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Scientific, Technical, and Ethical Considerations in Cardiac Transplantation

SIR,—Your leading article (30 December, p. 757) on cardiac transplantation prompts us to put before you our views on this subject, based on an experience in both transplantation and cardiac surgery just short of two decades, and particularly to attempt to define the reasons why we have not felt justified yet in carrying out heart transplantation in man.

We agree with your leading article that in the last few years progress has been made in the isolation of certain antigens in leucocytes. We also agree that some relationship can be demonstrated between leucocyte group compatibility and the behaviour of allotransplanted skin. We are disturbed, however, by the present growing assumption that by identifying strong antigens in the leucocytes accurate assessment of difference between other tissues of individuals can be made. Leo Loeb¹ in his monumental work using the lymphocyte as a test of biological individuality failed in a lifetime to define an individual; and it is significant that analysis of the antigenic composition of the red cell has still to be completed despite the lapse of over half a century since Landsteiner discovered the ABO antigens.

There is, on the contrary, some *prospective* evidence from a team very experienced in clinical kidney transplantation that this assumption may not be justified. The Denver group² state:

"It is equally discouraging to note that the use of prospective antigen matching for donor selection did not have more influence upon prognosis. . . . The latter finding emphasizes the futility, with the presently available therapeutic protocols, of envisioning effective and large-scale application of tissue-typing techniques in cadaver programmes."

The complexity of the present situation is

ably summarized by Hamburger,³ of Paris:

"It is remarkable that a certain degree of correlation is found between a rough classification of clinical results and leucocyte typing, with of course many individual exceptions, some patients doing well despite a major mismatch and some showing poor results without any known mismatch. This, I believe, means that our friends responsible for leucocyte typing are on the right road. But it also means that they probably are only at the beginning of this road."

Surely it is premature to overemphasize the value of tissue typing based only on the leucocyte as a test model.

If we now turn to the present immunosuppressive techniques used in kidney transplantation the outlook is no more encouraging. The Denver group² have concluded recently:

"The foregoing observations make it clear that, if renal homotransplantation has become a standard form of therapy for terminal renal disease, it has reached this status prematurely. Every active transplantation centre has its brilliant results, but the incidence of failure is high, and, what is worse, it seems to have reached an irreducible minimum employing the 'standard' immunosuppressive drugs."

Nor is the position ameliorated by the possibility of substituting a second, third, or fourth graft in the event of primary failure. Evidence has accumulated in the experimental animal and in man⁴ that individual specificity is no longer a rigid rule of transplantation biology, and we are not surprised to find that in two leading American centres^{5,6} successive kidney transplants in man have brought disillusionment.

Past Experience

In this hospital we have been engaged in both experimental and clinical cardiac sur-

gery since its infancy. The development of the heart-lung machine and perfusion techniques have been pursued throughout this period, the behaviour of the cadaveric heart has been studied by perfusion and conservation techniques, and much has been learned from animal cardiac transplantation. Access to a dead human donor could have been arranged—technically, human cardiac transplantation could have been done.

No less determined have been our efforts in the field of organ transplantation, and much of the present technique of renal transplantation was pioneered by our experiments. By 1951 we had developed the technique of kidney autotransplantation, we had described in great detail the natural history of the kidney allotransplant, the syndrome of rejection, including the hypertension which it elicits, and the likely technical complications.⁷ Further, we had developed immunosuppression by both total body and local x-irradiation and by high steroid dosage. By this time we had stated:

"Clinically the homotransplant problem is of vital importance and its solution is increasing in urgency. The problem is so obscure that the widest research co-operation between experimental surgeon, clinical surgeon, serologist, and geneticist will be required for its solution; yet it is so vital that an organization for the co-operation of these specialists, with the aim of achieving successful homotransplantation in man, would seem opportune."⁸

It is of interest to note the recent imaginative move by the Ministry of Health in designating kidney transplant hospitals, which indicates a desire to promote vigorous research in the whole field of transplantation. This should not be interpreted as an indication that the biological problem has been largely solved.