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EX AEDIBVS ACADEMICIS IN CIVITATE VATICANA

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CHANGES IN REACTION PATTERN ACCOMPANYING BACTERIAL ADAPTATION

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SVMMARIVM — Contendit Auctor, cum bacteria nonnullas habent aptationes (ut cum resistentiam adversus medicinas acquirunt), evenire quasdam mutationes in generali ipsorum enzimaticarum relationum aequilibrio.

The adaptability of bacteria is a very remarkable phenomenon, which has aroused much controversy. One theory about cells which have become resistant to drugs is that they have simply lost the power of taking up the drug at all. In one or two examples there is evidence that an explanation of this kind is probably correct. But more generally it seems that there is a physiological adaptation in which the entire pattern of chemical reactions used by the cell in the building of its constituents is modified.

The object of the work which Dr. D.J.W. GRANT has carried out in Oxford has been to detect changes in enzyme activity accompanying various adaptations and so to obtain clues as to the nature of modifications in the cell metabolism.

The enzymes chosen for study were representative of different types. *Glucose dehydrogenase* is a major catabolic

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enzyme used by the bacteria in their normal growth medium. *Lactose dehydrogenase* and β-*galactosidase* play a major role in the utilisation of lactose. *Succinic, lactic* and *acetic dehydrogenases* are involved in a well-known biochemical reaction path usually referred to as the tricarboxylic acid cycle, *asparagine deaminase* was selected as an enzyme representative of those concerned in nitrogen metabolism, and *catalase* is one primarily concerned with the protection of the cell against toxic products of its own working. The organism studied was *Aerobacter aerogenes,* and the various adaptations considered were those connected with he utilisation of lactose, and resistance to streptomycin, crystal violet, chloramphenicol and proflavine.

During the adaptations most of the enzyme activities change in a way strongly suggestive of a coordinated pattern. The most clear-cut result is that in cells resistant to streptomycin or crystal violet the whole metabolism seems to have been shifted to paths resembling those followed in anaerobic growth. In these there is a much greater consumption of substrate, whether of lactose or glucose, and this is provided for by expansion of the relevant enzymes, β-galactosidase or the dehydrogenase concerned with the substrate. This type of response is not shown in the cells adapted to proflavine, where on the other hand an expansion of the nitrogen metabolism (asparagine deaminase) appears to compensate for an actual reduction in the level of the enzymes concerned in the breakdown of the carbon source.

Some enzymes normally not fully mobilised in the cell seem to be sacrificed in part during the establishment of the new reaction scheme, as though some compromise is brought about between competing demands. Catalase, whose function in the cell appears to be a special one which only assumes importance as the environment becomes adverse, shows in general little change as a result of the adaptation to drugs.

During adaptation to lactose the enzymes directly concerned show an expansion, but the behaviour of succinic, lactic

and acetic dehydrogenases is complex. At first they increase in activity, but as the cells become more completely acclimatised to lactose they sink back again, reflecting the known fact that lactose adaptations is a process of some complication.

Though necessarily fragmentary, being based upon the study only of a few representative enzymes out of the innumerable enzymes of the cell, the results give clear indications that drug adaptation, like adaptation to new substrates involves a purposeful and coordinated redeployment of the resources of the cell.