surface areas and so on, and different times of dialysis—two, three or four dialyses a week—naturally we need objective data on the clinical status of the patient. I think Dr. Kennedy made a very good contribution on this point: could you comment on this?

KENNEDY (Glasgow): Thank you, Dr. Michielsen. As you know, I feel quite strongly about this and I think the present terms ‘rehabilitated’ or ‘partially rehabilitated’ used in publications and in reports are capable of varied interpretation. I should imagine that Dr. Drukker’s slide this morning which showed a certain percentage of patients rehabilitated on R.D.T. was representative of a very heterogeneous population indeed and that they would not all be comparable if we got down to a strict analysis. I think there is need for an objective grading system which would allow the patient data of one unit to be compared objectively with that of another unit. It would allow comparison between different methods of treatment—the number of hours of dialysis a week and so on. In Glasgow, we have devised such a system on the basis of allocating points to a patient if he develops any of the known complications of R.D.T. No accurate statistical assessment is available so far, because we do not really know what determines success or not, but we have given a large number of points for the development of complications that are known to be positively harmful and a rather smaller number of points for those that are apparently, at our present state of knowledge, relatively less harmful. The system is quite a comprehensive one: it ranges over the various systems of the body and the biochemical data that one would collect in these patients and, depending upon the number of points a patient collects, he is graded into one of four categories—A, B, C or D, A representing a well patient on the basis of this objective system. This is shown in some detail in the demonstration and I would be very interested indeed in any comment on it.

The CHAIRMAN: De ce qui vient d’être dit par le Dr. Shaldon et le Dr. Kennedy je voudrais retenir deux points: tout d’abord la dialyse chronique ne donne jamais de réhabilitation à 100%, ensuite la nécessité de mettre au point une évaluation du degré de réhabilitation des malades sur des bases objectives.

I think it is the opinion of the members of the panel that they should devise a single master sheet on which, with a monthly entry, all the data concerning the type of dialyser used, laboratory data and the clinical status of the patients could be reported. This master sheet could then be used with or without a computer: this is just a matter of design. I think if we make up a sheet at this moment it should be prepared so that it could be used by a computer and, on a basis of this sheet, the yearly report on dialysis could be compiled.

Now I should like to ask the members of the Assembly, if such a master sheet was developed, how many members would use it? Can we have a show of hands of those in favour of this master sheet? Well, I think a large majority is in favour of one single master sheet which could be used by the majority of members, so I think the next point is to ask some of the people to make up such a sheet and then this could be submitted to the members, maybe at next year’s meeting.

IMMUNODEPRESSIVE THERAPY IN KIDNEY TRANSPLANTATION

Chairman: Prof. J. HAMBURGER, Paris

The CHAIRMAN: Notre Président, le Dr. Walsh, nous a demandé s’il était possible de répondre à la question suivante: existe-t-il actuellement, en 1968, une méthode idéale d’immunosuppression en transplantation rénale?
ROUND TABLE DISCUSSION

As you know, the coming year will be the tenth anniversary of the two first successful renal allografts, one in Europe and one in America, so that Dr. Walsh, our President, thinks that the time has come to consider renal allografts as a therapeutic measure and not only as research operations. The question he set is: Is there an ideal way of using immunosuppressive methods for renal transplantation. I suppose the answer is NO, because none of the present methods is satisfactory. I suppose, however, that it may be useful to study these methods and to discuss each of them.

Je suggère le plan suivant: (1) le sérum et les globulines antilymphocyte; (2) les drogues, telles que la 6-mercaptopurine et l’Imuran; (3) les corticoïdes; (4) les autres méthodes; (5) le problème de savoir s’il est ou non possible d’arrêter l’administration des immunosuppresseurs à un moment donné de l’évolution d’une allogreffe rénale bien tolérée; (6) enfin, le problème de savoir dans quelle mesure les progrès de la sélection immunologique du donneur peuvent permettre d’atténuer l’intensité de notre action immunodépressive.

I shall now ask Prof. Traeger to introduce the question of antilymphocyte serum.

TRAEGER (Lyons): Les résultats cliniques vous ont été mentionnés dans la précédente communication, aussi je me bornerai à vous donner quelques détails sur l’application pratique, les effets toxiques et aussi la préparation des globulines antilymphocytaires.

Les globulines antilymphocytaires sont préparées à partir des lymphocytes obtenus par un drainage du canal thoracique. Les lymphocytes ainsi collectés sont conservés, congelés et utilisés pour l’immunisation des chevaux. Le sérum absorbé sur les globules rouges humains, précipité par les sulfates d’ammonium, conduit à l’obtention de globulines antilymphocytaires.

La standardisation du sérum est réalisée par des mesures de lymphocytoxicité (1/1024 taux habituel), les tests de lymphoagglutination et de lymphostimulation en culture étant pour nous moins importants. L’activité immunsuppressive des lots de sérum ne peut être affirmée que par des essais chez l’animal ce qui a été réalisé dans le service du Dr. Balner chez le chimpanzé. Les types d’intolérances que l’on rencontre lorsque l’on utilise les globulines antilymphocytaires par voie intramusculaire à la dose de 5 ml/jour sont les suivantes:

Il y a constamment des modifications locales avec une douleur parfois très vive. Cette réaction inflammatoire dure quelques heures et disparaît. Elle s’accompagne en général de température assez élevée qui dure 2 ou 3 heures. Nous n’avons vu qu’un seul cas de réelle maladie sérique ayant obligé à l’arrêt de la thérapeutique. Les cas de choc après l’injection sont exceptionnels. Il faut souligner que nous n’avons jamais perdu aucun malade alors que plus de 2000 injections ont maintenant été appliquées depuis plus de 2 ans. Les globulines antilymphocytaires ainsi utilisées ne présentent pas de caractère de néphrotoxicité: en effet chez 10 malades atteints de syndrome néphrotique et dans le but de réaliser la cure de celui-ci, ce syndrome étant résistant aux thérapeutiques classiques, il a été injecté des doses quotidiennes de SAL pendant 1 à 2 mois. Nous n’avons constaté chez ces sujets aucune modification des fonctions rénales, pas de modifications de l’aspect histologique au niveau des glomérules, ceci étant déterminé par des biopsies rénales avant et après le traitement.

La stimulation ganglionnaire réalisée par un tel traitement est assez intense et ceci a été prouvé par de nombreuses biopsies ganglionnaires avant et après traitement. Malgré cette stimulation intense aucun signe permettant de soupçonner un processus tumoral n’a été constaté chez 20 malades ainsi étudiés.

Le schéme thérapeutique que nous utilisons chez nos transplantés est le suivant: le sérum antilymphocytaire est administré 10 jours avant la transplantation et parfois plus longtemps chez les malades qui attendent un rein de coma dépassé. Les corticoïdes ne sont pas utilisés avant 2, 3, 4 ou même 6 à 8 semaines après la transplantation afin d’éviter au maximum les complications infectieuses et les ennuis de cicatrisations. Le SAL est injecté tous les jours pendant 1 mois, tous les 2 jours le mois suivant, tous les 3 jours au cours du 3ème mois. Puis
les doses sont continuées de manière variable. L’Imuran est donné 4 jours avant la transplantation et continué régulièrement.

VAN ROOD (Leyden): I would like to make one remark, and put one question to Prof. Traeger. First, it is not my own work but that of Balner, who has also been mentioned this afternoon, who has been testing numerous antilymphocyte sera in chimpanzees. Chimpanzees and humans have, to a large extent, the same leucocyte tissue antigens, and it is probably for this reason that you can use the chimpanzee to assess the effectiveness of your antilymphocyte serum. We think this is a very important point; we think too much work since Balner has tested more than 10 different batches of antilymphocyte serum. It turns out that you can divide antilymphocyte serum into three groups; the first group of antilymphocyte serum might have antibodies against human lymphocytes but there is no biological activity. In other words, it is not able to prolong skin grafts in chimpanzees. The second group of antilymphocyte sera which has been found prolongs skin graft survival for about twice the normal length of time. But then, even if you continue giving antilymphocyte serum, the skin graft is rejected. The third group of antilymphocyte serum is very effective and will prolong skin graft survival as long as you continue to give antilymphocyte serum.

I think this is a very important point because many of these studies which have been published about antilymphocyte serum give really so little, objective data to evaluate the antilymphocyte serum which was used. This is no of course the case for Prof. Traeger, because his antilymphocyte serum was tested by Balner and found to be in the top quality group.

I have two questions, however, for Prof. Traeger. First, you have a batch of antilymphocyte serum, it has been tested in chimpanzees — and you know your antilymphocyte serum is good. Then you go back to your horse and bleed it a month later. Will it be at good? There has been conflicting evidence on this point.

Secondly would you again state why you decided that the antilymphocyte serum was responsible for the very good results you obtained, and not, for instance, the greater experience which you have also gathered in the meantime?

TRAEGE (Lyons): 1. La raison principale pour laquelle nous pensons que le SAL est actif lorsqu’il est utilisé chez l’homme en transplantation rénale est le très faible pourcentage d’épisode de rejet pendant les 3 premiers mois après la transplantation. En effet chez 22 malades nous n’avons eu que 1 rejet aigu aboutissant à une perte des fonctions rénales. Le pourcentage de malade n’ayant présenté aucun épisode de rejet est de 60%. Si l’on élimine les cas de rejets classés “type I”, c’est-à-dire qui ne représentent que des suspicions de rejets, le pourcentage de malade n’ayant présenté aucun épisode s’élève à 87%. Les statistiques comparables de Hume, portent sur les 3 premiers mois après la transplantation signalent que le pourcentage de sujets n’ayant jamais eu de rejet n’est que de 12%.

Bien entendu ces arguments ne sont pas parfaits; n’ayant pas de groupe de contrôle, c’est-à-dire de malades qui n’ont été traités que suivant des méthodes classiques (Imuran, corticoïdes), il nous a été impossible d’établir par des propres malades une étude statistique précise. Cependant la comparaison de ce que nous avons constaté, alors que nous représentions une équipe de transplantation relativement jeune, avec les statistiques publiées par des équipes beaucoup plus expérimentées que la nôtre, nous incite à penser que l’utilisation du SAL représente un élément de valeur dans les transplantations rénales.

2. Dans notre expérience, il ne nous semble pas que le fait d’immuniser à long terme un cheval et de le saigner de manière répétée, modifie la qualité du sérum obtenu. Dans notre cas particulier, un cheval a été saigné pendant plus de 18 mois, il a toujours fourni un sérum dont le taux cytotoxique était élevé et dont les qualités immunosuppressives étaient constantes. Ceci a été vérifié d’ailleurs par le Dr. Balner sur le chimpanzé.
CROSNIER (Paris): Les exposés du Prof. Traeger et du Dr. Fries montrent combien il est encore difficile de se faire une idée claire sur l'efficacité réelle du sérum antilymphocytaire dans l'obtention d'une tolérance satisfaisante d'un homotransplant chez l'homme.

Dans notre expérience sur les 26 dernières transplantations effectuées à l'Hôpital Necker entre le 1er Juin 1967 et le 1er Juin 1968, 22 malades sont actuellement en vie, ce qui représente 84%.

Notre expérience sur les deux dernières années donne une proportion de 72% de reins fonctionnels chez des malades n'ayant jamais reçu de sérum antilymphocytaire et qui ont été traités uniquement par l'azathioprine ou la 6-mercaptopurine.

Si l'on essaie d'adopter comme critère d'efficacité du sérum antilymphocytaire la nécessité ou non de recourir au traitement par les corticoïdes, 55% seulement de nos malades, non traités par le SAL, ont reçu des corticoïdes au cours des premiers mois post-opératoires.

The CHAIRMAN: I think we have to leave this first question with the conclusion that we cannot assess the exact value of antilymphocyte serum, and we shall ask Mr. Walsh to give us one, two or three more years before we can answer the first question.

The second question, what about drugs? Le Prof. Calne, vous le savez, a été l'un des promoteurs de l'usage des drogues immunosuppressives. Puis-je lui demander d'ouvrir la discussion à ce sujet par un rappel introductif.

CALNE (Cambridge): Thank you Dr. Hamburger.

The trouble is that there are more than 100 methods of producing immunosuppression in different specific experimental models. Some of these methods are very effective, and other methods have very dubious effects, but when one tries to translate this into clinical practice the situation becomes terribly difficult. This is no argument against trying to find the truth, but I think that it is a very strong argument against jumping to conclusions with any particular agent.

There are many nitrogen mustard derivatives which are quite effective in rodents as immunosuppressive agents which do not seem to be effective in dogs with kidney transplants, and as far as they have been used in man again do not seem to be very effective. The thiopurines, which have almost no effect in rodents, are moderately effective in dogs with renal transplants and seem to be moderately effective in man. Steroids do not seem to work very well in dogs with renal transplants, but would seem to be extremely valuable in man. Antilymphocyte serum is miraculous in mice; if mice got burned and needed therapeutic skin grafts, antilymphocyte serum would save them. But its application to dogs with renal transplants shows that its effect is comparable to Imuran.

Speaking now as a clinician, what I think is important in immunosuppression, and in new methods of immunosuppression, is that they should be additive in effect without being additive in toxicity. The fact that you add a new immunosuppressive agent, which you know is effective, to a regime which you already have does not mean to say that it is worth while using this until you can prove that your overall results are better. Results may well be better with antilymphocyte serum, and I hope so; I am very disturbed by the reports of tumours appearing in patients—I think all but one of those patients that you referred to earlier had had antilymphocyte serum—and it will certainly be very helpful when this is published.

I do not think it is worth repeating any of the works on drugs—I think it is common knowledge how to use Imuran, and the fact is that you get better results the more experience you have with the agent. I would just make one point again; if one is using a new agent, it takes a long time and a large number of cases, and very careful control of other variables before you can say even that it looks good, rather than saying that it is proved to be good.

The CHAIRMAN: The accidents you were referring to were accidents of antilymphocyte serum. Would someone like to comment on accidents due to Imuran and related drugs?
WOLF (Richmond): One point with regard both to Imuran and to the decreasing of drugs. We had a patient recently who had a kidney transplant for four years; she has been matched, and she is a good match; she has never had a rejection in 3–3½ years; she was getting her pills by mail. As you know, Imuran comes as 50 mg and 25 mg. The girl is not terribly bright, and instead of taking two pills when she got the 25 mg tablets she continued to take one pill. Within about three months her function deteriorated quite significantly. She was brought back to the hospital, the accident was discovered, the drug was restarted in its usual dosage, and the function has since returned to normal.

CALNE (Cambridge): Could I just add to that experience, quoting from Prof. Woodruff’s Edinburgh series? He had an even more remarkable case of a child who had a kidney for five years from his father; the child was on 25 mg of Imuran on two days in the week. This is an incredibly small dose, and he wanted to see what would happen if it was stopped. Three weeks after the Imuran was stopped, the patient had a violent rejection which was very difficult to control. So the balance between the organ and the recipient and the immunosuppressive drug is a very delicate one. The penalty of taking two pills a week seems a very small one, and I would certainly caution anybody against stopping immunosuppression on any of their patients.

The CHAIRMAN: Yes, we had also a similar case, after three years, a rejection after having stopped the drugs. On the other hand, we have some patients with a perfectly stable situation with no drug. De tels faits sont d’autant plus importants que ces drogues sont loin d’être dépourvues de toxicité à long terme: j’aimerais que nous revenions à ce problème des accidents toxiques des médicaments tels que l’Imuran.

CROSNIER (Paris): Il est très difficile de répondre à cette question. Sur le plan hémato logic, certains de nos malades qui avaient parfaitement toléré les drogues immunosuppresseuses pendant deux ou trois ans ont vu progressivement cette tolérance diminuer, ce qui nous a obligé, chez deux d’entre eux en particulier, à diminuer progressivement les doses d’azathioprine ou même à les supprimer totalement, à partir de la quatrième année. L’un de ces malades n’a reçu aucune drogue depuis 13 mois et garde une fonction rénale parfaite.

La toxicité hépatique de ces drogues ne doit pas non plus être négligée et dans notre expérience près de 20% des sujets traités pendant plus d’un an par les drogues immunosuppresseuses ont des troubles hépatiques. Dans ce cas, il est toujours d’ailleurs difficile de savoir si ces troubles sont le résultat d’une toxicité hépatique des drogues immunosuppresseuses ou s’ils ne sont pas le reflet d’une infection virale hépatique déclenchée ou favorisée par le traitement immunosuppresseur.

VAN ROOD (Leyden): In connection with the case quoted just now by Prof. Calne, I would like to add one bit of information relevant to that case.

The boy, and his father who was the donor, were studied by us, and found to have identical leucocyte groups. Thus, in this case of a parent/child combination which was identical, even in the face of identity we could not do without immunosuppression. This of course does not imply that the same situation holds in two sibs: here the situation might be quite different.

The CHAIRMAN: So, Mr. Walsh will see that the second answer is not much more brilliant than the first one. Is there an ideal dosage for Imuran? Certainly not. One may even be in a situation where, if Imuran is stopped rejection occurs, and if it is not stopped, death will result from hepatitis or bone marrow depression after three or four years.

Let us go to the third point: Prednisone and other cortisone-like drugs. Le Prof. Crosnier accepterait-il de présenter ce problème des corticoïdes?
CROSNIER (Paris): Nous avons adopté comme principe, à l'Hôpital Necker, de ne jamais utiliser systématiquement les corticoïdes. Or, malgré cette restriction théorique, 70% de nos malades transplantés reçoivent ou ont reçu, à un moment quelconque de leur évolution, des corticoïdes.

Les indications sont essentiellement portées dans les trois conditions suivantes:
1. L'indication la plus formelle est provoquée par la survenue d'une crise aiguë de rejet, crise que nous traitons par de fortes doses de prednisone, 5 à 6 mg/kg/24 heures, pendant une dizaine de jours.
2. Une autre indication moins fréquente est provoquée par la survenue d'une complication hépatique par exemple, qui nous oblige à renoncer momentanément à l'utilisation des drogues immunosuppresseurs. Pendant cette période de sevrage de l'azathioprine ou de la 6-mercaptopurine, les corticoïdes peuvent être utilisés comme 'solution de relai'.
3. Enfin, une troisième indication encore plus rare peut être portée sur les résultats de biopsie que nous pratiquons systématiquement le 6e mois, à la fin de la 2e année et à la fin de la 4e année. Dans certains cas, alors même que la fonction rénale est normale, l'examen histologique peut montrer un certain degré d'œdème ou la présence d'infiltrats du tissu interstitiel, ce qui nous conduit à prescrire des corticoïdes à faibles doses, ne dépassant pas, en général, 1 mg/kg/24 heures, pendant des périodes assez prolongées.

The CHAIRMAN: In summary, you do not like corticoids. You use them when you are forced to do so, but you dislike them even more than Imuran. Is that right?

CROSNIER (Paris): Quite right, yes.

The CHAIRMAN: Any more comment on the corticoids?

CALNE (Cambridge): I entirely agree with Prof. Crosnier.

WOLF (Richmond): One comment: in Richmond we are not quite so brave. We do not know the 70% that do not need it, and which are the 30% that do need it. I think in a clinical situation it is difficult to find out until the patient rejects, and perhaps, if you wait until rejection, the barn door is already open and the horse has gone. So I think for this reason, at the present time, we are beginning to administer all steroids at the day of transplantation, and only if the patient demonstrates no rejection over a 4-5-6 month course do we drop the steroids.

The CHAIRMAN: Well, Dr. Wolf, we have seen rejection crises with the use of previous 'prophylactic' prednisone. Since then we have given up the prophylactic use of corticoids except in cadaver kidney grafting. The incidence of rejection crises did not increase. Besides, the crises respond equally to a very high dosage of corticosteroids in patients with or without a previous prophylactic moderate dosage of prednisone.

WOLF (Richmond): I quite agree, but I think it is difficult in the individual case to assess beforehand which patients will have the vigorous rejection. Perhaps when the tissue-typing people can tell us this it would be easier at that point to prescribe the treatment before rejection. But at the present time perhaps the wisest course might be to use whatever therapy we have at hand, and only decrease those therapies after the patient has demonstrated a smooth course.

CALNE (Cambridge): I think the management of steroids depends on what kind of patients you are dealing with. If you are using live donors, then the methods that Prof. Hamburger suggested seem to be reasonable; if you are using dead donors, the tubular necrosis makes the
management difficult, and the difficulty of assessment of the patient in this situation has made us use prophylactic steroids. Using prophylactic steroids and Imuran, and no other immunosuppressive agents at all, we have had no clinical evidence of rejection at any time in more than 30% of our patients—I am sure there have been microscopical changes, but this is of the order of results that Prof. Traeger was talking about, with the use of antilymphocyte serum in addition.

The CHAIRMAN: Any more comment on corticoids?

TRAEGER (Lyons): J’aimerais souligner que les doses de corticoïdes utilisées chez nos malades traités par le SAL sont beaucoup moins importantes que celles données par le Prof. Crosnier et même qu’en cas de rejet nous ne dépassons jamais 1 mg/kg/24 h; comme traitement d’entretien, nous utilisons 5 à 10 mg/24 h.

CROSNIER (Paris): Les doses habituelles utilisées à l’Hôpital Necker en cas de crises de rejet sont de 5-6 mg/kg/24 h de prednisone pendant 10 jours, puis à doses dégressives jusqu’à un taux de 30 mg par jour. Le problème est de savoir si de très hautes doses de corticoïdes sont plus nocives que de fortes doses de sérum antilymphocyte.

TRAEGER (Lyons): J’ai montré que le SAL ne présentait aucun danger au cours des premiers mois: on peut évidemment se poser le problème de ses inconvénients au cours des traitements prolongés mais dans notre expérience nous n’avons jamais eu d’incidents. Nos malades n’ont aucune complication secondaire due aux corticoïdes sauf le cas dont j’ai déjà parlé où une nécrose des têtes fémorales est survenue justement parce que la malade avait reçu de fortes doses de corticoïdes en raison de l’arrêt du sérum antilymphocyte.

The CHAIRMAN: We are now coming to various auxiliary methods such as thoracic duct drainage.

TRAEGER (Lyons): Nous considérons dans notre expérience le drainage du canal thoracique comme une méthode immunosuppressive accessoire. Ce n’est d’ailleurs pas dans un but d’immunosuppression que nous pratiquons les drainages du canal thoracique mais uniquement avec l’intention d’en récolter des lymphocytes qui serviront à immuniser les chevaux pour l’obtention de globulines antilymphocytaires.

Cependant il faut noter un certain pouvoir immunosuppressif des drainages prolongés du canal thoracique puisqu’on a constaté à plusieurs reprises la négativation des tests tuberculiniques chez l’homme après drainage.

The CHAIRMAN: What about local irradiation?

WOLF (Richmond): We in Richmond have been interested in local irradiation for some years, and in 140 out of 145 transplants have given local graft irradiation, 150 rads on days 1, 3, 5 and 7 post-transplant. Before Prof. Calne comments on this, I realise it is very difficult to assess this in man, particularly with the use of Imuran/prednisone, but at least in dog studies, we have shown by various studies that local graft irradiation alone can prolong renal homograft survival.

In a recent experiment that we did in dogs, we placed two kidneys from the same donor to the same recipient, one in the neck and one in the pelvis, then we irradiated one of these two kidneys on days 1, 3, 5, and 7, leaving the other kidney as the dog’s control. The control kidney was selectively rejected, as expected, between days 5 and 7. The other kidney has continued to function for as long as two and a half weeks after the first kidney has been rejected. I think this suggests at least some local effect of immunosuppression from this experiment.
ROUND TABLE DISCUSSION

We think it probably works in three ways, one is that, from an experiment published several years ago, it probably interferes with the afferent arc of sensitisation, if that is the only kidney in. It also probably interferes with the efferent arc of graft destruction; this may be a specific immunologic reaction, that is, the death of the lymphocytes going to the graft to destroy it or it may be the non-specific anti-inflammatory effect that is well known for all irradiation in low doses. There is no way of assessing which mechanism is at work in man; we probably cannot show that it is effective, but at least in dog work it certainly suggests that it can give some immunosuppression. We have had no evidence in any patient that we have had any ill-effects from these doses of irradiation.

The Chairman: The reason why a number of people are a little frightened by this local irradiation is that the dosage may be more than 1,000 rads.

Wolf (Richmond): The most has been 1,350.

The Chairman: That is very near the lower limit of toxic dosage of X-ray; as you know, with 2000 rads one may completely destroy the kidney and the destruction is not immediately seen. It is after 12-18 months, or two years. So it would be extremely useful to check whether two years after this treatment the kidneys are as good as if they had not received local irradiation. Would anyone comment on that?

Calne (Cambridge): Dr. Wolf sounded a little sensitive, and I would like to put him at ease straight away by restating my tremendous enthusiasm for the scientific integrity of Richmond. I entirely believe the dog results that he obtained, but this form of immunosuppression falls into the category that I mentioned before. Although it is definite, when you add it to the other methods of immunosuppression, does it improve the results? We cannot really answer that yet, but it will be possible to answer it when there are large enough series with irradiation that can be compared with series without, such as our own.

The Chairman: Now, you must know that Prof. Calne has recently discovered another way of immunodepression which, as you will see, is not very convenient but very interesting from the theoretical point of view.

Calne (Cambridge): Well I have good news for pigs with liver disease! And also for pigs that might be suffering from kidney disease. It is no use their just having a kidney transplant because they will reject a kidney, as they will a skin graft, in the same way as any other animal, but the liver grafts will consistently last for long periods of time—our longest pig at the moment is 11 months, and we have a group of pigs between 6-11 months and have not seen rejection of a liver in any pig unless the pig had been previously sensitised by a kidney graft. What is interesting is that if a kidney from the same donor as the liver is transplanted at the same time, then the kidney is also protected. Our longest pig with hepato-renal transplant, bilaterally nephrectomised and hepatectomised, is now 7 months, and there are four other animals of 1-7 months.

So this is a form of immunosuppression which is exceedingly potent, appears to be non-toxic, and we have no idea how it works.

The Chairman: Now we are coming to the last part of our discussion, i.e. the role of the donor selection.

Van Rood (Leyden): It has not been mentioned so far that the recipients might differ strongly in their immunological capacity. This is evidenced by the following: almost all our recipients have been treated by dialysis, and this includes blood transfusions. Many of them
have been immunised by this, but not all of them. Some of them make, quickly, strong antibodies against leucocytes, others do not. We do not know the clinical importance of this capacity, but it might be of importance.

A second point which has not been mentioned is that probably the only drug which is really effective in suppressing the homograft sensitivity which (contrary to our earlier thoughts on this point) can be induced by blood transfusion, is probably antilymphocyte serum, and this might in future be one of the main indications for antilymphocyte serum in renal transplantation.

Then a second general point I would like to make is this: from our retrospective studies it is quite clear that the classical forms of immunosuppression, such as prednisone and Imuran, are quite able, even with a mis-matched kidney, to keep a kidney going for 18 months to two years. It is only after that period of time that the mis-matched kidneys do significantly less well than the well-matched ones. I bring up this point because it is of direct relevance to the evaluation of old and new drugs. It is only after you have used your drug for two years or more that you really can start making comparisons.

The Chairman: Thank you, Dr. Van Rood. You will surely know that the Montreal group and some others claim that multiple blood transfusions before grafting may have an exactly opposite effect, that is, improving the results of the transplantation exactly as if they had some enhancement effect.

THE CIMINO-BRESCIA FISTULA

Chairman: Mr. Anthony Walsh, Dublin

The Chairman: The Cimino-Brescia fistula has been claimed by many people to be one of the great advances of recent years in the technique of dialysis. Others say they have tried it and cannot make it work. So we thought it would be a good idea to assemble here on the panel a number of people who among them have a considerable experience of using the Cimino-Brescia fistula, to see if we can find out why some people make it work and some people do not.

I shall start by asking Dr. Hanson to show the 'classical' technique of the Cimino-Brescia fistula.

Hanson (Dublin): The normal procedure is to cut down on the cephalic vein some 2-3 inches proximal to the wrist (Fig. 1). There are two important points (1) to make adequate mobilisation of your vessel (2) to keep the opening in your fistula to 5 mm or less. Here you see both the radial artery and cephalic vein dissected, and the orifice, which is about 5 mm.

Figure 2 shows the fistula completed. There is no angulation in either vessel; they come smoothly together. Figure 3 shows the fistula in use.

The Chairman: Thank you. Dr. Hanson's points are that the fistula should not be more than 5 mm and that one must take care and time to get adequate mobilisation of the vessels so that there is no kinking, particularly of the vein. I think your emphasis is that it must not be kinked by fascia?

Hanson (Dublin): Yes. You must get adequate undermining of the superficial fascia so that the vein swings deep to the superficial fascia. Without adequate undermining of the skin flaps this will not happen and you will get kinking and subsequent clotting in the vein.