Book Reviews

WHAT IS AGEING?

An Inquiry Concerning Growth, Disease and Ageing

By Philip R. J. Burch. Pp. vii+213. (Oliver and Boyd: Edinburgh, November 1968.) 63*s*.

A MEDICAL physicist, in this book, expounds a theory which seeks to bring into a single conceptual framework some of the most puzzling problems of biology and medicine; among them, the regulation of growth, deviations of normal growth (cancer), ageing and the origin of certain chronic or remitting diseases of hitherto unknown aetiology. In the first chapters Burch describes the way in which he came to formulate ideas which derive both from Macfarlane Burnet's "forbidden" clone theory of auto-immune diseases and Burwell's suggestion that the growth of mammals is centrally regulated by the lymphoid system. After detailed and complex analyses of the mechanisms at work, and of the application of his theory to biological and medical problems, the author observes in the course of his final reflexions: . . . "the would-be synthesizer is obliged to survey fields in which he has no specialist training, and he cannot always distinguish . . . that which is scientifically established from that which is mythology and dogma".

I find myself in the identical position, and I have had to take on trust, among many biological and highly specialized medical matters, the author's mathematics. An adequate critique of this book would require a multidisciplinary symposium. All that can be attempted here is to give through the reviewer's eyes a bald outline of the theory and of some of its implications.

Briefly, then, the organs of the body consist of anything between 10^6 to 10^{10} of distinctive tissues; for example, every single dermal ridge of the finger print, every component of the kidney, has its distinctive pattern of growth and final morphology. Originally, these characteristics are, of course, laid down in the genes of the fertilized ovum, and they are then passed on to groups consisting of fixed numbers of mesochymal stem cells. Each of these groups guides the development of each distinctive tissue, and later on is thought to regulate its growth and, in the case of many tissues, its regeneration. These growth control stem cells form what amount to comparators, and are thought to transmit to the growing target tissue a substance which stimulates mitoses. Each distinctive tissue responds to a stereochemically specific and thus recognizable mitotic control protein (MPC), which reaches it on the outer membrane of certain small lymphocytes, or electrophoretically in humoral form in the case of tissues beyond the blood-tissue barrier (for example, in the brain). In return, the cells of the target tissue secrete another protein (tissue coding factor, TCF), which is equally specific and unique in structure, and which homes on to the related group of mesenchymal stem cells (that is, the comparator). Growth and its cessation can thus be regulated by phase reversal within a feedback system.

The antithesis to growth is ageing, and for this there have so far been opposing types of theory. On the one hand, ageing has been regarded as a programmed phenomenon; on the other, as the result of the accumulation of random errors, most likely the result of spontaneous somatic mutations leading to chromosomal defects. Burch adduces convincing evidence against either type of theory, but gives support to an intermediate (both stochastic and programmed) "auto-immune" theory of ageing. He and his colleagues appear to suggest that mutations occurring in growth control stem cells give origin to "forbidden" clones, which in turn secrete mutant MCP. This is the primary "auto-antibody" which attacks the related target tissue. Hence it is suggested that an auto-aggressive rather than an auto-immune disorder results.

Numerous observations in the field of pathology appear to support the role of mesenchymal stem cells and of random changes in their chromosome materials. To give but one or two examples, dental caries occurs almost exclusively in certain sites of certain teeth in fixed patterns of distribution, though all teeth and their entire surfaces are equally exposed to external agents favouring decay. This localization is explained in terms of the dentition being made up of different distinctive tissues, several of which contribute to the make-up of individual teeth. Mutations in the stem cells of one growth control centre will thus cause auto-aggressive changes only in certain portions of several teeth. Another application arises from the assumption that mutations occurring in a fixed number of stem cells are random events, the frequency of which is expressed by the same type of differential equation as other stochastic events, such as the decay of radium. In fact, surprisingly good fits can be demonstrated between the age incidence curves of many diseases and curves representing stochastic differential equations, after the addition of certain factors. These allow for genetic predisposition, the time that has to elapse between the initiation of the auto-aggressive process in the tissue to the manifestation of the disease, and the number of mutations required for the process to get started. Burch's theory helps to understand difference in the sex incidence of certain diseases, keeping in mind that women have two X chromosomes as against the male XY constitution. Trisomy of chromosome 21 in mongols (Down's syndrome) is related to a considerably higher incidence of a certain kind of leukaemia. There is room in Burch's theory for an explanation of known genetic mechanisms and also for the role of immunological defences. In addition, modifiable pathogenic factors are recognized, ranging from viral and bacterial infections to mental stress. For instance, infection alone results in a symptomless carrier state, unless several other factors are present, among them the occurrence of a requisite number of mutations, the absence of immunity due to earlier infections and the like. In the absence of medical prophylaxis, chance events determine whether or not, and at what time, we fall ill.

Apart from its comprehensiveness and elegance, Burch's theory bears another hallmark of quality: it leads to numerous testable predictions, and is thus wide open to decisive rejection, to confirmation or, most likely, to modification.

F. POST

ALL THE STARS

The Molecular Basis of Life

An Introduction to Molecular Biology. With introductions by Robert H. Hayes and Philip C. Hanawalt. (Readings from *Scientific American*.) Pp. 368. (Freeman: San Francisco and London, January 1968.) 84*s* cloth; 42*s* paper.

THIS book, the latest volume in the series "Readings from *Scientific American*", needs no introduction; it will