perhaps they can. Does that negate brain death? I do not see how it does.

### *Shewmon's Rejection of All Brain-Based Criteria for Death*

Shewmon is entitled to reject all brain-based criteria for death. I want to make it clear this is not an *ad hominem* attack on Alan Shewmon, quite the contrary, he is offering us the opportunity to refine, clarify, bring to a fine point brain death as a medical entity. The starting point of his discomfort appears to be the issue of the appearance of a warm body. That is a reasonable starting point but we have heard that medicine is allowed to have a logical progression based on evidence, not on thought experiments, and medicine is permitted, if not obliged, to change our notions of death over time.

An essential diversion here is the idea that the body is dying but not yet dead, and that an irreversible phenomenon occurs when we recognise brain death, the same way that a physician who stops cardiopulmonary resuscitation recognises that he has reached the point of no return. I find this idea of 'dying but not dead' appealing but, either way, it creates an entity which is

de facto dead. The Repertinger meningitis case, which Dr. Shewmon utilizes, ironically demonstrates that it is possible to keep a body and organs perfused for a long period of time. I would like to point out that that patient did not have an apnea test, at a time when you could have presumed that he was brain dead. We know that some time, perhaps in a brief epoch before the autopsy, there was necrosis of the lower brain stem, completing the brain death notion, but there is no testing to confirm that. One possibility, although I am uncertain, is that that patient may not have been brain dead for a long period of time.

Another problem that has caused people to reject brain death is the operational motivation in transplantation. We are familiar in medicine and in society with withdrawal of supportive care to avoid the prolongation of suffering of the corpse, or 'beating a dead horse', as it were. It is cruel. I think there is a point at which one can remove the ventilator and can take out the organs but the two are disconnected and really remain so. Shewmon says that he can imagine going about transplantation in a different way, so that removal of the vital organs neither kills nor harms the donor; I do not really understand that. There is not a lot of middle ground: either the patient is dead, and all you are doing is taking the organs, which is seemingly permissible societally, or they are not dead and you have to make a whole new conceptual system around it.

### *Thought Experiments All Lack Context*

All of the thought experiments that have been proposed by Shewmon and others lack context. The first is the apnea-coma idea, namely that brain death is simply coma and apnea, or destruction of the top and the bottom of the brain. These thought experiments are querying why a cervical section is not dead, or if somebody has cortical damage and is comatose and they happen to have a cervical cord transection that we are claiming that that patient is dead. Of course, no neurologist would diagnose either of such cases as dead. These are just ideas that lack neurological context. The pupils, the corneal responses, the eye movements, deep coma, and so forth are all required for the diagnosis of brain death.

An extension of the apnea-coma notion is vagotomy and cardiac denervation. This creates a different type of disconnection of the brain and the body. It again lacks context and misrepresents what we are doing when we determine that somebody is brain dead. Further extensions of this idea to severe Guillain-Barre syndrome or motor neuron disease in which the



patient cannot signal that he is awake, similarly have no context. There is, of course, in these instances no coma, no brain stem damage etc.

The decapitation notion is very interesting and still fascinating. It was apparently Alan Shewmon who at a Vatican meeting proposed decapitation as the most compelling reason for making an analogy of brain death to death. No one can imagine that a decapitated body is alive, so why not extend that to brain death? Now the decapitation notion is being used for the contrary argument that says a decapitated body can have vital energy of some sort, and therefore that brain death is not death. I cannot grasp this logic. Similarly, White's monkey brain transplant attempts, while complicated philosophically, are not a problem medically. Unless such work is going on somewhere in the world, I do not think we are even going to have to grapple with it and I am not going to open the conundrum of putting a new brain in somebody. Is the person in the brain or in the new body? There is a very old joke about a woman who was angry that her husband was buried in a brown suit so she argued with the funeral director until he finally got fed up. When she returned she saw her husband in the blue suit she wanted for him. She asked 'so, finally you put him in the blue suit that he liked', and the funeral director replied 'no, we just switched heads'. It has no context.

The problem of a longer time frame has been raised. By this I mean that the 'irreversibility' of death does not exist until the ventilator is withdrawn. The analogy was made weakly, that the ventilator is supportive the way dialysis is supportive and obviously we do not dismiss somebody on dialysis because they are on a machine. Again, this is the wrong context and the Harvard Commission, when it framed brain death was simply catching up to medical resuscitative science. Incidentally, from discussions with Dr. Raymond Adams, the work of the Harvard group was not meant as a way to drive transplantation. It was meant as a response to futility. If there were to be a perpetuation of the brain death idea solely for the expedient purpose of transplantation, then we have a problem. I would submit, that it simply *allows* for transplantation, and it would be tragic if we rolled back the clock and transplantation went away, but there is a curtain between them and there always has been one.

#### *Loss of 'Somatic Integrative Function'*

The loss of somatic integrative function, or the unity argument, which has been expressed in many different idioms, is medically weak. It was perhaps unfortunate that was included in the President's Commission (1981).

However, even arguing against this does not negate brain death as death. Did the commission mean something different from a higher manner of unity; were they talking about soul? I think the loss of somatic integration is best considered as a supportive element for brain death.

*For Medicine, a Practical Science, Death is what Medicine Makes of it, but With Good Reason!*

For medicine, which is a practical science, death is what medicine can make of it, and with good reason. All pronouncements about death are based on what is possible and not possible currently in human physiology. Ideas are based on accurate and formalised practical clinical criteria which do not tell us that every cell of the brain is dead, do not tell us that there is no blood flow to the brain (those are additional emphatic confirmatory features), but tell us that that organism is not sustainable in most cases and that that dissolution is inevitable, inexorable, not just permanent. And medicine always has had to make practical distinctions by using the cessation of observable signs such as spontaneous breathing or pulse or brain function as the sensible time to declare that the patient is dead.

Brain death can be very precisely defined from a clinical perspective. It should remain an extension of the traditional consultation by the physician to a family to confirm death. It may alter the traditional sense of death as derived from common experience but with good reason. Practical life and observation eventually trump casual notions and customs. It is not simply an expedient to declare death on brain criteria and it is neither philosophically lazy nor self-contradictory. Thank you to the Academy and to my esteemed colleagues.

## GENERAL DISCUSSION

DR. ROPPER Dr. Shewmon is entitled to reject all brain-based criteria for death. I want to make it clear this is not an *ad hominem* attack on Alan Shewmon, quite the contrary, he is offering us the opportunity to refine, clarify, bring to a fine point brain death as a medical entity. The starting point of his discomfort appears to be the issue of the appearance of a warm body. That it is this Cartesian idea, again, that the body looks like it is alive. It is the Frankenstein arguments. That is a reasonable starting point but I think we have heard that medicine as a science is allowed to have a logical progression based on evidence, not on thought experiments, and medicine is permitted to change our notions over time. The timeframe for brain death of course has been short, 40 years. An essential diversion here, again in my own view, is the idea that the body is dying but not yet dead and that the irreversible phenomenon that occurs when we recognise brain death, the same way that a physician who stops cardiopulmonary resuscitation recognises that they have reached the point of no return, I find this idea unappealing but if it works for everyone, either way, it still creates an entity which is de facto inexorably dead. The Repertinger meningitis case, which Dr. Shewmon endorses, in fact ironically demonstrates that it is possible to keep a body and organs perfused for a long period of time. I would like to point out that that patient did not have an apnea test, at a time when you could have presumed that they were brain dead. I hope I am putting that clearly enough. We do not know about that patient. We know that some time, in a brief epoch before the autopsy, there was necrosis of the lower brain stem, completing the brain death notion, but there is no testing at all to confirm that for us. My first presumption, although I am uncertain, is that that patient may not have been brain dead for a long period of time. The operational results of brain death are the other problem that has caused people to reject brain death philosophically, specifically that this is being done solely for transplantation. We are quite familiar in medicine and in society with withdrawal of supportive care to avoid the prolongation of suffering of the corpse, or 'beating a dead horse', as it were. It is cruel. So, I think there is a point at which you can remove the ventilator and can take out the organs

but the two are disconnected and really remain so. Shewmon says that he can imagine going about transplantation in a different way, so that removal of the vital organs neither kills nor harms the donor, I do not really understand that. It is a little self-contradictory. There is not a lot of middle ground: either the patient is dead, and all you are doing is taking the organs, which is seemingly permissible societally, or they are not dead and you have to make a whole new conceptual system around it.

All of the thought experiments that have been proposed by Shewmon and others lack context completely. The first is the apnea coma idea, namely that brain death is simply coma and apnea, or destruction of the top and the bottom of the brain. These thought experiments are asking if you made a cervical section why is that patient not dead, or if somebody has cortical damage and is comatose and they happen to have a cervical cord transection that we are saying that that patient is dead. Of course, no neurologist would diagnose that patient as dead. It is irrelevant, it is just an idea, but it lacks any context, it ignores all of the neurology that has been hard fought. The pupils, the corneal responses, the eye movements, the deep coma, and so forth are all required for the diagnosis of brain death. The decapitation piece is very interesting. It was Alan Shewmon of course who proposed decapitation as the most compelling reason for making an analogy to brain death. No one could imagine that a decapitated human body is alive, so why not extend that to brain death. Now the decapitation notion is being used as an end run for the contrary argument, that yes, a decapitated body could have vital energy of some sort, and therefore that brain death is not death. I am lost here. I have read it five or six times, I cannot grasp the logic. An extension of the apnea-coma piece is the vagotomy and cardiac denervation, that the brain and the body can be disconnected in terms of autonomic control, it again has no context at all, that is not what we are doing when we determine that somebody is brain dead. I will not even dignify the analogy of brain death to Guillain-Barre or motor neuron disease which is given in another thought experiment, that somebody has no ability to innervate anything, and why is that patient not dead? It is not the context, there is no coma, the brain stem, etc., is preserved. ... I do not have to repeat this for you but I am obliged to enumerate them.

Similarly, White's monkey brain transplants attempts, while very complicated philosophically, is not a problem medically. Unless it is going on somewhere in the world, I do not think we are even going to have to grapple with it and I am not going to open the conversation of putting a new brain in somebody. Is the person in the brain with a new body? There is a

very bad and old joke about a woman who was angry that her husband was buried in a brown suit and she argued with the funeral director and he finally got fed up and she came back and said, finally, you put him in the blue suit that he liked and he said, no, we just switched heads. It has no context.

The longer timeframe has been suggested. What do I mean by that: that the irreversibility is not there until the ventilator was withdrawn. The analogy was made weakly, that the ventilator is supportive the way dialysis is supportive and obviously we do not write off somebody on dialysis because they are on a machine. Again, it is the wrong context and the Harvard Commission, as I alluded to, was catching up to medical resuscitative science. It was meant not primarily as a way to drive transplantation, it was meant as a response to futility. Why do I say this? Because in all humility I see Dr. Raymond Adams every Friday on my way home and we have discussed this for a very long period of time. I think, Eelco, you called him did you not at some time? There is no question that when Beecher, Adams, Schwab, sat down to write these criteria of irreversible coma they were not doing it for transplantation, emphatically. Now, it is mentioned in the discussion but I think that in a way it is important to know motivations and the motivation was not transplantation. Now, if there is a perpetuation of the brain death idea solely for the expedient purpose of transplantation, then we have a problem. But I would submit, that it allows for transplantation, and it would be tragic in a way if we rolled back the clock and transplantation went away but there is a curtain between them and there always has been one.

The loss of somatic integrative function, which has been expressed in many different idioms, or the unity argument, is medically soft, by which I mean weak, and perhaps an unfortunate argument that was included in the President's Commission, I would again submit that even arguing against this does not negate brain death as death. Did they mean something different from a higher manner of unity, were they talking about soul, I do not know. I think it is best considered as a supportive element for brain death.

So medicine recognises the withdrawal of support of a severely injured patient, in special circumstances. This is in the interest of the patient, particularly if they have previously expressed a desire not to be sustained in this manner, even without a loss of that unity. Brain death is an extension of that circumstance; if the circumstance is futile, it is inexorable, and it is so because it is unique in medicine and really it is not part of a continuum, it is over a line.

So for medicine which is a practical science, death is what medicine can make of it, but with good reason. It is based on what is possible and currently not possible in human physiology, it is based on accurate and for-

malised practical clinical criteria which do not tell us that every cell of the brain is dead, do not tell us that there is no blood flow to the brain, those are additional emphatic confirmatory features, but tell us that that organism is not indefinitely sustainable in most cases and that that is inevitable, inexorable, not just permanent. It is beyond permanent, and of course it requires ethical and proper behaviour of physicians. And medicine always has had to make practical distinctions by waiting for the permanent cessation of something like spontaneous breathing or pulse or brain function as the sensible moment to declare that death has occurred. Of course death has occurred before the physician writes the note and does the testing. Brain death can be very precisely defined from a clinical perspective; it is an extension of the traditional consultation of the physician to a family to confirm death. It does alter the traditional sense of death from common experience but with good reason, because reason with observation trumps casual notions and customs. It is not simply an expedient to declare death on brain criteria and this is neither philosophically lazy nor self-contradictory, I would submit, but those are broad strokes that again I cannot make a substitutive judgement for other people. Thank you to the Academy and my Esteemed Colleagues.

PROF. SPAEMANN Would you please say something about the Repertinger case?

DR. ROPPER I had two comments about the Repertinger case. The first is that, at some time, at some moment, that patient, if we could have examined him exhaustively we would show all of the clinical manifestations of brain death but we do not know, because he never was examined in that manner, he never had the full series including apnea testing. Am I wrong Jerry, do you have the paper? I have no way of knowing that but I think we can say it is highly unlikely, that is all, no more than that, not definite, highly unlikely that that patient was brain dead for seventeen years or however many years because either it is the most exceptional case ever, or we are missing something. And that is really the problem, is that we do not know when that patient became brain dead, we have no idea. The other thing it shows, the ironic thing as I suggested was, that it is possible for a period of time to keep perfusing organs, but I do not know whether it was a minute, a day, a week, a month or a year. It could be a year, I have no trouble with that, in a young patient. Those are my comments. That case was never subjected to neurologic scrutiny. It is true he was examined but his medulla was not clinically examined, it was pathologically examined after the fact. Have I been able to transmit this?

PROF. SPAEMANN Yes, thank you. I am only astonished that in 40 years doctors did not make these experiments. There was time enough.

DR. ROPPER Well, we have experiments of nature all the time. We try, at times very hard to keep somebody whose medulla, the bottom of the brain, is damaged, I would go beyond damaged, has no nerve cells left in it. We try to keep those patients perfused and we usually fail, but occasionally it is possible to go on and on and on, not indefinitely but occasionally. The question is, that case does not prove the point that the body can survive for a very long period of time and be brain dead because we do not know when that patient became brain dead.

DR. POSNER I think it is very important at least to look at this, because I agree with you it is entirely irrelevant but I think we ought to know. Let me read one paragraph, 'multiple EEGs have been isoelectric and no spontaneous respirations or brain stem reflexes have been observed over the past fourteen and a half years. Multimodality evoked potentials revealed no intracranial peaks, magnetic resonance angiography disclosed no intracranial blood flow and neuroimaging showed the entire cranial cavity to be filled with disorganised membranes, proteinaceous fluids, and ghost-like outlines of the former brain'. So I think this child was dead for a long time before the autopsy was done. The fact that we can perfuse peripheral organs and keep them alive for a greater or lesser period of time, requires enormous effort. Remember some of the slides I showed yesterday indicate that in Japan, Taiwan and in other places, attempts to keep the body functioning for a period of time after the brain has died have inevitably failed in twenty days or thirty days. Young, healthy, pregnant women, who are brain dead and in whom major attempts are made to keep the peripheral organs alive so that the fetus can come to viability, can go on for perhaps a hundred days but at great effort and usually with failure.

PROF. BATTRO Thank you so much, Prof. Ropper, for your talk and I really appreciate the way you put it. I am a medical doctor too and I agree that thought experiments are not useful in medicine, but we can focus on natural experiments related to very extreme cases. For instance, concerning the whole brain death, what happens if the person has only half a brain? There are hundreds of hemispherectomised persons and some may die perhaps by an accident, and only half a brain will be enough for saying that the brain is dead, that the half brain is dead. This is a point.

Half-brain people were not frequent some fifty years ago but today someone with half a brain could arrive at a clinic being brain dead. This is a perfect demonstration that we do not need 'the whole brain death' because in that case the whole brain was only half a brain. Thank you.

DR. ROPPER Monsignor, I do not know whether you want to extend this discussion to the actual questions that you have posed, because I listed them and found that all but one or two were answered, but this is your part of the conference, not mine.

BISH. SÁNCHEZ S. For me it is very well if we spend all the time that is necessary to understand exactly the neurological level, because afterwards we can make philosophy but we need to be sure at the neurological and biological level. For example, for me, it is completely impossible to understand that, if you have a person who is decapitated or a brain dead individual, the body could be considered an organism with somatic life. At biological and neurological level, is this hypothesis possible? I think not. This for me is very important.

DR. ROPPER I think that, generally, there would be agreement on the part of the neurological community and in fact you could leave the face, you could leave the ears, you could leave everything below the frontal bones, even take it further, but there is a point at which you have to stop slicing because then you are looking at the vegetative state, severely disabled and so on. The unique thing about the brain death entity is that it marks a threshold phenomenon in neurological life. It is not part of a continuum. And decapitation is even going further than you have to, it is sort of kicking the dog when he is already down but I would only respond in the affirmative, that we would have to start over from square one in neurology if the death of the brain is not death and is not the loss of personhood and is not the loss of the personal entity that is embodied in each individual, not collectively. No brain, no person. For neurology, that is a neurological issue, not a philosophical one.

DR. BERNAT Regarding the Repertinger case, I agree with Dr. Posner that we, as a neurological community, should accept that this represents a valid case of brain death that was confirmed by exhaustive pathology. I saw the videotape nine years ago of Dr. Shewmon examining this patient and it was clear the patient was brain dead. All of the testing that Dr.



Posner just summarised was performed about nine years ago, so he was certainly brain dead at that point. The parents would not permit an apnea test because of their fear that it might harm their child. The absent evoked potentials, the flat EEG, and the basically absent intracranial blood flow as well as all the clinical tests were consistent with brain death. So I think if we try to attack the case and assert the patient was not really brain dead, we are on shaky ground. I think that we, as a community, should agree to accept that it is a validly documented case of brain death that was pathologically confirmed. It makes the point that, in extraordinarily rare circumstances, this kind of thing can occur. With the technologies that we have in the modern intensive care unit we may be seeing more of this type of case, as physicians develop the technological prowess to reproduce some of the functions of the brain stem and hypothalamus in the integration and coordination of all the subsystems of the body. But I do not think that this case in any way disturbs the conceptual validity of brain death as being equivalent to human death.

DR. ROPPER Thank you for taking me back to a neutral position.

DR. BERNAT May I ask a simple technical question? After your impassioned defence of brain death as human death I hate to backtrack into a highly technical area, but the first part of your talk was about apnea testing and I noticed that you did not discuss the CO<sub>2</sub>-augmentation option of apnea testing.

DR. ROPPER Yes, I think it is just another option. One of the reasons I am hesitant to endorse it too strongly is that it has simply not been tested. That is, we have no idea about whether the rate of rise of CO<sub>2</sub> is an element in stimulating medullary function and it may well be that it is a time function, it is not just an absolute number and I would love to see it tested. It is a reasonable way to conduct the test if your premise is you just have to get to an absolute number but, frankly, I could imagine that it is not instantaneous, you are going to raise the CO<sub>2</sub>, then you change the pH of the spinal fluid, then you have a step where you change the pH of the cellular environment of the medulla and then you have to have electrical activity. There will be a latency. So, I am a little worried that if you, say, had a servo mechanism that just made CO<sub>2</sub> 60 through some kind of feedback loop, and you said, well, it is 60 and we are done, you might miss an opportunity to stimulate the medulla more slowly. But it is at the edges, I do not have an answer, Dr. Bernat.

DR. BERNAT The test does allow, as you know, a more rapid rise in PaCO<sub>2</sub>. It basically has people inspire 5% CO<sub>2</sub> instead of 0.5% (or whatever the amount of CO<sub>2</sub> is in room air) and it can be safer in some cases, such as when a prolonged apnea test, that might take seven minutes, could produce hypoxemia, hypotension, or other complications. It has been advocated in those cases.

DR. ROPPER I think it is a valid point, it should be studied.

DR. DEECKE My comment was meant as an *ad hoc* to the decapitation story. The Shewmon paper was distributed to us all and in the title there is already the expression 'physiological decapitation'. So, in my opinion, both expressions are wrong. Brain death is not physiological but highly pathological and it is not decapitation because the head is still there. What does he mean? Is it just a provocative term?

DR. ROPPER I presume so, it is legitimate though because the arguments that are made under it are the coma plus cord sectioning and oxygenation argument and the vagotomy plus denervation argument and then the motorneuron disease argument. I think it is just provocative and I cannot speak for my colleagues, but I think at he is circling back to his original notion, when he was involved in persuading the Academy that decapitation was an appropriate way to view brain death and it would have made me uncomfortable at the time, because it is again a little bit of a partial thought experiment. It is ersatz.

DR. ESTOL I just wanted to address the point requesting clarity by Msgr Sánchez Sorondo, but the other way around. Instead of quoting a theory of models like that posed by Dr. Alan Shewmon, I would like to emphasize the unanimity that has been shown here by many scientists from very distant and different regions of the world. We have representatives from South America, North America, Europe, Australasia and they have shown strong agreement and, when we heard similar things in similar talks, it was not redundancy, each time we were expressing that we agree on the fundamentals and not just among us. Many described what their societies state and what their governments have as rules and laws. There has been only one strong disagreement. In the paper by Dr. Alan Shewmon there is a mix of philosophy, theology and biology and I was concerned because I did not understand it. Now I know that at least two

of us, Dr. Ropper and myself, supposedly know the biology but could not get through the paper, and Dr. Ropper said he read it five times. I did the same, and I really did not understand it, but when I hear that Cardinal Martini, who knows the philosophy and the theology, could not get through the paper either, as he said this morning, then I thank you, Allan, because in your slides you clearly explained the problem, which is that the analogy and theory by Dr. Shewmon is out of context.

DR. WIDDICKS Allan that was wonderful. I do not have much else to say other than I think that there is in general a disconnect with what is in the literature and what is the interpretation, maybe it would be better to use the word 'extrapolation' of the literature and what professional neurosurgeons and professional neurointensivists see when they see patients who are brain dead. When we say that it is not easy to maintain those patients, we know that it is extraordinarily difficult and that these patients rapidly deteriorate, or what is left of the body rapidly deteriorates, through a sequence of events. We know that, for example, lung transplant surgeons are concerned if lungs are not transplanted after 48 hours, not because they had an initial neurogenic pulmonary edema, that was present at the onset, but because they develop neurogenic pulmonary edema after they are maintained. So there is a disconnect between what is in the literature and what we, as professionals in our own experience, see. I think that is concerning and I think that is an important point to mention. I have a few points about the apnea test. I think the apnea test is a safe procedure. When we published the data on the complications of apnea test it was before the American Academy guidelines that provided those preconditions to the apnea test. I do have unpublished data that those numbers are much better when these patients are oxygenated. I have concerns using CO<sub>2</sub> because I think that much of the cardiac arrhythmias and potential cardiac arrests can occur with an extreme hypercarbia I still prefer just simply waiting for the arterial CO<sub>2</sub> to rise in a very controlled manner.

DR. ROPPER I tend to agree with you, I think that is an open issue right now. I do not do it because of those kinds of problems but that is more anecdotal and we could settle it.

DR. HUBER I enjoyed your presentation very much and I have understood and learned now that also the phenomenon of death will change perhaps in the future, from the biological and from the medical point of view.

But for the clinician, who has to make decisions everyday, today and tomorrow, in a very hard field, for our decisions at the moment we have only one Rubicon to differentiate between this and life, and this Rubicon is brain death and the signs of brain death. I think it is very important to discuss also from the theological and philosophical point other aspects, but for the clinician it is very important to have guidelines, also for ethical reasons, and therefore I believe, at the moment, of course this can change in the future, at the moment there is only one Rubicon between death and life and this Rubicon is brain death.

DR. ROPPER I think you would get a general endorsement of that.

DR. TANDON As a medical student I was taught never say never in medicine. If there is an exception, it is paramount that we look at it. However, having made that statement, I must say that experience of not one or two but thousands of neurologists and neurosurgeons around the globe has come to the conclusion that brain stem death or brain death is death, it is not equivalent to death, it is death. This is an extremely practical issue and as just mentioned by Dr. Huber, it is a practical everyday question and we have to answer. I would like to make a comment here, the fact is in historical terms these tests were not developed with the idea for transplantation. All these tests, which we carried out years before any successful transplant was carried out, were based on our desire to be able to give prognosis of our patient to the family. If we could be more precise, how much more efforts we could put in, we never gave up efforts, that is one thing, at that time because there were no such laws that we could give up, as long as the patient was with us, heart was beating, we continued. But the fact is, as I mentioned earlier today, that when you examine the brain of most patients who have been diagnosed as all the brain stem functions lost, who were on a ventilator, the degree of autolysis of the brain that was seen at autopsy was directly proportional to the number of days for which the person had been on a ventilator. So the ventilator, while on the one hand perfusing many other organs which may be utilised for transplantation, the fact remains that it itself, more often than not, damages the very tissue that we wish to preserve, that is, the brain, and that has been repeatedly shown in a series of autopsies that have been carried out in so-called 'brain dead people'.

DR. ROPPER Thank you for your comment. I suppose bringing these two comments together simply would be by way of saying, it is practical but it

is not an expedient, it is not a means to an end of transplantation. But it is practical and, as you said, there will be a change in the future, potentially.

PROF. ZICHICHI Thank you. I have been following this extremely interesting discussion. I am sorry not to have been here during all of the meeting; I was engaged in other scientific activities. Nevertheless, I have been following these arguments even outside this meeting. It is interesting what you write there, i.e. the question of whether brain death in historical terms was the result of the independent study of the brain and thus unconnected with the related subject of the transplant.

DR. ROPPER This is Monsignor's question from the original conception of the conference.

PROF. ZICHICHI From the scientific point of view, to know exactly the time T1 of the brain death is a problem that cannot be disconnected from the consequences which go into the theological field. The brain is made of about  $10^{27}$  of atoms. Roughly speaking, billions of billions of billions of atoms. If I have exactly the same atoms and molecules and I put them together I do not have the brain, because science is unable to go from inert matter to living matter; so this famous T1 has as profound meaning, which corresponds to the transition from inert matter to living matter. Here the consequences are very large. The problem of a transplant is not existing in the sense that, if it was decided to have a strong support in technological developments for artificial organs there is no question that what we know today allows us to conclude that any organ can be artificially constructed and therefore this connection from the ethical point of view disappears. So, from the fundamental point of view, the relation between the study of this time T1, which has been discussed here, has as a consequence our understanding of the relation between inert matter and living matter. You can study the brain as much as you want, you will never be able to produce, with the same number of molecules, the brain you are studying. And this is the big bang of the so-called evolutionary theories, which are unable to explain this extremely important point.

What I have learned here, is that you have been studying what happens to the brain in a passive way, using positron emission technologies or other technologies, but the fact that our friend Battro has pointed out, namely that half a brain can be as good as a total brain, has again enormous consequences and therefore my question to you is why nobody studies (there is no ongoing R&D) the so-called active methodology, tech-

nology to stimulate the brain, not from outside, from inside. The modern mathematical models of the brain are now not anymore in terms of electronically connected systems but of antennas and this can explain, from the qualitative point of view, why a half brain can be equivalent to the total brain. So, from the technological point of view, this is my second question to all of you, why no one does R&D in the active analysis of the brain and all the results that I have been listening to with extreme interest are on the passive technology. What is the reason? Why is no one engaged in this field, due to the fact that, from the fundamental point of view, the brain is a system consisting – as I said before – of  $10^{27}$  in number of atoms. The mathematical model of the brain is not anymore in terms of an electronic sequence but of an enormous number of antennas, and the technologies used are all passive. Thank you.

DR. ROPPER Thank you. I do not know that I can respond for everyone but I would say the emerging field of cognitive neuroscience, which is one of the most exciting outgrowths of clinical neurology, is oriented towards first an understanding and then a mechanistic change in brain function. I think the nascent or the incipient features of this are coming out in the Owen paper and in the Shiff paper but beyond that, although it is considered a little bit fringy, I think the brain stimulation experiments with implanting electrodes to activate parts of the brain, deep brain stimulation, in hopes of substituting for the loss of some elemental piece of brain hardware, even though it is very primitive. I think it is easier said than done. This is beyond wet lab work, because it requires even having a new vocabulary about connections in the brain and relationships that we do not have. But there is no doubt that it is one of the goals of clinical neurology, because at the end of the day clinicians want restorative medicine, not just passive diagnostic medicine.

PROF. CABIBBO Prof. Zichichi posed some fantastic philosophical physical questions, futuristic. My understanding, which I tried to collect during this day is that when you speak of brain death you are speaking of a very physical, macroscopic event. There is overpressure, herniation...

DR. ROPPER That is correct.

PROF. CABIBBO It is not a continuous transition from atoms to molecules.

DR. ROPPER It is a physical decomposition of the brain, top to bottom.

BISH. SÁNCHEZ S. I think that it is a very good idea to distinguish the questions. This new question is very important and very interesting but for me, also for the wish of the Holy Father, I think it is very important to finish with the first question, the relation of brain death and the death of the individual. When we finish this we can go back to Prof. Zichichi's question that is in another line of fundamental questions.

PROF. CABIBBO My understanding is yes, that brain death is death, this is the answer we are receiving. It is a different clinical situation from the classical one, where certain events appear and the doctor is close to the patient – if the patient is lucky enough to have a doctor close to him – and he looks at the clinical signs and at a certain point says, 'this patient is dead', after testing pulse, respiration etc. In the case of patients who are under intensive care, so they are under a ventilator, you have a different set of tests that bring you to the conclusion that this patient is dead. And this is what is called brain death, essentially, because this conclusion cannot be reached by the usual tests, which are presence of respiration, presence of pulse, because these are artificially provided, in a way, by the machine. So it is an alternative set of tests that satisfies you, as responsible physicians, that the patient has indeed died at a certain point. So you say, I have to make these tests, I have a list of tests, since this is a new matter these tests are much more formalised than the classical ones, which are passed on from master to student, but it is a similar problem in a different situation, how you declare that a patient is dead in this very artificial situation provided by the ventilator. This is what I have understood.

DR. ROPPER I believe that is accurately said. I think you understood the sense of clinical medicine, anyway. But, ironically, these criteria are more rigid, stricter, more refined than the classic criteria.

PROF. CABIBBO I would like to add that I am convinced also of the fact that transplants have nothing to do with this, because you have the problem, the guy is on a ventilator, when is he dead? I mean, normally, in the movies, the doctor is close to the patient, he says he is dead and the cover is pulled over his face, or the eyes are closed, etc.

DR. ROPPER I hate to make this analogy because it sounds like a thought experiment, but imagine that the ventilator was not invented and in order

to accomplish the state of a sustained body in the intensive care you had to blow into someone's mouth, over and over and over. At one point you would say, 'it is over'. Cardiologists do it with the heart. It is the same. But a machine has arrived and the machine relieves the burden for the physician, the nurse, society, everybody. It interposes itself between what we all have as a Cartesian common sense notion of death and the dissolution of the corpse. That is all that has happened and we have been trapped by it.

CARD. COTTIER Je veux remercier pour avoir été invité à ce symposium où j'ai beaucoup appris. J'ai été frappé par la grande convergence existant entre tous les scientifiques, comme le Prof. Estol l'a déjà souligné. A mon avis, un problème auquel nous devons nous efforcer de répondre est celui de l'insuffisante communication entre le monde scientifique et l'opinion publique.

Il serait nécessaire également que l'on arrive à une convergence sur les définitions. Il convient d'être précis. Par exemple, plusieurs ont souligné le danger de parler de "mort cérébrale". On se demandera inévitablement: différent-elles de la mort tout court? En réalité, cette formule, qui peut porter à équivoque, indique un fait indubitable: le cerveau, lui aussi, et pas seulement le cœur et les poumons, sont des signes de la mort advenue. Ces signes sont particulièrement sûrs. On chasserait bien des phantasmes qui empoisonnent l'atmosphère si on prenait la peine d'expliquer aux gens le sens de la formule ou si on parlait simplement de la mort dûment constatée. Qu'une forte charge d'émotion entoure la mort, cela est normal, cela est humain, car la mort est pour chacun une chose dramatique.

Autre point à souligner: faire en sorte que la machine ne devienne pas un écran entre le médecin et le malade ou, dans certaines circonstances, les familles. Les rapports interpersonnels sont une nécessité.

Ne pourrait-on pas intéresser les grandes organisations mondiales à l'effort d'unification du vocabulaire et des définitions. Cela aiderait le travail législatif. J'ai été frappé par l'observation faite par plusieurs que, rien qu'à s'en tenir aux pays occidentaux, la législation varie notablement d'un pays à l'autre. Une unification des législations, avec l'aide de l'OMS ou du Conseil de l'Europe, aiderait l'opinion publique à ne pas s'effrayer de choses qui ne doivent pas effrayer. Mais on me dit que le projet pour le moment est utopique. Encore une fois: merci!

DR. ROPPER I do not feel I am in a position again to speak for the group, I am humbled by the fact that I am the one left standing here, but I agree,



I think the World Health Organization or the European Union would go a long way and yet it might take generations of conceptual change about the brain and society for people to get beyond the sense experience of the warm body. It will take a conceptual leap in understanding the meaning of the brain. That is probably when there will be a natural acceptance of brain death, but in the meantime we have a problem. I think we have a problem in a way because we are still here talking about brain death thirty-five years later, *déjà vu* all over again, as they say.

DR. RAICHLE I would only have said, in relationship to your comment, that deep brain stimulation is now widely used in movement disorders, it has recently been implemented in the treatment of depression and I think it is only a matter of time before it is applied in many other circumstances and experimentally it has been tried on patients in the persistent vegetative state so, at that level, a lot of work is going on to not only apply it but to understand it. As well there are attempts not only to examine the brain by stimulating it with magnetic fields but to treat depression. So I think manipulating it, if I understood your comment, is definitively moving in the direction you are suggesting. And, completely changing my comment, in relationship to this matter of how the public and families understand the situation here, I think we need to appreciate the depth of this challenge; the impact of the warm body and the face and the arm that moves is so integral to the way our brains work as we judge other people that, to dissociate that from the fact that there is no brain behind the face is an exceedingly difficult thing to comprehend. It is an intellectual challenge that we will have to deal with, which is the non conscious response of ourselves to what we perceive to be the mind intentions of another human being. If they are laying there and if they look like an awake, aware human being we will have the inherent tendency to make judgements that do not fit with the scientific reality, which is, tragically, that there is no brain there.

But I think the first step is to recognise the challenge, it is a scientific issue, people have discussed this, it is very actively being investigated in cognitive neuroscience under the rubric of theories of mind, but it seems to be conspicuously absent in these kinds of discussions. Yet, as I commented earlier today, the one word that kept coming up over and over and over again was the word perception and we need to understand, when we say that we perceive something, we must be aware of the tricks our own brains are playing on us.

DR. BERNAT Thank you very much. I would like to pick up where Dr. Ropper left off in terms of the rebuttal of Dr. Shewmon's paper, recognising that it is not entirely fair, since Dr. Shewmon does not have the opportunity here to defend himself. However, his paper does so quite ably and, since it is here representing his position, it is fair for us to further comment on it. What I would like to do is, at the risk of offering a thought experiment (which both Dr. Ropper and Dr. Battro do not think is necessarily a good idea) because his paper basically turns around and rebuts his previous thought experiment of physiological decapitation. I would like to go on record as saying that the physiological decapitation argument, when it was first proposed in the 1980s, was and remains one of the most powerful arguments supporting the equivalency of brain death with human death. In brief summary, it proposes that if there were a controlled surgical decapitation and the two halves of the human being were treated in an experimental way, such that there was endotracheal intubation at a time that the heart continued to beat, that the neck down portion of the human would represent something similar to the brain dead patient. If the head portion immediately was put on a cardiopulmonary bypass so that oxygenated blood could flow to the brain, such that there was no interruption of consciousness, and there was a way to establish a communication using EEG signals (such as is being currently done in medical centres in people who are utterly paralysed from a high spinal cord transection or ALS), the question would then arise, which of these two halves represents the patient. I have said earlier that I think that the conceptual definition of death is the loss of the critical functions of the organism as a whole. There is an important distinction to be made between the organism as a whole on one hand, and the whole organism on the other. If you remove a limb from a human, that in no way disturbs the organism as a whole. Although it is true that some of the aspects of the organism as a whole may not be present solely in the head portion of this thought experiment, I think most of us would have to side with those who claimed that the head portion, who is able to communicate, think and experience, would represent the person and not the body portion which is analogous to the brain dead patient. So, I would compliment Dr. Shewmon on his original thought experiment, which I think remains a powerful defence for the conceptual equivalency of brain death and human death. I feel that his current attack on that thought experiment is not adequate to diminish its staying power.

DR. ROPPER I think, again, trying to represent a group rather than myself, that is extraordinarily lucid and, at the risk of being a little bit glib, Stephen

Hawking comes to mind. Brain without a body; who is the person, but the body without that brain? It is certainly not Stephen Hawking but it is ostensibly no one, but there I think we are creeping into the philosophical.

PROF. SPAEMANN Ich möchte eine Bemerkung machen zu Herrn Kollegen Raichle. Es scheint mir gefährlich zu sein, in Bezug auf elementare menschliche Phänomene die Gültigkeit unserer menschlichen Wahrnehmung abhängig zu machen von dem jeweiligen Stand der Wissenschaft und ihrem Urteil. Wenn cartesianische Wissenschaftler leugneten, dass Tiere Schmerzen haben, dann wären diejenigen Menschen im Recht, die sich ihre unmittelbare Wahrnehmung des Leidens von Tieren nicht ausreden ließen von einer Wissenschaft, die auf einer strikten Dichotomie von Subjektivität und Objektivität gleich Materialität beruhte und die den Begriff des Lebens als ontologischen Grundbegriff aufgegeben hatte. Oder denken Sie heute an die Diskussion um den Freiheitsbegriff, der von Neurologen in Frage gestellt wird. Denken Sie an das Libet-Experiment. Hirnforscher sage uns, dass Willensfreiheit eine Illusion des *common sense* ist, die vor dem Urteil der Wissenschaft nicht bestehen kann. Diese Wissenschaftler sollten erst einmal Kants Analyse studieren, der dieses Wissenschaftstheoretische Problem bereits genau gesehen hat. Wir müssen uns klar machen: Wenn unser Freiheitsbewusstsein, das eng mit dem moralischen Bewusstsein verknüpft ist, eine Illusion ist, und als Illusion erkannt ist, dann gibt es keine Dankbarkeit mehr, keine Schuld, keine Rechtsordnung, und statt Bestrafung der Schuldigen wird es vorbeugende Arretierung aller Menschen geben, die auf Grund genetischer Disposition potentielle Straftäter sind. Wir müssen dann leben in einer Welt „beyond freedom and dignity“ wie der Titel eines berühmten Buches von Skinner lautete. Skinner war tatsächlich der Meinung, dass Begriffe wie Freiheit und Menschenwürde archaische Relikte des *common sense* seien, die eine wünschenswerte Organisation der Gesellschaft nur behindern können. Für den Scientismus ist das Alltagsbewusstsein der Menschen eine Art Slumbereich der Welt, der der Sanierung der Wissenschaft bedarf. Aber diese Ansicht bedeutet die Zerstörung unserer Lebenswelt. Und so ist auch die Todeswahrnehmung, die wir alle haben, ein Zugang zum Phänomen des Lebens. Wir müssen nicht auf die Wissenschaft warten, um zu wissen, was Leben und Tod ist. Die Aussagen der Wissenschaft müssen sich vor der elementaren menschlichen Erfahrung rechtfertigen und nicht umgekehrt.

[I would like to make a consideration to colleague Raichle. To make elementary human phenomena dependent on the respective standard of science and its judgement seems dangerous to me. If Cartesian scientists

denied that animals feel pain, those people were right whose immediate perception of pain of animals could not be removed by a science based on a strict dichotomy of subjectivity and objectivity coinciding with materiality, and that has given up the concept of life as an ontological basic idea. Or just think about the idea of freedom under discussion today and made doubtful by neurologists. Think about the Libet Experiment. Brain researchers say that free will is an illusion of the common sense that cannot continue to operate in front of the judgement of science. Those scientists should study Kant's analysis; he had recognised exactly that scientific-theoretical problem. We have to realise that: if our consciousness of freedom, which is closely associated with moral consciousness, is an illusion and if it is recognised as an illusion, so there does not exist any gratefulness, no guilt, no legal order, and instead of penalty of the guilty there will be preventive locking of all those people who because of their genetic predisposition are potential criminals. Then we have to live in a world 'beyond freedom and dignity' as runs the title of a famous book by Skinner. In fact it was Skinner's opinion that concepts like freedom or human dignity were just archaic relicts that could only hinder a desirable organisation of society. For scientism, everyday consciousness is a certain kind of slum-sphere of the world, which calls for rehabilitation by science. But this view stands for the destruction of our living world. And so our perception of death, that all of us have, is an access to the phenomenon of life. If we want to know what life and death are, we do not have to wait for science. The statements of science have to justify themselves in front of the basic human perceptions and not the contrary.]

DR. ROPPER Is a response proper? Because, again, I think we are talking about the neurological sensibility. We do not want to get too far a field, but it might be worth considering that many of the human behaviours, I will not say the human condition, but the behaviours that you enumerated do have a neurologic basis. They are not free-floating, they are not emergent. Rage, criminal behaviour, sociopathy, etc. have a basis in the brain. Now, that might not be the whole basis, there could be a spiritual element to them but there is no doubt that certain physical activities of the brain create these behaviours. Now, you could talk about what is behind them, maybe something even deeper, but it is possible to begin to understand these things. And the Cartesian analogy may not work here, because now we see with our own eyes, as we are seeing in PET scanning or the more sophisticated type of scanning, what the brain is doing as experiences occur and as the brain initiates activity and thought. So it may not be contradictory to your sensibility that you cannot see these behaviours and therefore

they lack primacy. It is further than we wanted to go in this discussion, I know, but I think there may not be a duality here.

BISH. SÁNCHEZ S. I think that the idea of a body without a brain is more contrary to common sense than the idea of the death of the brain. It is a fantastic idea to think there could be an organism, a living organism, without the brain. That is impossible in the superior animals, I do not know in the other animals, but it is clearly against common sense, I think.

DR. DEECKE When Professor Zichichi said this wonderful proverb of the billions of molecules in the brain and if you take the same bunch of molecules and try to entangle them, you will never come close to what is the brain, I remembered that someone said: 'the human brain is probably the most complex 1.5 kg of the Universe'.

DR. MASDEU I would like to make a very brief point. It is scientific, going back to some of the previous discussions and I think it is relevant because it has to do with this single case, the Repertinger case. We know that the patient had a neurological examination except for one quite important test, which is the apnea test; we all know that he did not have it, correct? In the account of the MRI findings that is in the paper we are told that the MRI revealed a number of things inside the brain that you could not identify but there was intracranial blood flow adjacent to the clivus. There is only one place where that flow could be, and that is in the basilar artery. That is a fairly distal vessel so again supporting the possibility that there was a small remnant of the medulla functioning in that individual. I do not think we have the answer in this case as clear-cut as Dr. Bernat said before. I think the evidence we have still leaves a question mark in that particular case.

DR. ROPPER By the same token I do not think we want to get too embedded in the idea that every respiratory neuron has to be gone. I agree with you actually, José, I mean, that is what I was trying to transmit, you have these circuits of reverberating neurons that control the rhythmicity of breathing, maybe some of them are in the upper cervical cord, however if we are addressing the Repertinger paper per se I agree, I am not sure we know everything we need to know and it is not meant, again, to engage in a polemic with Shewmon, it is more just in the interest of accuracy or, let us say, specificity, but I get it.

PROF. BOUSSER You have rightly alluded to the publication bias in favour of such very prolonged cases; I was wondering if there was in the US or in Europe a kind of registry of these 'brain dead' but artificially maintained patients. This would help to have a better idea of the duration. You mentioned 100 days in a pregnant woman but this is very likely to be an extreme situation.

DR. ROPPER I am fairly certain there is not an organised registry that would be a complete data set. I think we know it does *not* exist, we cannot even answer this rudimentary question, how many patients are declared brain death, in the world, in the US, in one state of the USA but Dr. Wijdicks has the closest experience, an aggregate experience. Maybe you want to comment. I think before we endorse that, though, we want to take a moment to think about what we would do with the data, but it would be interesting for us.

DR. WIJCKICKS In the United States, patients who are declared brain dead are seen by organ procurement agencies and it is not only when transplantation is agreed upon, it is actually the organ procurement agencies are involved with asking for permission to go ahead with organ donation, actually take over the care of that particular patient before the transplantation surgeon takes the organs to move them into a recipient. Most of these organ procurement agencies cover two to three states, some four states. Where I live, in Minnesota, there is an organ procurement agency called LifeSource, and has total data, I think, of about five hundred patients that are seen in three states over a ten-year period and most of those cases are coming out of the Mayo Clinic. We have the clinic numbers, we have all the basic data on those patients and these can be easily retrieved. Not sure if that is going to be important data. We do know in patients that it became very clear within the first two or three days that there was a 'somatic disintegration', a very clear-cut rapid disintegration indeed.

DR. ROPPER Would it be accurate if we stated that the Repertinger type case is an extreme rarity, an anomaly?

DR. WIJCKICKS You know, a twenty-year support of a brain dead body I think would be an unheard observation and therefore the first intuitive response is, that cannot be true, that cannot be brain death, something must have happened that caused this to happen, there must have been something there that maintained vascular tone. I am not so much interested in whether

or not the patient was breathing, I am more interested if the vascular tone was maintained by an intact medulla, which at that point would create an effective circulation, which would make it far more easier to keep the rest of the body in the state that the patient was in with all the antibiotics that the patient received in those 20 years, with all the increasing dose of vasopressors these patients have a major autonomic disconnect and therefore are very unstable, we think that they are so stable but they are lying flat in bed with not much movement, nurses know that the moment they take care of the patient the patient's vital signs change at that time.

DR. ROPPER Would it be further fair to say, to return to the original theme, that it probably does not matter that this patient survived for this period ... that there is no way to contort this case into an argument against brain death?

DR. WIJDICKS Yes.

DR. ROPPER Should that be elaborated on?

DR. WIJDICKS Well, it is not only this particular case, it is the combination or the so-called 176 cases that are interpretation of an extrapolation of many papers in which supposedly patients were found that could be maintained for a long period of time. That is the problem I have and I am sure that is the problem I think every neurosurgeon and every neurointensivist and any neuroanesthesiologist and any pediatric intensivist who sees these patients would argue against, that is not their observation, their observation is entirely different from what we see and therefore we question these patients.

DR. DAVIS Thank you. I have the feeling that we are all saying very similar things and we heard this comment before, I would endorse virtually everything that Dr. Ropper has said, I do not believe that if the beating of the heart and sustenance of the circulation by artificial machinery lasts one minute, one hour, one month or one year it makes any difference, death has occurred, and I would agree with Professor Shewmon in one sense and that is the communication issue with the non medical and the non scientific people. I think the concept of brain death is critical but, in communicating with the public, these are the signs of death, this meeting is in fact called 'The Signs of Death' and these are the signs of death: death in these

patients, in my view, has occurred. We are all saying it in different ways, that signs are masked by this artificial machinery but the signs of death are there, death has occurred, and the brain criteria but it is death and I think that this is the message that we need to convey now. I think we are convinced, medically and scientifically, I believe overwhelmingly that this is the message that we need to convey to the public.

PROF. CABIBBO This is very clear. The question about what our conclusions should be. I must say I am extremely grateful to our Chancellor for all the work he put in preparing the meeting, he did a fantastic amount of work, essentially, in stating also what were the questions that the Pope posed, because the Pope posed the question why do you not study this problem again. So, having heard the Pope or having read his letter, are you satisfied now? Do you think he will be satisfied? What should we write to him?

BISH. SÁNCHEZ S. I think that we can perfect a little the questions, maybe, and the answers, as you suggested, this could be very good to add these two questions.

DR. ROPPER It would be wonderful if they could put the slides back on, you would have the opportunity to go through them, I just listed them for you in a paraphrased way. I think the questions originally posed were terrific. When they first came out I thought they were disembodied but they are very logical in the end.

BISH. SÁNCHEZ S. We can add these two questions and answers and also, of course, our idea is to publish this meeting, with all of the papers, also that of Professor Shewmon, and of course it depends on our authority because we can propose but the conclusion is of our relative authorities. However, I think, in this line of questions and answers, and if we can also publish the papers and the discussions, this could be very important. Of course, if we can arrive at a general statement or common conclusion, if we can arrive at an understanding with Professor Shewmon and with Professor Spaemann in the philosophical, that would be the best. But if we put this, I think it is a very good orientation for the Congregation of Faith that is studying these questions. We can study these questions also and we can ask our relative authorities to know exactly what is the meaning and what is the wish about the conclusion of our meeting. I think. What is your



idea, President? We already have a substantial agreement but we can perfect this. We need your collaboration and your help because you are the great specialists in this.

DR. ROPPER Would you like us to quickly cycle through these? Ok, I will just moderate, I am not going to comment, and people can stop me. We do not have statistics. The historical issue I think we have resolved, the motivation was not transplantation.

*Additional questions and answers to the list published in the booklet.*

DR. ROPPER [returning to question 9] *Is it true that brain death is synonymous with the death of the cells of the brain?* (I am paraphrasing the questions of the booklet). I think we have concluded that it is not exactly synonymous but it is so close that, for practical purposes, medicine being a practical science, it is all we need. If somebody were to insist on that as a standard, there would be no way to establish it.

PROF. CABIBBO My understanding after the meeting is that the basic question that the meeting answered is, is brain death equal to death, is it the same thing, and that is an overarching question. I think that, from what I heard, this has been qualified in a positive sense.

DR. ROPPER But it has been exposed to challenges on a number of fronts. So I suppose the answer is, yes, and the response to those challenges are as follows. Some of them are embedded here.

DR. BERNAT I would like to refine Dr. Ropper's answer slightly. We are talking about the brain's clinical functions and that the cells that have to die are those cells that are responsible for conducting the clinical functions of the brain. That quantity is not every single brain cell, so we need to clarify that there may be some residual surviving brain cells but not enough to contribute to the production of any of the measurable clinical brain functions.

DR. ROPPER [returning to question 10] *What evidence is employed to demonstrate the cells of the brain are dead?* There is clinical evidence, it is not always utilizable and there are additional tests that are used to get beyond the limitations in a very small number of cases.

DR. ROPPER [returning to question 12] *Does the lack of blood circulation to the brain lead directly to death?* (Again paraphrasing the question in the booklet). Yes, it does. It may not be the causative mechanism in every case but it certainly does when it occurs.

DR. ROPPER [returning to question 13] *Is death as the irreversible cessation of spontaneous cardiac and respiratory functions – following classic definitions – a consequence of the lack of blood circulation to the brain?* In most cases, yes. But there are some subtleties behind it because there are times when the supply side is the problem – cardiac arrest or asphyxia – and there are times when the supply is squeezed out because of swelling of the brain – head trauma, cerebral haemorrhage, massive strokes, when the brain swells. So in most cases our understanding is yes, but they are not synonymous of course.

DR. ROPPER [returning to question 14] *If the irreversible cessation of spontaneous cardiac and respiratory functions is the result of the lack of blood circulation to the brain, do we agree that it is evident that the lack of blood circulation is the cause of the irreversible cessation of spontaneous cardiac and respiratory functions?* Through the intermediate mechanism of destruction of the medulla, yes. Is that fair? Again, I am only acting as the vessel for the group.

DR. DAROFF Without ventilation there is deoxygenation, and the heart fails; it is as simple as that.

DR. ROPPER So, I think the answer is yes but it requires a mini explanation as it were.

PROF. SPAEMANN Es stellen sich in der Debatte zwei Immunisierungsstrategien heraus. Die eine besteht darin, zu bezweifeln, ob weiterlebende Hirntote wirklich hirntot waren. Man bezweifelt die Zuverlässigkeit der Untersuchungen. Dahinter steht eine *petitio principii*: es kann nicht sein, dass jemand noch lebt, wenn sein Gehirn vollständig ausgefallen ist. Die zweite Strategie stellt in Frage, ob man ein Leben, das nur durch künstliche Mittel erhalten wird, Leben genannt werden soll. Die Frage, ob der Hirntod der Tod des Menschen ist, hängt letzten Endes an der Frage, ob künstlich erhaltenes Leben künstliches Leben – also kein Leben – ist, oder ob es fortführt, natürliches Leben zu sein, auch wenn es nur mit künstlichen Mitteln erhalten wird.

[Two strategies of immunisation are put to the debate. One consists in doubting if a surviving brain dead person has really been brain dead. One has doubts about the results of the research. Behind that there is a *petitio principii*: it is not possible that a person is still alive, if his brain has completely passed away. The second strategy doubts whether a life, maintained only by artificial means, should be called life. The question whether brain death means the death of a person finally depends on the question whether artificially maintained life is artificial life – whether it means no life, or whether it continues to be natural life, even if just maintained by artificial means.]

BISH. SÁNCHEZ S. I think the first question is whether brain death is the death of the individual. If someone thinks otherwise, we can add their thoughts and state the reasons. The following question would be, what is, from the point of view of neurologists, the body without the brain? I think that these two questions raised by Prof. Spaemann are very central questions. For me, I can say, after this discussion, but it is only my opinion, that we have two scenarios. Using Prof. Shewmon's example of the ventilator, when the person is alive, the ventilator is an instrument of the person, which serves to improve or prolong the life of the person. On the contrary, when the individual is dead, the ventilator is the principal cause to delay the corpse's inexorable decomposition process, maintaining an artificial somatic reality. In this case, in my opinion, we cannot say that it is properly a human body, because of brain death or of the lack of a brain. When an architect builds a house, the form he gives to the various materials is not natural but artificial, because he does not give life to them. Something similar happens with the ventilator, which is used to maintain a dead individual. In short, in my opinion, the same reality, i.e. the ventilator, could be either an instrument to improve and prolong the life of a living person or a cause to maintain the inexorable decomposition process of a somatic reality.

DR. ROPPER [returning to question 15] *Does evidence demonstrate that cardiac and respiratory functions cannot take place after brain death, without artificial means (a ventilator)? What has the Repertinger case taught us?* As I have already said (Cf. pp. 250, 253-4), the famous Repertinger meningitis case, which Dr. Shewmon endorses, in fact ironically demonstrates that it is possible to keep a body and organs perfused for a long period of time. I would like to point out that that patient did not have an apnea test, at a time when you could have presumed that they were brain dead. I hope I am putting that clearly enough. We do not know about that patient. We know that

some time, in a brief epoch before the autopsy, there was necrosis of the lower brain stem, completing the brain death notion, but there is no testing at all to confirm that for us. My first presumption, although I am uncertain, is that that patient may not have been brain dead for a long period of time.

DR. DAROFF I think that the neurologists in this room would agree with the statement, that this case simply indicates that a ventilator kept a heart beating in a corpse for possibly ten years. Does any neurologist disagree? We cannot be absolutely certain that it is ten years, but it may have been up to ten years. This extraordinary case is perhaps the longest report of maintaining a beating heart in a corpse with the use of artificial ventilation.

PROF. CABIBBO I am not a neurologist but I read the article and what they found in the autopsy looks like there was no brain at all, essentially, so he was not a man anymore for who knows how long. Regarding the distinction between corpse and cadaver, my English is not so good to grasp these subtleties. In Italian, a corpse is a 'cadavere' and we have no other word.

DR. BERNAT One way to approach the question is to consider subsystems of a person that can be kept alive through mechanical or other scientific means, such as in cell culture. We know that HeLa cells that were taken from a woman who died in 1951, are still kept alive in cell culture in laboratories throughout the world. Yet no one would make the claim that she was still alive, even though cells from her body clearly remain alive. One could extrapolate that argument to an organ: if we could keep a kidney or a liver going through perfusion over a long period of time, everyone would agree that it was someone's organ but it was not that individual who remained alive. As Dr. Daroff said, having a heart perfusing blood to a series of organs mechanically supported is really not materially different than either of those examples and does not necessarily prove that that preparation in question is a living human being.

DR. TANDON Neurologically-speaking a person has two major components: the vegetative component of the human body and the intellectual or brain function. They are interrelated and it is this integration that we call a person. In absence of that integration there is no person, there may be a physical artificially-controlled organ in culture. You can now culture organs taken out of the body as organ cultures. You can think of this body which has separated from a brain which does not exist as multiple organ cultures but we cannot call this a human person. Regarding the way you

put it in words, I leave it to you, but as a neurologist I think that will be acceptable to all people sitting here.

DR. WIJDICKS I would like to add that Dr. Bernat and I called it a magnificent cell culture.

DR. ROPPER There is a comment by Dr. Shewmon generally in reference to this that created considerable controversy, 'It is not true that brain death necessarily leads to imminent cardiovascular collapse ... To still claim that in 2006 would be to overlook the abundance of published cases of prolonged somatic survival following brain death'. He refers to his own paper. I think we want to go on record as saying that is not entirely accurate. It pains me that he is not here to have the conversation, but I do not think he is a critical care neurologist and people who do this for a living would say that is just not true.

DR. POSNER I think we should go on record saying it is not relevant. In the literature there are patients who have been kept with their body functioning a week, a month, a hundred days. The fact that Shewmon can say that there are some individual bodies that have been kept going for two months or six months is irrelevant. That patient was dead from the time the ventilation was started.

DR. WIJDICKS I think we should say it is not true and not relevant.

DR. ROPPER [returning to question 16] *What is the clinical evidence that there is no chance of recovery from brain death and that discussions regarding recovery from various states of coma must be separated entirely from brain death?* Certainly the latter part of that is true, I think that has been repeatedly emphasised. The first part is true but tricky to prove. There has never been a recorded case and, in fact, in a way again through a paradox of logic these few prolonged somatic survivals are evidence that there has not been such a case.

DR. BERNAT I would like to make a refinement to that comment also. I suspect that some of the cases of 'prolonged somatic survival' that have been reported were not examined properly. Physicians may not have performed state-of-the-art neurological examinations, including a proper apnea determination. In our institution we had such a case and I was asked

to review it. It was clear to me that the physician who performed the brain death determination did it incorrectly. So my mild refinement to Prof. Ropper's answer would be to add the qualification that the brain death determination has been done properly, using the accepted standards of medical practice that we have defined here.

DR. DEECKE We should add for the non-physicians the fact that brain tissue or brain cells cannot regenerate.

DR. WIJDICKS I think it is, in general, correct to say that the clinical examination was incomplete in those cases in which recovery has occurred but I would argue that in practice it is probably far more that preconditions were not met and that these patients recovered because they were intoxicated, rather than have patients who missed some part of their neurological examination then suddenly started to recover. In general, those patients are so severely damaged that there is very little recovery possible. I think that it is perhaps in practice more the failure to recognise the important preconditions, hypothermia and sedative agent and neuromuscular agents and several others were not met or not recognised and therefore the patient had a chance to recover even sometimes dramatically.

DR. POSNER I think it is fair to say that there is no recorded case of a patient awakening from properly diagnosed brain death. On the contrary, there are a number of recorded cases of autoresuscitation of the heart after the cardiologist has given up attempting resuscitation, so that brain death is a much more certain diagnosis than is cardiac death.

DR. ROPPER [returning to question 18] *What are the clinical evidence and implications of the recent reports on axon regeneration in patients with severe brain damage and what is the relationship of such reports to the criterion of brain death as death?* They are really two different entities, two different circumstances. The notion, particularly when you see the dissolution and liquefaction of the brain, that there would be regeneration of any sort would not be biologically feasible.

DR. DAVIS Just to reiterate, because we are making concluding remarks, we have all agreed that these patients are not dead, they are severely brain injured, it is a very challenging area in which there are some developments but these people are not dead and we have made that fundamental distinction, so it is not relevant to the criteria or the signs of death.

DR. ROPPER Moreover, there is a societal risk to suggesting that there is a continuum and there might be a relationship. It is at the moment beyond comprehension.

DR. MASDEU That is very important. The reports of axonal regeneration are on people who are not brain dead, so there is no evidence of any axonal regeneration in brain dead individuals.

DR. BERNAT Yes, the answer to that question is that you do not get axonal regrowth in the absence of functioning neurons and that the patient with diffuse axonal injury, who is in a minimally conscious state in which the tensor diffuse imaging showed the regrowth of axons was predicated on their being intact neurons that permitted this axonal regeneration, that is not the case in the brain dead patient where the neurons are destroyed, so any opportunity for axonal growth would be absent.

DR. TANDON The evidence of axonal regeneration that was claimed in the paper presented by Dr. Davis was not an evidence of axonal regeneration, it was only imaging which showed axonal flow, not necessarily that there was axonal regeneration. So far there has been no demonstrable acceptable proof that such an axonal regeneration will take to the extent that it will overcome the whole brain dead brain.

DR. DAROFF It is an absurdity, and absolutely inconceivable that axons can grow in a brain in the absence of blood flow to the brain.

DR. ROPPER [returning to question 19] *In addition, can one demonstrate that adult stem cells in the brains of brain dead people are dead or is it possible to posit that some are still alive and could be used in the future for regenerative purposes?* I guess the follow on question has to do with stem cells and the theoretical notion that if stem cells were somehow preserved in the brain dead brain there might be the potential for the reconstitution of the brain in some fashion. I think it would meet with the same answer, but I was rebuffed early in the conversation yesterday about where those stem cells came from so I do not want to dominate that answer either.

(PROF. SPAEMANN suggests a new question that in the list of questions corresponds to n. 5, cf. p. XLV) *Es besteht, wie mir scheint, heute Einigkeit über die Irreversibilität des Hirntodes. Allerdings gibt es einige Neurologen, die glauben, das müsse nicht für immer so sein. Ich kann das nicht beurteilen.*

*Aber alles scheine doch hinauszulaufen auf die Frage, ob künstlich erhaltenes Leben des Gesamtorganismus eines Hirntoten Leben ist oder nicht.*

*[It seems to me that today there is a consensus about the irreversibility of brain death. Nevertheless there are some neurologists who think that should not be forever. I am no judge of that. But all that seems to amount to is the question whether artificially maintained life of the whole organism is life or not.]*

DR. BERNAT To respond to Professor Spemann's question of whether it is life, I would say that it is a living organ or an organ subsystem but it is not a living human organism. The human as the integrated, interrelated organism as a whole is no longer alive and what is still living are human organs that are being perfused by a beating heart.

(BISH. SÁNCHEZ S. suggests a new question that in the list of questions corresponds to n. 6, cf. p. XLVI) I asked one question to Prof. Spaemann who is great philosopher and could clarify also for me these questions. *Do you think that a body without the brain or a brain dead body has a soul?*

PROF. SPAEMANN Die Frage von Mgr. Sánchez ist identisch mit meiner Frage: ist ein solcher Körper ein lebender Organismus? In traditioneller Sprache: „hat er eine Seele – ja oder nein?“

[Msgr Sánchez's question is identical to my question: is such a body a living organism? In traditional language: 'Has it a soul – yes or no?']

BISH. SÁNCHEZ S. What is your answer?

PROF. SPAEMANN Der lebende Körper ohne funktionsfähiges Gehirn ist nicht ein Sack voll lebendiger Organe, sondern ein hochkomplexes System, das viele Subsysteme nach wie vor koordiniert. Und diese Einheit stiftende Koordination heißt Leben. Ich würde Ihre Frage also mit „ja“ beantworten.

[The living body without a working brain is not a sack full of organs, but a system which is highly complex and which coordinates many subsystems now as before. And that coordination causing unity is called life. Therefore I would answer your question with 'yes'.]

DR. DEECKE I would answer the question in the following way: on the way to brain death is what happens what we call dying and I think, if you believe in a soul, in a spiritual principle, then the soul leaves the body



already in the moment of brain death. And I agree with my colleague Dr. Bernat that the remaining body is dead because there is no coordinator, no head of the whole system available any more. So it is a corpse. And I would not say that this remaining body is *beseelt* (German for animated, inspired) that it is animated or has this spiritual principle.

BISH. SÁNCHEZ S. Prof. Spaemann, can you use philosophy to support the idea that a body without a brain has a soul? Which philosophy? Because it is clear that in Aristotelian Thomistic philosophy it is impossible for a body without the brain or a brain dead body to be informed by a soul. This philosophy seems to me to support the idea of Pope John Paul II with his definition of death as the separation of the soul from the body and I think, with this definition of death, it is impossible for a body without a brain or without a head or, as it was said, a decapitated body or, again, a brain dead body, to be a living human and not a corpse.

PROF. SPAEMANN Was ist dann mit dem Embryo? [What is the case with the embryo?]

BISH. SÁNCHEZ S. But the embryo is a perfect stem cell with an individual DNA, what Aristotle would call 'form' containing within it a development programme, which is passing from a real potency to the complete development of the brain.

PROF. SPAEMANN The embryo in the first weeks is a human being without a brain.

BISH. SÁNCHEZ S. Sorry, but no; it is not that the embryo does not have a brain at all: the embryo has a potential brain under development. In the other case, be it brain death or decapitation, we no longer have a brain. It is a completely different ontological situation. One situation is the potential development of the complete body with the brain and the other situation is that you have only the body without the brain. Going back to Aristotle, we can say in his language that the embryo is a generated individual who, from an intrinsic principle – the form –, is developing everything that corresponds to his reality, and therefore also the brain, and in the other case, because of the lack of a brain or the destruction of the brain cells, we have the corruption of this individual with the separation of form from the body, and consequently a corpse.

PROF. CABIBBO This is a very difficult question because clearly medical doctors cannot tell us when the soul departs from the body. However, from what I read in the words of John Paul II and through what I heard at school in Catechism is that the Church accepts that the definition of death by physicians is correct. When a physician says that a person is dead, normally he or she is dead and the Church will say that the soul has already departed. We are not in the situation like in the famous movie 'Night of the Living Dead' where instead of departing the soul remains attached to the corpse and does horrible things to the living people. This is my understanding but certainly there is a point where the discussion is passed over to the theologians or philosophers.

PROF. VICUÑA This is not philosophy but something very practical. According to you, Professor Spaemann then, no medical doctor could disconnect a patient or a body that is being ventilated, since it would be a crime. As far as I know, there is no legislation that punishes the disconnection of a ventilator. Would you consider it a crime then to shut down a ventilator?

PROF. SPAEMANN Not at all. Es gibt keine Pflicht, jeden Menschen um jeden Preis künstlich am Leben zu halten. Das Abstellen des Ventilators ist zwar äußerlich eine Handlung und sieht so aus wie eine Tötungshandlung. Tatsächlich aber ist es nur die Beendigung einer Handlung, zu der wir nicht immer verpflichtet sind. Leider machen hier oft Juristen unberechtigte Schwierigkeiten. Ich beantworte also Ihre Frage mit „nein“. Die andere Frage aber ist: verschwindet die Seele mit der Gehirnfunktion? Es war Descartes.

Vorstellung, dass die Seele in einem bestimmten Körperteil sitzt, Descartes meinte: in der Zirbeldrüse. Die Seele ist also eigentlich nur die forma dieses Körperteils, der dann sozusagen causa efficiens – und nicht formalis – der Lebensfunktionen des Organismus ist. Wenn die Seele forma corporis ist, dann ist sie im Fuß ebenso unmittelbar präsent wie im Gehirn. Die Seele ist das Prinzip des Lebens. Fragen wir also: lebt der menschliche Organismus noch bei totem Gehirn? Bei der Erörterung dieser Frage besteht das Risiko, dass wir endlos um Worte streiten. Die Frage sollte dann eigentlich lauten: Wann sollten wir von „Leben“ sprechen und wann nicht? Wir müssen diskutieren über die Begründung unseres Sprachgebrauchs.

[Not at all. There is no obligation to keep any person alive at every cost. The removal of a ventilator is apparently an action and it seems to be a killing action. In reality it is only the termination of an action which is not always an obligation for us. Unfortunately jurists often make unfounded

troubles here. Therefore my answer to your question is 'no'. But the other question is: does the soul disappear together with the brain function? It was Descartes' idea that the soul had its seat in a certain part of the body, Descartes thought in the pineal gland. So the soul is just the forma of that part of the body, which is in a way *causa efficiens* – and not *formalis* – of the life function of the organism. If the soul is *forma corporis*, thus it is directly present in the same way in the foot as it is in the brain. The soul is the principle of life. So let us ask: is the human organism with a dead brain still alive? In discussing that question there is the risk that we endlessly struggle for words. In fact the question should be: when should we talk about 'life' and when not? We have to discuss the motivation of our linguistic usage.]

BISH. SÁNCHEZ S. In my opinion it is not correct to say that it is only Cartesian philosophy that says that the brain is the principal part of the body; this is a natural observation. We only need to say that if the brain is not in the body there is no soul either. Also Thomas Aquinas said, and I apologise because this is a philosophical question but it is important, that the soul is the form of the body and, for this reason, the soul is in all parts of the body, but as a motor the soul uses the first organ as an instrument to transmit energy to the body. This distinction of the soul as form and as motor is very important also for us. This means that the brain is not a medium between the soul and the body as form, but a medium as motor between the soul and the other organs of the body. Thomas Aquinas considered the first organ as an instrument that communicated movement to the other organs. Without this instrument, the body cannot receive life from the soul so the soul separates from the body. This instrumental mediation of the first organ in the causality of the soul as motor (and not as form) is not a Cartesian interpretation but a Thomistic one.

PROF. SCHAMBECK Wenn wir davon ausgehen, dass der Mensch ein Verstandeswesen ist, dann ergibt sich die Antwort auf die Frage nach der Dauer des Menschseins aus dem Umstand, dass das Menschsein endet, wenn der Hirntod eintritt. Mit der Erkenntnis des Todes im Zeitpunkt des Hirntodes ergibt sich auch nach dem treffenden Hinweis von Exzellenz Sánchez Sorondo, dass der Verstand auch im Dienst der Seele steht, eindeutig, dass damit das Menschsein endet.

Wenn wir uns, wie Herr Kollege Spaemann nach den Wortbegriffen fragen, würde ich meinen, dass zwischen der bloßen Existenz und dem Leben eben ein Unterschied gegeben ist. Dass hier vielleicht für den anderen Teil des Körpers eine Existenz gegeben ist, aber nicht ein Leben als Mensch.

Diese Grenzsituation, um einen Begriff von Karl Jaspers zu gebrauchen, hat sich für uns von Thomas von Aquin an, ich verweise auf seine Schrift „De Ente et Essentia“ durch den Fortschritt der Medizin und der Technik ergeben. Und daher ist es dankenswert, dass unser Heiliger Vater Papst Benedikt XVI. im Anschluss an Papst Johannes Paul II. uns aufgerufen hat, uns über das Lebensende Gedanken zu machen. Ich glaube, wir wären hier auf dem besten Weg von der Naturwissenschaft her unter Zuhilfenahme der Philosophie und des Rechts die Enzyklika *Fides et Ratio*, zu der auch Exzellenz Sánchez Sorondo kommentierend Bedeutendes geleistet hat, zu bedenken. Dazu möchte ich auch auf die Lehre von der Entelechie bei Aristoteles hinweisen. Wenn wir nämlich das menschliche Sein entelechial verstehen und das telos im ens erkennen, dann können wir feststellen, und damit darf ich meinen Diskussionsbeitrag schließen, dass mit dem Hirntod hier ein telos erreicht ist, das auch nicht fiktiv fortgesetzt werden kann.

Ich glaube, wenn wir diese entelechiale Betrachtung anstellen und das einschlägige Schrifttum des Heiligen Vaters Benedikt XVI. hier, auch in seinem Schrifttum schon als Professor und Kardinal betrachten, dann glaube ich, werden wir in einer entsprechenden Beantwortung seines Briefes zu einer mit ihm übereinstimmenden Auffassung der Seinsbetrachtung und der Lebensdauer gelangen.

Das ist ja eigentlich die Hamletfrage „Sein oder nicht Sein“. Wenn wir gläubige Menschen sind, dann sind wir ja aufgefordert, eine Antwort auf die Seinsfrage zu geben, die sich uns allen stellt. Ich freue mich, dies heute hier im gemeinsamen Bemühen mit Persönlichkeiten verschiedener Religionen feststellen zu können. Auch der Heilige Vater Johannes Paul II. und der Heilige Vater Benedikt XVI. waren immer nicht nur für eine ökonomische Partnerschaft, sondern auch für eine ökumenische Brüderlichkeit. Ich danke, und damit schließe ich, Exzellenz Sánchez Sorondo und Präsident Cabibbo, dass sie uns mit diesen Einladungen von Persönlichkeiten aus verschiedenen Erdteilen und außerdem Repräsentanten verschiedener Bereiche der Medizin, Bereiche der Philosophie und der Jurisprudenz auch die Möglichkeit gegeben haben, über die Grenzen der Wissensbereiche und der Religion eine Brüderlichkeit zu entfalten, die in einer Zeit, in der wir den Frieden dringend brauchen, von Wichtigkeit ist.

[If we presuppose that man is a rational being, the answer to the duration of human existence results from the circumstance that human existence finishes when brain death occurs. After His Excellency Sánchez Sorondo's appropriate comment that the mind is also subordinated to the soul, from the cognition of death at the moment of brain death it also results clearly that human existence ends here.

If we ask ourselves like our colleague Spaemann about semantic concepts, I would say that there is a difference between pure existence and life. Perhaps there is an existence for the other part of the body, but not a life as a human being. This borderline situation, to use a concept of Karl Jaspers, has emerged with St. Thomas Aquinas (and here I am referring to his work 'De Ente ed Essentia') because of the progress of medicine and technology. And therefore we have to be grateful that the Holy Father Benedict XVI, following Pope John Paul II, has called on us to reflect about the end of life. I think that starting with science and with the aid of philosophy and law and considering the encyclical *Fides et Ratio*, to which also His Excellency Sánchez Sorondo's comments have made has a significant contribution, we are on the best possible path. I would like to point to Aristotle's doctrine of the entelechy. If we understand the human being as an entelechy-being, and if we see the 'telos' in the '*ens*', we can realise – and here I want to finish my contribution to the discussion – that with brain death there has been reached a 'telos' that cannot be continued, not even fictitiously.

If we make this consideration about entelechy and if we reflect here on Pope Benedict XVI's writings, I think that already in his writings as a professor and a Cardinal on being and the duration of life, we will reach, with our answer to his letter, an identical understanding to his own.

This is essentially Hamlet's question: 'to be or not to be'. If we are believing persons, then we are called to give an answer to the question of being, which all of us are confronted with. I am glad that today I can achieve this together with people of different beliefs. The Holy Father John Paul II and the Holy Father Benedict XVI have always been not just for an ecumenical partnership, but also for an ecumenical brotherhood.

In conclusion, I thank His Excellency Sánchez Sorondo and President Cabibbo, through these invitations and to people from different continents and to representatives of different fields of medicine, philosophy and law, for having given us the possibility of developing a brotherhood beyond the borders of religion, which is of great importance in a time which has an urgent need for peace.]

BISH. SÁNCHEZ S. I believe that the detailed philosophical discussion can wait for another time. I think it is important now to know, from a neurological point of view, whether the body without the brain, the decapitated body, is a living organism as a whole, not as a single organ.

PROF. CABIBBO The business of the neurologists is... They are brain workers, it is like asking taxi drivers whether life without cars would be of

any interest. It is clear that if you ask neurologists whether life without brain is meaningful they would say no. I am joking, of course!

BISH. SÁNCHEZ S. I think that knowing what is a body without a brain is first and foremost a neurological question, absolutely for neurologists, not only for the human body but also for superior animals. In my opinion, according to common sense, it is impossible to think that a body without a brain, a decapitated body, is a living body as a whole. I am not saying as a single organ but as a unity.

DR. TANDON Not only neurologists but I do not think any medical man will accept the statement that a body separated from the head or the brain is a living body, as a unity, which you are mentioning. I think there will be no disagreement on that in this community.

DR. PUYBASSET I would just like to make a short comment regarding all this discussion. When we ventilate a brain death patient, we authorise ourselves to do that only for the purpose of organ donation. Otherwise ventilating a patient without a brain is, for me, a medical monstrosity, because we then create some tremendous problems that we should not. We overcome our role as doctors, which is not to ventilate brain dead patients, we do that only if it can serve the better purpose of organ donation and to help other people, otherwise we should not do that. All this discussion of ventilating people who are brain dead for me is unconceivable, it is much beyond what we should do as doctors. As doctors we should not authorise ourselves to do that. If we go beyond this limitation, beyond this red line, it is only for organ donation purposes, because then we think that we can save four persons, then it is worth it, for a short period of time, 10 hours, 12 hours, 24 hours, but not more, but I will never accept to ventilate a brain dead patient for a longer period of time, because then we have this semantical discussion regarding life and death. This should not occur, reasonable doctors should never do that, it is a crazy medical situation, it is Frankenstein. I would never ventilate a brain death patient after a refusal for organ donation, even if a family asked me to do that, because I think it is not in my role to do that.

DR. HENNERICI Just a short answer to your question. I think yesterday Werner Hacke and today Allan Ropper made it very clear: the situation, when we make a diagnosis of brain death, is a unique one, it is essentially in a person who is very severely ill and who has a severe lesion of the brain

and this person needed artificial ventilation. This is the only subgroup we are talking about. I think one basic misunderstanding, probably, with Dr. Spaemann and people like us working in this field is that we talk about death in general. It is not a general discussion about everybody's death but it is a very peculiar, specific situation. Once the diagnosis is made, the apnea test illustrates this specific situation, this is a short lasting test to show what happens if the artificial ventilation is stopped. Actually, the appearance of the body immediately becomes much closer to the general impression of a dead body because breathing stops and heart action can become arrhythmic, blood pressure falls down, so if you wait a little bit longer you have all the signs that you have in cardiorespiratory arrest. This is why Werner Hacke yesterday said, if this diagnosis is made with the complete standardised testing, then death can be declared and experienced and then we should behave like we do under these circumstances. The only delay that we accept is for transplantation and to collect the organs for transplantation, and this is only allowed for this purpose and the benefit of others we are ethically responsible for, otherwise we would have to stop ventilation at that moment, immediately, because the person is now dead.

DR. DEECKE I think Professor Spaemann addressed the neurological community. I think that, in this meeting, we did our homework, so to say. I think that we were very strict in our statement that, for instance yesterday it was said, you can live without a leg or without other limbs, you can even live with an artificial heart, but you cannot live without a brain. So, without a brain, life is gone, it is no human living any more, no human personality. I am not a dualist but if you believe in dualism, I would say this spiritual principle has left already when the brain is dead.

PROF. CABIBBO May I add a word that I take from John Paul II, he speaks of a correct anthropology in discussing the light in which you should examine this problem. I think the medical profession should be our scientific guide to understand this.

BISH. SÁNCHEZ S. I think it would also be important to hear Cardinal López Trujillo's opinion, because he is a Cardinal very interested in anthropological issues.

CARD. LÓPEZ TRUJILLO Devo dire che non mi aspettavo di dover prendere la parola; pensavo soltanto di ascoltare ma, su invito di Mons. Sánchez Sorondo, mi permetto di dire qualcosa di molto semplice.

Ho constatato, prima di tutto, il pensiero quasi unanime dei medici e degli scienziati che, nella loro autonomia scientifica, hanno concluso: quando c'è vera morte cerebrale, non c'è vita. "Vera" significa che, in casi particolari, dove esistono certi problemi, la diagnosi non si può considerare veramente completa, per un aspetto o per un altro. Ma dove c'è vera *morte cerebrale*, per un medico o uno scienziato non si può parlare di vita, anche tenendo in considerazione una nozione della vita che può benissimo avere il medico in un senso antropologico più completo: cioè che è un'unità coordinata e che si svolge in continuazione. La presenza di fatti o segni di una *disarticolazione irreversibile*, porta i medici ad una conclusione riguardante ciò che devono fare e possono fare.

Questo è il compito, secondo la scienza medica, che si presenta ogni volta che siamo di fronte ad un certo insieme antropologico, perché la vita è definita nella sua totalità, secondo una visione olistica, che non è quella che va soltanto a rispondere di una singola parte del corpo, cioè di un organo o dell'altro.

In questo senso, personalmente non vedo nessuna ragione di disaccordo tra il punto di vista scientifico, anche rispettando la vostra autonomia di scienziati, e il pensiero antropologico e filosofico.

Altro aspetto: la ricchezza di questa riunione sta nella ricerca di un dialogo anche con i filosofi e con altri scienziati. Dal punto di vista filosofico sono pienamente d'accordo con Mons. Sánchez Sorondo. La medicina da sola non può dare l'ultima spiegazione del perché c'è questa *disarticolazione irreversibile* e subentra così la filosofia a presentare un altro aspetto, la *forma sostanziale*. Tale forma sostanziale ha una forza, non soltanto col pensiero aristotelico, perché è impossibile avere una tale unità coordinata, sistematicamente in sviluppo, ecc., senza che vi sia un principio o una causa, che spiegherebbe con tutta la forza cosa si opera nel campo filosofico. Sappiamo che San Tommaso, nel suo pensiero, arrivava ad un certo punto, ma oggi grazie al forte sviluppo della scienza, la concezione della medicina è più vasta. Però la risposta a tutto il problema della morte non può essere offerta solo attraverso la medicina; si dà una risposta filosofica che possiamo trovare nell'ilemorfismo di una forma sostanziale del corpo (anima), che è una spiegazione nel pensiero di secoli.

Il livello teologico è più completo, in senso antropologico, nell'unità di fede e ragione. Di questo ha brevemente parlato il Cardinale Martini. Nella antropologia biblica, nella metafora della creazione dell'uomo, c'è il soffio di Dio nelle narici, un alito di vita. Così l'uomo diventa un essere vivente. Il *Nefesh* (anima) fa vivere. La morte è la mancanza di quell'alito di Dio, per cui l'anima diventa come un'ombra, *rephaim* che va allo *Sheol*.



Nella concezione cristiana la creazione fa splendere la totalità del potere di Dio. L'unità del corpo e dell'anima nella morte non c'è più: l'anima, che è immortale, si separa dal corpo. Xavier Zubiri offre un ricco approfondimento su questo argomento.

E la nozione della spiritualità dell'anima va unita proprio alla concezione profonda del mistero della creazione. Così nei grandi teologi, l'arricchimento del pensiero sulla persona umana, sulla vita e sulla morte, è un insieme affascinante per il principio della totalità della potenza di Dio nella creazione. Ciò permette anche che questa forma sostanziale, che è spirito, possa vivere separata dal corpo: è tutto il mistero della creazione, redenzione e risurrezione.

A conclusione di questo mio pensiero, che ho espresso sebbene non mi fossi convenientemente preparato su tale argomento, voglio aggiungere che è di grande bisogno per l'umanità intera una concezione integrale antropologica dell'uomo, che deve essere considerata dalla scienza, la quale deve riconoscere i propri limiti. Qui inizia il contributo della filosofia. È una risposta, sia dal punto di vista ontologico che metafisico, molto importante nell'insieme. Anche la teologia e la fede danno un tipo di risposta. Quell'insieme fa parte di un dialogo molto arricchente per tutti.

Ciò che vedo di molto positivo in questo giorno è che si apre la possibilità di un dialogo rispettoso dei diversi campi della medicina e della scienza, di una debita spiegazione e di un pensiero filosofico. Manca l'aspetto teologico del quale non si può parlare se non si prende in considerazione la totalità della creazione. In Cornelio Fabro possiamo trovare diverse spiegazioni sull'anima e sulla sua immortalità. È bello poter intraprendere un dialogo che porti ad una concezione globale, perché altrimenti, trattando questi concetti disgiuntamente, potremmo cadere in una totale separazione, che condurrebbe a ciò che Romano Guardini definiva "disumanizzazione", cioè l'uomo visto soltanto in un aspetto, considerato come una cosa, non come una persona. È la non personalità dell'uomo. In tal modo l'uomo diventerebbe uno strumento.

Sono stato felice di constatare la vostra preoccupazione per l'uomo nel contesto familiare. Si tratta di una preoccupazione profondamente umana, per poter avere una maggiore sicurezza e sapere se si tratta di una vera morte cerebrale della persona. Ma occorre andare ad una concezione più integrale, perché è di quella che c'è bisogno, come diceva il Cardinale Cottier, nella legge, nei gruppi internazionali, nell'ONU, nella Comunità Europea.

Se non si va ad un concetto più integrale di una antropologia ricca e totale, sulla quale la medicina dà una risposta valida, sebbene limitata, anche i

filosofi non sarebbero in grado di dare la loro risposta completa, perché la totale verità si trova soltanto nell'amore di Dio che crea l'uomo integralmente. Nel nostro Lexicon si può trovare una bella sintesi, al di fuori del pensiero di Romano Guardini, cioè quella presentata da Leo Scheffczyk.

Dunque penso che la cultura integrale, della quale si è trattato, deve essere concepita nella totalità della fede e della ragione, la quale deve prendere in seria considerazione sia la scienza, sia la filosofia, sia la teologia.

Esprimo la mia gratitudine per l'invito a questo incontro e per la possibilità di prendere la parola.

PROF. CABIBBO Siamo noi che la ringraziamo perché innanzitutto la ringraziamo di essere stato con noi in questo giorno, spero sia stato utile, abbiamo molto gradito il suo apprezzamento per il nostro lavoro che abbiamo cercato di fare al meglio, quindi la ringraziamo moltissimo.

BISH. SÁNCHEZ S. With regard to the following questions and answers, I think that Prof. Spaemann agrees on many of these. What I would like is to propose to Prof. Spaemann to draft with his precision two questions in relation to whether brain death is the death of the individual or otherwise, and what is a body without the brain. Then, I would like to suggest to him to also write the first answers to these questions. Afterwards, the participants will also be able to give their own answers.

PROF. SPAEMANN I did not understand well. You will formulate some new questions?

PROF. CABIBBO No, the proposal is that you, Prof. Spaemann, write the questions and write your first answers. We will put these questions together with those already formulated.

PROF. ZICHICHI I just want to make a remark. I have the feeling that, from what I heard, the scientific community of the specialists is unanimous in establishing that brain death is the end of human life from the point of view of medicine. This is extremely clear. So I think there is nothing to be added. From what I have heard, the consensus is unanimous that brain death establishes the end of human life. This is what I understood and from the scientific point of view this seems to me extremely consistent. I am not a philosopher so I cannot interfere with philosophical thought but I understood this meeting has as purpose to ask the specialists to give an answer which I think could not be more clear and unanimous. Thank you.

PROF. SPAEMANN Ich muss Professor Zichichi leider widersprechen. Es gibt hier keine Einstimmigkeit. Die Mehrheit, nicht die Gesamtheit der scientific community vertritt die Hirntoddefinition. Die annähernde Einstimmigkeit auf diesem Symposium beruht darauf, dass die Dissenters hier fast nicht vertreten sind. In Deutschland gibt es mehrere hervorragende Spezialisten, die der Harvarddefinition widersprechen. Die Publikationen, darunter eine Habilitationsschrift an der Humboldtuni-versitat in Berlin, die die Hirntodthese für überholt halten, mehren sich. Die Juristen, die sich speziell mit diesem Thema beschäftigen, haben sich von der Harvarddefinition nicht überzeugen lassen. Und auch auf diesem Symposium kann von einer Einstimmigkeit der Spezialisten nicht die Rede sein, solange Dr. Shewmon, der, was unser Thema betrifft, mit seiner empirisch fundierten holistischen These sozusagen die Galilei-Rolle übernommen hat, nicht wirklich widerlegt wurde.

[I am sorry to contradict Prof. Zichichi. There is no consensus. The majority and not the totality of the scientific community holds on the definition of brain death. The consensus at this symposium is based on the fact that there are almost no dissenters represented here. In Germany there are a lot of excellent specialists who contradict the Harvard definition. The publications, among them a thesis submitted for the habilitation certificate from the Humboldt University of Berlin, that consider the thesis of brain death outdated, are increasing. The jurists who are concerned with that thesis were not convinced by the Harvard thesis. And also at this symposium there is no consensus of the specialists as long as Dr. Shewmon – who, concerning our theme, has taken on the role of Galilei with his empirically founded holistic thesis – has not really been contradicted.]

PROF. CABIBBO If I may add something maybe on the problem of scientific evidence. It is clear that the whole subject is relatively recent, it is what, 45-50 years old?

DR. ROPPER The data we have, if I am not mistaken, is from 1987 to 1995, so it is the last ten years.

PROF. CABIBBO But just on this famous case of Dr. Shewmon which was a very early case, so sometimes in physics it happens that the first results of early experiments are wrong. I remember I had one example in my career, not that I made an error but that I did not believe a certain result because it did not fit with certain theories and in the end a new experiment

demonstrated the result was different. So in the very early experiments in physics you are testing an idea until you really understand perfectly your instruments. Also in the beginning maybe you have three cases, five cases, in our case 'events', now maybe instead of having five we have five thousand or five million etc. so the whole thing becomes a much safer scientific situation in the sense of giving an answer to certain questions. So, in this sense, I think it is not unreasonable to simply forget cases which were not studied with the kind of rigour which we now would require to say for example that a person was brain dead. The very situation that this boy was twenty years old and in the meantime a few years have passed, so it is really a case that started 30 years ago, 25 years ago if I understand correctly, so it is very early in the history of this subject. So I think we will learn much more when centres like the one Dr. Wijdicks mentioned get more statistics and these things will become more and more clear. I think already if we neglect the very early examples which might be dubious, the recent statistics seem to indicate that the conclusions are becoming very firm. That is my impression.

DR. ESTOL It is just important to state that the cases you are referring to do not challenge the question of brain death as death. As Allan Ropper has said, they actually serve to confirm the notion that these are corpses, cadavers with some body functions artificially sustained in a dead body, but nobody here thus far has challenged the concept that an accurate determination of brain death means death and after death there is nothing left but a corpse that is not the 'person' any more.

The President concluded the meeting by thanking all present for their active and fruitful participation. He also extended his thanks to the Chancellor, the secretarial and technical staff, the translators and the caterers.

# MENTAL DISCONNECT: 'PHYSIOLOGICAL DECAPITATION' AS A HEURISTIC FOR UNDERSTANDING 'BRAIN DEATH'<sup>\*,1</sup>

D. ALAN SHEWMON

## 1. STATEMENT OF THE PROBLEM

The important task entrusted to this Conference by Popes Benedict XVI and his predecessor John Paul II has been clearly articulated by Bishop Chancellor Sánchez Sorondo: 'The Academy is thus faced with the task of seeing whether the criterion of brain death (according to its full definition) indicates the biological state of death of an individual ...' (Conference Brochure, p. 4, 'The Purpose of the Meeting').

It is remarkable that in the last decade or so, the various position statements and official commentaries on brain death by neurological and other medical societies have failed to state *why* brain death should be regarded as death of the individual. The same can be said for many recent books and chapters by neurologists on the subject. The equivalence is simply taken for granted as common knowledge, and the discussions focus rather on such aspects as diagnostic criteria for determining that the brain is dead, controversies over how much of the brain must be destroyed for the brain as a whole to be dead, etc.

The American Academy of Neurology, for example, in its 'Practice Parameters for Determining Brain Death in Adults' (1995), which still remain the gold-standard diagnostic criteria in the United States, did not offer a single reason why it considers death of the brain to be death. Neither did fellow conferee Dr. Eelco Wijdicks in his accompanying commentary on the 'Practice Parameters' (Wijdicks, 1995) or in the chapter on brain death in his book on critical care neurology (Wijdicks, 2003, pp. 547-62). Nor, in his recent book on brain death (Wijdicks, 2001a), does he state why he him-

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences.

<sup>1</sup> Although not publicly discussed, this paper was added because Professor Shewmon sent it in before the meeting and it was privately viewed and discussed by the participants.

self believes brain death to be death; rather, that apologetic task was delegated to co-conferee Dr. James Bernat, who has become somewhat of the unofficial brain-death-theory spokesperson for mainstream neurology (not without good reason), in whose chapter only a single paragraph is devoted to answering what he himself characterizes as ‘the most serious challenges thus far to the brain death concept’ (namely my publications as of that time) (Bernat, 2001, p. 180). Neither does fellow conferee Dr. Allan Ropper, in the sections on brain death in his two widely read textbooks, state why he considers brain death to be death (Ropper and Brown, 2005, pp. 306-7, 961-2; Ropper *et al.*, 2004, pp. 157-64). Along similar lines, in their introductory essay for the conference brochure entitled ‘Why the Concept of Brain Death is Still Valid as a Definition of Death’, Dr. Ropper and colleagues concern themselves with rebutting the weakest arguments against brain death, while ignoring or glibly dismissing the strongest arguments, without in the end offering a single reason ‘why the concept of brain death is still’ – or ever was – ‘valid as a definition of death’.

Discussions at this conference regarding the history of brain death, disorders that are not brain death, neuroimaging, apnea testing, determination of irreversibility, determination of totality of brain nonfunction or destruction, controversies over what constitutes a ‘critical’ function of the brain, etc., interesting and important though they may be, will not bring the Church any closer to an understanding of whether and why death of the brain, so diagnosed, ‘indicates the biological state of death of an individual’.

I daresay that doctors in general, and neurologists in particular, have come to an overwhelming consensus that brain death is death, not because they have examined the evidence and concluded it for themselves, but purely and simply from a professional herd mentality. When queried about it, few can give a coherent explanation why brain death is death itself, as opposed to deep coma in a dying patient. In a revealing survey of physicians and nurses involved in transplantation, who surely ought to have a solid understanding of brain death for the sake of their own consciences, 58% did not use a coherent concept of death consistently and 19% held a concept of death that would logically classify patients in a persistent vegetative state as dead (Youngner *et al.*, 1989). This is a serious mental disconnect in professionals who should have clear and coherent thoughts on the matter.

## 2. FOUR CANDIDATE RATIONALES FOR EQUATING BRAIN DEATH WITH DEATH

Across the half-century of brain-death history up to the present, the many proposed reasons for equating death of the brain with death of the

individual have fallen into four basic categories:

(1) *because* death is not an objective physical state but a relativistic legal definition or custom based on what seems most useful to a given society at a given time (societal relativism); or

(2) *because* the brain is the organ of the mind, which is the essence of the person; therefore, the irreversible cessation of mind is cessation of the person, i.e., 'death of the individual' (person/mind reductionism); or

(3) *because* the brain is the central integrating organ of the body, so that without brain function the body ceases to be a unified biological organism and begins the irrevocable process of disintegration, thereby indicating cessation of 'the corporal reality of the person' (to quote Pope John Paul II, 2000) (somatic integration rationale).

(4) *because* the permanent loss of *both* mental functions *and* bodily unity, attendant upon death of the brain, constitutes – again in the words of Pope John Paul II (2000) – 'the total disintegration of that unitary and integrated whole that is the personal self' (psychosomatic integration rationale).

A fifth rationale is not listed, because it is only a pseudo-rationale, namely the 'fatal lesion fallacy' (brain death is death because it will imminently lead to death). Remarkably, some experts still offer this as an implicit rationale for brain death (e.g., Dr. Wijdicks, 2001b, p. 76): 'In the United States, primary brainstem death does not fit into the concept of whole brain death, but it has been accepted in the United Kingdom and rightly so, because no survivor has been reported when all brainstem function has been lost'.

There are no other broad categories of proposed reasons why death of the brain as an organ should constitute death of the individual person. Let us now examine these four rationales in somewhat greater detail.

(1) *Societal relativism* was the rationale of, among others, Dr. Henry Beecher, chairman of the Harvard Committee, as made clear in some of his commentaries following the revolutionary Harvard Committee report of 1968, which marked the beginning of the general acceptance of brain death as death (Beecher *et al.*, 1968). 'At whatever level *we choose to call death*, it is an *arbitrary* decision. Death of the heart? The hair still grows. Death of the brain? The heart may still beat. The need is *to choose* an irreversible state where the brain no longer functions. It is best *to choose* a level where, although the brain is dead, usefulness of other organs is still present (p. 120). ... Here we *arbitrarily* accept as death, destruction of one part of the body; but it is the supreme part, the brain (p. 121). ... Can society afford to discard the tissues and organs of the *hopelessly unconscious patient* so greatly needed for study and experimental trial to help those who can be

salvaged? (p. 122)' (Beecher and Dorr, 1971) (emphasis mine). Needless to say, societal relativism is incompatible with any sort of objective metaphysics of life and death, and as such is incompatible with the fundamental tenets of many of the world's religions, including Catholicism.

(2) *Person/mind reductionism* declares the person to be dead when there is no longer a personal mind or consciousness, even in potency (e.g., excluding states of sleep or coma from which there is a potential to awaken; whether human embryos are excluded or not varies across authors). According to this view, truly *irreversible* coma, as well as permanent vegetative state (defined according to the American Academy of Neurology and many other professional societies in terms of unawareness of self and environment – cf. Shewmon, 2004a; Shewmon, 2004b) are therefore death of a person, regardless of the biological life/death status of the (former) person's body (also prescinding here from the subtle controversies surrounding the terms 'irreversible' and 'permanent' (Cole, 1992; Lizza, 2005; Lizza, 2006, pp. 102-7; Tomlinson, 1993). This rationale is frequently referred to in the literature as the 'higher brain' formulation of brain death. It has had and continues to have many advocates. Such equating of person with mind is patently Platonic/Cartesian and contrary to the Aristotelian/Thomistic notion, which the Church endorses, that the human person is a corporal/mental hybrid, so that the spiritual soul is at once both the center and source of intellectual and volitional powers of the mind, as well as substantial form (life-principle) of the body (Council of Vienne [1312], 1957).

This psychological rationale was most strikingly articulated by one of the participants of the Pontifical Academy of Sciences' Second Working Group on Brain Death: '[T]he Cartesian 'cogito ergo sum' principle is still applicable in our days. Life means that the individual has the right and/or the ability to think freely. Death steps in when the brain is no longer able to think ... death can only arise from the cessation [of] the ability to think' (Gerin, 1992, pp. 91-2).

It is no secret that the philosophical world-view of most scientists today is material monism: only matter-energy exists, and all talk of any sort of spiritual 'soul' is meaningless nonsense, a holdover from previous ages of unscientific religious credulity. The fact that the brain is the organ of the mind, in this world-view, therefore translates necessarily to the thesis that the human mind is totally the product of physical brain activity (mysterious as that may be). Thus, most scientists today, and especially neuroscientists, are not only person/mind reductionists, but person/mind/brain reductionists, so that permanent unconsciousness from a brain lesion con-



stitutes cessation of personal existence. Perhaps the most succinct statement of such reductionism is to be found in the chapter on brain death in the influential textbook *The Diagnosis of Stupor and Coma* by Drs. Fred Plum and fellow conferee Jerome Posner: 'Agreement that the brain and the person are one has essentially removed the ethical conflict that otherwise derives from the almost universal respect for the dignity of the individual human being' (Plum and Posner, 1983, p. 325).

By contrast, according to the philosophical anthropology endorsed by the Church, the fact that proper mental functioning depends on the instrumentality of the brain translates rather to an interpretation of permanent unconsciousness as a severe mental disability, a paralysis of a person's psychological functions, but not an annihilation of the person, so long as the human organism remains biologically unified and alive, which is a sign of the continuing presence of the human soul in its other capacity as substantial form of the body. Catholic neurologists and neuroscientists are not immune to assimilating material-reductionistic ideas from their professional environment, despite the incompatibility with their faith.

(3) *Somatic* and (4) *psychosomatic integration*. Both of these rationales stand or fall on whether a developed human body (embryos and fetuses excepted) requires somatically integrative brain function to remain a unified biological organism, totally apart from the brain's role in mental functioning. In the 1970s and '80s this presumed physiologically integrating role of the brain was almost universally cited as a well established medical 'fact' by brain-death apologists (e.g., the U.S. President's Commission [1981], the Swedish Committee [1984], and the two Working Groups of the Pontifical Academy of Sciences [Chagas, 1986; White *et al.*, 1992]). Despite increasing challenges by new clinical and theoretical counterevidence over the last 10 years, many still cling to the somatically integrating role of the brain as a fundamental reason why brain death is supposedly death (whether the *only* fundamental reason as in the somatic integration rationale, or one of two fundamental reasons – *both necessary* – as in the psychosomatic integration rationale). Since societal relativism and person/mind/brain reductionism are incompatible with Catholic anthropology, it goes without saying that all endorsements of brain death by expressly Catholic apologists or Catholic institutions rely critically on the supposed medical 'fact' that without brain function the human body is no longer a unified organism and is therefore dead (and the person whose body it was is dead).

It was precisely the emergence of impressive counterevidence to this supposed medical 'fact' that caused me in the early 1990s to reverse my ear-

lier position defending brain death as death (as presented at the Second Working Group of 1989 [Shewmon, 1992]). Over the last 10 years an increasing number of brain-death commentators, including both advocates and critics of brain death as death, have rejected the somatic-integration thesis as no longer tenable. The October 2001 issue of *Journal of Medicine and Philosophy* was devoted entirely to the topic of brain death. In the preface, the issue editor acknowledged being convinced by my lead article (Shewmon, 2001) that '[e]quating brain death with loss of somatic integrative function, while useful for clinical, transplant, and policy purposes, is physiologically inaccurate and theoretically incoherent' (Lustig, 2001, p. 448). Moreover, the other authors, spanning a broad spectrum of philosophical and ethical opinions surrounding brain death, acknowledged being convinced that the brain-dead body is after all a living human organism (Dagi and Kaufman, 2001; Halevy, 2001; Potts, 2001; Youngner and Arnold, 2001). The same conclusion is accepted by most 'higher brain death' advocates (Lizza, 2006, p. 14; Spittler, 2003, pp. 91-2; Veatch, 2005) and other thoughtful critics of brain-death orthodoxy (Potts *et al.*, 2000; Truog, 1997).

At the Third International Symposium on Coma and Death, in Havana, Cuba, February 22-25, 2000, I gave a keynote address (Shewmon, 2004c), which in philosopher John Lizza's opinion 'delivered on [my] claim to 'drive the nails into the coffin' of the idea that organic integration requires brain function' (Lizza, 2004, p. 52). During the question-and-answer session Dr. Fred Plum himself, brain-death expert and co-author with Dr. Posner of the important textbook *The Diagnosis of Stupor and Coma* (Plum and Posner, 1983), stood up and said in essence, 'OK, I'll grant you that the brain-dead body is a living human organism, but is it a human *person*?' At which he proceeded to propound person/mind/brain reductionism as the *real* reason why brain death is death, insisting that the biological life/death status of the body is philosophically and ethically irrelevant.

It is not mere carelessness when prominent neurologists and neurosurgeons drop 'Freudian slips' regarding the life/death status of the brain-dead body, implying agreement with Dr. Plum's comment at the Cuba symposium.

*Dr. Albrecht Harders*, neurosurgeon: 'Transcranial Doppler findings were obtained in 15 patients who fulfilled the clinical criteria for brain death ... All of the patients *died* within 24 hours or upon discontinuation of the mechanical ventilation' (Harders, 1986, p. 115) (emphasis mine).

*Dr. Allan Ropper*, neurologist and first author of this Conference brochure's introductory essay: 'Dr. Ropper added that it has been suggested that children who are brain dead *can be kept alive* by artificial means for a

long period of time, but this is not true in adults' (*Neurology Today*, March 2002, p. 7) (emphasis mine). (We may give Dr. Ropper the benefit of the doubt that this was a misquotation on the part of the medical reporter; it is nevertheless provocative that that was the impression the reporter came away with). Of greater interest are the words Dr. Ropper and colleagues themselves chose, in their popular textbook *Principles of Neurology*, to describe long-surviving cases of brain death: 'In exceptional cases, however, the provision of adequate fluid, vasopressor, and respiratory support allows *preservation of the somatic organism in a comatose state* for longer periods' (Ropper and Brown, 2005, p. 962) (emphasis mine). This is precisely my thesis, that these patients are indeed comatose human organisms.

*Dr. Fred Plum*, neurologist: In a book chapter published in 1999, Table 2.4 is entitled 'Prolonged Visceral Survival after Brain Death', the fifth column of which has the heading *Mode of Death* (Plum, 1999, p. 38). Included in this column are entries of either 'spontaneous cardiac arrest' or 'respirator discontinued', implying that these patients were *not* dead by virtue of the brain death, which had taken place from 26 to 201 days before, but by virtue of the circulatory-respiratory arrest. Later in the same chapter, regarding a series of 73 brain-dead patients, Plum wrote: 'half experienced asystole by the third day but the bodies of 2 *lived on* until the 10th and 16th day' (Plum, 1999, p. 53) (emphasis mine).

The late *Dr. Ronald Cranford*, long-time chairman of the Ethics Committee of the American Academy of Neurology and prominent expert on brain death, was more forthright in not only his own endorsement of person/mind/brain reductionism, but even in opining that this was the ultimate, though tacit, conceptual driving force behind the widespread acceptance of brain death in the 1970s: 'It seems then that permanently unconscious patients have characteristics of both the living and the dead. It would be tempting to *call them dead and then retrospectively apply the principles of death, as society has done with brain death*' (Cranford and Smith, 1987, p. 243) (emphasis mine). I am indebted to Dr. Cranford for his bringing to my attention certain cases of prolonged survival in brain death and for his candid editorial commentary to my 1998 article on 'chronic brain death' (Shewmon, 1998), in which he agreed with my conclusion that these bodies are biologically living organisms, although he opined that this is ethically irrelevant because they are still dead as human beings (Cranford, 1998).

My impression from many Socratic conversations with colleagues on this issue is that most neurologists and physicians in general, when probed and pressed for a coherent rationale why brain death is death, regardless

what rationale they may offer at the beginning of the conversation, will ultimately end up saying something like Dr. Plum did in Havana: 'OK, I'll grant you that the brain-dead body is a living human organism, but is it a human *person*?' Nevertheless, 'cessation of the organism as a whole' still remains the tacit, semi-official rationale for brain death in most countries as well as the explicit rationale in Catholic circles.

### 3. BRAIN DEATH AS 'PHYSIOLOGICAL DECAPITATION'

In the effort to explain why brain death is death, authors of all persuasions have often made use of an analogy with decapitation, according to seemingly straightforward syllogistic reasoning:

- (1) A decapitated person is dead.
- (2) Brain death is physiologically equivalent to decapitation.
- (3) Therefore, a brain-dead person is dead.

I must preface this discussion with an apology for the distastefulness of the topic at a time when beheading is no mere historical curiosity of the French revolution, but a current and barbaric form of terrorism carried out on innocent hostages, sometimes even slowly and piecemeal in order to maximize the agony and the horror of it. Out of respect for these victims and their loved ones, I would prefer not to deal with the topic here in writing. Nevertheless, a thorough re-evaluation of brain-death orthodoxy is now very timely and necessary, and it cannot be done without addressing in depth the validity and explanatory utility of this traditional and powerful analogy. Therefore, I shall proceed, trying to keep the discussion as hypothetical as possible, but with a reverent awareness that some aspects of the analogy are sadly all too real.

#### 3.1. *Utilization of the Analogy by Advocates of Whole-Brain, Brainstem, and Higher Brain Death*

The analogy must get at something fundamental and important about the essence of brain death, since it has been utilized by all three of the major competing brain-death camps: 'whole brain', 'brainstem', and 'higher brain'.

Among whole-brain advocates, nothing less than the U.S. President's Commission itself wrote: 'Contrast such situations [heart or kidney transplants, dialysis, iron lung], however, with the hypothetical of a decapitated body treated so as to prevent the outpouring of blood and to generate respi-

ration: continuation of bodily functions in that case would not have restored the requisites of human life' (President's Commission, 1981, p. 36). In the Commission's critique of 'higher brain death', it also refers to the analogy: 'When the brain processes cease (whether due to decapitation or to 'brain death') the person's identity also lapses' (p. 39). Eighteen years later, the Commission's Executive Director, Alexander Capron, was still citing 'physiological decapitation' as '[p]erhaps the easiest way to think of brain death' (Capron, 1999, p. 125). Conferee Dr. James Bernat, one of the most prominent apologists for 'whole brain death', began his chapter on philosophical and ethical aspects in Dr. Wijdicks' book with a historical reference dating the *Anlage* of modern brain-death theory back to observations on decapitation: 'The idea that irreversible absence of brain function was the equivalent of death began in the 12th century with the writings of the famous Jewish physician and philosopher Moses Maimonides. Maimonides noticed that decapitated humans exhibited muscular twitches for a short time immediately following decapitation. He asserted that decapitated humans were dead instantly and that such muscle movements were not a sign of life because they lacked the central direction that was indicative of the soul' (Bernat, 2001, p. 171; cf. also Bernat, 2002, p. 244). Within Judaism the 'physiological decapitation' analogy of brain death was introduced by Rabbi Dr. Moshe Tendler, citing Talmudic support for it (Tendler, 1978, p. 395). The validity and consequences of the analogy remain controversial among Jewish authorities, but its importance as a heuristic device is clear (Rappaport and Rappaport, 2004, p. 135; Rosner, 1999, pp. 217-9).

'Brainstem-death' advocates in the United Kingdom make similar use of the analogy. As far back as 1975, the British medical literature cited decapitation by guillotine as a conceptual aid to understanding the new criterion of death (Thurston, 1975). A 1996 monograph by Pallis and Harley (Pallis and Harley, 1996), one of the most complete and vigorous defenses of 'brainstem death', goes so far as to include a photo of an actual execution by decapitation (date and place unidentified), showing a propped-up, sitting, headless body with distinct columns of blood spurting spectacularly into the air. (At least it is in black and white). The caption reads: 'Anatomical decapitation. Heart is still beating as shown by jets of blood from carotid and vertebral arteries'. The associated text reads: 'One type of event epitomizes the fact that death may precede cessation of the heart beat: decapitation. Once the head has been severed from the neck the heart continues to beat for up to an hour [citing here an 1870 French reference regarding execution by guillotine]. Is that person alive or dead? If those who hold that

a person can be truly dead only when the heart has stopped believe that a decapitated person is still alive simply because parts of the heart are still beating, they have a concept of life so different from ours that we doubt if bridges could be built. The example given is one of *anatomical* decapitation. Brain death is *physiological* decapitation and usually occurs when the intracranial pressure has lastingly exceeded the arterial pressure. Nevertheless, the implications of the two types of decapitation are similar. They are that the death of the brain is the necessary and sufficient condition for the death of the individual person' (Pallis and Harley, 1996, p. 4).

Advocates of 'higher-brain death' similarly make good heuristic use of the analogy and all sorts of hypothetical variations on it, such as surgical brain removal, head or brain transplants, partial brain transplants, isolated living brains floating in vats, replacement of parts of the brain with futuristic computer chips, etc. I based my own earlier defense of brain death largely on a thought experiment involving surgical decapitation and technological maintenance of both the isolated head and the headless body (Shewmon, 1985; Shewmon, 1988). Similar kinds of thought experiments have been used to support a consciousness-based 'higher-brain' notion of death by philosophers (Green and Wikler, 1980, pp. 123-5; Lizza, 2006, pp. 28, 107; Machado *et al.*, 1995, pp. 3-4; Wikler, 1988), ethicists (Youngner and Bartlett, 1983, p. 265), and neurologists (Machado, 1994, p. 214; Machado, 1995, p. 63-4; Machado, 2000, pp. 206-8; Spittler, 2003, p. 110).

Actual experimental decapitations of animals, with mechanical ventilation and prevention of exsanguination, have been performed to prove that such thought experiments in humans are in principle physiologically possible. In the Pallis and Harley monograph cited above, on the page facing the decapitation-execution photo, there is a photo of a decapitated chicken standing, with the head lying on the ground at its feet. The text reads: 'About 25 years ago a picture of an unsuccessfully decapitated chicken appeared in a leading magazine. The forebrain had been amputated and lay on the ground. The brainstem was still in situ. The animal, still breathing, was photographed some time after the decapitation. Was it alive or dead? In our opinion the animal must be considered alive so long as its brainstem is functioning' (Pallis and Harley, 1996, p. 5). A pregnant sheep was technologically maintained for 30 minutes following decapitation, when a healthy lamb was delivered by Cesarean section (Steinberg and Hersch, 1995). Neurosurgeon Robert White, consultant for the Pontifical Academy of Sciences' First and Second Working Groups on Brain Death and co-editor of the proceedings of the Second Working Group, performed experi-

mental head and brain transplants in monkeys to demonstrate the theoretical feasibility of such thought experiments in humans, and made use of these experiments in his arguments justifying brain death as death (White, 1968; White, 1986; White *et al.*, 1965; White *et al.*, 1963; White *et al.*, 1964; White *et al.*, 1971). Bernard Gert, co-author with Bernat on two important conceptual articles on brain-death (Bernat *et al.*, 1981; Bernat *et al.*, 1982), cited these experiments of White in his later independent defense of brain death (Gert, 1995, pp. 25-6).

What I intend to show in the remainder of this paper is that, when the 'physiological decapitation' analogy is properly dissected down to its essential features, it ironically proves just the opposite of what 'whole-brain' and 'brainstem' advocates have been using it for. Namely, I will show that the 'physiologically decapitated' brain-dead body is just as much a living 'organism as a whole' as a body with high spinal cord transection, the difference being that the former is comatose and the latter is conscious – but as far as the physiological equivalence goes, they are the same. If the focus of the analogy is on the headless body and its physiology, then the analogy completely backfires on the defenders of 'whole-brain' and 'brainstem death'. If, on the other hand, the focus is on the severed head, consciousness and personal identity, then the analogy has a powerful heuristic value for defenders of 'higher brain death'. I will argue, however, that the conclusions that can be drawn from thought experiments involving brain-body separation are highly speculative, depend in large part on one's basic philosophical world-view, and in the final analysis are irrelevant to understanding clinical brain death, in which no such separation is involved. Michael Reuter, in his recent monograph on brain death, comes to a similar conclusion about the lack of heuristic utility of the decapitation analogy (Reuter, 2001, pp. 54-5). Not only can such thought experiments not be taken as proof that brain death is death within the framework of a Catholic philosophical anthropology, but something much stronger can be said – that the somatic-physiology aspect of the analogy surprisingly proves that brain death cannot be death within a Catholic philosophical framework.

### 3.2. *Focus on the Body – Is it Still an Organism as a Whole?*

Let us begin by focusing on the headless body following decapitation, since, after all, that is the part where the 'physiology' occurs in 'physiological decapitation'.

### 3.2.1. *Irrelevance of Exsanguination and Esthetic Considerations*

First I want to quickly dismiss the relevance of references to actual decapitation-executions (such as mentioned historically by Bernat and sensationalized by Pallis and Harley). Everyone seems to take for granted that a person dies instantly upon execution by guillotine or swift sword swipe (the major premise in the syllogism at the beginning of section 3. above). I suggest that this assumption is essentially an unreasoned gut-reaction to the emotional shock effect: the extreme degree of mutilation (neither part *looks* like a human being ‘as a whole’) combined with the profuse and rapid exsanguination from both parts. True death no doubt occurs some seconds to minutes later after a critical degree of exsanguination and anoxia in whichever of the two severed parts (or both) is the person. One hardly needs guillotines to know that the heart has its own intrinsic pacemaker and can beat perfectly well without any influence from the brain (although unmodulated in rate [García *et al.*, 1995]). Hearts removed for transplantation will continue beating spontaneously for some time completely outside the body. Be that as it may, no one can seriously claim that the acutely exsanguinating, unventilated body shown in Pallis and Harley’s execution-photo is physiologically equivalent to a brain-destroyed body with normal blood volume, no bleeding, and normal blood gases maintained by mechanical ventilation.

Since neither grotesque mutilation nor exsanguination characterizes clinical brain death, there must be something else about decapitation that provides the supposed physiological equivalence with brain death. Moreover, that ‘something else’ must also be a reason why decapitation is death; otherwise the purported physiological equivalence would prove that brain death is *not*, rather than *is*, death.

A more plausible case for physiological equivalence can be made only if the decapitation analogy is ‘President’s-Commission style’, featuring the hypothetical details of immediate suturing of severed neck vessels and cauterization of tissues to prevent bleeding, plus mechanical ventilation through an endotracheal tube placed in the tracheal stump. The major premise in the decapitation-analogy syllogism is that such a headless body is dead. But this cannot simply be assumed without question. One possible reason for saying that it is dead is to draw attention to the mind/brain-body disconnection: to look over at the severed head and argue that the person is with the head, because the head contains the brain; therefore, what is left



of the person's true 'body' following decapitation is actually the head, while the rest (whatever it may be) is no longer the person's body. But note that this is not an argument that the headless body is biologically dead (not an 'organism as a whole'), but rather that it is not the original person's body. The question presently at hand is whether the headless body is a mutilated 'organism as a whole' or is a non-organism with the metaphysical status of a severed limb. If it is deemed to be an organism, the question *whose* body it is, if anyone's, is a completely separate issue that will be taken up below in section 3.3.

The question presently at hand is therefore: Is the ventilated, non-bleeding, headless body a mutilated and terminally ill 'organism as a whole' or a mere unintegrated collection of living organs and tissues? To answer *that* question, we must look directly at the biological properties of such a body. This is rendered difficult by the fact that, thankfully, no such preparation of a human body has ever been or (hopefully) will ever be carried out. Two approaches come to mind to investigate the physiological properties of such a hypothetically maintained headless human body: (1) its physiological equivalence with a brain-dead body, and (2) determining the 'essential' anatomical component of such decapitation (*vis a vis* brain-death theory) and examining the physiological properties of cases of 'critical' ('essential') partial decapitation.

### 3.2.2. *Somatic Physiology in Brain Death*

The first approach sounds strangely circular: to understand whether a brain-dead body is an 'organism as a whole', we investigate a decapitated, ventilated, non-bleeding body, which is physiologically equivalent. But there are none to investigate, so to understand whether such a hypothetically maintained body is an 'organism as a whole', we investigate brain-dead bodies, which are physiologically equivalent. There are plenty of the latter to investigate, and the amount of physiological data accumulated over the years is vast. The interpretation of such data has led to conflicting conclusions regarding whether such a body is a very sick organism or a non-organism (and consequently for our purposes, whether the hypothetically maintained headless body is a very sick organism or a non-organism).

#### 3.2.2.1. *Acute Instabilities*

Those who conclude from the somatic physiology of brain death that

such a body is a mere collection of organs and tissues, not an 'organism as a whole', point to several aspects: multi-system dysfunction and corresponding difficulty maintaining such bodies for any extended period of time in ICUs (e.g., the maintenance of brain-dead pregnant women for weeks to bring the fetus to viability is always a technological *tour de force*), extreme cardiovascular instability, and the alleged imminence of cardiovascular collapse despite all technological means to prevent it. Such reasoning is faulty. If brain-dead bodies are in fact unintegrated collections of organs, then such physiological properties would surely follow. But the fact that such physiological properties occur with brain-dead bodies does not prove that therefore they are unintegrated collections of organs. 'If A, then B' is not equivalent to 'B, therefore A'.

Indeed, there are other explanations for the multiple physiological instabilities of acute brain death that have nothing to do with the putative explanation of the brain being the central integrating organ of the body, without which the body literally dis-integrates. In many cases of brain death the etiology that damaged the brain directly damages other vital organs as well (e.g., severe hypoxia-ischemia, massive trauma). In my meta-analysis of 56 cases of brain death with survival at least 1 week, one of the two factors that statistically significantly influenced survival potential was indeed etiology (multi-system damage had shorter survival potential on average than primary brain pathology) (Shewmon, 1998). Even in cases of primary brain pathology, the very process of brain herniation, prior to actual death of the brain, can produce a 'sympathetic storm' resulting in subendocardial microinfarcts and neurogenic pulmonary edema (Wijdicks and Atkinson, 2001, pp. 32-8).

Thus, there could be several reasons why these patients are often so unstable in the acute phase that have nothing to do with loss of integrating brain function. Moreover, there are many kinds of severe brain lesions short of brain death, as well as non-brain lesions (e.g., high spinal cord injury, severe Guillain-Barré syndrome, septic shock, etc.) that result in similar degrees of cardiovascular instability and multisystem dysfunction, but no one concludes from the requirement of a similar level of high-tech ICU care that such patients are already dead. No more does such acute somatic instability *per se* prove that brain-dead patients are already dead.

Another reason for the systemic instability in many cases of acute brain death is spinal shock. As far as the spinal cord is concerned, brainstem infarction down to the level of the foramen magnum has the same effect as transection of the spinal cord at the level of the foramen magnum

(Jørgensen, 1973; Jørgensen, 1995; Shewmon, 1999b; Shewmon, 2004c). Spinal shock lasts days to weeks and involves not only hypotonia and loss of tendon reflexes but also, and more importantly, autonomic areflexia, which exacerbates the instabilities already due to intrinsic or secondary multisystem damage.

### 3.2.2.2. *Some Brain-Dead Patients Are Dead, But Not Because Only Their Brains Are Dead*

I am quite sure that some brain-dead patients *are* in fact already dead by virtue of associated supracritical multisystem damage, and the mechanical ventilation merely masks this fact. (This ‘masking’ theory of brain death – that there is only one kind of death, and the only difference between traditional ‘cardio-pulmonary’ criteria and the new neurological criteria is that in the latter the death-state is ‘masked’ by the artificial ventilation – is one of the earliest proposed rationales in the history of brain death. It was originally popularized by lawyer-ethicist Alexander Capron (Capron, 1987; Capron, 1999, p. 125; Capron and Kass, 1972) and promoted by the President’s Commission (of which Mr. Capron was Executive Director) (1981, pp. 33, 35, 58) as applicable to *all* cases of brain death. This theory of brain death was obliquely alluded to by Pope John Paul II in his discourse to the Transplantation Society, when he described ‘the traditional cardio-respiratory signs’ and ‘the so-called ‘neurological’ criterion’ as alternative signs for the same physiological state (John Paul II, 2000). I suspect that such ‘masking’ of death by the ventilator is in fact the case with many brain-dead patients who experience rapid cardiovascular decompensation and cardiac arrest, from which they cannot be resuscitated by any means. If such patients (or some subset of them) are dead, it is not *because* their brains are dead, but because they suffered supracritical multiorgan damage, including the brain. The diagnostic problem with such cases is that one can’t know that they fall into this category until they actually undergo the cardiovascular collapse from which they can’t be resuscitated.

### 3.2.2.3. *Chronic Stability*

Contrary to an endlessly repeated dictum in the earlier brain-death literature, and parroted even as recently as 1996 by Pallis and Harley (Pallis and Harley, 1996, ‘Preface to the second edition’), *not all* brain-dead patients undergo imminent, irreversible cardiovascular collapse. The pro-

portion that could in principle survive longer than a few days with ICU care will never be known, since the huge majority either become organ donors or have the extraordinary-disproportionate life support ethically discontinued. What is known is that with therapeutic motivation (e.g., brain-dead pregnant women to bring the fetus to viability; cultural reasons – especially in Japan, for example, where many of the long-surviving cases have been reported; respect for family sensitivities and beliefs; etc.), some brain-dead patients have been maintained long enough for many of the acute instabilities to resolve: blood pressure stabilizes and pharmacological cardiovascular support is no longer needed; intestinal ileus resolves and nourishment can be maintained through enteral tube feedings; diabetes insipidus, if initially present, may spontaneously resolve.

As of 1998 I collected some 175 cases of brain death with survivals at least 1 week, not just 56 as is often stated about my article (Wijdicks and Atkinson, 2001, p. 39) by those who must not have examined the accompanying Tables 1 and 2, which detail all the cases and references (Shewmon, 1998). (These tables were too bulky for inclusion in the published article but were available to anyone interested). The 56 cases were a subset of the 175 with sufficient individual information available to include in a meta-analysis, which identified two factors that statistically predisposed to longer survival potential: primary brain pathology (as opposed to multisystem damage) and young age. The other 119 cases were from published series with aggregate, rather than individual data; many were from Japan.

This provocative research has been both praised and criticized. Most of the critics have expressed doubt regarding the reliability of brain-death diagnosis in all the cases, whether an apnea test was performed properly, etc. (Bernat, 2001, p. 180; Bernat, 2002, p. 257; Bernat, 2004, p. 161; Wijdicks and Bernat, 1999). All I can say is to repeat what I wrote in the article itself and quoted in my reply to letters to the editor: 'If patients were 'brain dead' enough to qualify as organ donors, they were surely 'brain dead' enough to qualify for this study' (Shewmon, 1998; Shewmon, 1999a). Even if, for the sake of argument, some of the 175 cases were misdiagnosed, surely the majority were not; and even more surely still, the *longest surviving* cases were not.

I will not repeat here the case history of the record survivor, 'TK', who at the time of my meta-analysis had been brain-dead for 14 years and on a ventilator at home. I presented a video of my complete neurological examination of TK at the Task Force on Brain Death of the Pontifical Academy for Life (1997-98), as well as at the Third International Symposium on

Coma and Death in Havana (Shewmon, 2000). Everyone who saw the video agreed that the patient met all the clinical criteria for brain death short of a formal apnea test, which could not be ethically performed because there would have been no benefit to outweigh the risks. (He had never been observed to breathe spontaneously for up to 1 minute off the ventilator during suctioning or tracheostomy changes). Confirmation of total brain destruction (including the entire brain stem) was obtained, however, by an MRI scan, which showed no identifiable brain or brain-stem structure, making the apnea test a moot point. TK finally expired after 20 years in the brain-dead state. A brain-only autopsy was performed, with singularly remarkable findings that confirmed still more definitively the totality of brain and brain-stem destruction (Repertinger *et al.*, 2006).

I am glad that the autopsy and publication were done by physicians with no relationship to me and with no previous special interest in brain death. It is clear from their multiple choices of words what all four co-authors consider TK's life/death status to have been. He 'died at age 24 years of complications of *H influenzae* type b meningitis acquired at age 4' (p. 591). 'During the rest of his life, he was ventilator dependent ... He required chronic care for most of his life ... In his final 2 months of life ... [H]e experienced a cardiac arrest in January 2004. Following his death, a brain-only autopsy was performed' (p. 592). 'Our pathologic findings at autopsy confirmed that his brain had been destroyed by the events associated with the episode of *H influenzae* type b meningitis, whereas his body remained alive (brain death with living body) for an additional two decades, a duration of survival following brain death that far exceeds that of any other reports' (p. 594). I have no doubt that anyone else who might have seen TK prior to his cardiac arrest would have used similar terms to describe his body: a clearly living human organism, deeply comatose, with vigorous spinal reflexes (both neuromuscular and autonomic) – in no way a disintegrated collection of organs and tissues, or a 'corpse' whose death was masked for 20 years by a mechanical ventilator.

It takes only a single property at the level of the 'organism as a whole' to prove that there is a 'whole'. But the bodies of TK and other long-term survivors in brain death demonstrate many holistic properties, such as, for example: complex homeostasis of hundreds if not thousands of interacting chemicals and enzymes, assimilation of nutrients and elimination of wastes, proportional growth, maintenance of body temperature (albeit subnormal and with the help of blankets), wound healing, overcoming of infections, ability to recover from illnesses serious enough to require hospital-

ization and be discharged home again, systemic stress responses to noxious stimuli, feedback balance of various endocrine functions, etc. (Shewmon, 2001). A 13-year-old boy in my series, whom I personally examined in a skilled nursing facility, began puberty while brain-dead (Shewmon, 1998, Table 1, 'BES').

These chronic cases, though rare, teach several important lessons about the nature of brain death. (1) The systemic instabilities associated with acute brain death are due to a combination of factors other than mere lack of brain control over the body: primary multisystem damage (depending on etiology), secondary cardiac and pulmonary damage from the process of brain herniation, and spinal shock. Therefore, these often transient instabilities cannot be cited as evidence that the body's integrative unity depends on brain function *per se*. (2) Whereas some brain-dead patients may in fact be dead by virtue of supracritical multisystem damage, some are clearly living organisms, albeit severely disabled and dependent on a mechanical ventilator, tube feeding and nursing care. (Again, the question of *whose body* such an organism is, if anyone's, is a separate issue, primarily philosophical rather than biological in nature, which will be taken up in section 3.3. below). (3) 'Chronic brain death' would no doubt be more common if not for the fact that in the huge majority of brain-death cases, either organs are harvested or the extraordinary/disproportionate care is terminated within hours of the diagnosis.

#### 3.2.2.4. *The Body Has no 'Primary Integrating Organ'*

Why do so many people think that if there is somatic integration, there has to be a single, primary organ responsible for it? Plants and embryos have no central integrating organ; rather, the integration is clearly a non-localized emergent phenomenon involving the mutual interaction among all the parts.

Two kinds of distinction have to be made: on the one hand the distinction between a healthy, optimally functioning organism and a sick and/or disabled organism; and on the other hand the distinction between a very sick, marginally functioning organism and a dead one (a non-organism). For human organisms the brain is clearly the primary organ as regards the first distinction: it is the organ that gives humans superiority over all other earthly creatures, the organ most intimately involved in the human mind, personality, and spirit (cf. Aquinas: *Quaestiones Disputatae de Anima*, a.8 co; *Quaestiones Disputatae de Spiritualibus Creaturis*, a.2 ad 7). The human

brain is regarded by many as the most awesome structure in the entire physical universe, and it is the reason why most neurologists, like myself, chose neurology as a career.

But the distinction 'healthy vs. sick' (or 'optimally functioning vs. disabled') has little if anything, physiologically or philosophically, to do with the distinction 'marginally alive vs. dead'. Therefore, the primacy of the brain regarding human health and mental life in no way implies that the brain is also, and necessarily, the primary organ for life vs. death of the human organism, or even that there is a 'primary organ' for life vs. death.

### 3.2.3. *The Essential Component of 'Physiological Decapitation'*

We have already determined that exsanguination is not a component of 'physiological decapitation'. What aspect of decapitation, then, is the essential one that supposedly makes it death? A related but distinct question, to be taken up later, is: What aspect of decapitation is the essential one that supposedly makes it physiologically equivalent to brain death? We shall see that the answers are not the same, which is a major problem for the analogy.

Insight into the first question (What essential component of decapitation makes it death?) may be gained by considering two extremes of partial decapitation. If the guillotine blade got stuck after penetrating only 1 mm into the epidermis of the back of the neck, it is obvious that the intended victim is still alive. On the other hand, if the blade passed through almost the entire neck and got stuck 1 mm from the surface of the front of the neck, leaving the head attached to the rest of the body only by a small sliver of skin, it is obvious that for the heuristic purposes of the analogy, this would be just as much death as a 100% complete decapitation (if, in fact, it is death). Now we have a conceptual dilemma, because life and death are generally understood as mutually exclusive categories, whereas the degrees of partial decapitation are along a continuum from infinitesimal to 100% minus infinitesimal, and the possible anatomical patterns of each degree are infinite. Where along such continua does life pass to death (assuming the analogy's utility as an explanation of brain death), and what non-arbitrary explanation can be given for the answer?

#### 3.2.3.1. *Candidate Components*

One consideration that may help is that the cross-sectional anatomy of the neck is not homogeneous, so the relevant question may not be in terms

of distance traversed by the blade, but rather what anatomical structures are or are not severed. It would be more meaningful and heuristically fruitful to forget about instantaneous decapitation from a large guillotine blade and imagine instead a slow-motion decapitation from precise serial cuts from a surgical scalpel. The question can then be rephrased, whether there is a critical structure or set of structures, severance of which is the 'essence', so to speak, of decapitation, insofar as that alone suffices to produce the death of decapitation, whereas severance of any or all 'non-critical' structures does not produce death. Let us consider the following most likely candidates for 'critical' structures: (1) the non-neural, non-vascular tissues of the neck (skin, fat, fascia, muscles, cartilage, ligaments, bone); (2) the major blood vessels passing through the neck; (3) the neural elements (spinal cord, phrenic and vagus nerves); (4) all of the above (i.e., the total separation of head from body). We now consider these one by one.

(1) Non-neural, non-vascular tissues are clearly not critical: selective severance of these, with preservation of blood vessels, spinal cord, phrenic and vagus nerves, would produce a severe mechanical instability, in essence a severe cervical vertebral fracture with extreme soft tissue injury. Such a patient would be perfectly conscious, able to breathe and move all extremities normally. If the patient were brought to an emergency room in such a condition, a neurosurgeon would place him or her in a metal 'halo' device to immobilize and stabilize the head to allow the cervical fracture to heal over ensuing weeks (the juxtaposed severed soft tissues would also gradually reconnect by scar formation, no doubt with the help of surgical sutures). Clearly such a patient is not dead by virtue of the structures severed, and this form of partial decapitation is not death.

(2) Severing of the major blood vessels in the neck is not death, but certainly will very quickly *produce* death from exsanguination, beginning with loss of consciousness within a few seconds from the sudden, total lack of blood flow to the brain, followed by progressive damage, at first reversible and soon irreversible, to all the organs and tissues of the body due to hypovolemic shock and complete exsanguination. The organs succumb not all at once but in a well known sequence, depending on their selective vulnerability to ischemia, beginning with the brain, then kidneys, liver and heart, then soft tissues, and much later skin and bone. When along this sequence of ischemic damage death actually occurs is not entirely clear, but it is certainly at least some minutes after the severing of the vessels. As pointed out above, such death from exsanguination has no resemblance to brain death, and in fact the most 'physiological' version of the 'physiological decapita-



tion' analogy has the vessels sutured closed as soon as they are severed, to prevent blood loss. A vessel-focused physiological analogy with brain death would be the simultaneous ligation (rather than severing) of all the major blood vessels to the brain, resulting in total brain infarction. But such ligation is not a physiological *analogy* of brain death; it would actually be a particular *cause* of brain death some minutes later. Blood vessels are not the essential core of the 'physiological decapitation' analogy.

(3) Selective sectioning of the neural elements produces apnea and quadriplegia. Such a patient brought to an emergency room would be placed on a mechanical ventilator and admitted to an ICU for stabilization of blood pressure, and management of a variety of systemic complications of acute spinal cord injury. After some days or weeks, the patient would be transferred to a rehabilitation unit. Clearly this form of partial decapitation is not death.

(4) Complete physical separation into two parts (abstracted from the exsanguination issue) seems the only possibility left. In other words, there is no essential core of partial decapitation that is *per se* death. If both head and headless body are technologically kept alive through attaching the body to a ventilator and keeping the head perfused with oxygenated blood by attaching its major vessels to a cardiopulmonary bypass machine, then we can legitimately question whether even complete physical separation is *per se* death or rather a condition that would quickly lead to death if heroic medical intervention had not taken place. Whether the original person is with the head-part, the body-part, both, or neither, is again a philosophical issue to be taken up later; here we are focusing on the biology of the body-part.

Surprisingly, when we search for the essential anatomical core of decapitation that makes it death, we find that, not only is it elusive, but not even complete decapitation may *per se* be death after all (as opposed to an injury that would ordinarily quickly lead to death).

### 3.2.3.2. *Brain-Body Disconnection in High Cervical Cord Transection*

That having been determined, we now address the second question posed above: What form of partial decapitation captures the essence of the physiological analogy with brain death (setting aside whether either is death or not)? The answer is clearly the sectioning of the nervous elements: spinal cord, vagus and phrenic nerves. If the sectioning is above the exit level of the phrenic nerves, then we need concern ourselves only with high spinal cord and vagus nerve. Theoretically, the somatic physiology of brain

death and that of high spinal cord transection plus vagotomy ought to be identical, apart from the influences of pituitary function, which are variable in brain death but intact in spinal cord transection. This comparison was astutely drawn by Youngner and Bartlett back in 1983 (1983, p. 254), and it still remains perfectly valid. To make the somatic analogy conservatively complete, we could compare brain death with the combination of high spinal cord transection plus vagotomy plus hypothalamic hypopituitarism. This is necessarily so in principle, because in both cases the body ‘sees’ only the parts of the nervous system distal to the foramen magnum: in the one case because the rostral parts are missing, and in the other case because they are disconnected.

The theory is also borne out by clinical data. A detailed point-by-point comparison of the pathophysiology of brain death and the pathophysiology of high spinal cord transection reveals that the two conditions are indeed clinically identical (particularly if the spinal cord lesion is combined with vagotomy and hypopituitarism, or if the brain death does not involve much pituitary dysfunction). The *only* difference is consciousness (by no means a minor difference, but we are focusing here strictly on the issue of somatic physiology). In fact, a typical textbook chapter on the ICU management of brain-dead organ donors and a typical textbook chapter on the ICU management of high spinal cord injury patients are so nearly identical that one could be transformed into the other simply by switching the terms ‘brain death’ and ‘spinal cord injury’. This is the case not only in the acute phase, when spinal shock plays a major role in the instabilities of each condition, but also in the subacute and chronic phases, when spinal reflexes and spinally mediated integration return. (For a detailed itemization and discussion of these parallels, see Shewmon, 1999b; Shewmon, 2004c).

The essential core of the ‘physiological decapitation’ analogy with brain death is high cervical cord transection plus vagotomy. But patients with high spinal transection are clearly not dead – and *not only* because they are conscious. It is not that they are conscious mind/brains within a jumble of unintegrated organs and tissues; rather, they are clearly still living mental/corporeal beings, with biologically living bodies, although ventilator-dependent and severely disabled due to the brain’s lack of influence over the rest of the body.

Two conclusions follow: (1) If high-cord-transected bodies are disabled ‘organisms as a whole’, then brain-dead bodies are equally disabled ‘organisms as a whole’, the former being conscious organisms and the latter being unconscious organisms. (2) Loss of somatic integrative unity is not a viable

rationale for either brain death or the decapitation analogy. If brain death is death, it can only be so by virtue of permanent loss of consciousness, as maintained all along by the 'higher brain death' advocates. This would imply that not only 'brain death' but any neurological lesion producing permanent unconsciousness (e.g., permanent vegetative state) is also death.

#### 3.2.4. *Logical Disconnects Between Brain-Death Theory and Practice*

Brain-body disconnection, which is the essence of the 'physiological decapitation' analogy, brings to light a number of paradoxes or mental (logical) disconnects between mainstream brain-death theory and mainstream brain-death practice.

1. What is so magical about the cervicomedullary junction that brain-stem mediated somatic integration 'counts' for life/death status, but spinal-cord-mediated somatic integration does not 'count'?

2. In the context of all other criteria for brain death having been met, why should the presence of a somatically irrelevant sluggish pupillary reflex mean the patient is alive, whereas the presence of a somatically integrative hypothalamic function (e.g., maintenance of water balance through regulated secretion of antidiuretic hormone) does *not* mean the patient is alive?

3. Some patients with all the clinical signs of brain death (on the basis of primary 'brainstem death') can have prominent electroencephalographic activity, including even patterns resembling physiological sleep (Esteban *et al.*, 1995; Grigg *et al.*, 1987). Therefore, when the American Academy of Neurology practice parameter states that brain death is a clinical diagnosis and that electroencephalographic confirmation is not necessary, it implies that it doesn't matter whether the cerebral cortex is functional or not so long as the brainstem is nonfunctional, thereby tacitly aligning itself with the British 'brainstem death' notion and disconnecting its brain-death diagnostic criteria from all U.S. statutory laws defining the neurological diagnosis of death in terms of the totality of brain nonfunction.

4. If the mainstream rationale for equating brain death with death is still integrative unity ('organism as a whole'), why do the mainstream diagnostic criteria for brain death not require a single somatically integrative function to be checked and why do they explicitly allow some integrative functions to be present without invalidating the diagnosis (e.g., absence of diabetes insipidus, cardiovascular stability, autonomic and endocrine stress responses to unanesthetized surgical incision)? When Ropper *et al.*, in their essay on page 5 of the Conference brochure, state that residual hypothalamic func-

tion is a 'spurious argument' (Ropper *et al.*, 2006), why should hypothalamic function be any more 'spurious' than a gag reflex, if what is supposedly to be diagnosed is total brain nonfunction? And why should such a somatically integrative function as secretion of antidiuretic hormone be more 'spurious' than a somatically non-integrative function such as a corneal reflex, if the rationale for equating brain death with death is supposedly the loss of the brain's integrating and unifying control over the body? (Cf. Brody, 1999, p. 73; Halevy and Brody, 1993; Truog and Fackler, 1992). Furthermore, it is not true, as claimed by Ropper *et al.*, that such hypothalamic function is always a 'transient phenomenon[on]'. In the majority of the 56 cases in my meta-analysis no mention was made of diabetes insipidus. I'm sure that some of these patients had it and the case reports simply omitted mention of it; I'm equally sure that many did not have it. In the record case of 'TK', what was transient was the presence of diabetes insipidus at the beginning, not its absence. It then spontaneously resolved, so that during most of his 20 years in brain death, he did *not* have diabetes insipidus, despite having no residual hypothalamic tissue identifiable at autopsy. To dismiss such a somatically integrative function, which is generally considered a brain function, as 'spurious' amounts to dismissing the mainstream rationale of integrative unity itself as 'spurious'. And what can possibly be meant by asserting that such 'technical arguments can be dealt with on a practical level'? It seems to imply that, for the sake of practicality, we should disconnect our minds from (i.e., ignore) this serious logical disconnect between mainstream brain-death theory and mainstream brain-death diagnosis, and simply forge ahead with mainstream brain-death practice and organ harvesting despite the incoherencies at its theoretical basis.

5. Another mental disconnect has to do with the cardiovascular instability in acute brain death, which is often cited as supportive evidence that brain death is death – so much so that one unusually coherent brain-death defender went so far as to state that, if there is cardiovascular stability without pharmacologic support, then the patient cannot be truly brain dead even if all the other signs are present, and that in such a scenario the heart cannot be ethically harvested (Cervós, 1991, p. 13). On the other hand, the American Academy of Neurology diagnostic guidelines (1995) explicitly regard cardiovascular stability without pharmacologic support as *compatible* with the diagnosis of brain death, and cardiac surgeons regard the best hearts for transplant as coming specifically from brain-dead donors with cardiovascular stability without pharmacologic support (Darby *et al.*, 1989; Guerriero, 1996). Thus, the very physiological qualities of the best heart donors logically conflict with the theoretical reason why they are suppos-

edly dead in the first place in order to donate ethically.

6. Yet another mental disconnect is the fact that, although mainstream neurology still semi-officially endorses the integrative-unity rationale, many experts in their heart of hearts endorse the consciousness-based rationale (dead person despite a live body). (See above quotations from Drs. Plum and Cranford; also personal impression from many conversations with colleagues on this issue).

7. Finally, there is the mental disconnect surrounding the 'physiological decapitation' analogy itself. The thought-experiment analogy is supposed to help us understand why brain death is cessation of the organism as a whole. But in the final analysis, we need to examine the actual pathophysiology of brain death in order to determine what the pathophysiology of a headless, ventilated, non-bleeding body would be like – and when we do, we are forced to conclude, after overcoming the instinct of revulsion at the mutilated appearance, that the decapitated body is after all an organism as a whole, to the same extent that a high spinal cord-transected body is, to the same extent that a brain-dead body is. *Whose* body the headless living organism is, if anyone's, is a totally different question, to which we shall turn now.

### 3.3. *Focus on the Head – Who's there, if Anyone?*

In our thought experiment, let us arrange things so that not only the ventilated body does not exsanguinate, but also the severed head, which is kept alive by attaching the major vessels to a cardiopulmonary bypass machine. Since nothing has been done to interfere with the brain's mediation of consciousness, we can reasonably assume that the head is conscious, with the same personal consciousness as before the operation, and that it can communicate with us through facial and eye movements. In my first brain-death publication, I argued that, since bone and soft tissue do not contribute to consciousness, the thought experiment would be just the same, and produce a greater external resemblance to brain death, if only the brain were removed and kept alive floating in a vat, by means of attaching the major blood vessels to a cardiopulmonary bypass machine (Shewmon, 1985). Based on what we know about brain and consciousness, this would result in the same personal consciousness associated with the isolated brain as with the full head, except now the conscious mind is cut off from all communication with the rest of the world and remains alone in its thoughts and memories. The brainless body is phys-

iologically identical to a brain-dead body.

### 3.3.1. *The Challenge of the Thought Experiment*

Given that the headless (or brainless) body is a living organism, as established in the foregoing section, and that the head (or isolated brain) is the putative locus of the original conscious person, what conclusions can be drawn regarding the personal status and/or identity of the body? At first glance it would seem that the person's true 'body' is the brain plus whatever is physiologically integrated with the brain (the head, or the entire intact body pre-decapitation); conversely, whatever is physiologically and spatially disconnected from the brain is not that person's body, regardless whether it is a living organism or not. Therefore, if now the isolated brain were disconnected from its life-support and allowed to die, the still living brainless body would remain just the same: a living organism but not the body of the original person. This is exactly what obtains in brain death, except that the total brain infarction takes place *in situ* rather than following surgical removal and temporary maintenance in a vat. Thus, the analogy lends strong support to the consciousness-based rationale for brain death, namely that the brain-dead body is a living organism but no longer a living human person: the original person died when the brain died. This line of argumentation was very convincing to me in the decade of the 1980s, and it formed the core of my defense of brain death, initially of 'higher brain death' (Shewmon, 1985) and later of a modified version of 'whole brain death', which I presented at the Pontifical Academy of Sciences' Second Working Group in 1989 (Shewmon, 1988; Shewmon, 1992).

At the time I had not yet realized that the headless (or brainless) body was a living 'organism as a whole' in its own physiological right, although a severely disabled one. Since the isolated living head (or brain) was the original person, I assumed without much further consideration that therefore the rest of the 'body' could not possibly be a true body but rather something with the metaphysical status of a severed limb, only larger and more heterogeneously structured. In 1992 the physiological equivalence between brain death and high spinal cord transection first dawned on me, forcing a difficult re-interpretation of the thought experiment in the new light of the headless (or brainless) body being rather a permanently comatose, living human 'organism as a whole'. For several years I was not sure how to reconcile these two apparently conflicting theoretical arguments for and against brain death being death of the individual, but I was surer of the empirically demonstrable somatic equivalence with spinal cord transection

than of philosophical speculations on a hypothetical thought experiment.

After 5 years of laying low on the topic, I ventured forth again in the literature with my new, iconoclastic position against brain death as death. In the autobiographical narrative of my intellectual journey, I realized that the thought experiment had to be seriously dealt with, and I attempted a reinterpretation of it in keeping with my new attitude toward brain death (Shewmon, 1997, pp. 70-5). That attempt received various criticisms, largely from higher brain death advocates, and in retrospect I concede that certain criticisms were valid (Lizza, 2006, pp. 102-7). I was never fully satisfied with my own reinterpretation even at the time, but was simply unable to come up with a better reconciliation between what seemed an unassailable physiological conclusion of 'organism as a whole', on the one hand, and death of the person with death of the brain in the thought experiment, on the other hand. Since then, my writings have focused on the organism as a whole, showing that brain function is not after all necessary for integration of the body, and that somatic integration is not localized to a particular master-organ but is diffuse throughout the body in the mutual interactions among its parts. This paper represents my first dealing with the decapitation analogy since 1997; hopefully the intervening 9 years have occasioned some additional insights and perspectives on the matter.

### 3.3.2. *Reductionistic Interpretation*

I am now convinced that the interpretation of the thought experiment is highly dependent on one's basic philosophical world-view. For a material monist and person/mind/brain reductionist, the solution is clear. The person is with whatever part contains the functioning brain. In case the analogy is extended to separation of only part of the brain (as proposed in my original *Thomist* paper [Shewmon, 1985]), then the person is with whatever contains the part of the brain that is conscious. That is now the person's true 'body', severely mutilated and hardly recognizable as a human body, but one nonetheless; the rest is not the person's body, no matter how much it might look like a human body. Given that it is biologically an 'organism as a whole', it could be called a 'humanoid organism' (Lizza, 2004, p. 52; Lizza, 2006, p. 15; Shewmon, 1985). The person dies when the part with the conscious brain dies, not when respiration and circulation irreversibly stop in the headless (or brainless) body. Since this is exactly what obtains in brain death, except that the brain dies *in situ* rather than after separation from the body, it follows logically that clinical brain death is just as much personal death as is death

of the separated conscious brain in the thought experiment.

### 3.3.3. *Catholic-Compatible Interpretation*

From the basic philosophical world-view of the Catholic Church, however, the interpretation of the analogy becomes much more complicated, because the human soul must also, and primarily, be taken into account. Of the various notions of 'soul' proposed in the history of philosophy, the one most compatible with the Judaeo-Christian tradition and officially endorsed by the Catholic Magisterium is the Aristotelian-Thomistic concept of soul as 'substantial form' or life-principle of the body (Council of Vienne [1312], 1957). In distinction from plant and animal 'souls', the human soul has a spiritual dimension which is the ultimate basis for hybrid spiritual/physical mental acts (which necessarily involve brain activity but are intrinsically irreducible to physical brain activity alone), such as reflective self-awareness, abstract concept formation, and volition. The brain is necessary for the interaction between the spiritual ego-center and the rest of the body and the world, but the person and the person's mental activities are more than mere electrochemical brain activity and involve a whole immaterial/spiritual dimension of existence, which the reductionist does not recognize. It should be emphasized that the concept of soul endorsed by the Church is *not* that of Cartesian dualism, in which a purely spiritual soul/mind somehow interacts with an essentially mechanical body. Rather, the soul is at one and the same time the spiritual basis for the immaterial dimension of mental functions *and* the life-principle of the body, making it an 'organism as a whole'. Separated from the body at death, the human soul is incomplete; it is in some sort of conscious state but cannot perform properly human mental functions without the instrumentality of the brain (cf. Aquinas' thoughts on separated souls: *Summa Theologiae*, Ia, q. 89; *Quaestiones Disputatae De Anima*, a. 15). This emphasizes the importance of the doctrine of resurrection of the *body* for Catholicism. (Contrast this with the Platonic notion of the soul as a spirit imprisoned in the body, which is not its fully functioning self until released from the body at death into a purely spiritual realm of existence).

For Catholicism, then, the human soul: (1) has an immaterial dimension that allows it to persist after bodily death; (2) utilizes the brain as an instrument for properly human mental functions, but is itself the basis for those spiritual/immaterial aspects of mental functioning that are intrinsically irreducible to electrochemical or other physical brain activity; (3) is also by nature the life-principle ('substantial form') of the body; and (4) as such is



present throughout all parts of the body, not only in the brain (which would be a variation on Cartesianism, with the brain as a whole taking the place of Descartes' pineal gland). An important corollary is that brain lesions producing unconsciousness, even if permanent, *paralyze* the mental powers of the soul but do not annihilate them, no more than the cutting of all the strings of a piano would make the performer any less of a pianist. This is a key difference between Catholic anthropology and person/mind/brain reductionism: the former admits of such a notion as a 'permanently unconscious person', whereas the latter does not. For the Catholic, as long as there is evidence that the body is alive (an 'organism as a whole'), then the soul and person are present, even if rendered permanently unconscious by a brain lesion. For the reductionist, if such a body is alive, it is simply not the original person's body any longer (a nonpersonal 'humanoid organism'), and the person is still dead by virtue of the permanent unconsciousness. For the reductionist, the notion of a 'permanently unconscious person' is a contradiction in terms, whereas for the Catholic (and of course many others who share the Catholic view of soul) there is no contradiction at all.

Approaching the thought experiment from this Catholic world-view, we can make the following observations. Since mental functions (presumably) continue to be mediated by the isolated brain, the soul must be 'informing' the brain (or the head with the brain, depending on which version of the thought experiment). This seems clear enough. The difficulty has to do with what to make of the brainless (or headless) body, given its biological status as an 'organism as a whole'. Several theoretical possibilities present themselves: (1) The brainless (or headless) body has a new 'soul' or life-principle, but not a new spiritual human soul – rather, some kind of animal 'soul', albeit not that of any naturally occurring animal species. (2) The brainless (or headless) body has a new human, spiritual soul, something analogous to twinning during early human embryogenesis. (3) The one original soul, because of its immateriality, transcends the limitations of space and informs *both* the brain (head) and the brainless (headless) body, even though they are physically separated. (This would seem to invoke a somewhat unorthodox notion of Aristotelian hylomorphism and its Thomistic application to the human soul).

### 3.3.4. *Need for a Refinement of Aristotelian-Thomistic Anthropology*

Such a thought experiment falls into a class of related philosophical problems involving the splitting and fusing of biological organisms, such

as: planaria and other lower species that can regenerate a whole organism from a severed part, twinning of human or animal blastocysts, and Siamese twins. When a planarium is bisected and each part grows into a new whole planarium, how would Aristotle have answered the question which of the two resulting worms has the original substantial form and which has a new substantial form that was educed from the potency of matter at the moment of bisecting? (Or was the original form lost, and two new forms educed?) Probably he was not aware of this remarkable biological phenomenon, and his system of hylomorphism was developed based on the ordinary things of nature that he observed. Perhaps hylomorphism is not a fully adequate metaphysical system for explaining what happens when a planarium is bisected. The same dilemma applies to human twinning, only worse, because the human soul's spirituality cannot be simply 'educed from the potentiality of matter' as animal souls are, but each human soul is created *ex nihilo* by a special act of God when the material conditions are appropriate (Aquinas: *Summa Theologiae*, Ia, q. 90, a. 2&3). Thus, with human twinning, it remains mysterious and probably intrinsically unknowable whether there were two souls already present prior to the twinning – and that's precisely why the twinning happened – or only one soul prior and two afterwards, in which case it remains obscure which twin kept the original soul and which got a newly created soul. And in the case of Siamese twins that share many vital organs and blood circulation, there seem to be two human souls but only one body, which is hard to reconcile with hylomorphism; or else there are two bodies, each 'informed' by its respective soul, but with complex domains of overlap that seem to be informed by both souls.

Traditional Aristotelian hylomorphism and its Thomistic application to Christian anthropology do not seem philosophically adequate to account for such phenomena. Whether what is needed is a further development of hylomorphism, or a completely new philosophical framework that better accounts for such biological phenomena without conceptually sacrificing the spirituality of the human soul or its essential relationship with the human body – I do not know. I am not a philosopher, and I am not ashamed to admit that I have no definite, logically defensible answer for the thought experiment any more than I do for the related questions regarding planaria, twinning, and Siamese twins. In the end, especially regarding the human examples, we may have to be content simply remaining agnostic about one or two souls, which soul, etc., and sim-

ply stand in respectful awe of the mystery of human life.

### 3.3.5. *The Thought-Experiment is Actually Irrelevant to Clinical Brain Death*

This sounds like an intellectually rather weak alternative to the reductionists and 'higher brain death' advocates. But I would also assert that the inability to definitively, non-arbitrarily, solve the thought-experiment dilemma within the context of traditional Christian anthropology is actually *not* a problem at all for understanding brain death within the same philosophical framework – because in real brain-death cases, there is no separation into two parts, so the question never arises which part has which soul (or which kind of soul). Throughout the entire pathophysiological process of total brain infarction, there is only one 'part' (i.e., the entire body), and as long as it remains a living organism, then we can be sure that the soul is there as its life-principle, even if the soul's mental powers are suspended due to the destruction of the organ through which those powers are designed to operate.

Thus, when examined in depth, the decapitation analogy sheds no heuristic light at all on brain death, but only confuses things by diverting philosophical attention to interesting but tangential questions, the answers to which do not determine the ultimate understanding of brain death. The 'essential' *partial* decapitation analogy, on the other hand, does shed considerable light on the subject by highlighting the physiological equivalence between brain death and high spinal cord transection (plus vagotomy, plus-or-minus diabetes insipidus), which is the critical essence of 'physiological decapitation'.

In summary, for the reductionist, the brain-dead body is a living 'humanoid organism' but no longer the body of a person, who is dead by virtue of permanent unconsciousness. For those who accept an Aristotelian-Thomistic type of spiritual soul, some brain-dead bodies are indeed dead by virtue of supracritical multisystem damage, whereas others (with pathology relatively limited to the brain) are permanently comatose, severely disabled, still living human beings; in either case, death of the brain *per se* does not constitute human death.

## 4. BRAIN DEATH AND THE NEW CARTESIANISM

The brain-death literature is full of word-choices that juxtapose 'brain' and 'body' as though the brain were not part of the body but rather an entity unto itself that governs the body, which in turn is regarded as essentially a complex machine in need of external governance and coordination. An

illustrative example is the phrase, encountered frequently in the more recent brain-death literature, 'brain death with prolonged somatic survival', which clearly implies that the *soma* or body does not include the brain. Moreover, the mechanistic view of the body so permeates modern biology and medicine that one can hardly get a manuscript or a grant application accepted without some reference to 'basic mechanisms'.

There is much structural similarity between Descartes' mind-body dualism and the 'brain-body' dualism which is currently in vogue. An important difference is that Descartes' dualism involved a purely spiritual mind and a purely mechanical body, whereas the neo-Cartesian dualism is purely materialistic, with the brain operating on 'mechanical' principles just as much as the rest of the body. Another important difference is semantic, regarding the term 'body': for Cartesianism the 'body' includes the brain, whereas for the type of neo-Cartesianism under discussion, 'body' includes everything *except* the brain.

Keeping these differences in mind, the structural similarities are fascinating and illuminating. For both, there are two distinct entities in a hierarchical relationship, with the mental entity governing the mechanics of the non-mental entity. For Descartes, the anatomical locus of interaction between mind and body was the pineal gland; for neo-Cartesianism it is the cervicomedullary junction. Descartes could not comprehend that human mental functions are a spiritual-physical hybrid, neither reducible to nor separable from bodily (brain) functions. Neo-Cartesians cannot comprehend that the human body is a unified hybrid of neural and non-neural elements, and that the neural elements are continuous with each other, so that the brain is a separate entity from the spinal cord only in diagrams, not in reality (cf. the many white matter tracts passing through both, and the transition zone between upper cervical cord and lower medulla). Even if the brain is destroyed, there is still the rest of the nervous system: the spinal cord with its intrinsic integrative functions and its two-way communication with almost all other parts of the body via peripheral and autonomic nerves. Just because these parts of the nervous system are not associated directly with mental function, they should not be underestimated in terms of their role in the maintenance of an 'organism as a whole'.

The intellectual sin of both 'isms' is to reify and compartmentalize what are in reality two inextricable components of a single hybrid entity. No doubt the very language we use (with distinct words for these components: 'mind', 'brain', 'body'), plus our tendency to think with our imagination in simple diagrams and compartments, are strong temptations in the reifying

direction, but our intellects must overcome such conceptual laziness.

##### 5. WHAT IS DEATH, IF NOT BRAIN DEATH?

So far, this paper has expounded on what I think is *not* death. It should not conclude without stating succinctly what I think death *is*. In keeping with the traditional tripartite distinction introduced by Bernat and colleagues between 'definition' (concept), 'criterion' (anatomical substrate), and 'tests' for death (Bernat, 2001; Bernat *et al.*, 1981), I would say that my *concept* of death of a human person is the same as expressed eloquently by the late Pope John Paul II, namely, 'a single event, consisting in the total disintegration of that unitary and integrated whole that is the personal self. It results from the separation of the life-principle (or soul) from the corporal reality of the person' (John Paul II, 2000, §4). I also agree with the Pope that the exact moment of this event cannot be precisely determined empirically, but that there can be 'biological signs that a person has indeed died' (John Paul II, 2000, §4).

Turning now to the level of *criterion* or anatomical substrate, there could be many possible valid criteria ('biological signs') that a person has already died. But the closer one tries to get to the unobservable moment of death itself, the more difficult it becomes to formulate a universally valid and certain criterion. Rigor mortis is a valid criterion far from the moment of death and therefore not a clinically very useful one. A probably valid criterion close to the moment of death might be something like: 'cessation of circulation of blood for a sufficient time (depending on body temperature) to produce irreversible damage to a critical number of organs and tissues throughout the body, so that an irrevocable process of disintegration has begun'. At normothermia, the minimum sufficient time is probably somewhere around 20 minutes, although there are insufficient data to support a precise duration with certainty (Lynn and Cranford, 1999, p. 108). I do not believe that the critical number of organs and tissues can be universally specified, as it will no doubt vary from case to case; surely the brain is included, but not *only* the brain.

This is similar to the traditional 'cardio-pulmonary' criterion, but it is a refinement of it, because neither heart nor lung function is necessary for life (people with artificial hearts, on cardiopulmonary bypass, extracorporeal membrane oxygenation, etc. are most certainly alive). The above proposed criterion is better called 'circulatory-respiratory', emphasizing what is really critical for maintaining the integration of the organism as a whole. 'Respiratory' is to be understood in this context not as 'breathing' but in the biochemical sense of exchange of oxygen and carbon dioxide in the mito-

chondria of every cell throughout the body (the enzymes involved are often collectively called the 'respiratory chain'). Perhaps a still better term could be devised that avoids the ambiguity inherent in 'respiratory'.

The precise sequence of organ failure can be highly variable from one death to the next, depending on the cause and overall context of death. I also think that the moment death can be legitimately 'declared' and acted upon can vary, depending on the type and context of the death (Shewmon, 2004d; Shewmon and Shewmon, 2004).

## 6. CONCLUSION

As admitted by brain-death defenders and critics alike at the 3rd International Conference on Coma and Death and in the October 2001 issue of *Journal of Medicine and Philosophy*, the accumulation of clinical evidence and theoretical considerations have indeed undermined some of the sacred mantras of traditional brain-death theory and driven 'the nails into the coffin' (Lizza, 2004, p. 52) of a biological, organism-as-whole rationale for equating death of the brain with death of the individual. Whether official neurology acknowledges it or not, the active debate among experts in brain-death theory has shifted from the biological to the philosophical domain, where the key question is: Is a permanently unconscious living human being still a human person? The answer to that depends on one's fundamental philosophical world-view and cannot be further elucidated by scientific investigation. It is in this philosophical arena that material reductionists and the Catholic Church must respectfully part company, the former answering 'No' and the latter answering 'Yes'.

Such affirmation of the existence of human life in its most fragile, disabled and dependent state is by no means an implicit mandate to 'therapeutic obstinacy' or 'vitalism'. Intensive care in the context of 'brain death' is one of the clearest possible examples of ethically 'extraordinary' ('disproportionate') means, which can (and in most cases should) be legitimately foregone, in keeping with traditional Catholic moral principles (John Paul II, 1995, §65; Sacred Congregation, 1980, §IV). Cases where it could be appropriate to employ such 'extraordinary' means include brain-dead pregnant women to bring the fetus to viability, respect for cultural sensitivities (e.g., in Japan) or personal convictions (as with the mothers of 'TK' and other chronically brain-dead children, some orthodox Jews, etc.), empathy in allowing time for family members to arrive and come together to grieve,

etc. Issues surrounding justice (who pays for these very expensive treatments) are also important, extremely complex, vary according to each country's health-care structure, and are far beyond the scope of this paper.

That brain death *per se* is not death carries profound implications for the field of transplantation. Regardless of the early history of brain death, its post-1968 history has been driven largely by the demands of transplantation: the rapid development and implementation of diagnostic criteria without adequate validation, the precipitous revision of statutory death laws without a real consensus on the fundamental rationale why brain death should be death, and now the huge momentum of transplantation making everyone reluctant to face squarely the accumulated evidence that the semi-official integrative-unity rationale was all along based on faulty biological assumptions and can no longer serve as an intellectually viable basis for the death of brain-dead organ donors.

But the demise of brain death does not necessarily imply the death-knell to transplantation that so many of its defenders seem to fear. It does, however, imply going about the transplantation procedure in a different way, so that the removal of 'vital' organs neither kills nor harms the donor if the donor is not yet dead (ethically analogous to live donors of blood, bone marrow, a single kidney or lobe of liver). At face value this sounds self-contradictory, but it is not – for reasons beyond the scope of this paper and already developed elsewhere (Shewmon, 2004d; Shewmon and Shewmon, 2004). I emphasize this in conclusion, to dispel the fear that surrounds accepting solid counterevidence against a 38-year-old medico-legal sacred cow. To admit that many brain-dead patients are deeply comatose, severely disabled, living human beings is progress, not regress. It will force a refinement in our understanding and diagnosis of death, a clarification in our fundamental philosophical principles regarding human life, and a realignment between our understanding and our consciences in dealing with these most vulnerable human lives.

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## ANNEX

# THE DETERMINATION OF DEATH IN THE CONTEXT OF ORGAN TRANSPLANTATION\*

*Medical Ethical Guidelines of the SAMS  
approved by the Senate of the SAMS on 24 May 2005*

SWISS ACADEMY OF MEDICAL SCIENCES

## INTRODUCTION

In 1969, the SAMS first published a set of guidelines concerning the definition of death. These guidelines were mainly concerned with the determination of the moment at which death occurs, and they were developed for use by teams of physicians performing organ transplantation from deceased donors. The original SAMS guidelines thus dealt with a special situation, i.e., the physicians' need to determine with certainty that a person's brain had sustained a total and irreversible loss of function, coupled with the simultaneous need to preserve the integrity of the organ or organs to be transplanted by means of short-term perfusion and oxygenation. The utility of these guidelines, not just in the context of impending organ transplantation, but also in the entire field of intensive care medicine, has since been demonstrated by their official adoption and regular use, not just in Switzerland, but in other countries as well.

The new Swiss Federal Law on the Transplantation of Organs, Tissues, and Cells, which went into effect on 8 October 2004, defines death as follows: a human being is dead 'if the functions of his or her brain, including the brainstem, have irreversibly ceased'. Death of the individual, as defined here, inevitably leads to the death of all of his or her organs, tissues and cells, regardless of whether brain function has ceased because of direct brain injury or as the secondary result of irreversible cardiovascular arrest.

\*This is an English translation of the original German version.



The Law further stipulates that the modalities for the determination of death, as well as the conditions to be met by the physicians who determine death, are to be defined by an executive order of the Federal Council.<sup>1</sup>

In view of this new legislation, and because the SAMS's Guidelines on the Determination of Death, as last revised in 1996, were no longer fully applicable to the present situation, the Central Ethics Committee (CEC) of the SAMS, in 2000, entrusted a new subcommittee with the task of revising and reformulating certain parts of these guidelines, which would henceforward be called 'The Determination of Death in the Context of Organ Transplantation'. The present document, containing revised guidelines, is the result of the subcommittee's work.

In the current, revised guidelines, as in the Federal Law which will come in effect probably in 2007, the determination of death is based on the observation of signs indicating the irreversible cessation of all functions of the brain, including the brainstem. New to this document, in comparison with the 1996 version, is the specification that death cannot yet be said to have occurred after a single clinical observation that all brain functions have ceased, but only after such an observation has been confirmed by a second one performed after a defined interval of time, or, alternatively, after ancillary tests have been performed to demonstrate circulatory arrest in the brain.

These Guidelines are intended to help physicians in a difficult situation make a determination of death in accordance with the highest ethical standards. The physician caring for the dying person bears a paramount responsibility for that person's well-being and the protection of his or her interests. Yet, if the physician, in the light of his or her own experience, considers that a cure or recovery are impossible, then organ transplantation may be considered, as it offers a means of benefiting another patient, or patients, for whom this physician is not directly responsible. The previously determined death of the patient is, both ethically and legally, an indispensable precondition for the explantation of an organ or organs. These Guidelines describe the procedure to be followed for the death of the patient to be diagnosed with certainty.

<sup>1</sup> The Federal Council, composed of seven members, is the highest executive authority in Switzerland. It is comparable to the Cabinet in other countries.

In view of the experience gained to date, the Guidelines specify not just the precise procedures to be followed (sections 2 and 3), but also, in particular, the ethically and psychologically appropriate attitude to be adopted by all persons involved in preparing for the removal of an organ or organs (sections 4 and 5).

Death and dying are natural processes. There is usually no reason to intervene in the course of these processes, nor are the patient's family or the therapeutic team usually subject to any time pressure or other type of psychological pressure. Due respect can be paid to the dignity of the patient both before and after death, and, afterward, the family has the opportunity to grieve in peace.

Impending organ transplantation interferes with these natural processes by adding time pressure and/or the need for various diagnostic and therapeutic procedures, including surgical ones. The therapeutic team must always take account of the feelings of the patient's family, and of their grief. The treating personnel must listen to them, empathise with them, and keep them informed (see section 4).

The determination of death is based on a comprehensive assessment of the patient's history, the findings of ancillary tests, and clinical evidence of the cessation of brain function. These Guidelines define the clinical criteria and ancillary tests that enable the determination that the cessation of brain function is irreversible. They are meant to ensure the full reliability of any determination of death, whether it is made in a regional hospital or in a major medical centre.

The present Guidelines deal exclusively with the determination of death. Other, related questions of medical ethics, particularly those dealing with organ donation and with the discontinuation of life support, are discussed in two other SAMS documents: the Guidelines for Organ Transplantation and the Guidelines on Ethical Issues in Intensive Care Medicine.

## GUIDELINES

### 1. *General Remarks*

From the medical point of view, the best definition of death is the complete and irreversible cessation of all brain function, including brain-stem function. The brain is the controlling organ of the entire organ-

ism, and the loss of its function inevitably results in the death of all of the body's organs, tissues and cells.

When vital functions such as respiration, cardiac activity, or blood circulation temporarily fail, various resuscitation techniques can often be used to sustain the patient until these functions return. In contrast, there are no measures whatsoever that can remedy the effects of complete and irreversible cessation of brain function.

Death can be due to either of the following causes:

- *a primary injury or disease of the brain* that causes the complete and irreversible cessation of all brain function, including brainstem function, or
- *persistent cardiovascular arrest* reducing or totally abolishing the blood supply to the brain long enough to cause irreversible cessation of all brain function, including brainstem function (death after cardiovascular arrest).

The removal of organs is permitted only if a determination of death has been made on the basis of the clinical examinations and ancillary tests described below.

In the situations discussed in these guidelines, the time of death is legally defined as the time at which death is determined. This time must be entered on the death certificate.

Physicians and other members of the transplantation team must not be involved in the determination of death, nor may they exert pressure or influence of any kind on their colleagues who are responsible for the care of the dying person.

## *2. Determination of Death Due to Primary Brain Injury or Hypoxic Injury After Transient Cardiovascular Arrest*

### *2.1. Clinical signs*

If there is definite evidence of a primary brain injury, a determination that the brain has ceased to function can be made only if the following seven clinical signs are present:

- a) coma
- b) bilateral dilation of the pupils and absence of pupillary light reaction
- c) absence of oculocephalic (=cervico-ocular and vestibulo-ocular) reflexes
- d) absence of corneal reflexes

- e) absence of brain-mediated responses to noxious stimuli
- f) absence of the cough and swallowing reflexes
- g) absence of spontaneous respiration (apnea test)

A determination of death can only be made when the *irreversible* cessation of brain function has been demonstrated by one of the following two methods: either by a second determination that clinical signs a)-g) are present after a defined interval of time has elapsed (2.2.1.), or by ancillary tests demonstrating the absence of blood circulation in the brain (2.2.2.).

## 2.2. *Demonstration of Irreversible Cessation of Brain Function*

### 2.2.1. *By Clinical Examination*

The determination of death requires two clinical assessments separated by the following minimum intervals (see also Appendix 1: Model protocol for the determination of death due to primary brain injury or hypoxic injury after transient cardiovascular arrest):

- a) An interval of 6 hours in adults and in children over the age of 2 years, as long as the following conditions are met: the coma is of known cause and is not due to a metabolic disturbance; intoxication has been ruled out as a possible cause; the patient is not hypothermic; and there is no clinical suspicion of an infectious or inflammatory disorder of the nervous system, such as cranial polyradiculitis. Furthermore, any muscle relaxants or other medications that may have been given that depress the functioning of the central nervous system cannot be present in a concentration that would be sufficient to produce coma or the appearance of coma, in the light of general clinical and pharmacological experience.
- b) An interval of 24 hours in children under the age of 2 years, as long as the following conditions are met: the coma is of known cause and is not due to a metabolic disturbance; intoxication has been ruled out as a possible cause; the patient is not hypothermic; and there is no clinical suspicion of an infectious or inflammatory disorder of the nervous system, such as cranial polyradiculitis. Furthermore, just as for adults, any muscle relaxants or other medications that may have been given that depress the functioning of the central nervous system cannot be present in a concentration that would be sufficient to produce coma or the appearance of coma, in the light of general clinical and pharmacological experience.

- c) An interval of at least 48 hours in adults and children, if the cause of the coma is unknown, if a metabolic or toxic cause cannot be ruled out with certainty, or if any of the other criteria of a) or b) are not fulfilled.

#### 2.2.2. *By Ancillary Testing*

The cessation of brain function is determined by clinical examination (for exceptions, see section 2.5., below). The *irreversibility* of the cessation of brain function can be determined either by a second clinical examination (see 2.2.1., above) or through the use of ancillary tests. If the latter demonstrate total circulatory arrest in the brain, the cessation of brain function is thereby demonstrated to be irreversible, and the death of the individual is confirmed. The following are suitable methods of demonstrating total circulatory arrest in the brain:

- transcranial Doppler sonography or colour-coded Duplex sonography
- spiral computed tomography
- <sup>99m</sup>Tc-HMPAO scintigraphy
- intra-arterial digital subtraction angiography (IA-DSA)<sup>2</sup>

#### 2.3. *Requirement That Death be Diagnosed by Physicians (Medical Doctors)*

If death is to be diagnosed according to the criteria of section 2.2.1., the clinical examinations must be carried out by two different physicians (medical doctors). One of them must be a neurologist or a neurosurgeon, or, when a child is involved, a paediatric neurologist.

If death is to be diagnosed according to the criteria of section 2.2.2., the clinical examination must be carried out by, or with the participation of, a neurologist or a neurosurgeon, or, when a child is involved, a paediatric neurologist. None of these physicians may belong to the transplantation team. The ancillary testing must be carried out by a physician with the speciality certification of the FMH (Swiss Medical Association) that is appropriate for the particular test in question, or with the equivalent knowledge obtained in postgraduate speciality training or continuing medical education.

<sup>2</sup> Methods for the definitive determination of circulatory arrest in the brain are subject to ongoing re-evaluation and revision.

#### 2.4. *Documentation*

The findings of the clinical examination(s) and (in some cases) ancillary testing that are required by section 2.2 must be documented in writing. The SAMS model protocol for the determination of death due to primary brain injury or hypoxic injury after transient cardiovascular arrest (see Appendix A3.1) may be used for this purpose.

#### 2.5. *Situations in Which Ancillary Testing Must be Used*

Ancillary testing is mandatory for the determination of death in patients with suspected cranial polyradiculitis and in those whose cranial nerve function cannot be tested clinically.

Extensive brainstem injury without any injury to the remaining parts of the brain can produce a clinical picture that closely resembles that of death and that might be mistaken for it if no further testing is performed. In this situation, electroencephalography or a suitable study of another type should be performed to determine the presence or absence of function of the cerebral cortex. If cortical function is absent, the procedure for the determination of death can be continued and completed as described in sections 2.1. and 2.2.

A determination of circulatory arrest in the brain is mandatory for the determination of death in the following situations, in which the brainstem reflexes are not accessible to clinical examination:

- a) if craniofacial injuries render the clinical examination of the brainstem reflexes difficult or impossible, or
- b) If cranial polyradiculitis is suspected and an electroencephalogram reveals the absence of bioelectrical activity in the brain, including the cerebral cortex.

#### DETERMINATION OF DEATH DUE TO PERSISTENT CARDIOVASCULAR ARREST ('NON-HEART-BEATING DONOR', NHBD)

This heading refers to a situation in which the blood supply of the brain is abolished or reduced (as during cardiopulmonary resuscitation) for a long enough time to cause irreversible cessation of all brain function, including brainstem function, i.e., long enough to cause death.

### 3.1. *Clinical signs*

The determination of death due to persistent cardiovascular arrest or after unsuccessful cardiopulmonary resuscitation can be made only if all of the following eight clinical signs are present:

- a) absence of central pulses on palpation of the femoral and/or carotid artery
- b) coma
- c) bilateral dilation of the pupils and absence of pupillary light reaction
- d) absence of oculoccephalic (= cervico-ocular and vestibulo-ocular) reflexes
- e) absence of corneal reflexes
- f) absence of brain-mediated responses to noxious stimuli
- g) absence of the cough and swallowing reflexes
- h) respiratory arrest

### 3.2. *Period of Observation for the Determination of Death*

A determination of death due to persistent cardiovascular arrest, with or without attempted resuscitation, can only be made after clinical observation of uninterrupted cardiac arrest, with total circulatory arrest, for at least 10 minutes.

In persons undergoing cardiopulmonary resuscitation, the blood continues to circulate, albeit to a reduced extent. Therefore, in this situation, the determination of death requires at least 20 minutes of uninterrupted (though ultimately unsuccessful) resuscitation measures, followed by at least 10 minutes' observation of uninterrupted cardiac arrest with total circulatory arrest, under normothermic conditions.

Resuscitation is judged to be unsuccessful if it has been performed correctly but nonetheless has not resulted in a recovery of cardiac activity and spontaneous circulation within 20 minutes, and if the patient presents all the clinical signs listed in section 3.1, above. If spontaneous cardiac activity and circulation are temporarily restored at some point during attempted resuscitation, but then cease once again, resuscitation attempts are continued for at least another 20 minutes.

In special situations (e.g. in children under the age of 2 years or in hypothermic patients (central body temperature  $<35^{\circ}\text{C}$ )), resuscitation measures should be continued for 45 minutes before death can be confirmed. In persons with hypothermia, the body temperature should be raised above  $35^{\circ}\text{C}$ . In persons with suspected intoxication, the treating physician holds the responsibility of deciding how long the resuscitation measures should be continued.

### 3.3. *Requirement That Death be Diagnosed by Physicians (Medical Doctors)*

Death must be determined by two different physicians whose formal medical speciality training (FMH) includes training in resuscitation and in the determination of death. One physician establishes the fact of cardiovascular arrest and the presence of the clinical signs listed in section 3.1. The second physician confirms these findings after a 10-minute interval.

### 3.4. *Documentation*

The clinical findings and the resuscitation measures that are carried out must be documented in writing. The SAMS model protocol for the determination of death due to cardiovascular arrest (see Appendix A3.2) may be used for this purpose.

## 4. *Information and Assistance to the Patient's Family and the Therapeutic Team*

Special attention must be paid to helping the patient's family and the therapeutic team deal with the emotional stress surrounding these events. The patient's family, in particular, is faced with unusually severe stress if the patient's death is unexpected, as it often is in such cases. The physicians caring for the dying person should therefore name, as soon as possible, a competent member of the team (either an attending physician or a house-staff physician) to inform and assist the relatives and the rest of the team, before, during and after the patient's death and organ removal. Ideally, this role should be played by the same member of the team at all times.

It is essential for the patient's family to be thoroughly informed by an attending physician or a house-staff physician, in a suitable environment and without time pressure, about the patient's impending death and about the subject of organ donation (with details concerning the organs that would be removed).

It is best to inform the family of the cessation of brain function due to primary brain injury only *after* the first formal examination for the determination of death has taken place. This should be done in a calm environment and with empathy. Then, after an appropriate period of time, the family can be asked about possible organ donation. If the family wishes to ask other persons (e.g., clergy) for advice, these persons should be made available to them.



The member of the team entrusted with contact with the family should discuss with them, openly and frankly, the inevitable changes in the nursing staff (shifts) during the care of the dying person, the purpose of certain investigations and interventions that will be carried out both before and after the determination of death, and the reasons for transfer to another hospital, if necessary.

This team member should also be aware of the family's other needs and anxieties and should attempt to allay them, as far as possible. If organs are removed for transplantation, the family of the deceased person should be able to take leave of him or her afterward in an appropriately calm environment.

When organs are to be removed for transplantation, the hectic activity that surrounds the person who has just died, in order to ensure the survival of the organ(s) to be removed, creates an extraordinary degree of emotional stress both for the patient's family and for the therapeutic team. Special attention must be paid to this stress.

It is therefore essential to adhere to the following points, presented here in the form of a check-list:

- Death must be determined according to the state of the art.
- The patient's family must be informed of the death frankly, completely, and with empathy by an attending physician or a house-staff physician.
- The question of organ donation should be raised before the determination of death.
- Investigations and measures to be taken in preparation for an organ removal (see section 5) are to be begun before the determination of death, if the patient has previously given explicit informed consent for this to be done. The member of the therapeutic team speaking with the patient's family should explain this to them.
- If the deceased has not given any advance directive with regard to organ donation, the family's explicit consent to organ removal must be obtained. If the family consents, preparations for organ removal may be undertaken once a determination of death has been made.
- Assistance and advice must be offered to the patient's family before, during and after organ removal.
- After organ removal, the patient's family must be able to take leave of the deceased in a calm, dignified environment and without time pressure.
- The professional ethics of all persons involved in the care of the patient and of his or her family are to be respected.
- Psychological support must also be available to the therapeutic team.

### 5. *Preliminary Measures for Possible Organ Explantation*

Medical measures that are taken exclusively for the purpose of preserving organs, tissues and cells for transplantation are permissible before the death of the individual only if he or she has previously given fully informed consent for this to be done. If the patient's declaration of consent does not cover such measures, then they may be taken only after the determination of death.

## APPENDICES

### A1 EXPLANATION OF THE MODALITIES OF THE DETERMINATION OF DEATH

#### 1. *'Brain Death'*

Consciousness, i.e., the awareness of oneself and one's environment, is a biological phenomenon originating in the cerebral cortex. If the functioning of both cerebral hemispheres is impaired, consciousness becomes clouded. Complete cessation of the function of the cerebral cortex results in coma. If, in this situation, the brain stem remains intact and the body's respiratory and circulatory functions persist, the affected individual is said to be in a vegetative state. If the brainstem stops functioning as well, spontaneous respiration ceases, while the circulation can continue to function as long as the body's oxygen supply is intact. An irreversible situation of this kind is called death due to primary brain injury, or 'brain death'.

The cerebral cortex can function only if it is constantly stimulated by impulses coming from lower brain centres. The biological 'pacemaker' for the cerebral cortex lies in the reticular formation of the brain; if it fails, the cortex ceases to function. Thus, a brainstem lesion damaging the reticular formation exerts the same biological effect as a bilateral cortical lesion. If the brainstem suffers a total and irreversible loss of function, then the cerebral cortex will never be able to resume functioning either. This situation is termed 'brainstem death'.

These two situations cannot be distinguished from each other on clinical grounds alone. In bihemispheric dysfunction, just as in brainstem dysfunction, the electroencephalogram shows a flat tracing, and blood flow measurements show supra- and infratentorial circulatory arrest.

## 2. *Persistent Cardiovascular Arrest*

In everyday practice, the determination of death is based on clinical investigations enabling the diagnosis of cardiac arrest (absence of pulse) and respiratory arrest (permanent apnea). Unambiguous signs of death, such as rigor mortis and livor mortis, make their first appearance 20 to 30 minutes after death and are fully developed only several hours later. Patients in intensive care units, however, are connected to monitoring equipment and are often receiving artificial respiration, so that their circulatory and respiratory functions are under continuous control. Under these circumstances, cardiac arrest with circulatory arrest can still be confirmed by the absence of a pulse. In some cases, when the mechanical cardiac contractions have ceased and there is, consequently, no pulse, the heart may yet possess electrocardiographically detectable electrical activity. This situation is called electrical activity without pulse (previously known as 'electromechanical dissociation'). The possible persistence of electrical activity for some time after the heart has stopped beating has no bearing on the definition of death, which is confirmed by pulselessness and apnea.

In Switzerland, there are no uniform regulations specifying under what circumstances resuscitation should be undertaken after primary heart failure in a dying patient. Like all other major clinical decisions, this one must be made individually, based on the patient's condition and on the locally available infrastructure. The SAMS recommends that hospitals establish their own internal guidelines concerning this matter.

## 2. *Clinical Signs*

The clinical evaluation for the signs of cessation of brainstem function is of central importance for the determination of death. The circumstances and modalities of this evaluation are as follows:

- a) Coma of known cause
  - *Traumatic lesions*, massive supra- or infratentorial haemorrhages and other structural brain injuries must be demonstrated with a neuroradiological imaging procedure (CT or MRI).
  - In the presence of *hypothermia* (i.e. body temperature below 35°C), the clinical evaluation alone is not sufficient for the determination of death. In this situation, death can only be diagnosed if the body is warmed above 35°C and the clinical signs of death persist despite ade-

quate blood circulation.

- *Anoxia* of known aetiology may be considered the cause of coma as long as there is no simultaneous indication of a metabolic or toxic disorder.
  - In cases of possible *metabolic, drug-induced, or toxic coma*, appropriate laboratory tests must be used to show that brain function is not impaired (or apparently impaired) by muscle relaxants or central neurodepressant substances. In particular, toxicological studies must be performed to rule out a toxic concentration of alcohol, opiates, barbiturates, or benzodiazepines. Minimal metabolic testing must include electrolyte levels (Na, K, Ca), creatinine or urea, glucose, and hepatic enzymes.
  - *If an infection or inflammation of the nervous system is suspected*, particularly cranial polyradiculitis, appropriate ancillary tests must be performed to confirm or exclude this.
- b) Bilaterally dilated pupils, not reacting to light.  
Partially dilated or anisocoric pupils are compatible with the determination of death if they do not react to light.
- c) Absence of oculocephalic (=cervico-ocular and vestibulo-ocular) reflexes.  
If no eye movements are induced by with rapid, passive rotation of the head or by extension and flexion of the head, the oculocephalic reflexes are absent. This test may only be performed if cervical spine trauma has been ruled out. The vestibulo-ocular reflex is tested with caloric stimulation of the inner ear with ice water.
- d) Absence of corneal reflexes.  
The corneal reflexes are tested by touching the cornea with a compact cotton-wool bud.
- e) Absence of any reaction to strong noxious stimuli.  
The reaction to noxious stimuli can be tested by pressing on the point of exit of the second trigeminal branch at the lower rim of the orbit, on the sternum, or on the groove of the nail bed.  
(Sometimes there is a persistent withdrawal reaction of the upper and lower limbs to noxious stimuli. If brainstem reflexes are absent, these withdrawal movements are produced by spinal reflexes, and are not a sign of brain activity).
- f) Absence of the cough and swallowing reflexes.  
The examiner elicits the cough and swallowing reflexes by stimulating the mucous membrane of the trachea and the back of the throat.
- g) Absence of spontaneous respiration: apnea test.

The absence of spontaneous respiration must be proved by means of an apnea test. An apnea test can be carried out only if neuromuscular function is unimpaired. If a patient has been treated with muscle relaxants, the integrity of neuromuscular function must be demonstrated by electrostimulation. The purpose of the apnea test is to induce respiration, or to confirm the absence of induced respiration, by elevating the concentration of CO<sub>2</sub> in the blood. This is done by disconnecting the patient from the respirator (i.e., shutting off ventilation) while assuring adequate oxygenation by diffusion. The apnea test is carried out in the following steps:

- Arterial blood gas analysis to measure the baseline levels of PaCO<sub>2</sub> and pH<sub>a</sub>.
- Artificial respiration with 100% oxygen for 10 minutes.
- Disconnection of the patient from the respirator. The oxygen supply is assured through a catheter inserted into the endotracheal tube, with a continuous flow of oxygen at 2 to 4 litres per minute (in children, max. 2 litres per minute, through a narrow-lumen catheter); in order to avoid barotrauma of the trachea and bronchi, the catheter must not be inserted too deeply.
- Confirmation of the absence of respiratory movements.
- Confirmation that the partial pressure of CO<sub>2</sub> exceeds 60 mmHg (8 kPa) and the pH is below 7.3.
- Reconnection of the patient to the respirator, with the same ventilation parameters as before the test.

In patients with significant disturbances of oxygenation, the test can be modified as follows to shorten the period of apnea:

- Arterial blood gas analysis to measure the baseline levels of PaCO<sub>2</sub> and pH<sub>a</sub>.
- Artificial respiration with 100% oxygen for 10 minutes.
- Reduction of the respiratory volume by 30-50% per minute until the partial pressure of CO<sub>2</sub> exceeds 60 mmHg (8 kPa).
- Arterial blood gas analysis to demonstrate that the partial pressure of CO<sub>2</sub> exceeds 60 mmHg (8 kPa) and the pH is below 7.3.
- Disconnection of the patient from the respirator for 3 minutes.
- The oxygen supply is assured through a catheter inserted into the endotracheal tube, with a continuous flow of oxygen at 3 to 6 litres per minute.
- Confirmation of the absence of respiratory movements.
- Resumption of artificial respiration, with the same ventilation parameters as before the test.

#### 4. *Ancillary Tests*

As discussed above in section 2.2.2., the irreversibility of the cessation of brain function can be demonstrated with the aid of ancillary tests. Nonetheless, this purpose is better served by a second clinical examination after a suitable interval, rather than by ancillary testing, if any septic, toxic or metabolic factors are present or if central nervous depressants have been given to an extent that, in the light of general clinical and pharmacological experience, might produce coma.

The determination of death can be facilitated by ancillary tests that demonstrate circulatory arrest in the brain. These tests provide meaningful information only if the mean arterial blood pressure is high enough to ensure perfusion of the brain if the arteries of the brain are patent, i.e. at least 80 mmHg in adults and at least 60 mmHg in children up to the age of puberty:

- Doppler sonography.  
Transcranial Doppler sonography and transcranial colour-coded Duplex sonography are considered to demonstrate circulatory arrest in the brain if the transcranial ultrasound, performed to a depth of 55-65 mm on both sides, reveals pendular flow or only small systolic peaks (max. speed 50 cm/sec, max. duration 200 msec). If the acoustic bone window is insufficient, no reliable data can be obtained with regard to possible circulatory arrest in the brain, and another diagnostic method must be used. The study must be performed by a physician who has obtained the Certificate of Proficiency in Cerebrovascular Diseases of the Swiss Association of Clinical Neurophysiology, or who has undergone equivalent training.
- Computed tomography.  
Circulatory arrest in the brain can also be demonstrated by either of two techniques employing spiral computed tomography after the intravenous administration of contrast medium, namely, perfusion CT (for the measurement of brain perfusion) and CT angiography (for the visualisation of blood vessels). These studies must be performed by a radiologist with speciality certification of the Swiss Medical Association (FMH) or by a physician with postgraduate training equivalent to the FMH requirements for this certification.
- $^{99m}\text{Tc}$ -hexamethylpropylene aminoxime scintigraphy (HMPAO scintigraphy) at four levels and  $^{99m}\text{Tc}$ -HMPAO single photon emission com-

- puted tomography (HMPAO-SPECT) are procedures, in nuclear medicine, with which blood flow in the brain can be measured with radioactively labelled tracers. If no blood is circulating in the brain, the brain tissue cannot bind these tracers. These studies are to be performed by a physician specialising in nuclear medicine with speciality certification of the FMH, or by a physician with postgraduate training equivalent to the FMH requirements for this certification.
- Digital subtraction angiography after the intra-arterial injection of contrast medium (IA-DSA) can also be used for the determination of death. Proof of absence of circulation in the brain requires the injection of both carotid arteries and at least one vertebral artery with contrast medium. This must result in the filling of the external carotid artery and its branches on both sides, as well as of the extracranial segments of all vessels supplying the brain. If one vertebral artery is visualised and hypoplasia of this artery is suspected, then the vertebral artery on the other side must be visualised as well. Circulatory arrest in the brain, and thus death due to brain injury, is considered to have been demonstrated if the intracranial arteries and veins cannot be visualised either above or below the tentorium cerebelli. Angiography is to be performed by an FMH.-certified radiologist or by a medical doctor with appropriate training equivalent to the FMH requirements for this certification.

In some cases, the ancillary tests mentioned above may fail to confirm the diagnosis of death even if the individual is, in fact, dead (i.e., false-negative results are possible). If, for instance, there is a large defect of the bony skull as a result of head trauma or surgery, death will not necessarily be followed by a rise in intracranial pressure, and thus not necessarily by circulatory arrest in the brain. In these situations, the determination of death is based on clinical criteria, as discussed in section 2.2.1.

As for ancillary tests other than those mentioned above, some are not sensitive or specific enough for the determination of death (e.g. electroencephalography or evoked potentials), while others have not been sufficiently tested or are too time-consuming and costly (e.g. positron emission tomography or blood flow measurements with magnetic resonance imaging).

Methods for the definitive determination of circulatory arrest in the brain are subject to ongoing re-evaluation and revision.

## A2. REMARKS

### 1. *Organ Donation After Death Due to Primary Brain Injury*

The concept of 'brain death' is scientifically based and is recognised in countries where organ transplantation is performed. The correct application of the criteria for the determination of total, irreversible cessation of function of the entire brain ensures a high level of diagnostic reliability.

The ongoing controversies regarding the determination of death, both among the general public and in the health care professions, are largely due either to divergent convictions or to semantic misunderstandings. The very expressions 'brain death' and 'cardiac death', for example, are liable to create the misimpression that there are different types of death, and that 'brain death' occurs before the actual, definitive death of the individual. This misimpression is reinforced by the fact that, in these patients, certain physiological functions are artificially sustained with mechanical ventilation and circulatory support, so that, even though these patients are dead, they still display some of the traditionally recognised signs of life (e.g. warm body, pulse, and respiratory movements of the chest).

Thus, persons who are not well acquainted with these phenomena can gain the impression that persons whose brain function has ceased totally and irreversibly are, in fact, not completely dead, and that the criteria for the determination of death have been introduced merely to facilitate the early removal of organs. If such misunderstandings are to be avoided, the nature of death must be explained clearly to all persons involved, in language that everyone can understand.

In such situations, serious psychological difficulties may arise in the patient's family and even among the care-giving personnel (particularly nurses) if, for the survival of an organ or organs, the explantation must be performed with minimum delay. This can, understandably, generate opposition to organ removal. It is, therefore, particularly important that all persons involved should understand the ethical principles of transplantation medicine, and that the therapeutic team should apply these principles to their fullest extent.

Dying is a process, rather than an event that occurs at a single point in time. When the heart stops beating, all signs of life disappear very soon afterward, never to return. On the other hand, death due to primary brain injury (e.g., after head trauma or anoxia) often takes



longer, as the brainstem and the two cerebral hemispheres gradually cease to function.

Ancillary tests may be used as an aid to the determination of death only after the total cessation of brainstem function has been clinically confirmed. The purpose of ancillary testing is to demonstrate the absence of blood circulation in the brain. The clinical examination and ancillary tests described in the Guidelines (section II) provide the physician with the diagnostic certainty that recovery is impossible, and thus that death has occurred. In particular, the second clinical evaluation, which is to be performed after a specified interval (section 2.2.1.), serves to confirm the irreversibility of cessation of function of the entire brain and thus to confirm death, despite the possible continued functioning of the extracranial circulation. The second clinical evaluation is the only possible means of making a determination of death if the specialised equipment and personnel for ancillary testing are not available

In rare cases where the clinical signs are not sufficiently reliable for a determination whether all functions of the brain have ceased (sections 2.5. a and b), circulatory arrest in the brain must be demonstrated with ancillary testing (see also section 2.2.2.). The demonstration of circulatory arrest in the brain confirms that death has occurred.

The techniques presented here for the reliable and unambiguous determination of death can also be used in children. It must be stressed, however, that the brain lesions and pathophysiological mechanisms leading to coma in newborns, infants and children under age 2 differ from those that affect adults. Because the juvenile brain has a greater capacity for recovery than the adult brain, the required interval between the two clinical evaluations for the determination of brain death is longer in children up to age 2 than in adult patients.

## *2. Organ Donation After Death Due to Cardiovascular Arrest ('Non-Heart-Beating Donor', NHBD)*

Here too, death occurs because of the complete and irreversible cessation of brain function, but as the *secondary* result of a lack of blood supply and an ensuing deficiency of oxygen. If death is caused by cardiac arrest with circulatory failure, respiratory arrest and the absence of central pulses are the first clinical signs to be observed. As the circulation can be partially sustained by cardiac massage and other methods of resuscitation, cardiac arrest is potentially reversible, and

spontaneous circulation can, in some cases, be restored. The success or failure of resuscitation after cardiac arrest is difficult to predict. Therefore the duration of the cardiovascular arrest, determined empirically, or the duration of the continuously applied, but ultimately unsuccessful, resuscitation effort should be used as a criterion for the determination of death.

The brain is more sensitive to a deficiency of oxygen than other organs, and a lack of perfusion of the brain causes death within a short time. The current universal scientific consensus holds that, in normothermic patients, the total and irreversible cessation of all brain function, including brainstem function, is an absolute certainty after 20 minutes of unsuccessful resuscitation followed by 10 minutes of observation with demonstrable circulatory failure.

For children under age 2 with hypothermia and certain types of intoxication, there are, as yet, insufficient data regarding the duration of cardiovascular arrest that is required to produce irreversible cessation of brain (including brainstem) function. This being the case, the resuscitation effort, and the monitoring of cardiovascular arrest afterward, must be continued for a longer period of time in children under age 2. The removal of organs cannot be considered until these measures have ended.

On the other hand, in certain precisely defined situations, there is probably no chance of survival even after a much shorter interval. Examples include the following:

- Deceased persons whose cardiac arrest occurred without witnesses, who initially manifested a cardiac rhythm other than atrial fibrillation or atrial tachycardia, and in whom a spontaneous pulse could not be detected at any time during the first ten minutes of attempted resuscitation.
- Deceased persons with continuing electrical activity of the heart, but without pulse, whose end-expiratory partial pressure of CO<sub>2</sub> 20 minutes after the initiation of further resuscitation measures was 1.4 kPa (10 mmHg) or less.

To date, resuscitation efforts have never succeeded in any case of either of these two types. Future clinical research will put us in a better position to decide, in individual cases, at what point further resuscitation is to be considered futile. If the removal of an organ for the purposes of transplantation is envisaged, the resuscitative efforts must always be continued for at least 20 minutes, according to the current, universal consensus, followed by

a 10-minute period of observation with confirmed absence of the circulatory function.

If resuscitation is temporarily successful, i.e., if spontaneous cardiovascular function returns at some point during the resuscitation effort and then ceases again, resuscitation is begun again for a further mandatory period of 20 minutes (see section 3.2.). Death due to persistent cardiovascular arrest is even more stressful for the patient's family and the therapeutic team than death due to primary brain injury, for two reasons: both because of the unexpectedness of the event, and because of the time pressure for impending transplantation (the patient's organs can only survive for a short time after the onset of asystole).

The donation of organs under these circumstances is widely viewed with misgiving, because of the fear that, in some cases, potential donors might be exposed to a higher risk that is difficult to quantify, or that the determination of death in such cases might be insufficiently reliable.

It is, therefore, essential when death is due to persistent cardiovascular arrest, just as it is when death is due to primary brain injury, that all of the relevant rules be strictly observed; that the rights and dignity of all persons concerned be fully respected; and that there be no doubt about the guarantee of absolute protection to the potential donor for as long as he or she is still living (the 'dead donor rule'), or about the correctness and ethical propriety of any measures that are taken.

The rules to be observed include, in particular,

- the rules regarding the duration of resuscitation and the periods of observation after resuscitation and after the determination of cardiovascular arrest (section 3 of the Guidelines), and
- the rules regarding the preparatory measures for organ transplantation and the required informed consent to such measures (section 5 of the Guidelines).

An essential prerequisite is that the therapeutic team and the patient's family have been informed, with candour and in timely fashion, of the patient's condition, of the expected course of the patient's condition and the measures to be taken, and of the rules that are to be adhered to in accordance with section 3-5 of these Guidelines.

## A3. MODEL PROTOCOLS FOR THE DETERMINATION OF DEATH

Though the emotional stress on all persons involved, as well as the unavoidable time pressure, can present special difficulties, it is nonetheless essential that all of the following measures be carried out correctly and in the proper sequence. It is equally important that the responsibilities of the members of the therapeutic team be clearly defined. Carefully drawn up checklists and protocols have proved to be invaluable aids toward achieving these goals. Two such model protocols are presented below. They are recommended for use (either unchanged, or with appropriate modification) in all hospitals where comparable protocols are not already available.

*1. Protocol for the Determination of Death Due to Primary Brain Injury or Hypoxic Injury after Transient Cardiovascular Arrest*

Name of patient (first and last names) .....

Date of birth .....

		Date	Time	Responsible physician and hospital	Signature	Proceed to Point:
1.	The treating physician makes a determination of death on the basis of the clinical findings.					2
2.	The expert examiner makes a determination of death. The treating physician and the expert examiner may be the same person (see section 2.3. of the SAMS Guidelines). Death must be confirmed at least once by a neurologist, a neurosurgeon, or a paediatric neurologist.					3
3.	Laboratory tests reveal no metabolic abnormality that could produce coma; the body temperature is at least 35°C; curarisation, shock, and relevant effects of central depressants are ruled out. There is no suspicion of CNS infection or inflammation, e.g., cranial polyradiculitis.					4

4	The expert examiner finds no evidence of pharmacological or toxic causes for the coma; if toxic causes are found, toxicological tests must be carried out or any possible intoxication must be allowed to subside over an appropriate period of observation.					5
5.	A properly performed apnea test reveals the absence of respiration in response to elevated PaCO <sub>2</sub> .					6
6.	Permission has been given for organ donation (the wishes of the deceased person were expressed in writing before death, or his/her presumed wishes have been communicated by the family).					7
7.	The relatives are informed about the organ donation procedure.					8, 9 or 10
8.	Ancillary tests confirm circulatory arrest in the brain (see section 2.2.2. of the SAMS Guidelines).					
	a) Ultrasonography reveals circulatory arrest in the brain.					11
	b) Computed tomography reveals circulatory arrest in the brain.					11
	c) <sup>99m</sup> Tc-HMPAO scintigraphy reveals circulatory arrest in the brain.					11
	d) Digital subtraction angiography reveals circulatory arrest in the brain.					11
9.	The expert examiner makes a determination of death at least 6 hours after Point 2, the cause of death is known, and the criteria for a 6-hour interval between the two clinical examinations are met.					
	Child under age 2: The expert examiner makes a determination of death at least 24 hours after Point 2, the cause of death is known, and the criteria for a 24-hour interval between the two clinical examinations are met.					

	The expert examiner may not be a member of the transplantation team (see section 2.3.). Death must be confirmed, at least once, by a neurologist, a neurosurgeon or a paediatric neurologist.					11
10.	The expert examiner makes a determination of death 48 hours after Point 2 and the cause of death is unknown. The expert examiner meets the criteria stated above in Point 9.					11
11.	Cause of death					
12.	The preconditions for organ removal are met.					

This protocol must be kept near the patient at all times.  
After death, it is to be placed in the medical record.

## *2. Protocol for the Determination of Death Due to Persistent Cardiovascular Arrest*

Name of patient (first and last names) .....

Date of birth .....

		Date	Time	Responsible physician and hospital	Signature	Proceed to Point:
1.	Cardiovascular arrest initially determined by the treating physician.					2
2.	Extracardiac causes (tension pneumothorax, cardiac tamponade, intoxication, pulmonary embolism) are excluded.					3
3.	Body temperature at least 35°C					4 or 5
4.	No spontaneous circulation for 20 minutes despite resuscitation measures.					6
5.	A reason exists for refraining from resuscitation measures or halting them after less than 20 minutes.					6

6.	After a further 10 minutes since the cessation of resuscitation measures, the expert examiner makes a determination of death. The expert examiner may not be the same person referred to in Point 1 as the treating physician (see section 3.3. of the SAMS Guidelines).					7
7.	Permission has been given for organ donation (the wishes of the deceased person were expressed in writing before death, or his/her presumed wishes have been communicated by the family).					8
8.	The relatives are informed about the organ-donation procedure.					9
9.	The preconditions for organ removal are met.					

This protocol must be kept near the patient at all times.  
After death, it is to be placed in the medical record.

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*Earlier Guidelines of the Swiss Academy of Medical Sciences Cited in the text:*

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All the medical-ethical guidelines of the SAMS are available on the website [www.samw.ch](http://www.samw.ch).

## APPENDIXES

## COMMENTS ON THE TRANSCRIPT OF THE DISCUSSION

D. ALAN SHEWMON

As I could not physically attend the conference and participate in the group discussions, I am grateful for the opportunity to make some comments regarding aspects of the discussion pertaining to my paper. Indeed, several aspects of my position seem to have been misunderstood or incompletely understood by the discussants. An inordinate amount of time seems to have been spent countering certain ideas that I do not hold, as though I held them, or emphasizing certain obvious things as though I disagreed with them. By contrast, no time was spent at all addressing some of the key conceptual challenges I raised in my paper.

*First*, regarding the Repertinger case and my 1998 article on ‘chronic brain death’, several points must be made. I agree with Drs. Ropper, Bernat and others, who opined that even if there are exceptional long-maintained cases of brain death, such duration does not undermine the concept that brain death is death. I never claimed that it did. Drs. Bernat and Daroff said that ‘having a heart perfusing blood to a series of organs mechanically supported ... does not necessarily prove that that preparation is a living being’ (see p. 275). I completely agree. Drs. Posner and Wijdicks dismissed all the chronic cases as simply ‘irrelevant’ (cf. p. 276). I agree that the duration *per se* is conceptually largely irrelevant, but I insist that the cases in their totality are highly relevant, *because of the holistic, integrative properties that they manifest*. But even the duration is not *entirely* irrelevant: I challenge Dr. Masdeu to maintain at normothermia a perfused finger in a flask (cf. p. 146), or Drs. Bernat and Daroff to maintain a series of organs in a vat, for as long as some of these brain-dead bodies were maintained.

I became interested in such cases in the late 80s and early 90s, because the medical literature up to that time uniformly and with absolute certitude asserted that cardiovascular collapse *necessarily* occurs imminently upon brain death, and this was put forward as a key piece of



evidence that brain death is death, even though various cases had already been published that contradicted this supposed universal fact. (When the doctrine of necessarily imminent collapse was believed to be true, it was considered highly relevant by brain-death advocates; now that it has been disproved, they call it 'irrelevant').

I always find it interesting when new evidence contradicts established scientific 'facts', but my interest in this phenomenon grew by orders of magnitude in 1992, when I was consulted by a skilled nursing facility on the case of a 13-year-old boy who had been transferred to them on a ventilator from a major academic medical center, where brain death from head trauma had been diagnosed 38 days before. After the parents had refused a request for organ donation, the physicians did not disconnect the patient from the ventilator, although they had a legal right to, because they wanted to avoid unpleasant confrontations with the parents, who belonged to the Hell's Angels motorcycle gang and were threatening legal action against the hospital if the boy was disconnected, and also because the physicians *were so sure that imminent cardiovascular collapse would supervene* and solve the problem naturally. To their complete surprise, days turned into weeks, and the longer the boy lingered, the more difficult it became to convince the parents that he was dead. I reviewed the hospital records and examined the boy, and – without going into details here – was satisfied that the diagnosis of brain death was accurate. CT scan showed massive cerebral edema with obliteration of basal cisterns. He had diabetes insipidus and initially required dopamine to maintain blood pressure, but eventually required no pressor support. While brain dead, he underwent onset of puberty with some phallic enlargement and development of early pubic hair. He was nourished by tube feedings and survived 27 more days in the nursing facility until he succumbed to an untreated pneumonia.

This case forced me to rethink everything I had read and been taught about brain death, not because 65 days is such a spectacular survival duration (longer cases had already been published), but because after the initial period of somatic instability, he stabilized and required no more support than what a skilled nursing facility provides. The long surviving cases are of interest, *not* because the duration proves that brain-dead patients are 'organisms as a whole' (it does not), but for two reasons: (1) The dogma of necessarily imminent cardiovascular collapse had long been held up in the literature as proof that brain death is death. Such cases undermine the dogma and the alleged proof. It is a service to medical science to correct false dogmas. (2) The chronic cases demonstrate holistic physiological

properties that contradict the assertion that they are unintegrated collections of organs, with the same status as an amputated finger (Dr. Masdeu, p. 146) or a 'magnificent cell culture' (Drs. Wijdicks and Bernat, p. 276). Such rhetoric has no logical connection to the holistic physiological properties demonstrated by these cases.

Thus, is it not at all true what Dr. Ropper said, that 'the starting point of [my] discomfort appears to be the issue of the appearance of a warm body' (see p. 250). Apart from the fact that I have no 'discomfort' regarding the topic of brain death, I have never written or said that the appearance of a warm body bothered me conceptually. It certainly does not. The starting point of my rejection of brain-based criteria for death was the case of that 13-year-old boy, whom any biologist, not primed that the case had implications for brain-death controversies, would surely have judged to be a comatose, living organism.

Part of the discussion was devoted to questioning the relevance of the 175 cases of 'chronic brain death' that I collected in 1998, on the grounds of insufficient diagnostic information available in many cases. What the discussion completely overlooked was the fact that *at least some* of these cases were indisputably brain dead and *demonstrated holistic physiological properties*. My paper gave a partial list of such holistic properties, but this seems to have been totally ignored in the discussion, with all the cases dismissed as irrelevant because the duration of maintaining perfused organs is conceptually irrelevant. I agree that the duration of maintaining perfused organs is irrelevant. My argument is that these bodies are more than collections of perfused organs, because they have holistic properties not attributable to any organ system but that are emergent phenomena at the level of a whole. No one took up this challenge in the discussion.

I want to thank Dr. Bernat for pointing out that there can be unusual clinical circumstances in which the diagnosis of brain death must and can be made in the absence of an apnea test (see pp. 208-9). To the medical contraindications to apnea testing which he mentioned, I would add ethical contraindication, such as obtained in the Repertinger case. In the total clinical context of the case, it is absurd to doubt that the boy was fully brain dead from the start, simply because an apnea test could not be performed. At age 4 he had such elevation of intracranial pressure from cerebral edema that the sutures of his skull split apart. After that he never had any cranial nerve function of any sort, on countless neurologic examinations. A CT scan at 10 days showed generalized cerebral edema, absence of ventricles and obliteration of the basal cisterns. He had four isoelectric EEGs: at one

and two days after initial admission, at 2 years and 11? years into brain death. During the entire 20 years of intermittently disconnecting him from the ventilator for up to a minute, to perform tracheal suctioning, to change the tracheostomy, etc., he was never observed to make a spontaneous respiration. The MRI/MRA and evoked potentials at 14 years into brain death have been endorsed by Dr. Posner as evidence that he was brain dead at least by then (see p. 254). It is preposterous to propose, as Dr. Ropper did, that the patient had undiagnosed medullary function for years, which spontaneously disappeared 'in a brief epoch before the autopsy' (see p. 250, cf. p. 254). This is really grasping at straws in an attempt to discredit glaring evidence simply because it does not fit one's preconceived notions.

I also want to thank Dr. Bernat for mentioning (see pp. 255-6) the video of my complete neurological examination of 'TK', which convinced him that the boy was indeed brain dead, as it convinced the entire audience of neurologists who watched it at the Havana symposium in 2000. It was irresponsible, and frankly insulting to me and to the physicians involved in his care over 20 years, for Dr. Ropper to have stated, 'That case was never subjected to neurologic scrutiny. It is true he was examined but his medulla was not clinically examined...' (see p. 253). Although Dr. Bernat corrected that statement, and Dr. Ropper graciously accepted the correction (see p. 256), I cannot let the statement remain in the transcript of the discussion without vigorously contesting it myself as well.

*Second*, Dr. Ropper characterized my paper as being about almost nothing but hypothetical thought experiments, which he dismissed because they lack clinical context (cf. pp. 250-1). I did not invent the decapitation analogy. Defenders of brain death, including the President's Commission, used it before me, and I merely developed the idea further in my first brain-death paper of 1985. I decided to re-address the analogy now, precisely because so many defenders of brain death have appealed to it. But there are important parts of my paper that are not about thought experiments.

One has to do with a comparison between the somatic physiology of brain death and the somatic physiology of high spinal cord transection. Both of these have very real clinical contexts. If Dr. Ropper prefers to omit the detail of vagotomy (see p. 251) that I added to make the comparison exact, he is free to do so (although pharmacological vagotomy with atropine is a perfectly plausible treatment for autonomic dysfunction from unopposed vagal tone in high spinal cord injury). As it is, neither he nor anyone else participating in the discussion took up my challenge to explain

why – if the brain is the central integrating organ of the body, without the coordinating function of which the body ceases to be a body – why does the body not equally dis-integrate when it loses brain-control due to disconnection from the brain, as much as it does when it loses brain-control due to destruction of the brain? This is not about a thought experiment. It is about logic applied to two well known clinical scenarios.

Why is this kind of argument so hard for some people to understand? Anyone who replies that the two conditions are different because the spinal cord patient is conscious, or that the two scenarios are not comparable because one is dead and the other is alive, is simply missing the whole point, begging the question, and not answering my question. Dr. Fred Plum and many others at the 2000 Havana symposium understood and accepted the point of this comparison perfectly well, and proceeded to argue vigorously in favor of brain death on a totally different basis from somatic integrative unity, namely the loss of personhood. Dr. Masdeu, who was not at the Havana conference, is simply incorrect in his characterization (see p. 146) of the interchange between me and Dr. Plum at that symposium regarding the organism-status of the brain-dead body; Dr. Plum's statement was public and witnessed by many. It also corresponds to statements he himself wrote, which I quoted in my paper, regarding his rationale for equating brain death with death. Dr. Estol is correct in asserting that Dr. Plum 'was furious at what he heard in Havana and spoke out loud his disagreement' (see p. 150). What he was furious about was not that the integrative unity rationale was challenged, but that a fellow neurologist would have the gall to disagree that human personhood resides entirely in the brain and is annihilated with destruction of the parts of the brain that mediate consciousness, regardless of the organism-status of the body. What there was 'surprisingly broad acceptance' about (quoting my own paper) was not that brain death is not death, but that the spinal cord transection comparison effectively undermined the 'organism as a whole' rationale.

Which brings me to a very interesting thing that Dr. Ropper stated in the discussion: 'The loss of somatic integrative function, which has been expressed in many different idioms, or the unity argument, is medically soft, by which I mean weak, and perhaps an unfortunate argument that was included in the President's Commission. I would again submit that even arguing against this does not negate brain death as death' (see p. 252). If only he would have come out and stated what he considers to be a stronger reason for equating brain death with death. Perhaps he hinted at it later, when he said: 'we would have to start over from square one in neurology if

the death of the brain is not death and is not the loss of personhood and is not the loss of the personal entity that is embodied in each individual, not collectively. No brain, no person. For neurology, that is a neurological issue, not a philosophical one' (see p. 255). Thus, Dr. Ropper seems to have broken ranks with Dr. Bernat and the integrative unity camp and joined Drs. Plum, Machado, and many others in the 'personhood' camp. And, pardon me, Dr. Ropper, but the notion of personhood is very much a *philosophical* issue, not a neurological one.

So the unanimity among participants (apart from Prof. Spaemann and myself) is only on the surface, agreeing that brain death is death; but when it comes to the fundamental reason *why* brain death is death, there is diversity of opinion. A group of equally illustrious neurologists could have been gathered, including Drs. Plum, Machado and Cranford (prior to his recent passing) for example, who would be unanimous in asserting that brain death is death *because* it is loss of personhood, despite the persistence of a biologically live human organism.

Another section of my paper that was not about thought experiments was 3.2.4 (see p. 314), in which I listed various incoherencies between brain death theory and practice. Yet no one took up any of these challenges in the discussion. I ask again now for someone to explain, for example, why the American Academy of Neurology Practice Parameters require every clinically testable brainstem reflex to be absent but explicitly allow hypothalamic function to be present without contradicting the brain death diagnosis. Drs. Ropper, Estol and Battro in their introductory essay for the conference brochure called such hypothalamic function 'spurious', but no one has answered me when I asked in my paper why a hypothalamic function should be any more 'spurious' than a brainstem reflex, given that the hypothalamic function is more integrating for the 'organism as a whole' than all the brainstem reflexes put together.

Something Dr. Bernat said in the discussion is relevant to a point of contention in the answers to Question 1 of the four questions submitted by Prof. Spaemann and myself. Most of the respondents dodged the conceptual challenge of the 'almost brain-dead' case by dismissing it as hypothetical and not existing in clinical practice. It is logically impossible that such cases do not exist. In the course of brain herniation, just before all brainstem reflexes are lost, all but one have been lost. Such a patient cannot be diagnosed as brain dead until that last reflex is lost. In the discussion Dr. Bernat also refers to cases of 'almost brain-death' (without using that phrase) in the context of heart-beating organ donation: '(Maastricht) Class

III donors are patients who are severely brain damaged, but not brain dead, who are on ventilators in intensive care units, whose brain damage is irreversible, and whose prognosis is hopeless' (see p. 180). There certainly *are* cases of 'almost brain death', some of whom are more unstable in the ICU than some cases of unusually stable brain death, and the conceptual challenge raised by them is not resolved by dismissing the comparison as purely 'hypothetical'.

One can ignore these incoherencies, just like one can ignore the chronic cases and their holistic properties, but they will not go away. I will keep asking such questions until someone provides straightforward and coherent answers.

*Third*, the discussion about acute instabilities and imminent cardiovascular collapse was largely misdirected against ideas attributed to me that I do not hold. Dr. Ropper stated that I claim 'that it is relatively easy to maintain a body that has a dead brain for an indefinite period of time' (see p. 147). I have never made such a claim. To the contrary, in my paper I described the maintenance of brain-dead pregnant women as 'always a technological *tour de force*' (3.2.2.1, p. 304). I have always acknowledged that the long-surviving cases are rare, and that brain-dead patients are typically very unstable during the acute period. An entire subsection of my paper (3.2.2.1) is in fact entitled 'Acute instabilities'. In it I offer reasons other than the pure absence of brain function why this should be the case.

In the following subsection (3.2.2.2) I even acknowledge that some brain-dead patients are no doubt dead, that their death is masked by the ventilator, and that their succumbing to imminent cardiovascular collapse from which they can't be resuscitated is a consequence of being already dead. Nowhere in the discussion about my ideas is this acknowledged, but I am generally mis-portrayed as claiming that *all* brain-dead patients are living organisms as a whole. Rather, I argue that the dead subset are dead for reasons other than the isolated fact that their brains are dead; because there is another subset, much smaller to be sure but existent nonetheless, with equally dead brains who are relatively stable during the acute phase. I have seen such cases in the pediatric ICU at UCLA (yes, including a valid apnea test). In one case, requiring neither pressors nor antidiuretic hormone, the pediatric intensivist commented to me during the apnea test, without any prompting whatsoever, 'Isn't it amazing how well a human body can function without a brain!' He said it half in jest, but half seriously too. If such cases did not exist, why would the American Academy of Neurology have gone out of its way in the 1995 Practice Parameters to state

that 'Normal blood pressure without pharmacologic support' is explicitly 'compatible with the diagnosis of brain death'? And why would a cardiac transplant surgeon have written that 'most donors can be withdrawn successfully from catecholamine support with vigorous volume resuscitation'? (Darby J.M. *et al.*, *JAMA* 1989;261:2222-8). And why would transplant surgeons prefer brain-dead heart donors with cardiovascular *stability*? (Darby J.M. *et al.*, *JAMA* 1989;261:2222-8. Guerriero, W.G. In: Narayan R.K. *et al.*, *Neurotrauma*. New York: McGraw-Hill, 1996: 835-40).

How then can Dr. Wijdicks be so emphatic that 'TK' could not possibly have been brain dead because he had vascular tone? (see pp. 269-70). During my videotaped examination, the patient was supine, but at other times the family had him propped in a chair for variable periods of time. I suspect this could not have been done successfully during his acute phase of autonomic instability; but he, like many of the other chronic cases, gradually stabilized in terms of vascular tone. I believe the most likely explanation for such stabilization is the return of spinally-mediated autonomic function upon resolution of the spinal shock that accompanies acute brain death.

Dr. Wijdicks stated that the problem he has with the chronic cases that I reported is that they do not correspond with his clinical experience as a neurological intensivist. Moreover, he 'think[s] every neurosurgeon and every neurointensivist and any neuroanesthesiologist and any pediatric intensivist who sees these patients would argue against' the validity of diagnosis of the long-surviving cases (see pp. 270). Similarly, Dr. Ropper stated: 'There is a comment by Dr. Shewmon ... that created considerable controversy, 'It is not true that brain death necessarily leads to imminent cardiovascular collapse ... To still claim that in 2006 would be to overlook the abundance of published cases of prolonged somatic survival following brain death'. He refers to his own paper. I think we want to go on record as saying that is not entirely accurate. It pains me that he is not here to have the conversation, but I do not think he is a critical care neurologist and people who do this for a living would say that is just not true' (see p. 276).

Excuse me, but I have 20 years of experience doing neurological consults in the pediatric ICU of a large university hospital, which is also a major transplant center. I also 'do this for a living'. My experience with cardiovascular instability in acute brain death conforms to that of Drs. Wijdicks and Ropper and everybody else, although it is probably fair to say that, as a group, brain-dead children tend to be relatively more stable than brain-dead adults. I have never claimed that stability is common, let alone the norm. Rather, I claim that what is uncommon is interesting, and it may

have something important to teach us. It serves the function of a mathematical proof by contradiction. It is unscientific to ignore what is in itself extremely interesting, simply because it does not fit into one's preconceived theories or mental categories. To Dr. Cabibbo's proposal 'to simply forget' all cases prior to a few years ago (see p. 291), I would reply that it is better to try to learn what we can from such cases, taking into account their various limitations, than to play the intellectual ostrich and bury our heads from all evidence that seems to threaten prevailing dogma.

Dr. Ropper's comment that I cited only my own paper as reference to the claimed 'abundance of published cases' is not fair. That one citation was a shorthand for all the references cited in that article, which would have been inappropriate to repeat in the present paper's bibliography. The two tables from my 1998 article cited 23 references from the medical literature, which yielded over 150 cases. Two references were from the nursing literature, yielding two cases. Two other cases had been personally examined by me. Six cases were brought to my attention by reputable colleagues, including Dr. Ron Cranford and the University of Pittsburgh, a major transplant center where the neurologists surely know how to diagnose brain death. The latter case was the fourth longest survival in my series, a 14-year-old girl with a glioblastoma. After brain swelling resulted in herniation, she was twice declared brain dead according to the standard protocol, including an apnea test with a  $p\text{CO}_2$  of 77. Remarkably, most of her >411 days in the brain-dead state were spent at home on a ventilator and tube feedings.

Besides, Dr. Ropper himself wrote in his 2005 edition of *Adams and Victor's Principles of Neurology*: 'In exceptional cases, however, the provision of adequate fluid, vasopressor, and respiratory support allows preservation of the somatic organism in a comatose state for longer periods' (p. 962). This is remarkable for three reasons: (1) he describes the brain-dead body as an 'organism'; (2) he describes the brain-dead patient as 'comatose' (an adjective that applies only to live people); and (3) it supports my statement that 'It is not true that brain death necessarily leads to imminent cardiovascular collapse', and contradicts his rejection of that statement during the discussion.

To dismiss all of these fascinating cases simply because they don't correspond with Dr. Ropper's and Dr. Wijdicks' clinical experience as intensivists is irresponsible. They don't correspond with my clinical experience either. They are rare cases, compared with the denominator of total brain death cases, but their undeniable existence points out the limitations of any one person's clinical experience, no matter how experienced he or she may be.



But I shall give a plausible reason for the discrepancy with our clinical experience, which will explain why the rarity of such cases does not undermine their conceptual importance for brain-death theory. I would be interested to know the proportion of brain-death cases in Dr. Ropper's and Dr. Wijdicks' vast experience in which there was motivation to try to maintain the brain-dead patient for weeks or months, as opposed to either discontinuing the ventilator or harvesting organs immediately upon the diagnosis of brain death. I suspect that they have relatively little experience with such cases, because the occasions come up rarely and no one has much experience with them outside of Japan, where unique cultural factors have provided the motivation (less so in recent years). In fact, at an earlier point in the discussion (see pp. 97-8), Dr. Wijdicks stated that he has had only one experience of a case in which the family asked him to continue ICU care of a brain-dead patient. Within the small subset of cases where such motivation exists, prolonged survival occurs with much greater frequency than compared to a denominator of total brain-death cases, the huge majority of which are disconnected or organ-harvested immediately upon the diagnosis and are therefore irrelevant for determining somatic survival *potential* without brain function.

*Lastly*, a few miscellaneous comments. Dr. Ropper stated: 'Shewmon says that he can imagine going about (transplantation) in a different way, so that removal of the vital organs neither kills nor harms the donor. I do not really understand that. It is a little self-contradictory' (see p. 251). I wrote this to be intentionally provocative, and immediately followed it by: 'At face value this sounds self-contradictory, but it is not – for reasons beyond the scope of this paper and already developed elsewhere'. Dr. Ropper would have done better to go to the two references cited and find out what I had in mind, before insinuating that I would seriously suggest a truly intrinsic self-contradiction about such an important topic.

Dr. Deecke asks what I mean by 'physiological decapitation' and whether it is 'just a provocative term' (see p. 257). I didn't invent the term, as is clear from my paper. I agree that the term is ambiguous, and that most interpretations of it do not apply to brain death, as also explained in my paper. In this we seem to agree.

I must interject something in the dialog between Msgr. Sánchez Sorondo and Prof. Spaemann regarding embryos (see p. 280), which Prof. Spaemann used as an example of a unified organism without a brain, and Msgr. Sánchez Sorondo countered by saying that it 'has a potential brain under

development'. Both points are true; they do not contradict each other, as Msgr. Sánchez Sorondo seems to imply. What is interesting about Prof. Spaemann's example is that it is an organism whose very obvious integrative unity is not mediated by any actual brain function, because the brain-in-potency doesn't even exist yet. As I wrote in my paper, 'Why do so many people think that if there is somatic integration, there has to be a single, primary organ responsible for it? Plants and embryos have no central integrating organ; rather, the integration is clearly a non-localized emergent phenomenon involving the mutual interaction among all the parts' (3.2.2.4). No one in the discussion answered my question why *integration* should necessarily require a single-organ integrator. Nor did anyone address the distinction I drew (also 3.2.2.4), which is critically important, between the primacy of the brain for the health and optimal functioning of an organism, and the alleged primacy of the brain for determining the life vs. death of a marginally alive and severely disabled organism. Neuroscientists are rightly enamored with the brain's primacy in the first sense, but the second sense does not logically follow from the first.

Again, thank you for the opportunity to participate in the discussion *post-facto* and at a distance.

DISSENTING STATEMENT  
ON THE SUMMARY DOCUMENT:  
'WHY THE CONCEPT OF BRAIN DEATH IS VALID  
AS A DEFINITION OF DEATH'

D. ALAN SHEWMON and R. SPAEMANN

As a former advocate of the concept of brain death and one who has studied the vast literature on this subject in great depth, I understand well the reasons for the wide consensus that brain death is death. Nevertheless, an accumulation of clinical evidence and incoherencies in the rationale have led me to reject this equation. I take respectful issue with a number of points in the majority statement, which will be identified below by the sub-headings in that document.

*Brain Death is Death*

I disagree that neurologists 'are perhaps in the best position to clarify the pitfalls of this controversial issue'. Neurological knowledge is obviously integral to the controversies, but the essence of life and death are ultimately philosophical concepts. Neurological expertise is clearly necessary for designing reliable criteria that the brain is dead, but neurologists have no particular expertise for explaining *why* a dead brain equals a dead patient, and in fact there is no consensus among neurologists regarding the rationale for that equation, since it is ultimately a philosophical question. Many embrace a philosophical rationale that is incompatible with Catholic anthropology. The final sentence of the subsection is not 'an important initial clarification' but a linguistic confusion between certain words ('brain death' and 'death') and their referents.

*Death is the End of a Process*

The Summary Statement refers to a process involving ‘... the failure of the integrative functions exerted by the brain and brain stem on the body. It ends with brain death and thus the death of the individual’. The body has many integrative functions not mediated by the brain, including those of the spinal cord. Failure of brain-mediated integrative functions certainly produces a very sick organism, but the preservation of at least some non-brain-mediated holistic integrative functions means that it is indeed a sick organism and not a non-organism (i.e., a dead organism). The Summary Statement gives no reason for limiting the relevant integrative functions to only brain-mediated ones.

*The Consensus on Brain Death*

The consensus is superficial and fragile. In the UK and certain commonwealth countries, only the brain stem counts, whereas most other countries require the entire brain to be irreversibly nonfunctional. In Japan, brain death is legal death only if the patient is to become an organ donor, but not otherwise. In Germany, the law does not state that brain death is legal death, but rather that organs can be legally removed from brain-dead patients (parliament could not bring itself to state explicitly that brain death is death). The Danish Council of Ethics rejected brain death as death. Moreover, the general consensus concerns the proposition that death can be diagnosed by brain-based criteria, but there is no consensus whatsoever regarding *the reason why* death of the brain (or of the brainstem) should be death. The Chairman of the Harvard Committee, among others, opined that the definition of death is essentially arbitrary and based on societal convention and utility. The mainstream, quasi-official rationale is loss of integrative unity of the body. For many health professionals, including many neurologists, their personally held rationale is that brain destruction entails a loss of personhood due to permanent unconsciousness (regardless of the biological life/death status of the body), entailing the logical implication that patients in a permanent vegetative state are also ‘dead’. Surveys of health professionals, including those involved in transplantation, have revealed a disturbing lack of agreement and logical incoherence regarding the life/death status of brain-dead and other neurologically devastated patients.

*Statistics on Brain Death*

The Summary Statement exaggerates the amount of ‘uncertainty’ regarding the diagnosis of brain death in the Repertinger case. People with long, illustrious careers built on a given idea are often close-minded to empirical challenges to that idea, and they will grasp at straws to discredit even the most impressive contradictory evidence. The Repertinger case holds the record in terms of survival duration, but many cases of brain death have been reported with survival durations longer than the usually cited ‘few days’, many of them from Japan, where the social ethos provides motivation to maintain these patients much more than in Western countries. As of 1998, I found some 175 reported cases of brain death with survivals longer than one week. The maintainers of the ‘party-line’ sweepingly dismiss most or all of these cases as ‘undocumented’, which in effect means that they themselves did not have the opportunity to personally examine each patient and the corresponding medical records.

Regarding the penultimate sentence in this subsection, it is not true that ‘the brain stem and hypothalamus’ carry out ‘the integration and coordination of *all* the subsystems of the body’. (emphasis mine) There are many subsystems that integrate through their mutual interactions in the absence of brain function.

Long-surviving cases of brain death are so rare in the Western world, not because the body loses its integrative unity without brain function, but rather because there is no therapeutic motivation to sustain these patients: almost invariably, very soon after the diagnosis of brain death is made, either they become organ donors or intensive care is stopped. Within the small subpopulation where there is motivation to maintain such patients (as in Japan, in cases of pregnant women, or in exceptional family situations like the Repertinger case), prolonged survivals are actually not so rare as the collective experience of experts would lead one to believe. Be that as it may, it is not the long survival duration *per se* of such cases that ‘disturbs the conceptual validity of brain death’, but rather the many integrative functions at the level of the organism as a whole that these bodies demonstrate, if anyone would care to look.

*The Apnea Test*

The Summary Statement downplays the potential risks inherent in the apnea test, even when performed properly. The risks of acidosis, hypotension and cardiac arrhythmias have been described even in textbooks of

some of the signers of the Statement. Informed consent is required for many medical procedures that entail less risk, yet informed consent for the apnea test is neither solicited nor given. Moreover, no defender of mainstream brain-death practice has yet given an adequate and reassuring reply to Dr. Cicero Coimbra's published concern about the apnea test further raising intracranial pressure in a theoretical subset of patients who appear clinically brain dead, but who still have marginal cerebral blood flow (what Coimbra calls 'global ischemic penumbra'), resulting in the apnea test actually precipitating the very brain death that it is supposed to be diagnosing.

#### *Antidiuretic and Other Pituitary Hormones*

Why should these somatically integrative functions be dismissed as 'spurious', and all the emphasis be given to somatically non-integrative brain-stem reflexes, if the rationale for equating brain death with death is supposedly the loss of somatic integrative unity? Moreover, these functions are not necessarily 'transient,' as this subsection states.

#### *The Loss of Heart Activity*

It may be true that the diagnosis of an irreversibly nonfunctioning brain can be made with greater certainty than that of an irreversibly nonfunctioning heart (although this no doubt depends on the details of the cases being compared). Nevertheless, the diagnosis of death is much *less* certain in the case of brain death, because it hinges on philosophical rationales (often tacit), on which there is no consensus among either philosophers or medical professionals, rationales which by nature are not susceptible to empirical verification.

I disagree that 'the reluctance to accept brain death may be mostly related to the fact that it is a relatively new concept'. Its novelty *per se* is not a reason for the reluctance; many other novelties over the last 40 years have been accepted more readily and more universally than brain death. I would posit, rather, that the reluctance is mostly related to the fact that the brain-death notion is counterintuitive, and no amount of rhetoric or propaganda will succeed in convincing the 'common man ... that a deep sleep-like state with a heartbeat ... is death' – and not only with a heartbeat, but with normal functioning of other vital organs as well, apart from the brain. (Cf. subsections 'A Counterintuitive Reality' and 'Education and Brain Death'). The Summary Statement fails to explain why total brain infarction is so radi-

cally different from not-quite-total brain infarction, so that the presence or absence of a non-somatically-integrating brainstem reflex could make the difference between a state of very deep coma and death itself.

It is not at all true that the brain has 'the role ... as the generator of the functioning of essential organs'. The signatories of the Summary Statement know this perfectly well, and it is disingenuous for them to write such a misleading sentence in such a document. The only organ that the brain 'generates the functioning of' is itself. By a stretch of language, one could argue that the brain generates (in the sense of proximately causes) the functioning of muscles and of the pituitary gland. It modulates the functioning of many organs, but certainly does not 'generate' the functioning of the heart, lungs, kidneys, liver, and other essential organs, which can operate quite normally on their own in the complete absence of brain function, so long as ventilation is artificially maintained.

#### *The Loss of Breathing*

'If one proposes that the loss of spontaneous breathing defines death, then all brain-dead patients are, by definition, "dead"'. Who would ever make such an outlandish and oversimplified proposal? That would make not only all brain-dead patients 'dead' but also all apneic, ventilator-dependent patients 'dead', including conscious patients with high spinal cord injury, amyotrophic lateral sclerosis (Lou Gehrig's disease) or diaphragmatic paralysis, as well as many cases of coma short of brain death.

#### *No Ventilator, No Heart Activity*

'If one removes the ventilator from a brain-dead patient, the body undergoes the same sequence of events ... as occurs in an individual who has undergone loss of heart activity'. The same could be said about removing the ventilator from any ventilator-dependent, non-brain-dead patient. Obviously the heart needs oxygenated blood to continue functioning. So what? This is hardly an argument that the patient is already dead before the ventilator is removed.

#### *Artificial Instruments*

'Thus, it is as illogical to contend that death is the loss of heart activity as it is to affirm that the loss of kidney activity is death'. The Summary

Statement seems to implicitly attribute such a contention to the critics of brain death. I agree that it would be illogical, and I do not know any critic of brain death who contends 'that death is the loss of heart activity'. The irreplaceability of the brain is a spurious argument; if the brain is in fact not necessary for the integrative unity of the body, then its irreplaceability is irrelevant to the life/death status of the body.

*No Circulation to the Brain Means Brain Death*

This is so obvious that it hardly needs stating. No circulation to any organ means death of that organ. On the other hand, the essential role of the brain in the cognitive life of the individual, as described in the third sentence of this subsection, does not imply that the absence of 'all sensory, cognitive, and emotional experiences' should constitute death itself, as opposed to a deep coma.

*The Camouflaging of Death*

I agree that this can be the situation in some cases of brain death – namely those involving supracritical multi-system damage (including the brain), resulting in loss of bodily integrative unity. In cases where the pathology is limited to the brain, however, there is no loss of somatic unity, and the ventilator is not camouflaging anything, no more than the ventilator camouflages 'death' in every non-brain-dead, ventilator-dependent patient.



## RESPONSE TO THE STATEMENT AND COMMENTS OF PROF. SPAEMANN AND DR. SHEWMON

A. BATTRO, J.L. BERNAT, M.-G. BOUSSER, N. CABIBBO, CARD. G. COTTIER,  
R.B. DAROFF, S. DAVIS, L. DEECKE, C.J. ESTOL, W. HACKE, M.G. HENNERICI,  
J.C. HUBER, CARD. C.M. MARTINI, J.C. MASDEU, H. MATTLE,  
M. SÁNCHEZ SORONDO, H. SCHAMBECK, E. SGRECCIA, J.B. POSNER,  
L. PUYBASSET, M.E. RAICHLE, A.H. ROPPER,  
P.N. TANDON, R. VICUÑA, A. ZICHICHI

Dr. Shewmon criticises many of the conclusions of the statement 'Why the Concept of Brain Death is Valid as a Definition of Death' and some of the views expressed during the general discussion. His points could be considered contributions to the debate. Aristotle teaches us to be grateful not only to those whose views we share but also to those who express different opinions, because they too have contributed to the stimulation of reflection.<sup>1</sup> We regret that Dr. Shewmon could not attend the PAS in September, so that we could have debated his criticism in person, rather than in retrospect.

Dr. Shewmon and Prof. Spaemann may never agree that death of the brain is the death of the individual. However, there are certain statements upon which we all agree:

1. Meeting the clinical criteria for brain death establishes that that individual will never, ever, recover any semblance of consciousness or conscious activity.
2. The vast majority of bodies meeting the brain death criteria will suffer multi-organ failure including cardiac arrest within a short period of time, despite major efforts to preserve somatic organs. This is true despite the original injury being restricted to the brain, as for example a massive cerebral haemorrhage.
3. In a small minority of such bodies, somatic organs, including the heart, may be kept functioning for a period of time, usually a few days, some-

<sup>1</sup> Cf. *Met.*, II, 1, 993 b 12 ff.

times weeks and in extremely rare instances for an extended period. No matter how long somatic function is sustained, when brain death has been appropriately diagnosed, no semblance of consciousness or conscious activity will ever occur.

4. That the phrase 'physiological decapitation' applied to brain death should be avoided because a decapitation is contrary to physiology, which refers to the normal functions of living organisms and their parts, and because brain dead subjects can still, indeed, have heads.

An overwhelming number of medical experts, including those attending the Vatican Symposium, agree with the above propositions. One finds it difficult to understand why Dr. Shewmon and Prof. Spaemann, while accepting these statements about brain death, do not accept that brain death is the death of the individual. However, we can say that their refusal is based on personal physical/biological and philosophical views. From the physical/biological point of view, they affirm that the integration and coordination of the bodily sub-systems are not performed exclusively by the brainstem and hypothalamus. And thus for them, there is a holistic vital unity of the organs of a body without the brain.

Perhaps this point can be further clarified if we contrast brain death with a vegetative state. Why is the persistent vegetative state different from brain death? Given the same supportive care as a brain-dead body, a patient in a vegetative state is unlikely to die, suggesting that the brainstem, and particularly the lower brainstem, is important for the integrative function of the rest of the body, whereas the cerebral hemispheres are not.

There are other differences between the vegetative state and brain death. 1) Functional MRI suggests that elements of consciousness may be present in patients who are vegetative. 2) There are reports describing recovery of at least minimal consciousness after many months in a vegetative state. Thus, we should not make the diagnosis of a 'persistent' vegetative state for the first three months, and for the first year following head trauma. 3) Several papers, addressing the issue of keeping somatic organs functioning after the brain has died, demonstrate that it is extremely difficult and, with rare exceptions (not, as Dr. Shewmon suggests, 'common' exceptions), fails after a few days. This contrasts with the relative ease of maintaining individuals with severe brain or spinal cord injury who are not brain dead. That an individual whose spinal cord has been severed at the high cervical level and is ventilator-dependent, can be sustained to live and work at home, indicates the importance of the brain in the integrative function of the rest of the body. That it is easier to maintain the somatic organs

of a vegetative patient than those of a brain dead subject also attests to the importance of the brain, in this case the brainstem, in integrating the function of the remainder of the body, which, in part, explains why the vegetative state is not equated with death.

Thus we believe that once the clinical criteria for brain death are present, the individuals are as dead as if their hearts had stopped.

In addition, as regards the precise issue of whether the brainstem and hypothalamus are the integrators of 'all' bodily function, Dr. Shewmon seeks to present evidence that the integration and coordination of the bodily sub-systems are not performed exclusively by the brainstem and hypothalamus. To what kind of integration and coordination does he refer? The vast majority of neurologists believe that all of the functions relevant to the state of life are performed there, in the brainstem and hypothalamus, structures that are indeed the integrators of the main systems and sub-systems of the body. The brain integrates all functions of the body, through nerves, neural transmitters and secreted substances, the latter a process that Dr. Shewmon ignores when he compares spinal cord sectioned individuals with those who are brain dead. Thus, it is unclear as to what sub-systems Dr. Shewmon is referring; the rare subjects who are brain dead, but whose organs survive for weeks or months, indicate that some organs such as the kidney and the digestive system can function independently of the brain, but whether they can integrate with each other is less clear. For that matter, as certain papers demonstrated, if the technical support is adequate, one can maintain certain organs (i.e. heart) isolated from the body in a system of perfusion for days. Thus, it should not be surprising that if these organs are perfused within the soma (their natural location), they can remain active within a corpse. One can accept that the holistic physiological properties of the soma in a brain dead subject are greater than in a collection of perfused organs, i.e. that the interaction between organs within the ventilated soma is greater than that occurring with separated organs maintained in a vat. However, these experiments do not imply that an integration and co-ordination exists without the brain. Whatever 'integrative sub-systems' the rest of the body may have, they are few, fragile, and poorly coordinated, and one cannot sustain them once the brain has died. The other bodily structures that effect some integration (nerves in the heart and bowel or bones that make up the skeleton, for example) are entirely irrelevant in discussions about brain death as the death of the individual. The ancients knew about these other integrative forms through their observation of hair and nail growth in corpses, but did not doubt that the individ-

ual was dead. Thus, in opposition to Dr. Shewmon's affirmations, with the death of the brain an inexorable process of disintegration of the body begins that a ventilator can only slow down. Therefore, as affirmed in the Statement, this process of disintegration is different from the death of the individual, which begins with an irreversible fact of health and ends with brain death and thus the death of the individual.

Moreover, if it is asserted that the brain in the embryo does not 'mediate' the integrative unity of the organism, then it is evident that the word 'organism' is being used in an inappropriate way. The embryo is the first stage in the development of a multi-cellular organism (it immediately follows the fusion of the pronuclei in the ovule) but it is not properly an organic body. What is specifically called an organic body is one that has a diversity of organs. This is not the case with an embryo because it has not yet developed a system of organs. Thus there cannot be mediation between the organs, either between the brain and the other organs or between the various organs, because the organs have not yet developed and are still in potency. There is, therefore, a radical difference, from the point of view of integration, between a situation of brain death and that of an embryo that has not yet developed its organs. This fact invalidates the parallel made between the embryo and a brain-dead body.

At this point, given their gross underestimation of the importance of the brain for the integrative function of the rest of the body, Prof. Spaemann and Dr. Shewmon affirm that the adoption of brain death as death by neurologists is not physical/biological but philosophical. In other words, according to Prof. Spaemann and Dr. Shewmon, since neurologists are not able to justify the presumed sub-integration of the body without the brain, to state that brain death is the death of the individual, neurologists are compelled to identify the brain with the mind or personhood, which is a philosophical statement.

It was clear from the direction of the meeting that the task was to focus first and foremost on the scientific approaches. Indeed, the only philosophical paper was that given by Prof. Spaemann who opposed brain death as the criterion for death. However, from the discussions during the meeting, it emerged (a point not answered by Prof. Spaemann) that although the mind is not the same as the brain, one cannot today reasonably doubt that human intelligence (and in part personhood) depend on the brain as the centre of the nervous system and other biological systems. Although we certainly do not currently have a detailed understanding of the physical modalities of human thought, it is an established scientific fact that human

intelligence depends on the support of nerve cells and the organisation of billions of connections between the billions of neurons that make up the human brain and its ramifications within the human body. This does not mean that one could conclude in haste that contemporary neuroscience has definitively demonstrated the truth of a materialistic monism and rejected the presence of a spiritual reality in man.

According to the post-Second Vatican Council and contemporary *Catechism of the Catholic Church*, 'The unity of soul and body is so profound that one has to consider the soul to be the "form" of the body:<sup>2</sup> i.e., it is because of its spiritual soul that the body made of matter becomes a living, human body' (n. 365). So, from a philosophical and theological point of view, it is the soul that confers on the body the unity and the essential quality of the human body, which are reflected in the dynamic unity of the cognitive (and inclinational) activities with the sensitive and vegetative activities that not only co-exist, but can also work together in a participation of the nervous system with the senses and the intellect (and in a participation of the biological and sensitive inclinations with the will). Thus, Aristotle, using a geometric analogy of contemporary relevance that is explicitly appropriate for this operative order as well, declared that the vegetative is in the sensitive and this is in the intellective in the same way that a triangle is in a square and this is in a pentagon, because this last contains the square and even more.<sup>3</sup> This dynamic organic unity between the activity of the intellect, the senses, the brain and the body does not exclude but, on the contrary, postulates, at a biological and organic level, that there is an organ which has the role of directing, coordinating and integrating the activities of the whole body. Each specific function carries out its activity as an integral part of the whole. In contrary fashion, the fact of suggesting a sort of equivalence or equality of functions and of their activities leads us to acknowledge their relative independence, which is contradictory to the idea of 'organism'. So the brain is the centre of the nervous system but it cannot function without the essential parts of its connectivity throughout the organism, in the same way as the organism cannot function without its centre. We are not brains in a vat, but neither are we bodies without a brain.

Therefore, brain function is necessary for this dynamic and operative physiological unity of the organism (over and above its role in conscious-

<sup>2</sup> Cf. Council of Vienna (1312): DS 902.

<sup>3</sup> Cf. *De Anima*, II, 3, 414 b 20-32.

ness), but not for the ontological unity of the organism, which is directly conferred by the soul without any mediation of the brain, as is demonstrated by the embryo. However, if the brain cannot assure this functional unity with the organic body because the brain cells are dead or the brain has been separated from the organism, the capacity of the body to receive the being and the unity of the soul disappears, with the consequent separation of the soul from the body, i.e. the death of the organism as a whole.

The formula constituting the source of the definition of the Council of Vienna that the soul is '*forma corporis*', postulates, from the operative and dynamic point of view, the other formula of St Thomas (for that matter not cited by Prof. Spaemann) to the effect that 'the government of the body belongs to the soul in that it is its motor and not its form'<sup>4</sup> and thus 'between the soul [and the body], in that it is a motor and the principle of operations, occurs something intermediary, because, through a first part moved first, the soul moves the other parts to their operations' ('*inter anima secundum quod est motor et principium operationem cadit aliquid medium, quia mediante aliqua prima parte primo mota movet alias partes ad suas operationes*').<sup>5</sup> Thus the overall formula obscured by tradition and by Prof. Spaemann is: 'the soul unites to the body as a form without an intermediary, but as a motor it does this through an intermediary' ('*anima unitur corpore ut forma sine medio, ut motor autem per medium*').<sup>6</sup> Therefore, when the cells of the brain die, the individual dies, not because the brain is the same as the mind or personhood, but because this intermediary of the soul in its dynamic and operative function (as a motor) within the body has been removed – 'that disposition by which the body is disposed for union with the soul'.<sup>7</sup> One must see this intermediation of the brain not as delegation from outside but as a part of reality and this is what the traditional notion of 'principal organ' or '*instrumentum coniunctum*' seeks to express. St Augustine, who was the source of this Thomistic doctrine of the government of the body by the soul through an organ which is the principal instrument, is very clear in asserting *avant la lettre* that brain death is the death of the individual: 'Thus, when the functions of the brain which are, so to speak, at the service of the soul, cease completely because of some defect or perturbation – since the messengers of the sensations and the

<sup>4</sup> St Thomas Aquinas, *Q. de spiritualibus creaturis*, a. 2 ad 7.

<sup>5</sup> *Ibid.*, *Q. de Anima*, a. 9.

<sup>6</sup> *Loc. cit.*

<sup>7</sup> St Thomas Aquinas, *S.Th.*, I, 76, 7 ad 2.

agents of movement no longer act –, it is as if the soul was no longer present and was not [in the body], and it has gone away' (*Denique, dum haec eius tamquam ministeria vitio quolibet seu perturbatione omni modo deficient desistentibus nuntiis sentiendi et ministris movendi, tamquam non habens cur adsit abscedit [anima]*).<sup>8</sup> Therefore, in reality the objections to the criterion of brain death as death advanced by Prof. Spaemann and Dr. Shewmon do not hold up either at a physical/biological or a philosophical level.

We also disagree with Dr. Shewmon's conclusion that the worldwide consensus on the equivalency of brain death with human death is 'superficial and fragile'. Although practices vary between countries, there does exist a consensus of sufficient strength to permit the successful declaration of brain death in dozens of countries in the developed Western world and the non-Western and developing world that have addressed this question and possess the necessary state-of-the-art technology.

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<sup>8</sup> *De Gen. ad lit.*, L. VII, chap. 19; PL 34, 365. It would appear that St. Thomas Aquinas arrived at the same conclusion about the centrality of the head when he stated: 'The head has three privileges in relation to the other members. Firstly, it is distinguished from the others in the order of dignity because it is the principle and it presides. Secondly, because of its fullness of senses in that all senses are in the head. Thirdly, because of a certain influence of sense and movement on the members': '*Caput enim respectu aliorum membrorum habet tria privilegia. Primo, quia distinguitur ab aliis ordine dignitatis, quia est principium et praesidens; secundo in plenitudine sensuum, qui sunt omnes in capite; tertio in quodam influxu sensus et motus ad membra*' (*Super Colossenses*, cap. 1, lect. 5, Marietti, Rome, 1953, vol. 2, p. 135, n. 47).

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Cancer Center since 1967 where he holds the Cotzias Chair of Neuro-Oncology. He has served as President of the American Neurological Association and is a member of the Institute of Medicine of the National Academy of Sciences and the American Association of Arts and Sciences. With Dr. Fred Plum, he authored a monograph called *The Diagnosis of Stupor and Coma*, a fourth edition of which is being prepared. The monograph extensively reviews scientific data on brain death and the prognosis of the comatose patient. Dr. Posner also wrote the original criteria for the brain death policy at Memorial Sloan-Kettering Cancer Center. His major scientific work has been in the field of Neuro-Oncology, particularly paraneoplastic syndromes.

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PROF. LOUIS PUYBASSET was born in 1964 in Paris, France. He obtained his MD in 1992 from Paris V Faculty. He graduated in Anesthesia and Intensive Care in 1993. He became Professor of Anesthesiology and Critical Care in 2001 at Paris VI University and is since the head of the 25-bed surgical neuro-intensive care unit of La Pitié-Salpêtrière Hospital. He is a member of the ICU Committee and of the Ethical group of the French Society of Anesthesia and Critical Care. He was auditioned by the French Deputy House and Senate regarding the drafting of the April 2005 new law concerning the medical care of the end of life and took a part in the choices that were made at the time. He participated in public conferences and media coverage on this topic. He has published more than 60 scientific papers in ICU care. His research efforts are now devoted to building up biological, radiological and electrophysiological tools to define the outcome of coma in order to proportionate care in comatose patients. In his daily clinical activity he is concerned with organ donation and especially the ethical issues that have emerged from this field. He is particularly concerned by the potential misuses of organ donation and by the links that are being made by some physicians between decision of care withdrawal in the ICU, euthanasia and organ donation.

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PROF. MARCUS E. RAICHLE. Over the past 20 years, the field of cognitive neuroscience, and more recently social neuroscience, has emerged as one of the most important growth areas in science. Its focus is the relationship between human brain function and behaviour in health and disease. Leading this research are the new techniques of functional brain imaging: positron emission tomography or PET and functional magnetic resonance imaging or functional MRI. The great contributions that these modern imaging techniques are making to cognitive neuroscience would not have been possible without the efforts of Marcus Raichle and his research group which originated as members of the team that invented the PET scanner in the early 1970s. Dr. Raichle and his research group were the first to describe an integrated strategy for the design, execution and interpretation of functional brain imaging studies in humans. This accomplishment was at the time the culmination of over 17 years of published research work by Dr. Raichle and his associates. The key elements of this strategy have guided the explosion in imaging research in cognitive and social neuroscience ever since, and provided unique new insights into important clinical conditions such as depression, Alzheimer's disease and altered states of consciousness, to name just a few. Dr. Raichle is a neurologist by training and is currently professor of Radiology, Neurology, Neurobiology, Biomedical Engineering and Psychology, and Co Director of the Division of Radiological Sciences in the Mallinckrodt Institute of Radiology at Washington University in St. Louis. He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the Institute of Medicine.

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PROF. GIOVANNI M. ROCCHI was born in 1939 in Rome, Italy, and is married with a son and a daughter. He obtained his MD from 'La Sapienza' University of Rome in 1963 and his PhD from the same University. He graduated from the Departments of Infectious Diseases and Internal Medicine in Rome, and was promoted to Associate Professor in 1983. In 1985, he became Professor and Chairman of the Department of Infectious Diseases. He is currently Professor of Medicine at 'Tor Vergata' University Medical School in Rome where he holds the Chair of Infectious Diseases in Internal Medicine. Since 1967, Prof. Rocchi has been consultant physician in internal medicine in the clinical department of the Vatican City. Since July 2005, he has been in charge of the Direzione di Sanità ed Igiene of the Vatican City where he acts as director with specific interest in the management of the clinical department. Prof. Rocchi's research and clinical interests are medical care in internal medicine and infectious diseases. He has authored over 150 publications and made contributions to several textbooks. He is a member of several professional societies, including the Italian Society of Internal Medicine and the Italian Society of Infectious and Tropical Diseases.

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DR. ALLAN H. ROPPER was born in 1950 in New York City, New York. He received his BA from Cornell University in Ithaca, New York and his MD from Cornell University Medical College in New York in 1974. Dr. Ropper trained in internal medicine at UCSF-Moffit Hospital and in neurology at Massachusetts General Hospital. His work has been mainly in the field of neurological intensive care and related disorders such as Guillain-Barré syndrome. His present focus includes studies of gene therapy as a potential treatment for peripheral neuropathy, and he is conducting an NIH sponsored study of vascular endothelial growth factor (VEGF) for the treatment of diabetic neuropathy. He has over 150 publications and is an author of the most widely consulted textbook of neurology, *Principles of Neurology*, which is in its eighth edition. He is a longtime contributor to several major textbooks of medicine, including *Harrison's Principles of Internal Medicine*. He has received numerous awards for teaching and service at both the medical school and hospital. Most

recently, Dr. Ropper became an associate editor of the *New England Journal of Medicine*.

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PROF. PAOLO M. ROSSINI graduated and received honours in Medicine at the Catholic University of Rome (July 1974). He was appointed Associate Professor in 1984 and transferred to the University of Rome at Tor Vergata where he taught Clinical Neurophysiology at the Neurology Clinic directed by Professor Giorgio Bernardi. From 1982, he actively participated in the development of clinical applications in transcranial magnetic stimulation, collaborating with many Italian and foreign colleagues. He was appointed Chairman of the Department of Neurology at the Fatebenefratelli Hospital 'San Giovanni Calibita' of Rome in 1990. Since then, he has led the clinical activity of the Department. He actively collaborates with research centres operating principally with the National Research Council of Italy in the field of neuromagnetic recording. Visiting Professor at SUNY in Brooklyn from 1980 to 1982 and at the University of Irvine (California) in 1989. Editor-in-Chief of *Electroencephalography and Clinical Neurophysiology* (later *Clinical Neurophysiology*) between 1995 and 2003. Scientific Director of a Scientific Institute on Dementia and Psychiatry appointed by the Italian Ministry of Health since 1997. In 2000, he was appointed Full Professor of Clinical Neurology at the Faculty of Medicine at the Campus Biomedico University of Rome. Member of the High Council of Health since 2003. From 2001-2003, he was President of the Italian Society of Clinical Neurophysiology. He has been Chairman of the European Chapter of the International Federation of Clinical Neurophysiology (E.C.-I.F.C.N.) since 2005. Author of 301 publications listed in PubMed with I.F., in the fields of neuroanatomy, experimental neurophysiology, clinical neurophysiology, clinical neurology and clinical neuropharmacology, on 40 different journals reviewed in the Med-line directory.

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PROF. D. ALAN SHEWMON was born in 1949 in Pulaski, VA (USA) and now resides in Los Angeles with his wife and daughter. He received his BA in 1971 from Harvard and his MD in 1975 from NYU Medical School. He completed pediatric residency at Children's Hospital, San Francisco, and neurology residency at Loyola University Medical Center, Maywood, IL. After a fellowship at UCLA in 1980, he has remained on the UCLA Medical School faculty ever since, in the Departments of Pediatrics and Neurology. From 1983 to 1999 Dr. Shewmon was Director of UCLA's Pediatric Clinical Neurophysiology Laboratory. In 2000 he became Director of the Clinical Neurophysiology Laboratory and head of Pediatric Neurology at Olive View-UCLA Medical Center, an affiliated county hospital. In 2003 he became Chief of Neurology there and Vice Chair of Neurology at UCLA. Dr. Shewmon's research interests include pediatric epilepsy and the interface between neurology and ethics. On the topics of brain death, coma and vegetative state alone, he has authored 28 publications and given 47 international lectures, in addition to his productivity in EEG and epilepsy. He is co-editor and part author of the book *Brain Death and Disorders of Consciousness*, published by Kluwer in 2004. Dr. Shewmon is a member of the American Academy of Neurology, American Clinical Neurophysiology Society, and other professional societies, and was past president of the Western Clinical Neurophysiology Society. He served on the Child Neurology Society's Ethics Committee and was a consultant for the Multi-Society Task Force on Persistent Vegetative State. He was on the Pontifical Academy of Sciences' Second Working Group on Brain Death in 1989. Since 1996 he has been a corresponding member of the Pontifical Academy for Life, and in 1997-98 served on that Academy's Task Force on Brain Death. He delivered keynote addresses at the 2nd and 3rd International Symposia on Brain Death, in Havana in 1996 and 2000, and served on the Organizing and Scientific Committees of the 3rd and 4th such International Symposia of 2000 and 2004.

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PROF. ROBERT SPAEMANN was born in 1927 in Berlin, Germany. He studied at the University of Münster, where, in 1962, he was also awarded his *Habilitation*. He was Professor of Philosophy at the Universities of Stuttgart (until 1968), Heidelberg (until 1972), Salzburg and Munich, where he

worked until his retirement in 1992. He was also Guest Professor at the University of Rio de Janeiro, Brazil and at the University of Paris (Sorbonne). Prof. Spaemann's philosophic work is characterised by a very unusual style, which is never apodictical and does not boil down to the simple proposal of a new philosophic anthropology, not even as a pure 'return to metaphysics'. What he attempts is always on the grounds of modern culture, under his own conditions, trying to prove what has gone wrong in it, and which are the premises of the repeated failures it has incurred in. The 'abolition of the human being' (as well as of all traditional cultures), which is threatened today by the universalisation of the scientific objectification of the world and by its rational-instrumental organisation, whose essential paradox is mistaking the means for the ends, placing at risk the very idea of human life, can be matched only by rediscovering a principle of transcendence and the sense of the absolute. Prof. Spaemann is a member of the Pontifical Academy for Life and honorary member of the Chinese Academy of Social Sciences and of the Academia Chilena de Ciencias Sociales. His books have been translated in thirteen languages. Among his titles: *Glück und Wohlfühlen: Versuch über Ethik*, Stuttgart 1989; *Personen*, Stuttgart 1996; *Reflexion und Spontaneität. Studien über Fenelon*, Stuttgart 1998; *Moralische Grundbegriffe*, Stuttgart 1999; *Grenzen. Zur ethischen Dimension des Handelns*, Stuttgart 2001.

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PROF. PRAKASH NARAIN TANDON was born in 1928 at Shimla. Education: K.G. Medical College, Lucknow; M.S. (1952) and FRCS (England, 1956); specialisation in Neurosurgery at Oslo, Norway and Montreal, Canada. He returned to India to start the first neurosurgical service at K.G. Medical College, Lucknow and founded the Dept of Neurosurgery at All India Institute of Medical Sciences, New Delhi. His scientific contributions were primarily concerned with neurological and neurosurgical conditions of direct relevance for the health needs of India, including tuberculosis of the nervous system, developmental defects of the brain, head injury, spontaneous subarachnoid haemorrhage and a variety of brain tumours. These have resulted in publication of over 200 scientific papers, 14 monographs and chapters in national and international text books.

Prof. Tandon has steered the establishment of a series of national facilities: Neuroinformatic Centre, Neural Transplant Unit, a Brain Bank, a national NMR facility for biomedical research, National Brain Research Centre (NBRC). Hon. Minister for HRD & ST nominated him as the first President of the NBRC Society and Chairman of its Scientific Advisory Committee. He serves on the committees of DST, DBT, CSIR, ICMR etc. and is Chairman of the Science Advisory Councils or Governing Body of CDRI, CCMB, NARI, NII, NIMHANS. He is the only clinician to be the President of the Indian National Science Academy, and the National Academy of Sciences, India. He is an elected fellow of the National Academy of Medical Sciences, National Academy of Sciences, Indian Academy of Neuroscience. He delivered the Inaugural address of IAP-2000 conference in Tokyo. He was invited as a member of the Review Panel of the International Council of Scientific Unions and was the founder Co-Chair of the Inter-Academy Panel of the World Academies of Sciences in which capacity he addressed the Plenary sessions of the UN conference on Population and Development, Cairo, 1994, and the UN conference on Habitat Istanbul 1997. Member of the J.W.G. of the Indo-US Vaccine Action Programme since its inception in 1986. Member of the Governing Body of Indo-US S&T Forum. Awards and honours: Distinguished Fellowship of Vijnana Parishad, Prayag and Honorary Fellow for Life, Indian Institute of Advanced Study, Shimla; Jawaharlal Nehru Fellowship, Bhatnagar Fellowship; Megh Nad Saha Distinguished Fellowship; B.C. Roy Eminent Medical Scientist, DSc (h.c.BHU); Sir C.V. Raman Medal, Jawaharlal Nehru Birth Centenary Award (ISCA); Basanti Devi Amir Chand Award (ICMR) among others. He has been Honorary Surgeon to the President of India and Member Science Advisory Council to the Prime Minister. He was awarded Padma Sri (1973) and Padma Bhushan (1991).

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PROF. EELCO F.M. WIJCKES was born in 1954 in Leiden, The Netherlands. He obtained an MD at the Medical School University of Leiden and a PhD (cum laude) at the Erasmus University in Rotterdam. He was a visiting neurologist and research fellow in the Neurological/Neurosurgical Intensive

Care Unit at Massachusetts General Hospital, Harvard University, Boston in 1988-89. He became a consultant at the Mayo Clinic in 1992. He is the founding Editor-in-Chief of *Neurocritical Care*. He has written over 400 articles and chapters and authored or edited 10 books including *Clinical Practice of Critical Care Neurology*; *Neurologic Catastrophes in the Emergency Department*; *Neurologic Complications of Critical Illness* (with Oxford University Press and in 2nd edition). He edited and co-wrote *Brain Death* published by Lippincott, Williams, and Wilkins in 2001. He authored the American Academy of Neurology Guidelines of Brain Death ('Determining Brain Death in Adults', *Neurology* 1995; 45:1003-1011). Other articles on brain death include: 'Neurologist and Harvard Criteria for Death' (*Neurology* 2003; 61:970-976), 'The Diagnosis of Brain Death' (*New England Journal of Medicine* 2001; 344:1215-122) and 'Brain Death Worldwide – Accepted fact but no global consensus in diagnostic criteria' (*Neurology* 2002; 58:20-25). He was the medical director of the Neurological-Neurosurgical Intensive Care Unit at Saint Mary's Hospital, Mayo Medical Center from 1992 to 2003, and is currently Chair of the Division of Critical Care Neurology, Mayo Clinic and Professor of Neurology, Mayo College of Medicine.

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## TABLES

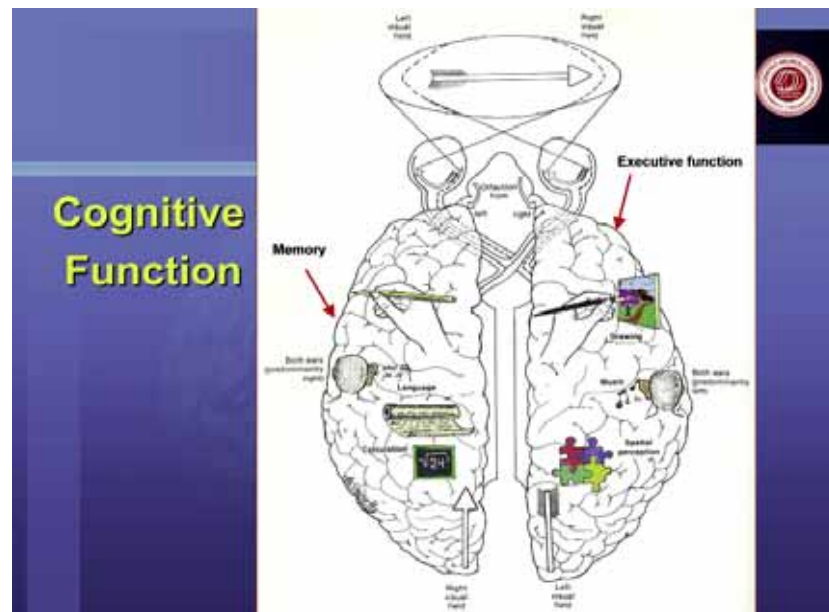


Figure 1.

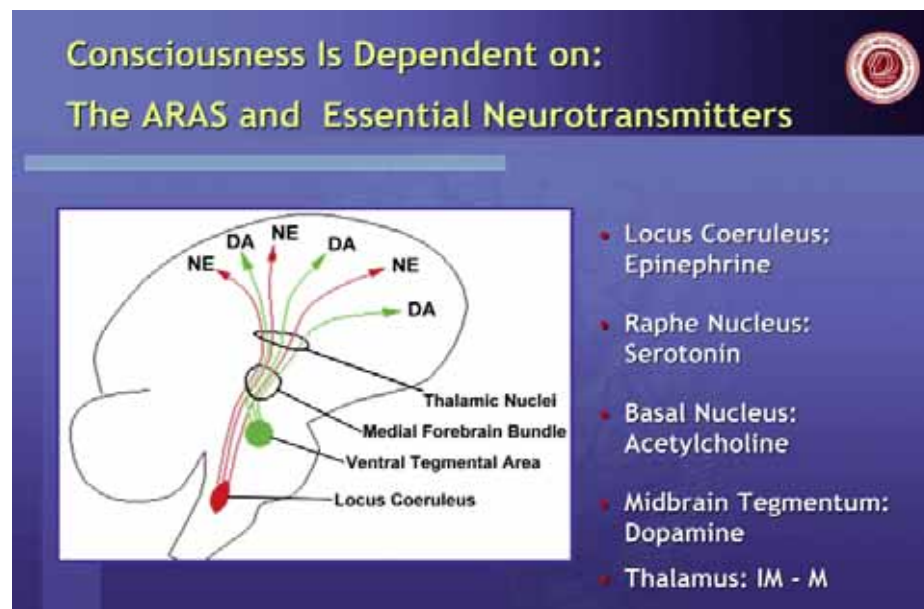
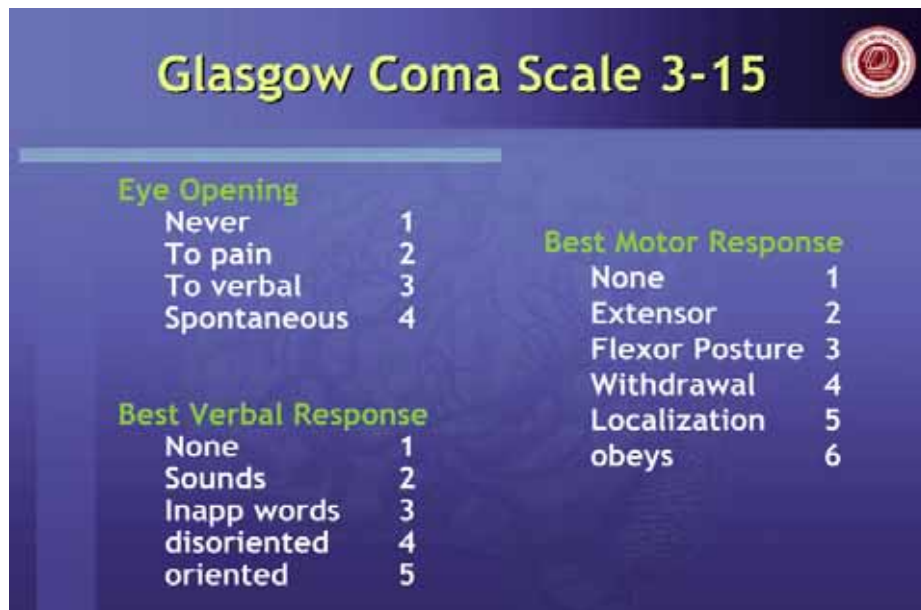


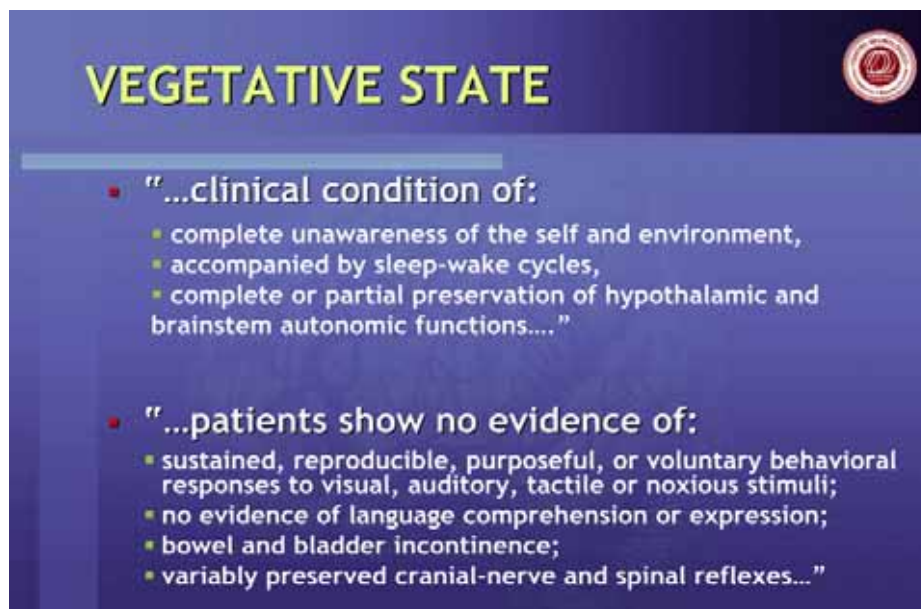
Figure 2.



**Glasgow Coma Scale 3-15**

Eye Opening		Best Verbal Response		Best Motor Response	
Never	1	None	1	None	1
To pain	2	Sounds	2	Extensor	2
To verbal	3	Inapp words	3	Flexor Posture	3
Spontaneous	4	disoriented	4	Withdrawal	4
		oriented	5	Localization	5
				obeys	6

Figure 3.



**VEGETATIVE STATE**

- "...clinical condition of:
  - complete unawareness of the self and environment,
  - accompanied by sleep-wake cycles,
  - complete or partial preservation of hypothalamic and brainstem autonomic functions...."
- "...patients show no evidence of:
  - sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile or noxious stimuli;
  - no evidence of language comprehension or expression;
  - bowel and bladder incontinence;
  - variably preserved cranial-nerve and spinal reflexes..."

Figure 4.

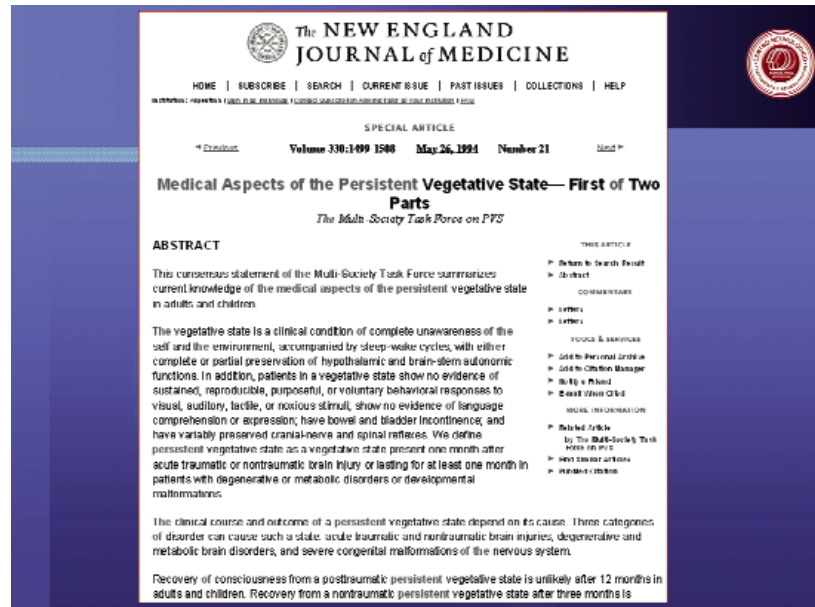


Figure 5.



Figure 6.

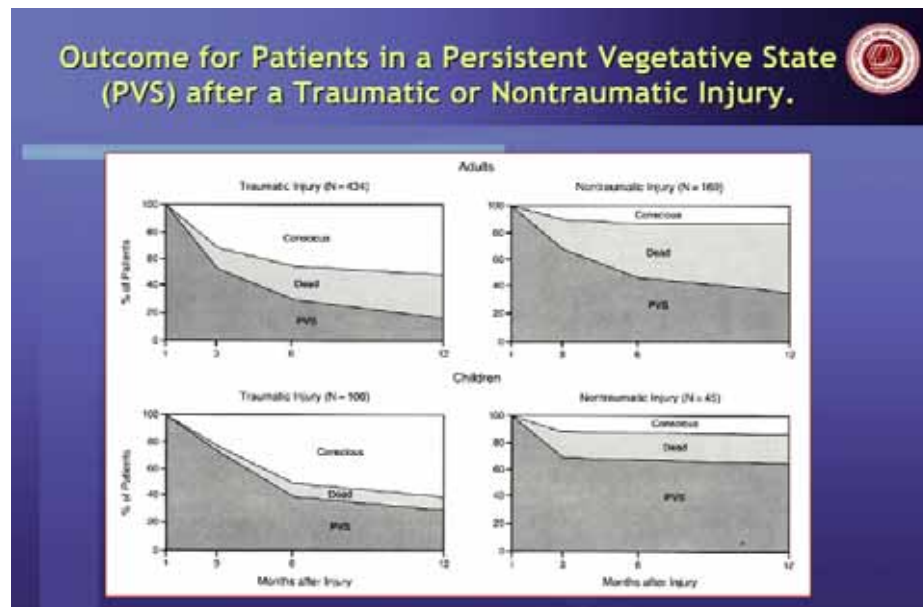


Figure 7.

AMERICAN ACADEMY OF NEUROLOGY®				
PRACTICE PARAMETER: ASSESSMENT AND MANAGEMENT OF PATIENTS IN THE PERSISTENT VEGETATIVE STATE (Summary Statement)				
Table 2. Probability of Recovery of Consciousness and Function at 12 Months in Adults and Children in a Persistent Vegetative State (PVS) Three or Six Months after Traumatic or Nontraumatic Injury.*				
OUTCOME	ADULT		CHILDREN	
	Traumatic (N = 434)	Nontraumatic Injury (N = 169)	Traumatic Injury (N = 106)	Nontraumatic Injury (N=45)
% of patients (99% confidence interval)				
Patients in PVS for 3 months+				
Death	35 (27-43)	46 (31-61)	14 (1-27)	3 (0-11)
PVS	30 (22-38)	47 (32-62)	30 (13-47)	94 (83-100)
Moderate disability	19 (12-26)	6 (0-13)	24 (8-40)	3 (0-11)
Moderate disability or good recovery	16 (10-22)	1 (0-4)	32 (15-49)	0
Patients in PVS for 6 months++				
Death	32 (21-43)	28 (12-44)	14 (0-31)	0
PVS	52 (40-64)	72 (56-88)	54 (30-78)	97 (89-100)
Moderate disability	12 (4-20)	0	21 (1-41)	3 (0-11)
Moderate disability or good recovery	4 (0-9)	0	11 (0-26)	0

Figure 8.



Figure 9.

## TREATMENT DECISIONS

- Artificial nutrition and hydration are forms of medical treatments
- No medical or ethical distinctions between withholding or withdrawing treatment

American Academy of Neurology 1989; 39: 125

- Death occurs within 10-14 days: dehydration/electrolyte imbalance (not malnutrition)
- Patients do not experience thirst or hunger
- Some patients progress from PVS to coma before death

Figure 10.



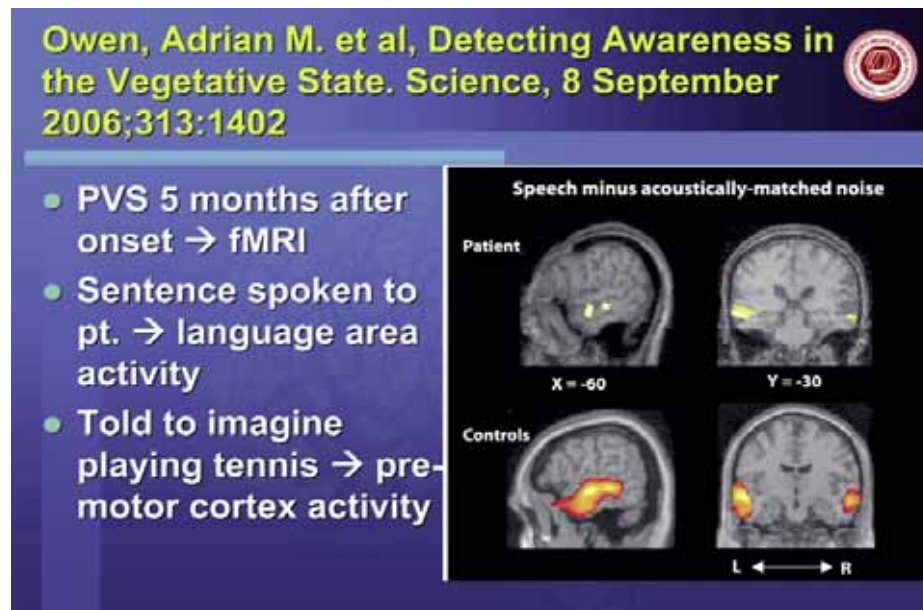


Figure 11.



Figure 12.

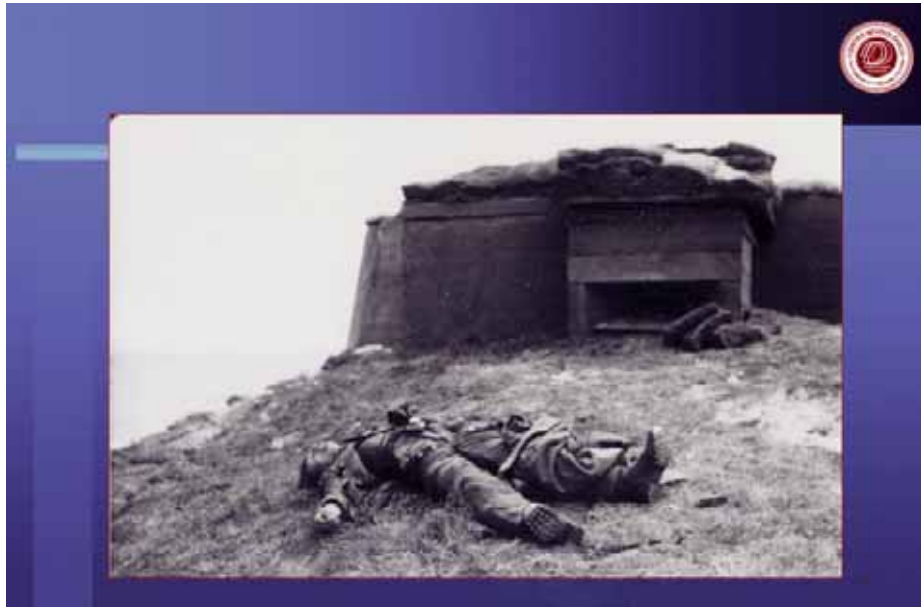


Figure 13.



Figure 14.





Figure 15.

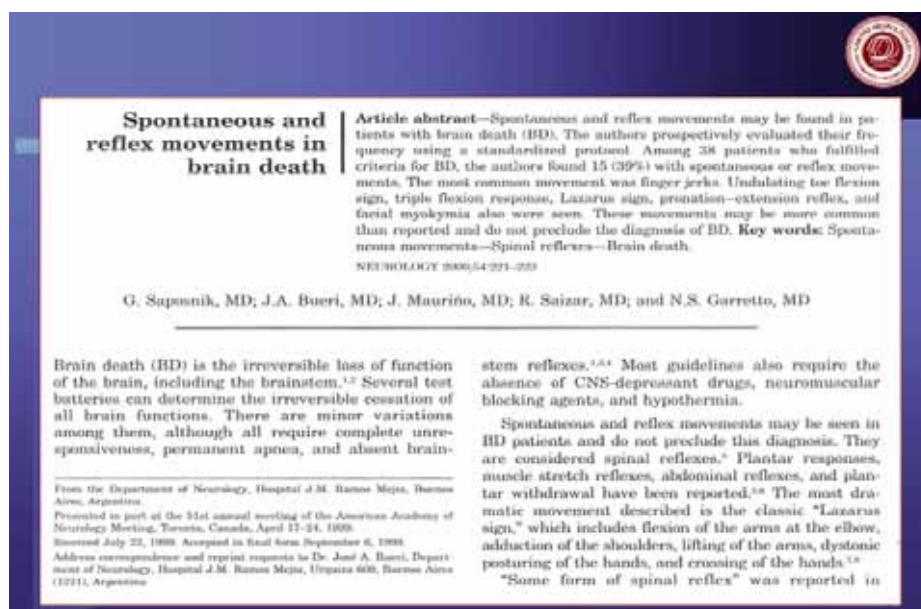


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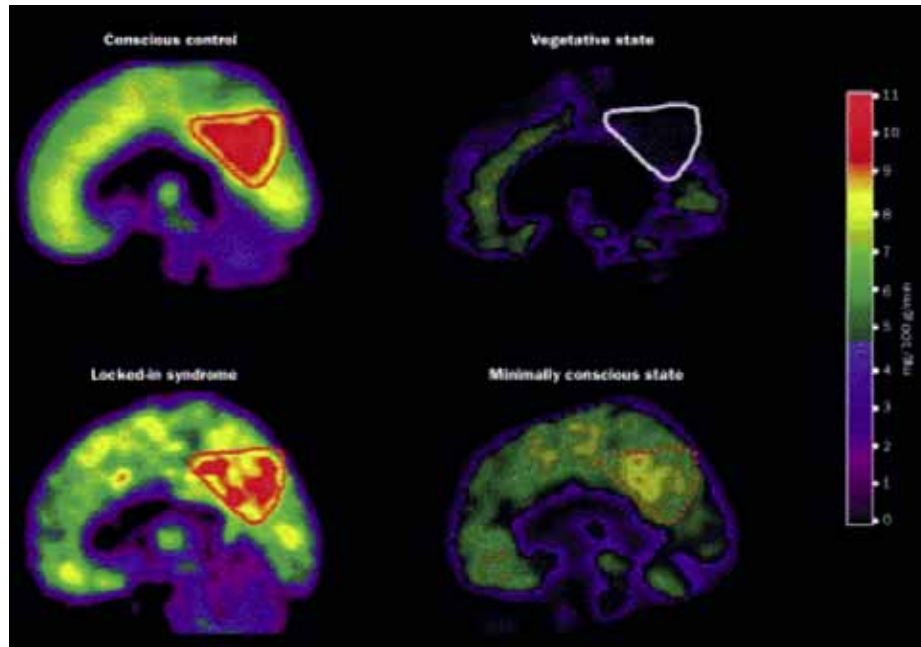


Figure 1. Resting cerebral glucose metabolism in healthy controls and patients in vegetative state, locked-in syndrome, and minimally conscious state. In healthy conscious individuals the medial posterior cortex is the most active brain region; in patients in VS who wake, this is the least active region. In MCS, there is an intermediate metabolism in this region, considered to be an important part of the neural network subserving consciousness. In locked-in syndrome, no brain region shows substantial metabolic suppression. From Laureys S. *et al.*, *Lancet Neurology*, 2004;3:537-54.

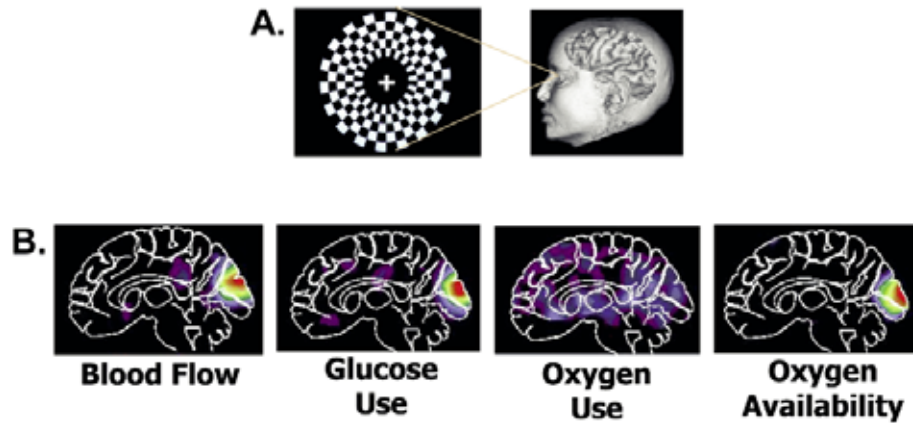


Figure 1. Stimulation of the human visual cortex with a reversing annular checkerboard when compared to a simple fixation crosshair (A) produces dramatic increases in blood flow and glucose use in the visual cortex that are unaccompanied by similar increases in oxygen use (B). The result is an increase in the local oxygen availability (B, right) because the increased supply of oxygen by flowing blood exceeds the increased local demand for oxygen. Functional neuroimaging with positron emission tomography (PET) has largely focused on the changes in blood flow (B, left) whereas functional magnetic resonance imaging (fMRI) has taken advantage of its sensitivity to the changes in oxygen availability (B, right). These data were adapted from our earlier published work (Fox, Raichle *et al.* 1988; Raichle and Mintun 2006).

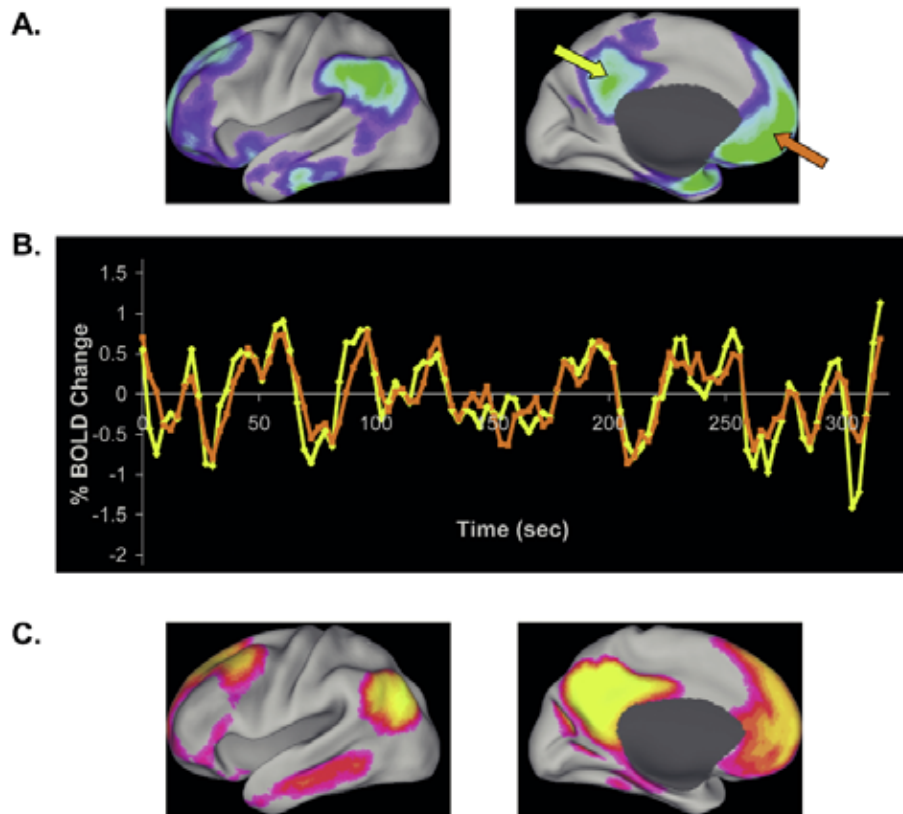


Figure 2. Performance of a wide variety of tasks has called attention to a group of brain areas (A) that decrease their activity during task performance in contrast to those areas in the brain that increase their activity as expected. What has been striking is the consistency with which these particular areas (A) behave in this manner. If one records the spontaneous fMRI BOLD signal activity in these areas in the resting state (arrows, A) what emerges is a remarkable similarity in the behaviour of the signals between areas (B). Using these fluctuations to analyze the network as a whole (Fox, Snyder *et al.* 2005; Vincent, Snyder *et al.* 2006) reveals a level of functional organization (C) that parallels that seen in the task related activity decreases. These data provide a dramatic demonstration of the ongoing organization of the human brain likely provides a critical context for all human behaviours. These data were adapted from our earlier published work (Shulman, Fiez *et al.* 1997; Gusnard and Raichle 2001; Raichle, MacLeod *et al.* 2001; Fox, Snyder *et al.* 2005).

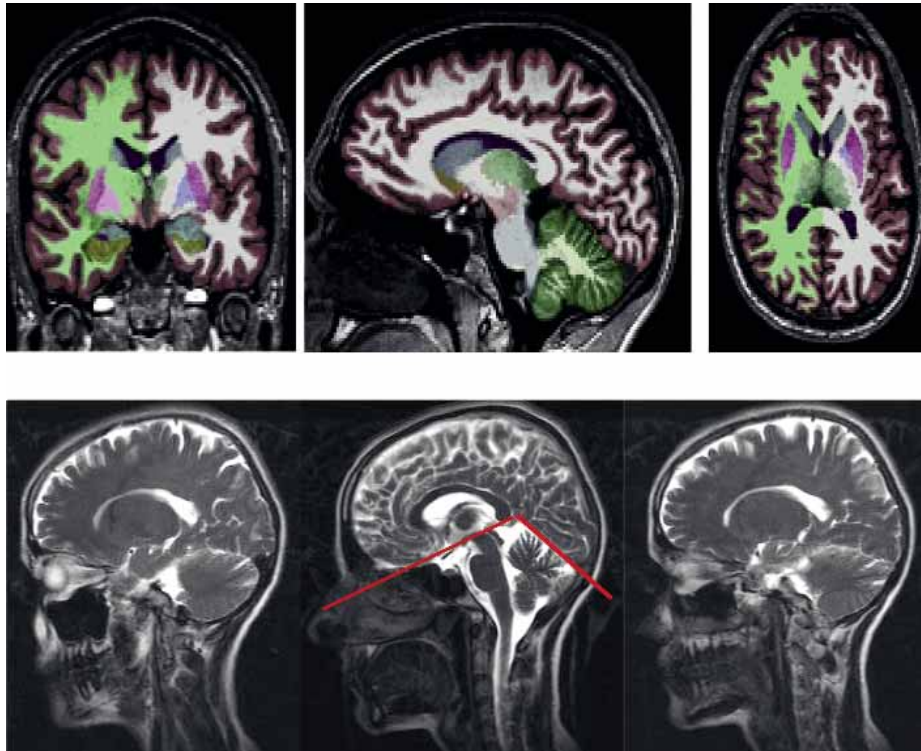


Figure 1. Sagittal, lateral and horizontal projections of the human brain in the MRI scan. Red lines separate cerebellum and brain stem from supratentorial structures.



Figure 4. Post-mortem brain of a patient who suffered a vegetative state for more than 12 years – severe destruction of the supratentorial brain structures with preservation of pontine and cerebellar segments.



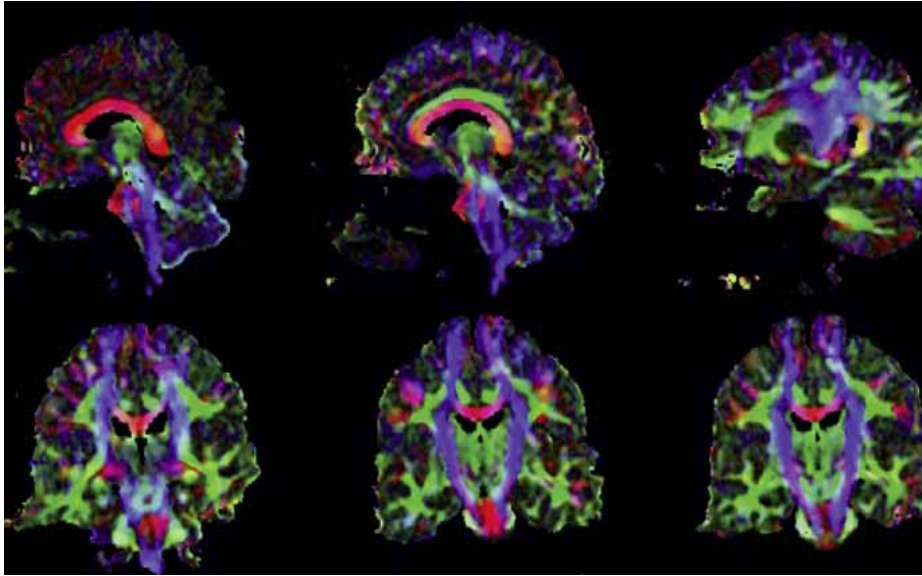


Figure 5. MR Tensor images of white matter pathways in a human brain (*red* indicates horizontal, *green* anterior-posterior and *blue* proximal-distal fibre connections).

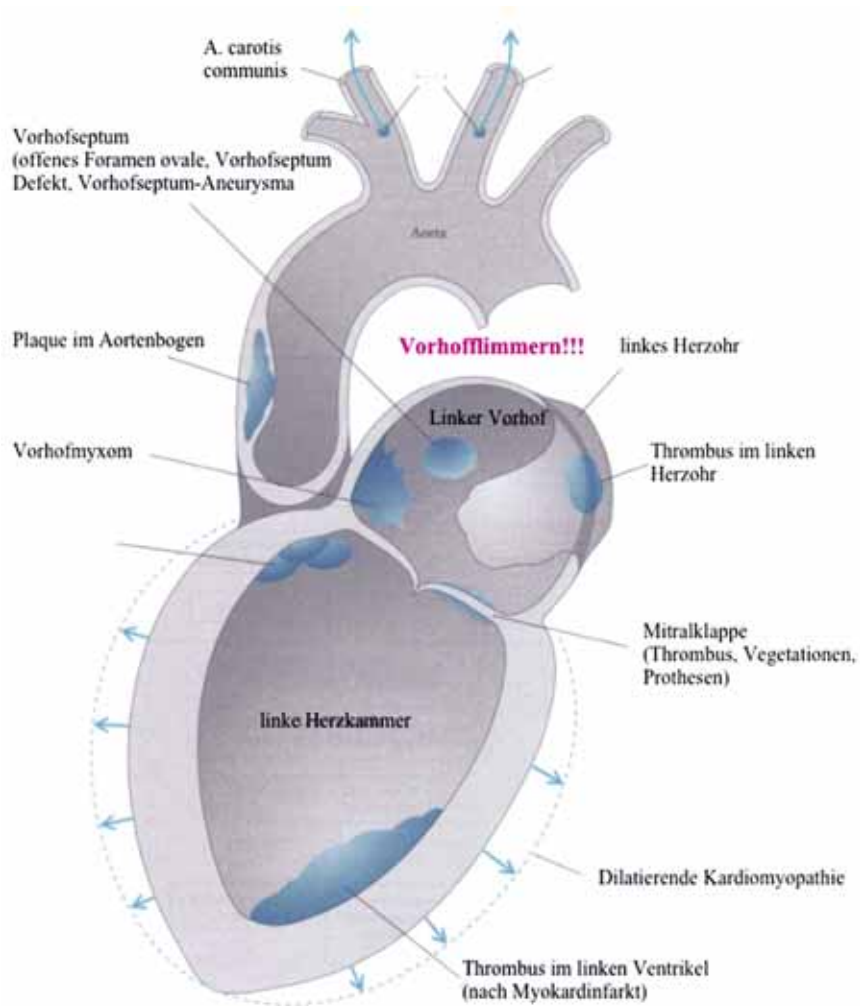


Figure 2. Possibilities of cardiogenic embolism.



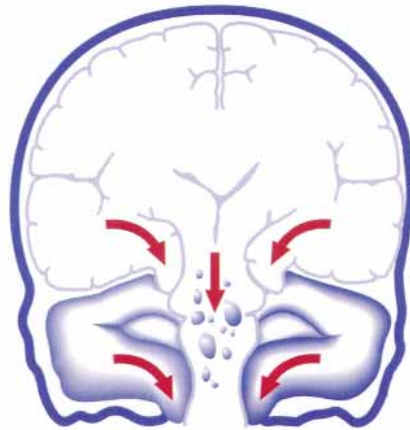


Figure 3.

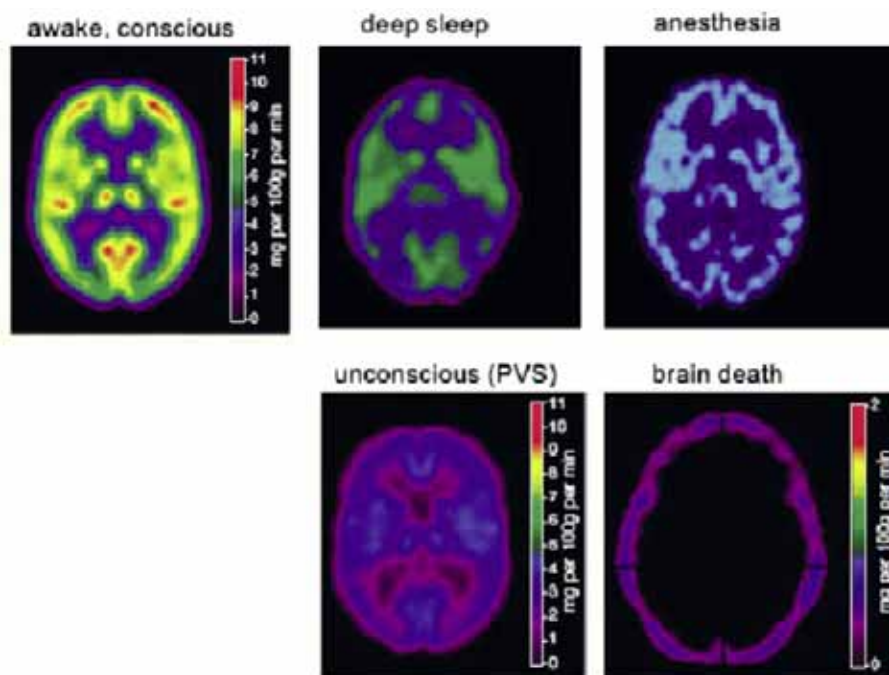


Figure 4. Regional cerebral metabolic rates of glucose (rCMRGlu) using positron emission tomography (PET). Lauryes S. *et al.*, *Nature Rev. Neurosci.* 2005; TICS 2005.

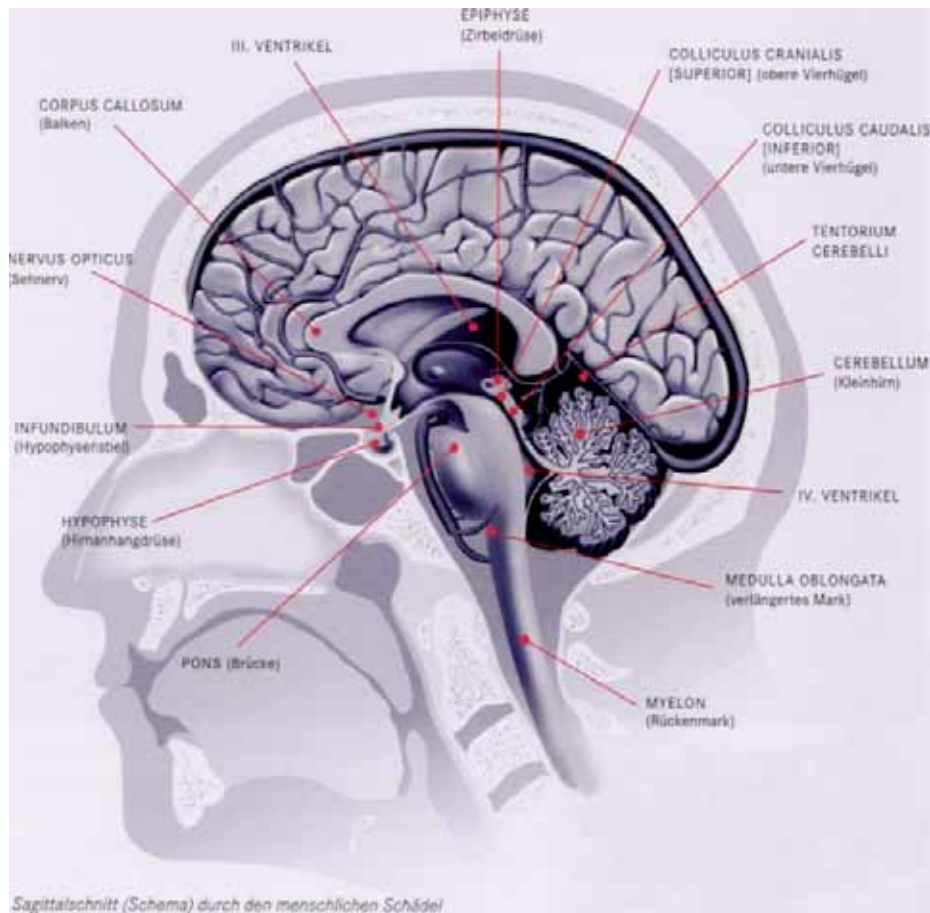


Figure 5. The Neurohypophysis (pituitary gland) separated from the brain, the *infundibulum* leads through the *diaphragma sellae* into the *sella turcica*.

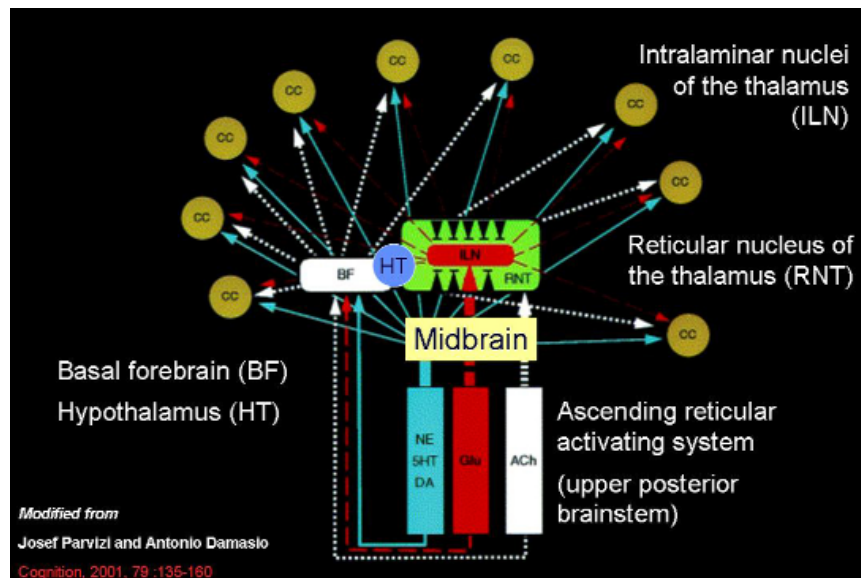


Figure 1.

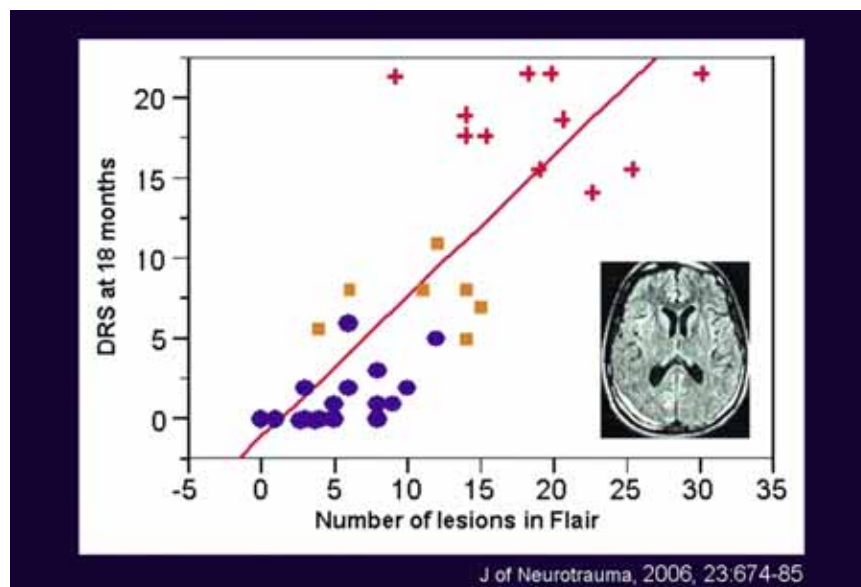


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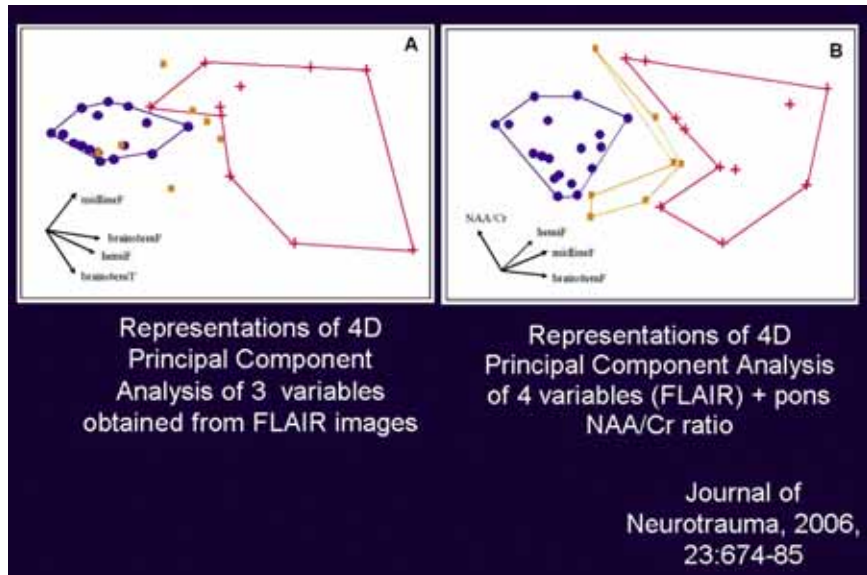


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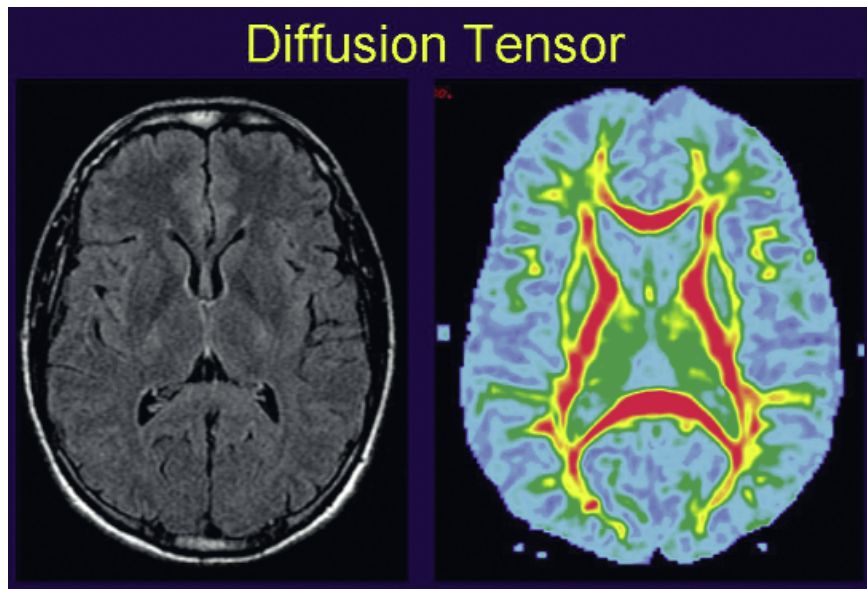


Figure 9.

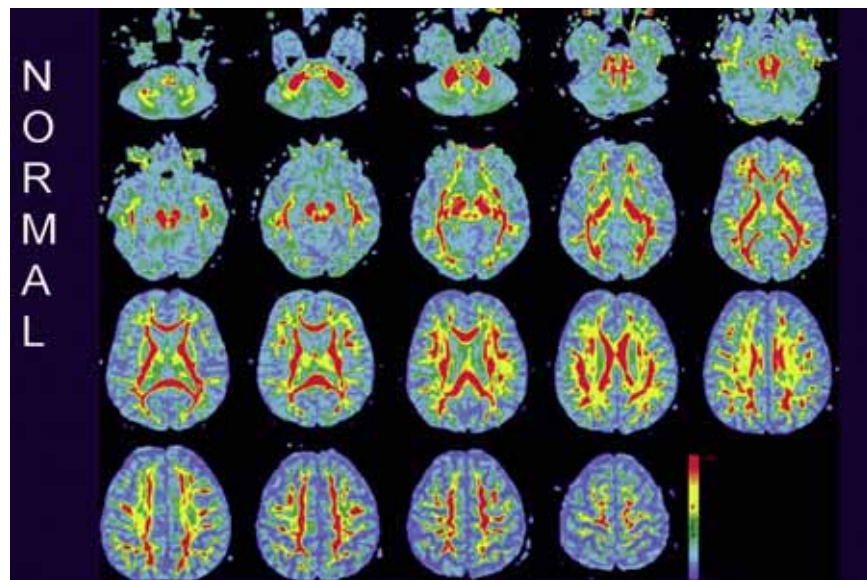


Figure 10.

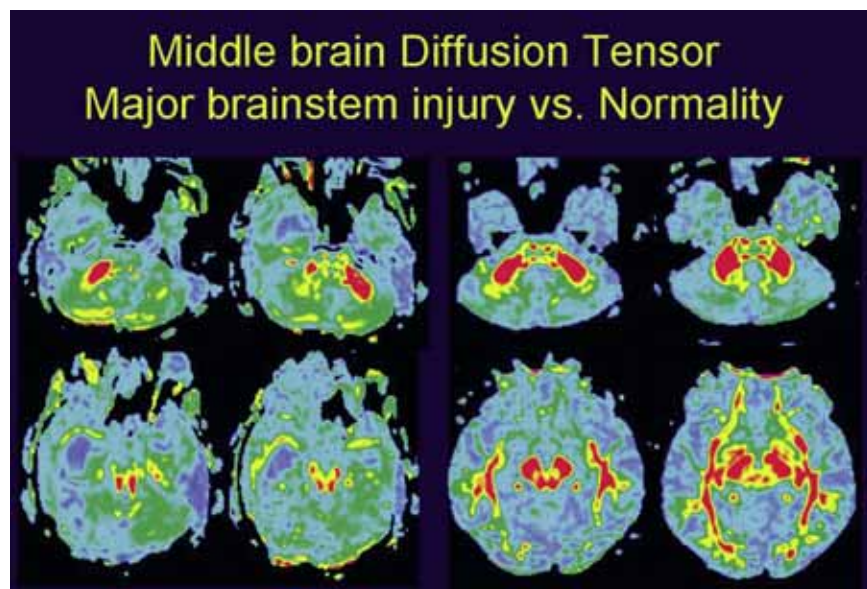


Figure 12.



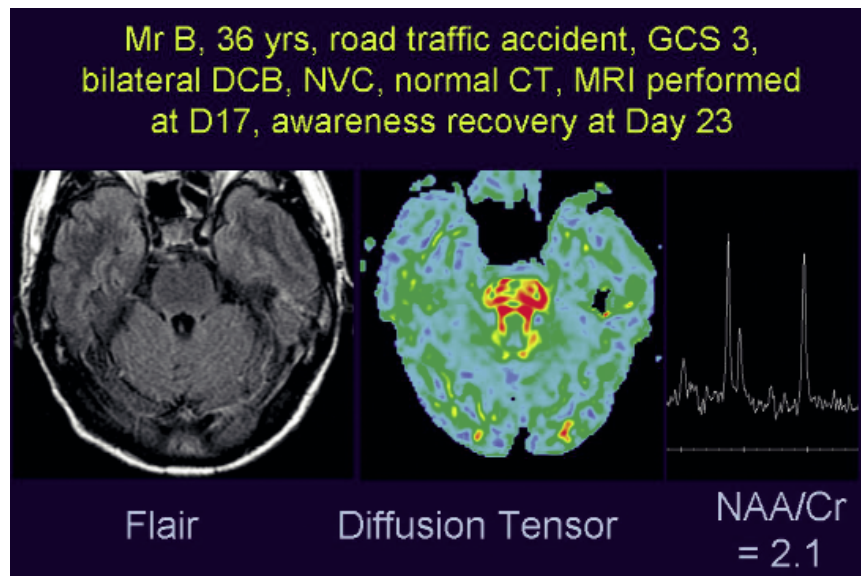


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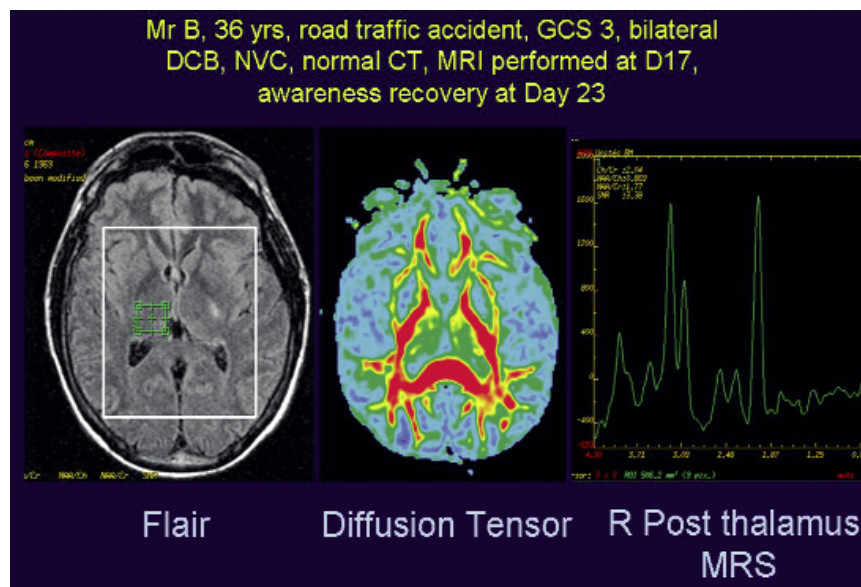


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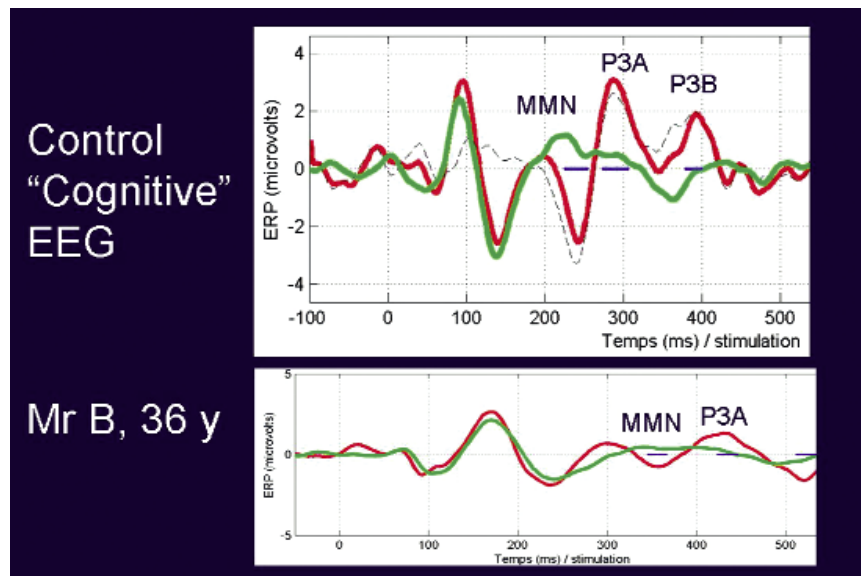


Figure 15.

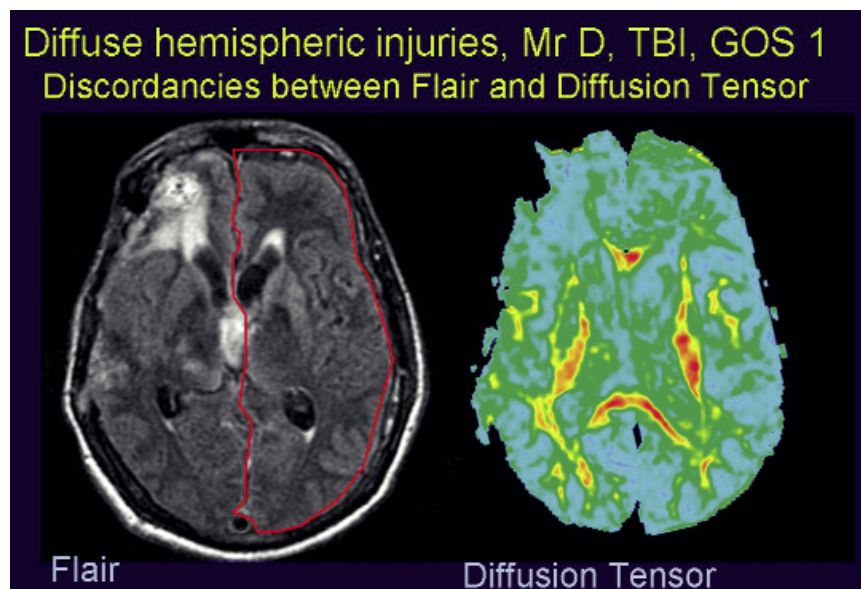


Figure 16.

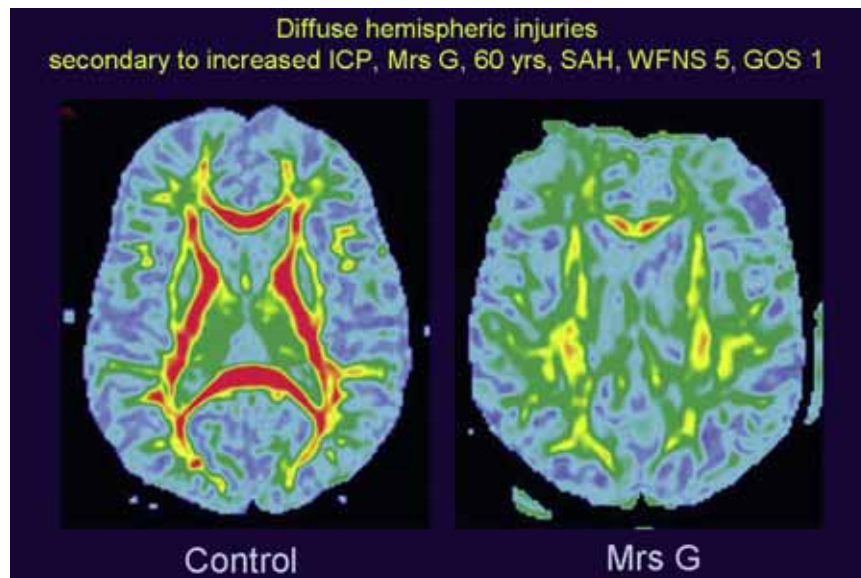


Figure 18.

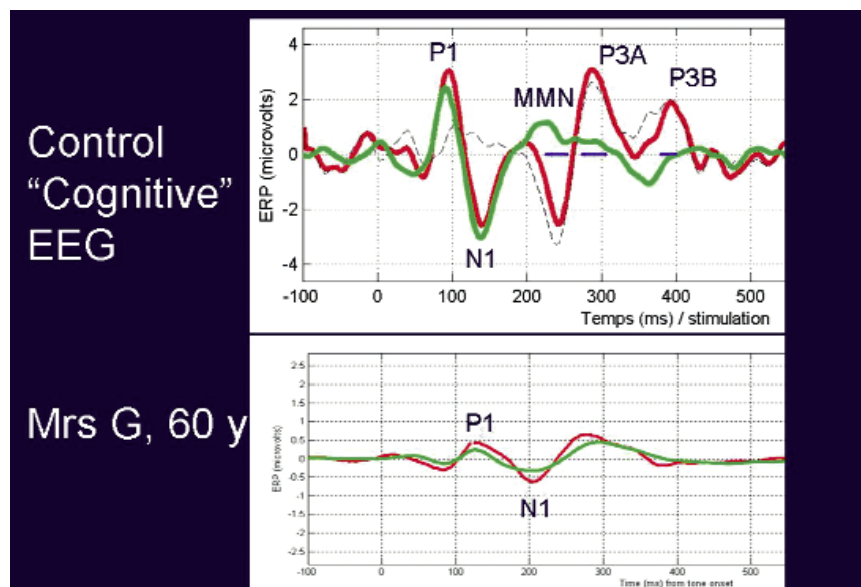


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