Letters

Metric System in Disguise

The letters of Schubiger and Baer (14 Feb., p. 638) bring to mind the fact that ball bearings have for decades been made to metric dimensions. While diameters and lengths have been expressed in inch units, they are actually round metric sizes translated into long fractions of inches.

W. B. SHEPPERD
621 Route 322,
State College, Pennsylvania

Mutations and Aging

Most of the conflict between Kohn and Curtis (*1*) would appear to be resolved by the autoimmune theory of aging (*2–5*). Although this theory does not cover all aspects of mammalian aging—it is, for example, inapplicable to the loss with age of fixed postmitotic cells such as neurones—it could nevertheless apply to the majority of those degenerative processes that culminate in death.

Cardiovascular diseases are important and representative examples of aging, and the possible etiological significance of age- and sex-specific mortality rate statistics is worth considering. When these rates are plotted against age on log-log scales, remarkably straight lines are obtained for most categories of cardiovascular disease over the whole, or greater part, of adult life (*4*). Depending on the disease, the slope of such lines may vary between about 2.5 and 11; in other words, these age-specific mortality rates are accurately proportional to a constant power of age for the greater part of the life span.

This mathematical form of age-dependence suggests that the initiation of most cardiovascular diseases depends upon a multistage stochastic process, where usually the number of stages or random pathogenic events cannot be greater than about 12. When we consider the pathology of such diseases—involving an astronomical number of cells—such a conclusion is at first sight nonsensical. However, Burnet's "forbidden clone" hypothesis (*2*) offers an escape from this paradox. A small number of "somatic mutations" affecting one or several stem cells could very well generate one or a few clones containing an enormous number of pathogenic cells. In this way several discrete primary events could be amplified, through clonal growth, into a widespread systemic disease. The two basic requirements of the theory are that (i) random events should initiate an amplification process, such as clonal growth, and (ii) the same random events should also produce a pathogenic incompatibility between the "forbidden clonal cells" (or their products) and normal tissue. It has been shown (*5, 6*) that the age-specific patterns relating to the phenotypic manifestation of recognized autoimmune diseases in man are fully consistent with Burnet's forbidden-clone hypothesis. It can be inferred that in some of these diseases the primary pathogenic agents are cell-bound and not humoral autoantibodies.

The statistics of autoimmune diseases (*5, 7*) reveal some interesting and rather complicated sex differences; from a consideration of such details it has been proposed (*4, 7*) that many cardiovascular diseases could be basically autoimmune. Burwell (*9*) has argued that the primary natural role of lymphoid tissue is related to morphostasis; if his view should be substantiated, then any tissue subject to mitotic regulation by lymphocytes ought, in principle, to be vulnerable to autoimmune attack (*5*).

Kohn rightly points out that damage to, or loss of, parenchymal cells can be repaired, even in old age, through regeneration from healthy cells. Although specific gene mutations in parenchymal cells might contribute to another aspect of aging—neoplastic change (and according to a recent analysis [*8*] they very probably do)—it must be presumed that many somatic mutations lead to the death and elimination of cells, followed normally by replacement through mitosis in the healthy stock of cells. Regeneration ensures that no permanent impairment of function occurs. If, however, lymphoid mitotic control cells (*9*) become aberrant through some form of mutation in stem cells, and if they overwhelm the natural defense system (*4–7*), degenerative changes can occur in target tissues through nonrecognition of "self" and an immunological incompatibility.

According to the autoimmune hypothesis, therefore, "somatic mutation" in the stem cells of the lymphoid series should be an important cause of mammalian aging.

P. R. J. BURCH
Department of Medical Physics, University of Leeds, General Infirmary, Leeds, 1, England

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NASA's Role Explained

The letter of Philip Siekevitz (31 Jan., p. 143) has typified an attitude which is not only irritating and insulting to scientists in and out of NASA, but, more importantly, potentially dangerous to our country's research efforts in space.

Siekevitz begins by asking, Why have "a middleman" (NASA) in research in geophysics, geomagnetics, solar physics, and so forth? Many of the observations necessary to answer questions pertinent to the universality of earth-bound observations must be made in outer space. Our atmosphere, although necessary for the maintenance of life, obscures a whole host of phenomena that bear on the structure and origin of the earth and the universe. No group in private enterprise or at an endowed institute can afford to build the necessary "middleman"—the booster rockets—to carry the instruments beyond the atmosphere where they can make their measurements. In many ways, NASA's program