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INFECTIOUS DISEASE AND HUMAN AGENCY: AN HISTORICAL OVERVIEW

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We have, because human, an inalienable prerogative of responsibility which we cannot devolve, no, not as once was thought, even upon the stars. We can share it only with each other.

(Sir Charles Scott Sherrington, *Man on His Nature*)

INTRODUCTION

The speed with which infectious diseases can now spread, the absolute number of humans at risk, and the rates of emergence of new pathogens: such parameters of global epidemics invite historical comparisons. Incurable, acute infectious diseases can now occur almost simultaneously across the globe, creating the further possibility that individuals who know what to do and how to intervene will themselves be compromised. SARS, for example, had its highest morbidity and mortality rates among medical personnel and hospital workers (NAC, 2003). The planetary ecosystem, meanwhile, may face many extensive global threats all at once, requiring a kind of global governance and compassionate collaboration of peoples that has never before existed. Finally, a substantial portion of humans alive today live in deep poverty, without access to material, social or political resources (Davis, 2006; UN-Habitat 2003).

This paper specifically reviews past human efforts in the understanding and control of infectious diseases. Within the past 500 years we do find justly celebrated successes. The imposition of barrier technologies to impede the spread and perceived contagion of plague, the invention of preventive vaccination and eventually eradication of smallpox, and the triumph of sanitation-based public health in the control of pandemic cholera epidemics: such are familiar examples among biomedical and public health communities. The evolution of effective epidemic controls and interventions, this paper will suggest, was linked to the perception of geographical and socioeconomic differences in mortality experience even during great epidemics. However the benefits of most interventions accrued to some segments of a population and to larger geographical regions. Ironically success in epidemic control created further differentials in vulnerability and risk among peoples and nations.

Retelling success stories does lend a helpful optimism about the capabilities of science allied to human political and economic will, for the global environmental problems before us require a belief that our concerted human actions can prevent catastrophe. Lessons of the 2003 SARS epidemic, for example, should include the speed with which a complex disease threat was recognized clinically and understood epidemiologically (NAS, 2004; NAC, 2003; Weiss and McLean, 2004). The full lethal potential of the epidemic was certainly blunted through a rapid infusion of research funding, a general international public awareness aided by the Internet, and broad interdisciplinary approaches to disease control, deftly implemented. Biomedical science and international surveillance are powerful tools, exponentially increased by recently developed knowledge and communications technologies.

Understanding the risks before us now requires a sophisticated environmental perspective that cause – and cure-driven medicine does not communicate well to consumers. The very successes of modern biomedicine facilitate both a false sense of security among those who expect to benefit, and a deep resentment among those who see technological progress as a threat. The illusion of safety among the currently privileged will further distance them from worries and fears that could mobilize resources to prevent novel pandemics. On the other hand, many people, when presented with a threat or crisis, will accept simplifying, familiar explanations from the past because the political and technological solutions adopted in a crisis threaten their livelihoods and social well-being. Unfortunately, many may repeat some reactions and responses from the past because they do not understand fully how the present global changes differ from the agrarian age of great epidemics. But they can easily grasp that the benefits of future breakthrough technologies will surely be inequitably distributed, disparities which reinforce the human experience of centuries.

I still find useful the dominant Western ideology of ‘progress’, because it is an antidote to inertia and denial before the current predicament. Thus I offer the argument that perception of differential mortality in the past led to successes in human health and longevity. In the remote historical past, mass suffering and dying were typically unseen outside stricken regions. Before the last century most humans could not see far enough in space or time to imagine their responsibilities to other humans on a global scale, even if they thought of their actions in such grand terms. Disease catastrophes progressed across regions within a time frame perceptible and measurable by humans' immediate lived experience. Progress followed improving communication networks, which highlighted disparities in health and disease experience. Recognition of differences among persons and groups led to useful interventions, if humans accepted a responsibility to act on these observations.

Seeing further than our predecessors did, in both time and space, carries ethical obligations. Not only are the economic connections among humans much stronger today than ever before, knowledge about the sufferings of others is not easily avoided. Great and catastrophic events, especially those that involve costs to people who regard themselves as non-responsible by-standers rather than as stakeholders, present disturbing ethical and economic dilemmas. However quickly we understood the biomedical parameters of HIV twenty years ago, and were then able to create new surveillance and control strategies, the longer-perspective of HIV/AIDS control is, unfortunately, already one that replicates historical patterns of inequitable distribution of resources and care, when assessed from the perspective of both incidence and prevalence of the infection (Farmer, 1999).

Residual apocalyptical thinking poses the greatest danger to the successful management of acute epidemic crises. The religion-driven acceptance that an end of days is foretold and possibly at hand has governed much human thinking about great epidemic infectious diseases over the past two millennia. Apocalypticism passively, and sometimes actively, dismantles our acceptance of an obligation to act collectively and collaboratively for the betterment and survival of all, because traditional religions tend to separate the saved from those whom they view as damned or evil. Fear is often used to rivet attention, attract resources, and shape political and economic actions, but can exacerbate converging natural catastrophes, which inevitably occur. Even though apocalyptical fears – including modern, secular environmental apocalypticism (Killingsworth and Palmer, 1996) – are often used to effect moral or behavioral reforms, historical evidence shows that living in the shadow of such fears reinforces violence and the dismissal of others' entitlements to either salvation or survival. Fear-driven assessments of current global change risk re-deployment of this dangerous ideological ordnance.

Three Historical Stages Linking Human History and Global Change

What impact has global change had upon human health in the past? With each significant change in humans' active manipulation of energy sources, initial health costs ensued, followed by aggregate improvements and significant human population increases (Szreter, 1997). These stages in human development may have happily coincided with geophysical stability, for the global climate of the last 10,000 years has for the most part supported human-driven changes-first changes to landscapes, then to the atmosphere, and finally to the oceans.

Similarly we might delineate three modes of anthropogenic production involving significant changes to the earth: hunting and gathering, agricultural, and industrial (Caldwell, 2004; Sieferle, 2001; Smil, 1994). Most recorded or archeologically accessible human experience with great epidemics lies within the agricultural era. Within this long phase of human history, the collective fate of all flora and fauna changed dramatically five hundred years ago. Regional economies, terrestrial ecosystems, and knowing scientific manipulation of the earth's resources altered the planet's landscape in this 'first global age', and altered human health and disease patterns forever. Effectively there were two worlds that humans manipulated before around 1500 CE. After that point one rapidly changing world emerged, and new human observations and ideas about infectious diseases accompanied post-Columbian global change. The underlying frameworks for analyzing and manipulating disease experience were also laid down before industrialization, justifying further attention to the interval that I call our 'first global age'.

Nevertheless the industrial transformation, beginning in Britain in the 1830s, was the single greatest change for both humanity and the planet, and most of the successful efforts at disease control lie within this ongoing era (Sieferle, 2001; Mokyr, 2002). Industrialization carried heavy initial penalties to the laboring population involved in production, much as had the transformation from hunting and gathering to agriculture (Szreter, 1997). Highly successful, combined English and French approaches to public health and sanitation overlap the industrial revolution temporally, but likely stem from the slower 'knowledge revolution' that preceded industrialization (Mokyr, 2002). These coincident developments fueled notions of 'progress', which led industrializing nations to accept their disproportionate wealth as inevitable and ordained.

The potential for global environmental catastrophe was created within advanced industrial modernity of the last fifty years, because human activities now can directly affect the oceans and atmosphere. Yet over the last fifty years we also have created the means to analyze and anticipate adverse consequences of our actions and choices. Within the last fifty years we have devised curative and preventive strategies, not all of which involve much expense. We have the capability of maintaining and improving health for all humans. As a consequence, life expectancies in many nations have increased dramatically (Riley, 2001). Global population has doubled over this miraculous and precarious half century (Whitmore *et al.*, 1990; Maddison, 2003). Since all the great acute epidemic catastrophes occurred before 1950, the points of comparison must focus on the general predicaments, explanations, and choices made in the past.

1. Global Change before the First Global Age

1.1. *Before agriculture: human planetary dominance*

For at least 40,000 years humans have deforested the earth, altered the course of streams, and fashioned tools and weapons to expand food-getting. Even before consolidation into early agrarian societies, humans effected global change with the megafauna extinctions of the late Pleistocene and their many uses of fire (Mithen, 2004; Williams, 2003; Chew 2001; Dean, 1995). Before the transition to permanent agricultural settlement, Paleolithic humans increased and multiplied globally by 'extensification', that is, increasing through dispersal the numbers, range and varieties of similarly sized human population groups (Christian, 2004). While the causes of the transition to agricultural are unclear, Sieferle (2001) argues that humans could always resort to plants and smaller game, when large game became scarce. As obligatory omnivores, we were thus ecologically more efficient than both carnivore and herbivore competitors, leading to multi-regional human dominance. The survival of a wide variety of tools and objects of ritual importance bears witness to sophisticated cultural strategies and human adaptation to many harsh environments, evidence of the further importance of knowledge transmitted over time to our species' global dominance.

Human global population, around six million at the end of the last ice age – around 12,000 years ago – doubled every 5,600 years over the period from 40,000 BCE to the appearance of agrarian civilizations, around 8000 years ago (Livi-Bacci, 2001; Mithen, 2004). During this long interval chronic infectious disease and disability, both traumatic and infectious, likely characterized most of the burden of illness in migratory groups (Cohen, 1989; Sieferle, 2001). There is simply no way to know how they faced, explained or managed temporally discrete disease and subsistence crises. Hunting and gathering human groups did not cook or store food, and they frequently removed to new locations. Relocations likely were prompted by the depletion of easily obtained food or game, typically through habitat destruction. Evidence from the relatively late colonization of Pacific oceanic islands often serves as a model of this much-earlier process (McNeill, 1994; Nunn, 1990).

1.2. *The Neolithic Revolution and Infectious Diseases*

The Neolithic revolution led to both agricultural and pastoral economies (Hughes, 1994; McNeill, 2004; Landers, 2003). After the agricultural transition humans multiplied in geographically concentrated localities, increasing the burden of gastrointestinal and respiratory pathogens. Evidence of chronic tuberculosis, smallpox, schistosomiasis infection can be found in ancient skeletal or mummy remains; descriptive evidence of periodic acute epidemics can be found in early written compendia (Grmek, 1989). Demographic costs in the move to settled agricultural societies were initially high, particularly in early childhood (Cohen, 1989). Rats, mosquitoes and other commensal species enhanced pathogen loads within settlements by adding vector capacity. A number of historically important zoonoses – measles and smallpox, for example – emerged with pastoralism and with the domestication of various animal species (Fiennes, 1978; McMichael, 2001). Such zoonoses mostly appeared in Eurasia and Africa, for the Americas and Micronesia had few animals to domesticate; Oceania had almost none. Whether farmers or herders, Neolithic humans transformed environments as much in their deliberate and inadvertent uses of animal species as in farming-driven alterations to landscapes. Northward migration into colder, wetter climates made the muscle power of livestock necessary to cultivation and facilitated a ‘secondary products revolution’ in the invention of multiple uses of large animals (Christian, 2004).

1.2.1. *Human Population Growth and Social Development: Unequal Burdens*

Global human population grew from 6 million to 50 million between 8000 BCE and 3000 BCE. The experience of recurrent acute infectious diseases, mostly evolved from animal pathogens, ubiquitously appeared in a context of differential command of agricultural surpluses. Novel disease burdens accompanied the later phases of the Neolithic revolution, but they were not wholly natural occurrences. Infectious disease was understood well enough to be deliberately manipulated by developing social and economic systems. Dynastic states relied on hierarchical distribution of power and resources, which raised the average standard of living in the population at the same time as it reinforced social stratification (Hughes, 1994; Christian, 2004, chapter 9). Within great civilizations the burden of infectious diseases fell heaviest on the poorest, particularly in urban settings. Heights of skeletal remains show greater final adult height among the wealthy than among those who lived in overcrowded or swampy locations, or were subjected to recurrent food shortages (Floud *et al.*, 1990), most likely because the privileged always ate first (Sieferle, 2001). Comparison of different dynastic states shows that greater social, political and economic organization minimized the overall cost in lives and resources of epidemics, famines, and natural catastrophes (Bawden and Reycraft, 2000).

Successful dynastic states accumulated material and knowledge resources, and built long-lasting regimes around increasingly sophisticated irrigation systems. Insuring reliable food production, irrigation permitted easy dissemination of waterborne pathogens. The history of early Japan provides a particularly good example of this overall pattern of change. Wet-rice cultivation first supplemented, then replaced hunting, fishing and gathering between 200 BCE and 300 CE in the islands that had greatest contact with the Asian mainland. Increasing hydrological sophistication decreased famines, but was accompanied by domestication of animals and consolidation of power and land in warrior clans. Between 600 and 800 CE, one clan successfully overpowered rival warlords, resisted naval assaults, and then created a structure to monitor its wealth, borrowing comprehensive systems of population registration and tax collection already invented by the Chinese. The written records of epidemics, in particular of widespread, costly smallpox epidemics first appear clearly in these court records (Farris, 1985). All aspects of agrarian state power were mobilized during epidemics – food relief, a central bureau of medicine dispatching medicines and doctors to the provinces, tax relief, rice loans, and religious ceremonies to appease angry deities were all used to combat the epidemic of the 730s CE, the first recorded smallpox epidemic in Japan.

Earliest strong evidence of the adaptive capacities of human societies comes from imperial China. A Chinese political ideology dating from the

Han Dynasty [c. 200 BCE] held that that rulers were legitimated by a 'Mandate of Heaven', and climatic or other environmental catastrophe provided the evidence that heaven had withdrawn its support for a ruling dynasty. Anxiety about the weather was thus longstanding, and Chinese phenological records exist for more than a millennium longer than do European climate records (Marks, 1998; Elvin, 1998; Kuriyama, 2000). The permission that heaven provided to a dynasty reinforced strongly hierarchical social organization and led to both unprecedented expansion of human population and great hydraulic engineering projects that transformed East Asian landscapes forever (Elvin, 2004, chapter 6). When the 'mandate' was withdrawn, through heaven-sent invaders or environmental catastrophe, hundreds of thousands died, vital irrigation structures went untended, and epidemics served mostly to accelerate demographic collapse (Elvin, 1993).

Using surviving population registers, tax collections, and conscription records, Deng (2004) has recently challenged earlier conservative estimates of Chinese population growth intervals, showing that patterns of unparalleled population growth in some periods before the seventeenth century are even more characteristic of Chinese society than are massive collapses secondary to disasters. Moreover, most of the known disasters were environmental or military reversals, rather than caused by exogenous novel disease organisms. This Chinese path to collapse is important to understand, because at least for the last four millennia, Chinese population has accounted for one quarter of humanity (Lee and Wang, 1999). The Chinese path is also a useful contrast to explanatory frameworks favored by Western historians of global catastrophes, for collapse was linked to converging (rather than linear, sequential) ecological disasters, followed by out-migration and political upheaval. Disaster responses in Chinese history illustrate the enormous buffering capacity of human social organization, as well as the rapid collapse after some tipping point within.

1.3. *Explanations and Patterns of Acute Epidemic Disease Experience in Early Agrarian Civilizations*

1.3.1. *Where are we Now? Apocalyptical Versus Scientific Discussions*

Most historians, social scientists, and scientists explain reversals of large, multi-century and/or multi-regional human demographic expansion by citing epidemics, climate change, the exhaustion of accessible natural resources, or by some combination of these factors. Many great religious traditions, however, include a view of time bounded by a predetermined beginning and end of days. The power of such ancient religious ideas cannot be easily excised from current scientific discussion. Not only did apocalyptical perspectives inspire much of the written evidence that investigators today use to discern patterns and explain collapse in earlier times. Also adherents to fundamentalism, steeped in ideologies created long ago and under very different historical conditions, have increased considerably within rich and powerful, as well as poor and struggling, political regimes (McGinn *et al.*, 2003).

Within the last two decades more extensive interdisciplinary study and collaboration helped to refine scientific understandings of distant times (Bawden and Reycraft, 2000). Scientifically we are beginning to know better what actually did happen in the more remote past. Yet both well-meaning environmentalist reformers and anti-technological, anti-scientific religious authorities have appropriated apocalypticism over the last half-century (Killingsworth and Palmer, 1996). Some hope to recapitulate ideas expressed in religious tradition; others hope to reverse or brake adverse global change. At issue in both cases is a view of time and human development that opposes the simpler versions of 'progress' in Western tradition.

1.3.2. *Historical Explanations of Great Epidemics and Environmental Disasters*

Great epidemics and uncontrollable climatic reversals are attractive explanatory events to account for sudden collapses of dominant societies. The particularly influential publications of William H. McNeill (*Plagues and Peoples*, 1976) and Alfred Crosby (*The Columbian Exchange*, 1972; and *Ecological Imperialism*, 1986), gave prominent place to plagues. More recent work has emphasized the extent to which ecological degradation eclipsed or stressed elites' exercise of power. Demographically successful cultures exhausted both forests and productive farmland, expanding the geographical compass of ecological degradation, making it difficult to separate the causal mechanisms and the timing of catastrophes (Chew, 2001; McNeill, 2004; Landers, 2003).

Urbanization, common in successful agrarian civilizations of the last 5000 years, effected profound environmental change over their hinterlands. Epidemics spread most briskly in cities and could economically destabilize distant regions dependent on these urban markets. This model resonates with new research on the way Native American agrarian empires collapsed. Haug *et al.* (2003) find climate change, specifically desertification, related to the collapse of Mayan civilizations in the 800-1000 CE, exacerbating social and environmental stress.

Chronic warfare was the motor behind social stratification, as well as the most common accelerant of both disease and ecological degradation. The retention of elite power relied on a parasitic approach to both food producers and forests. Forests in Eurasia were essential to the manufacture of metal weapons; the best agricultural land and the rights to its produce were secured through military and economic dominance. Urbanization required the maintenance of such military power, which in turn determined access to and acquisition of natural resources, even in regions, such as the Americas, where neither the wheel nor metallurgy had been invented. In some rare instances, warfare led humans of the agrarian period to go beyond control and exhaustion of organic resources (plants and animals), leading to the sporadic invention and use of chemical energy (Landers, 2003).

1.3.3. *Modern Malthusian Models of Catastrophes in the Agrarian Age*

Some modern economic historians and historical demographers place a high value on early epidemic accounts because they resonate with a widely-held Malthusian model of the more remote past. Ever since Thomas Malthus's first *Essay on Population* in 1798, many western scholars have seen depopulation crises as indicating perennially unwise choices of humans, principally their failure to control reproduction in the face of diminishing resources. Such a model gives a prominent explanatory role to great epidemics and subsistence crises. Watkins and Menken (1988), however, argue that demographically famines do not follow Malthusian patterns; Morineau (1998) debates the extent to which historical data ever supported Malthus's generalizations. Historians of Asia note the extent to which Malthus, and later Marx, were instead drawing a chauvinistic contrast with 'Oriental despotism'; Europeans in Malthus's day were still stunned by the tremendous wealth of non-European despots (Chaudhuri, 1986; Lavely and Bin Wong, 1998). In fact, the recent Eurasia Project shows, in full contradiction to Malthus's observations, that European harvest failures had greater impact on mortality than did harvest failures in China and Japan (Bengtsson *et al.*, 2004). Finally, the Malthusian model well explains mortality in great epidemics. Wrigley and

Schofield, in their path-breaking *The Population History of England*, 1541-1871 (1981, pp. 466-73) conclude that increasing population size is only weakly related to increases in mortality. Recent study of the horrific and extensive Asian famines of the 1870s and 1890s, in both cases associated with ENSO-related delay or absence of monsoon rains, has emphasized the extent to which Western acceptance of famines as a 'natural' consequence of unbridled population growth led those who could help to the conclusion that they were justified to do nothing (Morrison, 2000; Davis, 2001).

Malthusian models are not even universally applicable to the more remote past. Imbedded in western culture, they poorly explain population dynamics outside Europe, as Deng (2004) illustrates with data about Chinese population growth and decline. Even in western context, imbalance between resources and population size is insufficient to explain who dies in great subsistence crises. The earliest great famine for which we have fairly good social/historical evidence, the great European famine of 1315-1322 CE, does not follow a Malthusian pattern well. Mortality reached as high as ten percent, but affected the poor and powerless rather than the elite, and proceeded to cannibalism and other atrocities only in localities where the warrior elite persisted with military campaigns. The famine remained in popular memory three hundred years later (Jordan, 1996). Amartya Sen's model of modern famine survival through socially determined food entitlements thus seems to apply to this great medieval, agrarian famine (Sen, 1981).

1.3.4. *Exogenous Climate and Other Events Explaining Large-Scale Depopulation*

A few palynologists, dendrochronologists and historical climatologists have tried to discern intervals of global change that might explain large-scale regional depopulation events in frameworks linked to geophysical change. Impacts of meteors, changes in monsoon rains or northern oceanic storm patterns, and volcanic eruptions have all been postulated as potential disruptors of life systems across cultural and geophysical divides (Baillie, 1999; Atwell, 2001). Historical environmentalists have also reconstructed past El Niño patterns looking for evidence of the autonomous climate change in human history (Nunn and Britton, 2001; Grove, 1998). The disappearance of record-keeping and of evidence of economic and cultural production has also been ascribed to great epidemics. Only fairly recently has interdisciplinary research begun to separate and examine the extent to which plagues and pestilences reported as great and universal indeed had demographic, regional significance. The contribution of Ruddiman and Carmichael (2006) in this volume addresses this general issue in greater detail.

1.4. *Explanations of Epidemics in the Agrarian Age*

1.4.1. *Epidemics and Environmentalism*

Secular ideas about the meaning and significance of epidemics in the long agricultural era of human history were linked to social and religious systems that reinforced social hierarchies and controlled their uses of available natural resources. The tight interconnectedness of humans to the natural environment remained central to both medical and religious ideologies of the premodern past (Tuan, 1979). Traditional medical systems explained death from commonly-observed misfortunes with reference to individualized circumstances. These medical systems offered some useful generalizations about disparities in risk of ill health according to season, age, geographic particulars of one's residence, or variations in one's nutrition (Hughes 1994; Grmek, 1989; Glacken, 1967; Carmichael and Moran, 2002). Interventions in ill health and general health maintenance relied on strategies that individuals could take to manipulate their personal environments and choices. Great epidemics instead prompted collective action, including the mobilization of religious authorities. The serendipity of fortune, the capricious will of a deity, the result of sin or emotions, the violation of a taboo, or the individual's failure to observe accepted dietary or hygienic norms accounted for deaths that did not follow expected patterns.

1.4.2. *Apocalypticism*

Occurring rarely, catastrophes and natural disasters were also viewed as manifestations of divine displeasure, and were assigned religious meaning. While such explanations for an epidemic or environmental catastrophe could easily foster larger, apocalyptical predictions, blaming deities also exacerbated the feelings of helplessness, in both explaining and coping with an unexpected set of events (Rohr, 2003). Moreover reliable communications beyond a regional level were not possible, and therefore an epidemic could seem universal and world-annihilating. Viewing the world as coming to end mobilized efforts at religious conversion. Apocalypticism can, however, disable concerted human efforts in the face of calamity, or encourage believers to dissociate themselves from those assumed to be damned. Thus to the extent that such ideas have currency today, believers may be disinclined to take ameliorative actions when confronted with multiple serious epidemics or environmental challenges.

Ancient apocalypticism, particularly strong among Mediterranean cultures and deeply imbedded within early Christianity, imagined collapse as a battle lost, the divine actively in combat with mortals (Clifford, 2003). Religious devotion then and now powerfully motivates compassion, altruism, and philanthropy, as well as supplies stabilizing resolve to face fear and challenges. But many of the great global religions in the past encouraged resignation to catastrophe, or envisioned scenarios of an apocalyptical finale that separated the saved from the damned. Ancient apocalypticism also suffused some texts that have been used to support arguments about a late-Roman era of widespread plagues and pestilences. Stathakopoulous (2004) and Schamiloglu (2004) independently reviewed evidence related to the famous plague of Justinian in 541-2 CE, showing how this epidemic and its recurrences had geographically and demographically extensive effects. In the centuries before this pandemic, however, the evidence for widespread depopulation is not as clear, and apocalyptical texts should not be understood to reflect demographic collapse. Recurrent bubonic plague traveled along the Silk Road during the 600s (Twitchett, 1979; Deng, 2003). Schamiloglu (1993) claims that the disease was novel to steppe peoples.

2. European Responses to Plague: Epidemic Controls and Anti-Apocalypticism

2.1 *The Black Death: a Multi-Regional Epidemic with Global Implications*

In many accounts of global change, the great plague pandemic of 1347-1350 appears as one of the greatest demographic catastrophes of human history. Its initial appearance has been viewed both as an instance of Malthusian check on a population that had outstripped its agricultural capacity, and as an outcome of global climate changes. The ‘Black Death’ of the mid-fourteenth century was also geographically limited, and may not have extended to China. But it did sever frequent overland connections to East Asia, by causing extensive depopulation and political chaos among steppe-region successors to the Mongol Golden Horde (Schamiloglu, 1993). Dramatic depopulation simultaneously occurred in northern China during the Yuan, or Mongol, dynasty (1264-1368), though disease may not have been the primary cause (Deng, 2003). The 'Black Death' surely ravaged the Middle East, northern Africa, and all of western and central Europe (Benedictow, 2004). Nevertheless the brutal pandemic did not afflict peoples in the Western Hemisphere, in sub-Saharan Africa, or in South Asia (Chaudhuri, 1985), although Islamic cities and regions of the eastern Mediterranean and North Africa may have been even harder hit than western Europe (Dols, 1977).

2.2. *New Responses to Great Mortality*

Despite its less than universal geographical compass, the Black Death pandemic remains an historical event with global importance. The effect of plague among Eurasian steppe peoples was to re-separate Chinese agrarian civilization from European and Islamic agrarian civilizations (Schamiloglu, 2004; Dols, 1977; Chaudhuri, 1985, 1990). But above all, from the time of the Black Death in Europe, intellectual inquiry and practical responses to epidemics confronted the issues of local, differential mortality in epidemics alongside explanations for universal pestilence. Europeans living after this catastrophe invented novel ways of dealing with epidemics, developing technologies and ideologies that reshaped their perceptions of disease. Before this watershed, European medicine was but one of many traditional medical systems that depicted health as balance between humans and their environment. Dealing with recurrent plagues – which were always regional epidemics and could cause staggering loss of life in a few months' time – prompted new practices in European medicine.

The appearance of secular explanations to account for large-scale epidemic disease detached both traditional environmentalism and religious tradition from communal responses to epidemics, and led to aggressive local control policies. In Renaissance Italy, notions of a capricious or punishing deity were gradually replaced with explanations built around observable variations in risk and survival. The 'whole world' was not at risk in plagues. After the pandemic, Europeans increasingly saw and even created patterns of differential mortality, inventing ways of dealing with recurrent pestilence assured and reinforced differential risk of disease and death within communities (Carmichael, 1986). The deliberate manipulation of infectious disease experience begins with new practices in epidemic control.

However brutal the Black Death was, 60 to 65 percent of the population of Europe survived, also disconfirming apocalyptical expectations. Life went on. By the mid 1350s plague reports were scattered and survivors knew that the world had not ended. The mortality rates, ubiquity, symptoms, and suddenness of the Black Death distinguished it from previous epidemics and mortality crises. In these respects plague could thus be understood to reflect God's will and judgment (a punishment for human sins), but also an event explicable within the natural, created cosmos (Smoller, 2000; Rohr, 2003). Europeans also adopted the conviction that human actions to combat epidemics were both necessary and consistent with God's plan for humanity.

2.2.1. *Local Barrier Technologies*

The plague recurred in western Europe for over 350 years, and led to the invention of surveillance bureaucracies, which in turn supported the most enduring response to epidemics: flight. Advanced warning systems were predicated on the assumptions that plague could be predicted and that plague could be avoided. They obviously believed that not every person and not every place presented a risk of plague; thus information gathering was vitally important. Increasingly sophisticated study of the natural circumstances associated with plague appearances led Europeans to a complex array of proactive, protective, and self-defensive strategies. Together these anti-plague practices are the foundation of modern control of feared infectious diseases (Biraben, 1976), despite the fact that flight is no longer the principal security for the privileged.

Barrier technologies were designed to create boundaries between the sick and the well. They were not developed in a particular fixed sequence, nor under historically similar circumstances or time frames. Instead, these familiar public health practices were created and adopted piecemeal. Quarantine practices, public health boards, surveillance of travelers from infected areas, disinfection of goods and houses that the ill touched, isolation of the ill, protective garments for service personnel, and publicized reports of causes of death and illness are all social technologies invented in Europe to control the spread and the tremendous costs of recurrent plague. Bourdelais (2003) emphasizes that governing elites created most of these barrier technologies, and that little innovation accrued through medical advice or theory.

As political actions, plague controls addressed the personal, social and economic objectives of people in power. Carmichael (1986; 1998) argued as well that plague controls served to create strong differentials in plague risk within cities, such that plague was increasingly seen as a disease of the poor. By the sixteenth and seventeenth centuries, elite consensus was that plague was not a universal leveler. Even when the rich could not or did not flee to safer country retreats, their chances of dying were not as great as their poorer contemporaries (Champion, 1993). Aggressive uses of fire, perfumes, street cleaning, sea water, gunpowder and tobacco became popular in the seventeenth century (Biraben, 1976).

2.2.2. *Regional Barrier Technologies: Quarantine and* Cordons Sanitaires

Quarantine, invented in 1377, in Ragusa (now Dubrovnik, Croatia), is perhaps the most interesting of these anti-plague practices, and the one industrializing nations most needed to dismantle. Initially in 1377 well individuals and seemingly useable goods were passively sequestered, in order to determine whether plague lurked within (Grmek, 1980). Imbedded within the quarantine were thus modern ideas of healthy carriers and incubation times. But quarantine practices were not incorporated into a system of plague controls until the sixteenth century and later, when principal Mediterranean metropoles began to use passive quarantine isolation in combination with port lazarettos to confine the ill (Ciano, 1976). Concerted regional and national political control of plague spread, such as the imposition of regional *cordons sanitaires*, seems to have been the single most successful human intervention leading to the disappearance of plague from Europe. Brockliss and Jones (1997) illustrate that the systematic use of quarantine within early modern France effectively restricted appearances of plague to the port cities.

By the 1700s Europeans essentially concluded that plague was neither an act of God nor a naturally European problem, and so they built ever more elaborate regional security boundaries. Panzac (1986) and Rothenberg (1973) show the intensity of quarantine and lazaret systems along the Austrian Empire's boundary with the Ottoman Empire. Ottoman lands, both Egypt and Turkey, effectively became the pest houses for all of Europe. Baldwin (1999) examines quarantine practices and the *cordon sanitaire* in the wake of the first European cholera epidemic, 1831-1832, illustrating that western European nations benefited from observing the failed quarantine practices of Russians and eastern Europeans, for quarantine even rigorously enforced did not impede the spread of cholera. Echenberg (2002) has more recently described the retrieval of older quarantine practices in the plague pandemics of 1894-

1905, illustrating the extent to which re-used quarantine practices reinforced economic and racial differences in mortality around the globe.

Indeed, quarantine always imposed significant personal hardships, high economic costs, and political unrest. Opposition to quarantine from its inception stemmed from the absence of any medical rationale for the practice and the enormous costs involved, principally in housing, feeding, and policing those whose lives and livelihoods were temporarily suspended. Quarantine and other barrier technologies did contribute to the disappearance of plague from western Europe, and have a lasting presence in the control of epidemics to this day. International reaction to SARS in 2003 began to move this kind of barrier control away from national governments to international health authorities (Fidler, 2004).

2.2.3. *Anti-Apocalyptical Secularization*

The appearance of secular explanations to account for large-scale epidemic disease detached both traditional environmentalism and religious tradition from communal responses to epidemics, leading to a more aggressive pursuit of policies and interventions that focused on particular people or places. Francesco Petrarca, often called the 'father' of the European Renaissance or of European humanism, provides an interesting and original voice. He imagined a prosperous 'posterity', for whom accounts of the great epidemic would seem unreal. Petrarca also imagined that his own generation had obligations to these unborn generations, rather than they to their ancestors. Finally, Petrarca examined and then effectively rejected contemporary views of the world nearing the end foretold in religious texts. His perspective is elegantly written, and dismisses an apocalyptical view of the mortality:

> How can posterity believe that there was once a time without floods, without fire either from heaven or from earth, without wars, or other visible disaster, in which not only this part or that part of the world, but almost all of it remained without a dweller? When was anything similar either seen or heard?… Oh happy people of the future, who have not known these miseries and perchance will class our testimony with the fables. We have, indeed, deserved these [punishments] and even greater; but our forefathers also have deserved them, and may our posterity not also merit the same…
> (Petrarca, *Letter to his 'Socrates'*, Book VIII, no. 7 [tr. Bernardo, 1975]).

Petrarca thus rejected the bounded time of religious tradition in favor of a stance of hope and expectancy toward humans' future, temporal lives. His less articulate contemporaries parsed the universal with study of the particular, noting areas and peoples that had escaped the universal plague, rejecting notions of a capriciously acting, inexplicable deity in favor of humanly verifiable, terrestrial explanations of variations in survival. Thus for many historians the European Renaissance remains, in retrospect, an optimistic, watershed moment in human history. At the time it was, as Bowsma (1980) describes, an age of anxiety. Because anxiety is fundamentally related to time and the perception of an uncertain future, clocked time and a secular, scientific search for order and certainty about the knowable world were culturally new dimensions of recovery from near-catastrophe.

3. Global Change During the First Global Age

Christopher Columbus, often described as the discoverer of a 'New World', instead initiated the creation of one new world from two old worlds. Significant biological and cultural transformation of the planet dates from this expanded moment of European overseas trade and exploration. Western hemisphere flora first transformed great agrarian societies in Africa and Asia, through their gradual adoption of nutrient-rich staples (peanuts, potatoes and sweet potatoes, maize, and manioc) that grew well enough in poor soils and supplemented meager grain-based diets in subtropical zones (Ho, 1955; Crosby, 1986). East and South Asian populations rose between 1500 and 1800, as a direct result of the adoption of such foodstuffs outside the western hemisphere, while in Africa American crops prevented any net continental population losses from the accelerating Atlantic slave trade (Maddison, 2003). Interestingly as well, many of the addictive plants commonly used throughout the globe today – tobacco, coffee, tea, coca, chocolate – spread even more quickly than did new staple foods.

During the period from 1500 to 1850, human disease patterns and global environments changed rather dramatically and irreversibly. The change was both qualitatively and quantitatively distinctive in human history. Historical climatologists know this era as the Little Ice Age, reflecting global environmental changes, but not all regions were negatively impacted. Despite disruptions to longstanding Indian Ocean trade, the period from 1500 to 1750 was one of great expansion (Chaudhuri, 1985; Richards, 2003).

Historically this first global age is further important because humans began to take systematic notice of differences in disease experience, and from such observations they were able to invent new strategies of disease control and health improvement. Europeans, because they traded and traveled globally, were systematic observers of health disparities, and in many localities all written observations about disease and epidemics date from this period in time.

3.1. *Depopulation in the Americas and Oceania*

Numerous infectious diseases, particularly viral pathogens adapted to humans in Eurasia and Africa over the previous three millennia, spread unimpeded among indigenous peoples in great western hemisphere civilizations. Often European settlers regarded the disappearance of native Americans as providential, that is, reflecting God's intention that they increase and multiply in these newly discovered lands (Jones, 2003; Chaplin, 2001).

Recent research shows that brutal 'virgin soil' epidemics accompanied or followed, rather than instigated, demographic collapse. In the Caribbean and central Mexico smallpox did not arrive until population had already begun a precipitate decline, (i.e., in 1518, when first contact was 1492) (Livi-Bacci, 2003). To some extent the economic wellbeing of indigenous peoples may have been weakened before Europeans were actually present to witness the great die-offs. Because long-distance trade routes were crucial to the Aztec and Incan civilizations, economic stagnation likely had increased hardships among many indigenous peoples long before they encountered the novel viral infectious diseases. Alteration of trade patterns and re-orientation of North American native production (especially fur trading) toward French and English markets similarly altered livelihoods along the St. Lawrence river and seaway, all before the viral disease epidemics accelerated collapse (Richards, 2003).

Cooler global temperatures coupled to increasing frequency of extreme weather events in the seventeenth century destabilized subsistence economies even without the introduction of unfamiliar pathogens (Fagan, 2000). In sum, we need not invoke the particular virulence of discrete pathogens, nor the accidental vulnerability of a population to novel infectious diseases. But demographic collapse in the Americas had global economic (Dean, 1995) and environmental/atmospheric (Ruddiman, 2003) consequences, whatever the pathways.

3.2. *European Perceptions of New Disease Environments*

The unfolding global environmental transformation shaped Europeans' perceptions of disease and disease environments. In many colonial zones natives were fast disappearing without any comment from European observers. Dean (1995, p. 65) described such silences as 'an endless chain of complicity that enabled the neo-Europeans to claim the inheritance of an empty land'. Jesuit missionary accounts in New England and in Brazil are some of the few to express sustained regret and concern about the steady decline of native American populations. Pacific island changes, which for the most part began in the later eighteenth century, illustrate the massive and aggressive role of western traders, extracting resources and spreading chronic infectious diseases (syphilis and tuberculosis, especially) even before the viral pathogens accelerated population decline (Bushnell, 1993; McNeill, 1994; Igler, 2004). Interest in the mechanisms of ecological and demographic collapse in the Pacific islands has increased over the last decades because archaeological and historical analysis has been particularly collaborative, and because the various archipelagos offer documentation of a variety of starting and accelerating conditions.

3.2.1. *Observed Disease Differentials: a Stimulus to Disease Control*

Disease globalization during the first global age is easier to discern from our vantage point than it was at the time. Much as trade capitalized on differences in prices, commodities, and markets, less demographically significant differences in mortality and morbidity were heightened for contemporary observers during the first global age. Persisting across the first three centuries of European overseas trade and colonization were the high rates of shipboard mortality among sailors, and among early colonists outside Europe. Disability and death from 'sea scurvy' compromised military and exploratory missions from the sixteenth through the eighteenth centuries. Some of the earliest clinical trials of different therapies for scurvy, made by English ships' surgeon James Lind in the 1750s, stemmed from debates about the causes of mortality peculiar to those long at sea (Carpenter, 1986). The higher social status of officers did not necessarily protect them from this blight, but officers did have access to more food on board, as well as began these voyages better nourished.

During these centuries, some physicians focused on the ways in which particular built environments and occupations produced distinctive disease patterns. Traditional medical advice relied upon the avoidance of unhealthy environments and the consumption of food appropriate to the individual's humoral complexion, neither of which was an acceptable strategy for dealing with the increasingly observed diseases of miners, chimney sweeps, peat diggers, hatters, or cesspool cleaners – to name just a few of the European occupational groups that attracted novel medical observations at the time. In Great Britain dependence on coal for domestic uses was widespread by the late sixteenth century (Wrigley, 2000) and further contributed to the sense of human created, rather than naturally occurring, patterns of disease experience (TeBracke, 1975).

Native Americans' dramatic vulnerabilities to smallpox and measles led Europeans to early racial theories of human differences (Chaplin, 2001). When European colonists enslaved Africans to replace indigenous laborers, racialized theories of varying mortality and morbidity were further reinforced, because Africans were (wrongly) believed to be less vulnerable to 'intermittent fever' (malaria) and to yellow fever. Sugar cultivation in particular created new disease environments for all mosquito-borne diseases, which McNeill links to broader changes in early modern geopolitics (McNeill, 2005).

3.2.2. *Novel Research on the Medical Uses of Plants*

Commercially the most systematic observations of biological differences began in these centuries with the search for marketable botanical drugs among the remedies and plants found outside Europe. American guaiacum, hailed as a cure for the new 'French pox' was widely distributed in European markets before 1520, and facilitated the association of syphilis with the newly discovered lands (Arrizabalaga *et al.*, 1997). Peruvian cinchona bark, containing alkaloids from which quinine would be isolated in the 1820s and thus effective against malarial fevers, was transported to Rome and used in clinical experiments within the hospital of *Santo Spirito* (associated with the Vatican and the *Collegio Romano*) before 1630 (Freedberg, 2002; Rocca, 2003). These and other examples illustrate the useful observations of differences in disease experience as a stimulus to novel therapeutic approaches and commercial pharmaceutical success (Schiebinger, 2005).

3.3. *Realities of Disease Differentials in the First Global Age*

Hoffman *et al.* (2002) analyze the extent to which strong variations in standards of living occurred also on the European home front. While the per capita incomes of middle and upper class Europeans rose steadily, buoyed by trade wealth and slave labor colonies, in general the prices of luxury goods fell relative to the prices of staples, fuel and rents. The rich got richer, the urban poor visibly poorer (or at least shorter) (Floud *et al.*, 1990; Steckel, 2004). Some anthropometric and economic data from the eighteenth and early nineteenth centuries suggest that rural poverty, particularly if individuals had access to milk products and could consume some reliable portion of the crops they produced, may not have been as pernicious to overall health as was the poverty of urbanization (Komlos and Baten, 2004).

3.4. *Smallpox: Inoculation to Vaccination*

The most important therapeutic innovation of the first global age was the European adoption of first inoculation (or variolation) and then invention of vaccination against smallpox. Inoculation reinforced notions that particular diseases might be caused by particular substances, rather than by factors inhering within individuals or their specific environments. By the 1760s, physicians in French and English medical societies undertook statistical investigations of the utility of smallpox inoculation to populations, calculating survival and risk in cost-benefit terms (Rusnock, 2002). In 1796, English physician Edward Jenner invented the procedure of vaccination, offering a way to prevent creation of smallpox epidemics in protecting populations. The real benefits of smallpox vaccination occurred in the nineteenth century. Bantha and Dyson (1999) analyze the gradual and sequential imposition of variolation and vaccination in British India during the nineteenth century, and are able to show how smallpox alone caused between 16 and 24 percent of all deaths without such intervention. As with plague epidemics in Europe, recurrent smallpox epidemics made a significant contribution to demographic patterns independent of Malthusian pressure on resources.

3.5. *Eighteenth-Century Sanitary Campaigns*

Europeans were increasingly unwilling to accept starkly demonstrable mortality gradients. Rapid urbanization in Europe accompanied wealth from trade and overseas colonies, and cities were sites of observably higher morbidity and mortality than were rural. In the eighteenth-century elites launched great environmental campaigns to lower mortality and confront both epidemic and epizootic diseases (Riley, 1985, 1989; Wilkinson, 1992). The British also studied the population-level effects of smallpox inoculation, demonstrating by the 1760s that lives were saved and epidemic mortality reduced with inoculation (Rusnock, 2002). French and Italian engineers at this time were especially skilful in studies of water management, much of it in the service of urban street cleaning and refuse removal (Guillerme, 1988). Throughout Europe both cities and nation states systematized the collection of mortality statistics, causes of death, and records of disease occurrence.

The word statistics meant state management, and in an organic economy people and animals were essential components of a nation's wealth. European nation-states were not as successful in cooperative interregional epidemic or famine management at this time as the Qing Chinese state (Marks, 1998). But by the late eighteenth century limited initial successes in the reduction of death and illness rates in Europe convinced leaders that health was both a benefit and a measure of civilization. Actual reduction in mortality was elusive, however, because increased rural to urban migration with industrialization in the early nineteenth century outpaced the benefits of early, rudimentary public health interventions. Alter *et al*. (2004) show how industrial boom-towns of eastern Belgium were overwhelmed by recurrent epidemics, because public health housing and sanitation was not systematic until the later nineteenth century.

4. Global Change in the Industrial Age: Public Health and Medical Management of Epidemics

Industrial production created unprecedented wealth, quickly distinguishing human standard of living in industrializing nations from that in the great agrarian empires. Industrial production also began irreversible changes to global environments, first to the atmosphere, then to the oceans (Kates *et al*., 1990; Crutzen and Steffen, 2003; Sieferle, 2001; Andreae *et al*., 2004). This combined Western advantage was apparent to all before the end of the nineteenth century, and education and sanitary campaigns together reversed the longstanding demographic advantage that rural communities had over towns and cities by the early twentieth century; rural localities in the industrialized nations were the last to benefit from great sanitation projects (Bourdelais, 2003). But within this western, industrial context, sub-populations that were strongly disadvantaged socially and economically, such as African Americans in US cities during the early twentieth century, were able to benefit disproportionately from public sanitary campaigns, because it was not technically feasible to parse distribution of this social good (Troesken, 2004). Even British laboring classes enjoyed significant rise in overall health status during World War I, due to government investments in public health infrastructure and in well infant care (Winter, 1977).

Wealth alone did not insure health improvements even in the nineteenth and early twentieth centuries: there is only a very weak association between rising real wages and falling mortality levels. Kunitz and Engerman (1992) argue that rising per capita income was not the underlying explanation for falling mortality rates. Szreter (1997) points out that initially every industrializing region saw significant decline in population health. Instead from 1830 to 1880, the fall in mortality and morbidity from great infectious diseases and epidemics was the result of a national sanitary reforms and internationally orchestrated interventions to prevent the spread of feared epidemic diseases (Bourdelais, 2003; Baldwin, 1999). Large, public investments in sanitation and health education paid great dividends in health improvement.

These aggregate improvements in life expectancy partly masked persisting health inequalities caused by imbalances in the distribution of resources within rich nations. Riley (2001) emphasizes that industrial wealth and Western approaches to epidemic control (barrier technologies, vaccination and other biomedical technologies, and public programs based on a filth theory of disease) were not necessary routes for many lesser-developed nations in creating parity in life expectancy. Health education could be effective, even in poor nations (Riley, 2001). But as they had done for centuries, great pandemics exposed underlying disparities in risk and survival, even while generating the old fear that everyone was now suddenly at risk. Various public and personal strategies to control expected, understood risks might improve the prospects of longevity even in poor nations. In wars, natural disasters, great epidemics, larger differentials in health and disease were not as easily overcome. As Davis (2001) illustrates, the profoundly different health experience of an emerging 'Third World' came sharply into view in colonial settings. Only after the Second World War did rich nations make any concerted, large-scale efforts to improve the health of these lesser-developed nations. Great urban slums presently recreated the pre-conditions for health disasters as were seen in early nineteenth-century rapid urbanization (UN-Habitat, 2003; Davis, 2006).

None of the twentieth-century epidemics, including the great influenza pandemic, carried the mortality rates of recurrent plagues or even the costs from endemic, virulent smallpox. Wealthy societies, buoyed by the late nineteenth century optimism stemming from the germ theory of disease and successful public sanitary interventions, mobilized resources to further the analysis of cause and transmission. In this section of the paper, brief histories of pandemic cholera in the nineteenth century (at the beginning of industrialization) and the influenza pandemic of 1918 (concluding the first, industrialized global war) illustrate both the mobilization of collective resources to impede disease spread and the experience of differential mortality that both stimulated research and reflected longstanding disparities in health.

The histories of other great epidemics of the twentieth century, such as the histories of poliomyelitis vaccination and the WHO's malaria and smallpox eradication campaigns, might also be used to reflect biomedical gains that built on perceptions of geographical and seasonal differentials in mortality, to control as well as understand epidemics. But other contributions to this volume will explore in greater details the extent to which modern, successful control of epidemics has not relied on anti-microbial cures. Importantly, the successes and improvements of the human condition subsequent to industrial production and the health transition thus far have statistically overshadowed losses from the ancient four horsemen: war, famine, plague, and conquest. Nevertheless the twentieth century was one of sickening destruction and loss of life from warfare. Although wartime losses cause but brief reversals in the aggregate demographic patterns, wars provide atypical and extreme environments for the spread of infectious disease epidemics such as the 1918 influenza. Modern war and epidemics is also a topic beyond the scope of this overview.

4.1. *Cholera Pandemics*

We now know that *Vibrio cholerae* is globally distributed, particularly through infection of copepods, the food source for much marine life. But there is no written historical evidence of early, widespread cholera epidemics in the Indian Ocean trade zone (Arnold, 1991). Cholera suddenly appeared in temporally discrete pandemics during the early nineteenth century after the British consolidated their power in the Indian subcontinent.

Outbreaks initially called back into practice regional quarantine and other barrier defenses, which authorities in Britain and France resisted as scientifically-outdated and trade-unfriendly instruments of disease control (Baldwin, 1999). These plague-style epidemic controls also required international political cooperation, which proved more difficult to achieve than local and national improvements to general health (Bynum, 1993).

Cholera's clear origins in British India led the British to oppose many traditional barrier technologies during cholera years (Maglen, 2002). After the Suez Canal opened in 1869, and after further decreases in travel time that railroads and steamships allowed, Western powers increasingly saw the issues of cholera control as a matter of modifying quarantine and isolation practices to minimize mercantile costs (Hardy, 1993). Again they relegated application of such barriers to the Muslim nations that geographically separated South Asia from Western Europe (Howard-Jones, 1975; Fidler, 1999). Political solutions to global cholera pandemics, imposed by the rich, industrializing nations along lines similar to later plague controls once again created the sense of extra-territorial pest houses, rather than a global disease and environmental phenomenon.

Cholera also was viewed as an Asian invasion, rather than as either a global phenomenon or a consequence of British trade development in the Punjab. The evidence for global climate interconnectedness coalesced later in the nineteenth century, in part as recurrent cholera pandemics seemed to have some association with variations in monsoon rain patterns (Grove, 1998). ENSO [*El Niño Southern Oscillation*], first identified in the nineteenth century by English surgeons and climatologists in collaboration with Indian scholars, were noticed in part because epidemics of cholera could not be easily associated with either of the two presumed determinants of epidemics: trade and urban crowding. In the first half of the nineteenth century disruptions of seasonal monsoon rains could be linked to epidemics of cholera. Later in the century, simultaneous, virulent malaria epidemics in East Africa, South Asia, East Asia, and western South America coupled the rain and oceanic patterns of the Indian and Pacific Oceans to the phenomenon of monsoon-related epidemics (Davis, 2001).

4.2. *Public Health, Cholera, and Novel Sanitary Reforms within the Industrializing Nations*

Cholera's appearance in western Europe in 1830-32, evoked heated popular and scientific discussions of the origin and control of epidemic diseases. First-affected regions (Russia, Prussia, and Eastern Europe) deployed draconian quarantine procedures to impede the spread of the new disease, so that by the time the disease reached Paris and London, public officials knew that costly, politically destabilizing quarantines were not necessary (Baldwin, 1999). Knowing the futility of quarantining cholera, French hygienists used the epidemic to test their hypothesis that poverty caused higher morbidity and mortality. French public health had a strong commitment to state responsibility for the health of citizens, so hygienists heroically collected data door-to-door, as well as participated in care of the stricken (Bourdelais, 2003; La Berge, 1992). Despite more than 18,000 deaths from cholera in the city and suburbs of Paris, in 1832, the epidemic reinforced their conviction that polluted environments and non-hygienic behaviors exacerbated mortality, and that without their efforts the epidemic costs would have been much higher.

Neither did the English want to see the return of plague-style controls. Coming to power just after the first cholera epidemic, arguably the single most important architect of modern public health control, Edwin Chadwick, embraced a more restrictive view of the responsibilities of government than did the French. Advocating government-sponsored sanitation projects, Chadwick resisted any notion that the state had to solve the perennial problem of poverty in order to achieve protection from cholera (Hamlin, 1998; Baldwin, 1999; Bourdelais, 2004). When the second pandemic of cholera returned to Europe in 1848-1854, new surveillance mechanisms were in place. Cause-of-death reporting had become systematic, with debate settling now upon how those causes were to be assessed and assigned. Chadwick and his allies were instrumental in delimiting a focused approach on the provision of clean water, and the construction of sewage systems.

The second global cholera pandemic, 1848 to 1854, appeared at the same time as new microscopes, fueling interest in specific cholera-causing substances. Political and social debate about the causes of cholera mortality multiplied published data and discussion, which facilitated the elegant early epidemiological studies of an otherwise obscure London physician, John Snow (Carmichael and Moran, 2002). Snow's implication of water sources infected with a specific cholera substance was not widely appreciated until later in the century, with the more rigorous bacteriological proof that Robert Koch provided in 1884 (Carter, 2003; Hardy, 1993). Meanwhile, sanitary reforms in Britain and France reinforced the political and economic cost-benefit judgments of public health authorities (Hamlin, 1998). In 1851 the French and English called into being the first International Sanitary Commission to orchestrate Europe-wide responses to epidemic threats from outside Europe; and the first epidemiological societies were created. By the 1860s, before the third cholera pandemic of 1866, the English sanitarians created a radically modified 'English quarantine system', further elaborated into the 1880s (Hardy, 1993). Municipal sanitation created dramatic gains in survival for individuals in the wealthy, industrializing West (Baldwin, 1999).

Public health controls, by creating different expectations of health and risk, reinforced Westerners' sense of cultural superiority, when they witnessed economically struggling, unsanitary, famished backwardness of non-Western regions (Davis, 2001). Plague from 1894 to 1907 circled the globe, illustrating with the return of this dreaded, ancient scourge, that adherence to sanitation principles protected Europeans even when they were living in great squalid colonial metropolises (Echenberg, 2002).

Some important global consequences resulted in the way that cholera was handled in emerging international law. The first International Sanitary Congress of 1851 had placed oversight of cholera surveillance in the bailiwick of Ottoman Turkey and Egypt, regimes struggling to maintain economic prosperity in the rapidly changing world. Western nations became increasingly deaf to the political and religious conditions facilitating epidemics, and excluded non-Western nations from participation in international epidemic controls. Afkhami's (1999) analysis of late-nineteenth-century Iranian attempts to implement Western public sanitation and vaccination programs and his further work on cholera pandemics in Iran shows how important programs sensitive to local culture and political traditions were to the control of epidemics. Iranians not only did not see cholera as a disease threat from the potentially revolutionary, unwashed urban underclass, the importance that they placed on keeping open pilgrimage routes for devout Muslims created absolute resistance to Western plague protocols (Afkhami, 2003).

Between 1851 and World War I, International Sanitary Congresses met periodically to address feared, internationally spread epidemic diseases, focusing on bubonic plague, tropical yellow fever, and cholera (Howard-Jones, 1975; Bynum, 1993; Fidler, 1999). International legislation and protocols in the management of global epidemic threats were little revised even by the League of Nations Health Organization or the subsequent World Health Organization, and as a consequence stood as a somewhat archaic scaffolding underlying political and legal approaches, only recently overcome through WHO management of pandemic SARS (Fidler, 2004).

4.3. *Influenza 1918*

The severity and extent of the influenza pandemic in late 1918 came as a considerable surprise to medical and public health authorities throughout the world. Over 25 million persons died worldwide, and in rich, industrialized nations, the deaths among young adults were striking (Johnson and Mueller, 2002; Langford, 2002; NAS, 2004). Despite an exponential increase in 'population flux' – Cliff and Haggett (2004) create this measurement of population mobility to describe the increasing transmission of infectious diseases in the late nineteenth century – mortality rates in Europe had plummeted during the half century before the pandemic. Microbial causes and modes of transmission had been identified for most bacterial and protozoan diseases responsible for the adult deaths. Unanticipated measles epidemics among some of the World War I armies challenged medical and public health authorities, but otherwise epidemic infections among troops and on the home fronts were due to expected increases of sexually transmitted diseases, plus waterborne and vectorborne diseases (Smallman-Raynor and Cliff, 2004). In the US, wartime research on infectious diseases was meanwhile viewed as an opportunity for young investigators and clinicians, who might otherwise have traveled to exotic locations for such experience (Byerly, 2005; Barry, 2005).

Even today debate about the origins of the lethal strain of the influenza virus in 1918-19 is unresolved within both historical and scientific literature, providing a sophisticated and modern veneer to a story analogous to that of syphilis in the early sixteenth century. Shrouded in military secrecy, the focal appearances of virulent influenza cannot be discerned at the population level until late August, 1918. By then the name 'Spanish influenza', a French epithet for late spring cases of a severe, pneumonia-associated influenza reported uniquely in Spanish newspapers, had taken hold. Spanish journalists blamed the epidemic on French troops (Echeverri, 2003). The US civilian population was largely unaware of the Army camp deaths and high morbidity from pneumonia during the late winter and early spring of 1918, and military and public health authorities similarly suppressed reports of the widespread practice among camp commanders, transferring morbidly ill soldiers by train to other training camps (Barry, 2005; Byerly, 2005).

Most authorities have accepted three distinct waves of influenza infection, beginning with sudden deaths in a Kansas (USA) army camp in March 1918 (Patterson and Pyle, 1991; Johnson and Mueller, 2002). The origins of a second, more virulent mutation occurred somewhere during the late summer, and then spread from Brest, France (where US troops disembarked for the Western Front); from Sierra Leone; and from a military camp outside Boston. Crosby's (1989) history linked the origins of the severe influenza strain to the extraordinary survival environments of trench warfare and chemical warfare, an explanation that has long carried moral weight. A direct connection to the war has seemed plausible because of the degree of filth and degradation to which front-line soldiers were subjected. As recently as a decade ago epidemiologist Paul Ewald (1994) argued that the extraordinary virulence of the 1918 influenza strain is inconceivable without the Western Front conditions. More recently virologist John Oxford (2001) returned to accounts of severe pneumonia outbreaks in army camps from 1915 to 1917, implicating one British camp in France as the area of the new virus's emergence, thus much earlier than the 'three-wave' model postulates (Oxford, 2001). The balance of evidence about the pandemic's origins, however, still points to recombinant virus emergence in farming communities of central North America, particularly in rural Kansas, and thus is quite similar to instances of emergent infectious diseases today. In particular, the route of a novel epizootic from rural settings to urban markets, and from there global distribution is quite similar to SARS ecology and epidemiology (NAS, 2004).

The war, nevertheless, exercised a considerable role in the spread of the infection globally. 'Population flux' exaggerated mortality among young adult males: all combatant nations had a strong gender imbalance in influenza mortality. In all regional studies of the pandemic the spread of infection (as noted in the timing of observed cases) flowed from military enclaves and venues to civilian populations (Phillips and Killingray, 2003). The fundamental role of human contacts in the transmission of the disease has been studied rather closely using evidence from the South Pacific island nations. New Zealand and many of the island chains were seeded through trade and returning troop ships. While larger ports took some precautions, the young native men who provided labor services for merchant ships were largely invisible to the rudimentary public health observation, and so were permitted to travel from port to port as well as return home once they became ill. Communities with few medical services, such as the Maori of New Zealand and the Society Islanders, were especially hard hit in early November 1918 (Rallu, 1990). Australia's public health authorities, however, took advantage of the time differential between information about the epidemic and the arrival of crowded troop ships. Specifically targeted maritime quarantine, followed by household quarantines after soldiers disembarked, and military-style blockades along thoroughfares to the Australian outback successfully broke both the speed and the extent of the epidemic (Smallman-Raynor and Cliff, 2004; McCracken and Curson, 2003).

Secondly the war undermined civilian health indirectly, in the redirection of medical resources and personnel to the war effort (van Hartesveldt, 1992). Often the quantifiable aspects of a pandemic, including relief efforts orchestrated by those in power, give an incomplete picture of both risks and mitigating interventions. Previously impoverished areas remote from the conflict often suffered staggeringly high mortality and morbidity, unless the obstacles to mobility were great. Thus detailed, multidisciplinary local studies are now beginning to reveal these geographical and gendered differentials in influenza experience. For examples, access to female nursing care insured higher survival rates for many victims in the United States (Bristow, 2003); but women closest to the war front in France had much higher death rates than their male counterparts at any age (Zylberman, 2003). Data summarized by Johnson and Mueller (2002) illustrate further that overall mortality rates were much higher in lesser developed nations and regions.

The global reach of this epidemic had at least one positive effect, useful to note in the current century. Military and civilian scientists in the richest nations finally recognized the global interconnectedness of human populations confronting some epidemics: remote outbreaks became potential risks rather than research opportunities, and thus necessitated surveillance and investments in health.

Conclusion

This essay has offered a temporally very broad overview of human experience with globally significant acute epidemic infectious diseases. Past global climate changes, to the limited extent that they can be pinpointed with available evidence, appear not to determine the appearance and severity of identifiable global pandemics in the past. Before industrialization the link between climate and great pandemics instead seems the reverse: great depopulations may be linked to global cooling (Ruddiman, 2003; Ruddiman and Carmichael, 2006). But epidemics tend to play an important role in the ability of human societies to recover, once the balance between accessible food and natural resources on the one hand, and accessible human labor to exploit resources on the other, has been compromised. The realm of human ideas about catastrophic epidemics and natural catastrophes, however, has played an even more significant role in the gradual abandonment of religious ideas of a world-ending apocalypse, and the acceptance of secular, scientific ideas of human progress.

Global geophysical change is linked to the two radical changes in the mode of production over human history, agricultural/pastoral and industrial. Each transition came with initially high health costs, and in both instances those costs were redistributed and reinforced through warfare and differential access to resources. Here again mortality and morbidity experience in the past is not neatly aligned to changing ideas of epidemic causes. Since the Neolithic revolution, humans have largely assumed poverty and wealth occurred naturally. Thus the privileged paid greater attention to epidemics that could destabilize their power, particularly acute epidemic diseases that struck rich and poor alike. But experience first with recurrent plague in Europe, and then during the 'first global age' when European overseas ventures created multiple new and striking circumstances to observe disparities and differentials in mortality risks, propelled scientific observation, analysis, and experimentation with interventions. The rapid differences in wealth that industrialization subsequently created reinforced a sense of cultural, rather than mere economic superiority, among Westerners subscribing to ideas of secular 'progress'. Large-scale public health interventions within the West were undertaken because rich individuals learned that their own health in cholera epidemics could not be assured without such investment in sanitation. Aggressive surveillance, quarantines, vaccine development, and enhanced barrier technologies – the methods of the plague centuries – instead became the mode of epidemic response in western nations after the murderous influenza of 1918. After World War II, new international investments in disease eradication, economic development, education, and environmental manipulations returned to the cholera lessons of necessary public investment for private security.

The current challenges require cognizance of all these past approaches and fears. The most important historical and ethical issues to confront today relate to the ways that humans with power over resources make choices which determine the survival and well-being of those without power (Davis, 2004; Farmer, 1999). Over the last ten thousand years, human societies have displayed disappointing resistance to any truly equitable distribution of resources and risks. But success in the control and mitigation of demographically punishing infectious diseases was linked to ideas born in the perception of inequities and differentials in health and disease experience.

Most catastrophic declines in global population in the past were regional, because access to resources was regional. Exhaustion of accessible resources and the chronic attempts to address shortfalls in production through warfare in the more remote past destabilized trade networks, exacerbating great epidemics. Economic stability is now determined globally. Thus re-establishing the means of supporting very large populations after any acute, disruptive epidemic, even if does not reach the levels of the great pandemics and epidemics of the agricultural era, can pose protracted economic and public health challenges to recovery. Also apocalypticism, re-emergent among fundamentalist religions as well as in some ecological thinking, not only encourages inaction, it often carries an unexpressed agenda for a future that does not acknowledge the rights of all persons to exist within it.

Human choices and human actions have mattered. Pre-twentieth-century European history has a special place in the larger story of infectious diseases and global change in many well-known aspects: industrial production, the scientific method of inquiry, surveillance, isolation and containment practices in the management of epidemics, and the environmental sanitation approach to ongoing disease control. All of these were successes in part because governments subscribed to the public health investments and invested resources beyond those that individuals could make. In democracies of Europe and North America, tax payers rationally concluded that their own, individual well-being was more precarious if such investment in sanitary infrastructure was not made.

Finally, this essay has emphasized some novel early modern underlying ideas preceding industrialization: the rejection of bounded time, leading to the acceptance of obligations to future generations rather than the past; the idea of contagion, leading to the creation of boundary technologies to impede the rapid transmission of infectious disease; and the stepwise awareness and analysis of differential patterns in mortality and morbidity, seen first when Europeans understood that plague was not universal and elaborated as they expanded during the first global age, 1500 to 1850 CE. These novel ideas link also in these centuries to political ideas of justice and liberty that could not be discussed here.

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