NEWS AND VIEWS

The Nobel awards for medicine or physiology

from Sir Peter Medawar CH, FRS

THE joint award of the 1980 Nobel prize for medicine or physiology to Jean Dausset, George Snell and Baruj Benacerraf has been well received by immunologists and medical biologists generally. The general public and the scientific press also found the award easy to understand: Jean Dausset was prime mover in the discovery in human beings of an important system — 'HLA' — of tissue groups that affect the outcome of organ transplantation in a way analogous to that in which the principal blood groups — ABO — affect the outcome of blood transfusions.

Its relevance to tissue transplantation is not, however, by any means the most important aspect of the discovery of the so-called 'major histocompatibility complex' (MHC) of human beings and of the analogous — perhaps homologous — MHC of mice, known as H-2.

The great and abiding importance of the HLA system is twofold. First, it defines a system of polymorphism — of stable genetic differentiation — in human beings which has uncovered, as no other procedure could have done, the genetic basis of differences in susceptibility to multiple sclerosis, ankylosing spondylitis and the juvenile (insulin-dependent) form of diabetes. Even more important, it has become increasingly apparent that the MHC of man as of the mouse defines a whole system of cell-surface markers which are of the utmost importance for the organism's power to discrimate between self and non-self; indeed, an organism's power to react to a number of immunogens as antigens seems to depend on their being signalled by the gene products of the MHC.

Although Jean Dausset was prime mover in the recognition and definition of the HLA complex, this discovery — as with all others of comparable stature — was the work of a number of medical scientists standing shoulder to shoulder: the names that come instantly to mind are those of Bernard Amos, Richard Batchelor, Walter Bodmer, Ruggero Cepellini, Rose Payne, Jan van Rood and Paul Terasaki — a splendid example of international co-operation promoted by the Transplantation Society's generosity and good sense in organizing histocompatibility workshops at which all the principals met to exchange ideas, knowhow and reagents.

To explain George Snell's award we must go back to the early days of tumour transplantation. In the first decade of this century it was widely believed that a study of the factors promoting or retarding the growth of transplanted tumours held promise of a prevention or cure of malignant growth; but by the end of the decade, thanks mainly to the criticism of Peyton Rous, it came to be recognized that the study of tumour transplantation was a study of transplantation rather than of tumours, for in the days before homozygous strains of mice became available, tumour transplants were all of the kind known as 'allografts' and as such aroused immunological rejection reactions.

A very great deal of the work was done with what might be called 'any old mice'; it made no kind of sense and — what is worse — still cannot be interpreted today. This judgement applies with especial force to work on 'immunization' against transplanted tumours by the previous inoculation into their intended recipients of tumour cells of the same kind or of a variety of normal tissues.

Matters were in a desperate state until they were taken in hand by Little, Strong, Bittner, Johnson, Bagg and George Snell of the Roscoe B. Jackson Memorial Laboratory — the men who originated the inbred strains used throughout the world today. Using genetically uniform mice it became possible to formulate the elementary genetic ground rules of transplantation of normal tissues or of tumours. George Snell went further and worked out in great detail how the outcome of transplantations is governed by the genes that comprise the MHC of mice (H-2), first serologically recognized by Peter Gorer of Guy's Hospital, London, who if he had lived, would certainly have shared the Nobel prize. The study of H-2 provided the technology and the conceptual background that made possible the recognition of the MHC of man.

This has been the international year of the MHC, for the award to Baruj Benacerraf also relates to the MHC — in particular with that sub-region of it that has to do with '*Ir*' (short for immune response) genes. When Benacerraf and H.O. McDevitt first recognized this sub-region it was widely thought that they had discovered the gene that coded for the antigen-specific T-cell receptor, but it now seems more likely that the *Ir* region is involved with the presentation of antigen to T-helper cells.

The work of this year's recipients of the Nobel award for medicine or physiology has a twofold lesson to teach. The first is of the immense fruitfulness of collaboration between mice and men in the solution of medical biological problems. The second, not quite so obvious, is that the discovery of HLA provides an exemplary case history in rebuttal of the notion that scientific discovery can be premeditated. What advice, for example, should one give to a young man intent on finding out the genetic basis of differences in susceptibility to multiple sclerosis, ankylosing spondylitis or insulin-dependent diabetes? It would be the *reductio ad absurdum* of the notion that scientific discovery can be premeditated to recommend that the young research worker should embark on a study of tumour transplantation, specifying the use of heterozygous mice, until its contradictions and vicissitudes drove him nearly mad whereupon he should proceed at once to work out its genetic and serological basis, from which the results could be translated to human beings and the rest would follow.

In days when businessmen and others who ought to know better are advocating a diminution or even abandonment of 'pure' research in favour of its practical applications it cannot be too strongly emphasized that discoveries such as HLA — as of diagnostic X-ray radiography — were made by the ordinary processes of scientific discovery, slow, messy and uneconomic though they undoubtedly are. It is in fact only unworldly impractical daydreamers who think that scientific discoveries can be premeditated or can be arrived at by the working of some calculus, some organon of discovery. It was the tough practically minded, no-nonsense men of affairs — particularly of great affairs — the world's Rockefellers, Sloans, Nuffields and Wolfsons who proved to understand most clearly the need and to provide most generously the means for what is so mistakenly called 'pure' research. □

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