PANEL IV: DONOR SELECTION

Reporter - JOE MOSSEY

CHAIRMAN:	Jean Dausset	Laboratoire D'Immunohematologie Institut de Recherches sur les Maladies du Sang Universite de Paris
PANELIST:	John B. Dossetor	Director Renal and Urological Research Royal Victoria Hospital Montreal
	J. R. Batchelor	Senior Lecturer in Immunology Guy's Hospital, London
	Pavol Ivanyi	Institute of Experimental Biology and Genetics Czechoslovakia

In the time alloted to it, this panel discussed the subject of "Donor Selection" in surprising detail under two main points of view: the genetic aspects and the practical considerations involved in donor selection. The following is a brief summary of the presentations of the panelists.

The Chairman introduced the subject of the genetics of transplantation. He said that there were two and possibly four antigenic systems influencing the compatibility of a transplanted organ with its new owner. These systems are:

(1) the ABO blood groups,
(2) the HL-A tissue antigen system, and possibly
(3) the (P) or lymphocytic antigen, and finally
(4) the (LP) or lipoprotein antigen.

The last two entities were not discussed in any further detail as little was known about them at this time.

The significance of the ABO system was briefly illustrated by slides showing how immediate rejection of a skin graft occurred when the donor was type A and the recipient was type O. On the other hand no such reaction occurred in the same recipient if the donor was of the same type O.

The Chairman devoted the rest of his time to discussing the HL-A system. He said his laboratory was using three techniques in studying this system. These techniques are: (1) leuco-agglutination, (2) lymphocytotoxicity, and (3) complement fixation in platelets. Using these methods, the complexity and importance of the HL-A system is now being appreciated.

This system is not believed to be linked to any other antigenic system. In other words it is located in a different chromosomal pair than other antigenic system. Nevertheless, this system can be compared with the Rhesus system. In the Rhesus system there are a variety of antigens such as D, d, C & c and these antigens seem to act in groups with one group having a greater affect in the immune reaction than has another group. The same principle seems to apply to the HL-A system. There are at least seventeen different antigens in this system but they all fall into one of three groups. On a genetic basis, it is believed that each of these antigens behave as alternative alleles, so that no one individual would have more than two antigens from each group and may possibly have only one.

In summary then, Dr. Dausset presented a brief introduction into the genetics of immunology. From this we can appreciate its complexity, indeed it might be compared with the fingerprint in that it is so complex, it is possible that no two individuals are entirely alike, antigenically.

Dr. Dossetor said he would like to consider this subject from the point of view of a clinician. As a clinician, in 1964, he decided

to work with cadaveric donors for kidney transplantation. He made this decision for two main reasons: first of all little work of this nature had been tried as most workers were concentrating on live donor transplants and secondly, if successful cadaveric organs are more desirable for it removes the necessity of removing an organ from a healthy person who at a later date might require that organ for survival.

Once the clinician decides that a transplant is indicated he must look for a donor with certain properties. He seeks compatability with the ABO and other red cell antigens, as well as with the HL-A system. At the same time he must try to avoid preformed antibody either against the tissue antigens or against the red cell antigens or against other tissue or other antigens which may have nothing to do with the histocompatibility antigens.

In assessing the compatability of the donor and the recipient, he pointed out that the mixed lymphocyte culture test at this time was of little value. From a clinical point of view, the most valuable test is the tissue typing sera.

Dr. Dossetor devoted the rest of his time to discussing the significance of the preformed antibodies. He said that his laboratory has been able to show that in some cases of transplant failures, there was a cytotoxic antibody against the donor. There may also exist sensitization to several of the erythrocytic antigens such as the Kell factor, Duffy A and the Big E. Finally, in kidney transplants one should investigate the possibility of the existence of a preformed antibody against the basement membrane of the donor's kidney. This antibasement membrane antibody is not species specific and so if present in the recipient it is a contraindication to transplantation.

Finally, it is possible that there exists an enhancing preformed antibody or an antibody that enhances compatability. This is being investigated by cross circulation between donor and recipient. There is one case done to date that was cross circulated for seventy-two hours before the death of the donor. After transplantation there was no accelerated rejection and after three years the recipient continues to do well.

Summary:

This panel discussed in some detail some of the antigenic mechanisms influencing the compatability between the donor and the recipient. Despite the fact that each year new work is indicating that the complexity of the immune system will make it impossible to obtain complete compatability, the panel said that we should not be pessimistic in approaching this subject. Instead we should be encouraged by the success achieved in transplantation to date and using the knowledge gained by past experience: we should continue with transplantation seeking similar or parallel relationships between donor and recipient rather than absolute compatability.

Dr. Batchelor discussed the aspects of pool size and donor selection. He started by pointing out that because donors are few and far between, it is unreasonable that a pool of recipients be available so as to increase the possibility of being able to use every organ that becomes available.

The determination of the size of a pool of potential recipients would depend to a large extent upon the number of different genetic types. In other words one should attempt, at a minimum to have as many immunologically different recipients available as is possible. Therefore, it is necessary to adopt some method of typing. However, he pointed out that despite the complexity of the antigenic system one should not be too dogmatic in laying down rules. He said that in the past few years the Kidney Registry Bureau in Boston has reported steady improvements in all classes of transplant patients no matter whether the donor was related, unrelated or cadaveric. This improvement has occurred without any great change in the methods of donor selection.

The methods or rules used to date have been fairly simple, such as: never cross an ABO barrier and actual tissue typing has only been used recently. So that it would be dangerous to lay down hard and fast rules at this time for donor selection: as it might well exclude patients who might well experience clinical benefits from transplants.

Dr. Batchelor said that our knowledge and experience to date indicates that a pool of nine or ten patients who are immunologically different would ensure a 90% chance that any given organ that becomes available might be used. However, he also pointed

out that these figures should be considered as a minimum size for any given pool and the maximum size should only be limited by the resources of any given transplant clinic.

In closing he said those working in transplantation today should not expect absolute compatability between donor and recipient as this is probably an ideal which may never be achieved. On the other hand we can be encouraged by the success of some transplants done to date in which the donor and recipients were immunologically quite different.

Dr. Ivanyi started his presentation by saying he would like to discuss in more detail two points already mentioned: namely, the mixed lymphocyte culture technique and secondly the relative importance of the various HL-A antigens.

In the mixed lymphocyte culture technique, the lymphocytes of the donor and recipient are mixed together in a suspension. They are then examined by a variety of techniques for the presence of transformation into large lymphocytes which would indicate the presence of a significant difference in the HL-A systems of the donor and the recipient. This technique has proven reliable in assessing the compatibility between donor and recipients who are siblings but it has not proven accurate in studying unrelated transplants.

In discussing the relative strength of the different HL-A antigens; Dr. Ivanyi suggested that these antigens may act synergistically. However, he said this was very difficult to demonstrate but compared it with the example that if a donor and recipient are grafted who vary in two antigenic systems, the rejection is much more severe than it would have been had they differed in only one system. In the same way, the greater the difference in the HL-A systems of the donor and the recipient the smaller the chance of a compatible transplant.