CORRELATION OF TISSUE-TYPING TESTS IN BABOON RENAL ALLOTRANSPLANTS*

A PRELIMINARY STUDY

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This report deals with the frequency of occurrence of various human leucocyte antigens and their relative influence on the survival period of baboons subjected to renal allotransplantation, both with and without simultaneous immunosuppressive treatment. In all the experiments the compatibility of the donor and recipient pairs were matched in terms of their human (ABO) blood-group antigens.

In the absence of a safe method of inducing immunological tolerance to renal-graft antigens in man, it seems inevitable that non-specific immunosuppression will continue to be necessary in the management of graft recipients for the foreseeable future. The need for immunosuppression, with its attendant hazards, may be reduced if it becomes possible to select a donor compatible with the recipient in respect of the strongest antigens. Human leucocyte typing is at present advocated as a valuable method of tissue typing to obtain better graft matching.[1-5] Reports from large groups of human patients receiving renal homotransplants from pre-operatively matched donors are, however, not yet available.

The experiments reported here afford an opportunity to determine the relative significance of various human-type leucocyte antigens in immunologically competent subhuman primates, receiving renal allografts.

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MATERIALS AND METHODS

Renal allografts were performed on 34 adult male and female Chacma baboons (*Papio papio*, sub-species *Papio ursinus*). In 5 pairs of donors and recipients, grafts were exchanged without loss or sacrifice of the donor. A total of 22 pairs of renal allotransplants were thus performed (Table I).

The animals were housed and cared for in the Stellenbosch-Johns Hopkins Primate Project at the Karl Bremer Hospital in Bellville, CP. The details of the operative technique and various chemical tests have recently been described in detail.[6] As human blood substances are not found on the baboon erythrocytes,[6] the human ABO blood-groups were determined by two indirect methods. Saliva specimens were examined for the ability to inhibit the activity of human erythrocyte-typing antisera and serum specimens were examined for agglutinins to human erythrocytes. The animals were from heterogeneous troops trapped in widely scattered locations in the Cape Western Province and the grafts were performed between animals from different troops. The unknown effects of inbreeding and natural biological selection, more likely present within

TABLE I. LEUCOCYTE TYPING RESULTS

No.	*Treatment*	*Donor*	*Recipient*	*Day PO death*	*Human ABO groups*	*Number differences* D → R*	*Specific groups differences* D → R*	*Number differences* R → D*	*Specific groups differences* R → D*
1	Control	V-20	P-20	17	AB → AB	10	1, 5, 7, 9, 11, 17, 18, 20, 21, 22	None	None
2	Control	P-20	V-20	6	AB → AB	0	None	10	1, 5, 7, 9, 11, 18, 20, 21, 22, 17
3	Control	W-12	W-14	15	B → B	4	3, 6, 10, 12	None	None
4	Control	W-14	W-12	11	B → B	0	None	4	3, 6, 10, 12
5	Thalidomide	A-20	A-19	12	B → B	1	2	11	1, 4, 5, 6, 7, 8, 9, 10, 11, 15, 18
6	Thalidomide	C-17	C-18	6	B → B	1	1	5	5, 7, 8, 16, 21
7	Chloroquine	Y-6	Y-7	15	B → B	1	12	4	3, 13, 18, 20
8	Chloroquine	Z-9	A-11	5	B → B	8	1, 2, 3, 10, 14, 20, 21, 22	6	4, 11, 15, 16, 17, 18
9	Chloroquine	Z-3	Y-9	8	B → B	5	4, 17, 18, 21, 22	7	3, 9, 10, 12, 14, 19, 20
10	Imuran	B-21	A-27	7	B → B	0	None	2	3, 20
11	RNA-ase	R-12	Q-20	9	AB → AB	0	None	3	6, 17, 19
12	RNA-ase	T-20	U-11	6	B → B	0	None	14	1, 5, 8, 11, 14, 15, 17, 19, 20, 21, 22, 23, 24, 26
13	RNA-ase	Q-18	R-14	4	B → B	0	None	8	1, 2, 12, 13, 15, 19, 20, 22
14	Goat γ-globulin	I-20	K-18	11	B → B	14	2, 4, 5, 6, 7, 8, 9, 10, 14, 16, 17, 18, 25, 26	1	22
15	Kidney-cell fractions	W-16	L-11	7	B → B	0	None	0	None
16	Kidney-cell fractions	T-18	T-17	6	B → B	3	6, 12, 22	3	3, 4, 24
17	Kidney-cell fractions	T-17	T-18	6	B → B	3	3, 4, 24	3	6, 12, 22
18	Kidney-cell fractions	T-14	T-13	7	AB → AB	3	8, 18, 25	0	None
19	Kidney-cell fractions	T-13	T-14	8	AB → AB	0	None	3	8, 18, 25
20	Kidney-cell fractions	R-13	R-11	5	B → B	1	17	4	6, 13, 14, 26
21	Cortisone	A-27	B-21	5	B → B	2	3, 20	0	None
22	Cortisone	A-28	Y-15	7	A → A	2	7, 16	7	2, 4, 5, 6, 12, 21, 23

D = donor
R = recipient
*For + or greater agglutinin reactions.

a single troop, were therefore avoided. As a result of avoiding the possibility of blood relationship between the donor and recipient, the survival periods may have been shorter than those noted after transplantation between members of the isolated, inbred troop of animals in the Cape Point Reserve.[6]

At the time of surgery 10 ml. of EDTA blood were obtained from the donor and recipient. Baboon leucocytes were then tested against a battery of 26 human leucocyte antisera at the Cape Provincial Blood Grouping Laboratory.* This method of leucoagglutination as a test for tissue typing antigens has been described in detail.[3,4] The human antisera were originally obtained from a panel of pregnant women.[3,4] Agglutination reactions of baboon leucocytes in the specific antisera were recorded as W+ (weakly-positive), +, ++ and +++. Occasional stromal reactions were noted.

In the 22 paired baboon renal allografts, 4 were not subjected to immunosuppressive therapy, while the remaining 18 pairs were subjected to various forms of therapy. The following substances were administered by parenteral injection at operation and postoperatively, at varying intervals: Thalidomide (10 mg./kg.), chloroquine (5 mg./kg.), Imuran (3 mg./kg.), RNA-ase (300 mg.), anti-baboon goat γ-globulin (600 mg.), subcellular baboon kidney-cell fractions (2 ml.) and cortisone (60 mg.). The results of these forms of treatment and various other tests will be described in detail in a separate communication. Animals in the present series underwent renal rejection as determined by their clinical course, chemical tests, or gross and histopathologic postmortem examinations. None of the animals survived beyond 3 weeks and they are therefore comparable in terms of their response to renal allotransplantation, despite the differing modes of therapy.

The same battery of specific human leucocyte antisera were used in leucocyte agglutination tests on 100 other baboons. In addition, leucocyte matching tests were performed between human renal homotransplant candidates and baboons with similar human blood-groups. In one instance a modified third-man skin test was employed using two baboons of the same blood-group as the patient.[1] An autograft of skin was applied as a control and split-thickness skin grafts from the other baboon and the potential human recipient were transplanted. Other specific tests performed in special instances will be described in the text. Details of the various methods can be found elsewhere.[6]

Furthermore, in a series of experiments on organ preservation, 20 baboon kidneys were subjected to bloodless perfusion for 24 hours under hypothermic, hyperbaric conditions in a specially designed unit, using either helium or oxygen as the equilibrating gas.[7] The perfusate, a dextrose and water solution to which other substances were added, recirculates through the kidneys during the preservation. The fluid caused no reaction with the battery of 26 human antisera before or after the 24-hour preservation period.

In a further experiment a blood- and leucocyte-typed baboon was killed and various organs were then removed and washed out to remove all blood cells, and were then freeze-dried. Homogenates of these tissues were tested for reactions against the same set of 26 human antisera.[3,4]

The principles and practices of the South African Animal Welfare Society and the American National Society for Medical Research were observed throughout these experiments.

*The serological tests involved were carried out in the Provincial Blood Grouping Laboratory under the direction of Dr M.C. Botha.

RESULTS

Frequency Distribution of Leucocyte Agglutination Reactions Against Specific Antisera

Figs. 1 and 2 indicate the relative frequency of agglutination reactions observed in the 100 baboons used in a

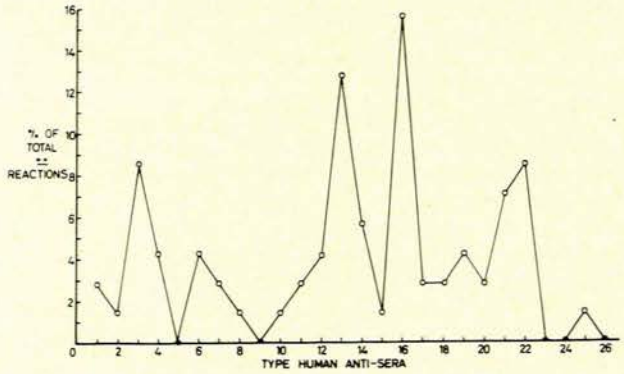

Fig. 1. The relative frequency of weakly-positive baboon leucocyte agglutination reactions to the battery of 26 human antisera.

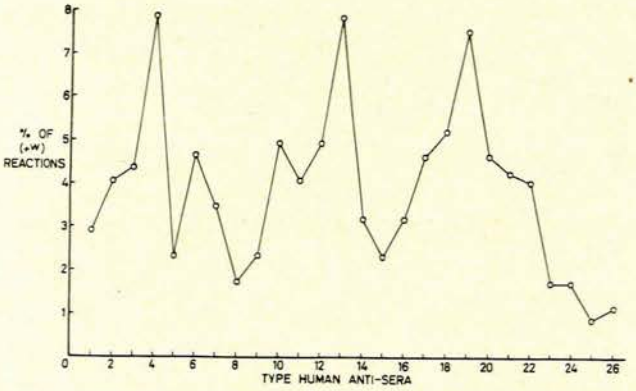

Fig. 2. The relative frequency of strongly-positive baboon leucocyte agglutination reactions to the battery of 26 human antisera.

screening test against each of the 26 human antisera. Fig. 1 illustrates the relative frequency of weak-positive reactions (W+), while Fig. 2 illustrates the relative frequency of stronger (++) agglutination reactions.

Fig. 1 shows that 3 main peaks of incidence are seen, indicating that the most frequently occurring leucocyte antigens are those reacting against the human antisera numbered 4, 13 and 19. It is not yet known how these 3 main groups may differ from one another antigenically, but it is possible that they may be similar.[3,4] The scale of reactivity was set at the lowest level (weak-positive) which may result in lower specificity than stronger reactions. However, as shown in Fig. 2, the strongest leucocyte reactions are also distributed into 4 groups, against antisera 3, 13, 16 and 21. Allowing for biological overlapping, this

is quite close to the groups most frequently found with those baboon leucocytes giving a weak-positive reaction (Fig. 1). The system of numerical identification of the human antisera used in the present study will be retained for future use, but it is unknown at present in what way these 26 numbered antisera are similar to or different from the antisera employed by other investigators.

In all the animals tested there were 1,197 negative reactions, 343 W+ reactions, 304 + reactions, 70 ++ reactions and one +++ reaction. These numbers thus constitute an extensive biological sample of the various types of leucocytes seen in 100 baboons as tested by our battery of 26 human antisera.

Donor and Recipient Leucocyte Typing Differences

Data on the survival after renal allotransplantation of the 22 pairs of grafted animals are shown in Table I. The correlation between donor and recipient leucocyte agglutination reactions with the antisera will be discussed separately.

Differences in survival of treated and untreated renal allotransplanted baboons were related to the observed discrepancies in leucocyte typing results. In the presence in the donor of more than 5 antigens not present in the recipient, only 2 of 22 (or 9·1%) of the recipients survived beyond 10 days, with or without antirejection therapy.

In the presence in the recipient of more than 5 antigens not present in the donor, only 1 of 22 (or 4·5%) of the recipient animals survived beyond 10 days, with or without antirejection therapy.

Assessment of lesser donor and recipient differences in leucocyte antigens were made by placing the 26 sera into 5 groups. Within each group the agglutination reaction was merely recorded as present or absent. The following regrouping of antigens were employed: division A, 1 - 15 (groups I, II and III); division B, 16 - 26 (groups IV and V); division C, divisions A and B (groups I - V); division D, any antisera (1 - 26); division E (no groups, no reactions). These divisions were applied to tests on both the donors and the recipients. Where the donor possessed one or more leucocyte antigens not present in the recipient, the following survival rates were recorded.

In division A (1 - 15) average survival was 12 days.
In division B (16 - 26) average survival was 5 days.
In division C (1 or more antigens not common to donor or recipient in both division A and division B) average survival was 8 days.
In division D (1 or more antigens not common to donor and recipient in entire tested groups) average survival was 8·9 days.
In division E (no antigens in donors) average survival was 7·2 days.

Similar correlations were made in regard to recipients possessing one or more leucocyte antigens not present in the donor. The following survival periods were noted in the 5 divisions:

In division A (1 - 15) average survival was 9 days.
In division B (16 - 26) average survival was 8·5 days.
In division C (1 or more antigens not common to recipient and donor in both division A and division B), average survival was 7·3 days.
In division D (1 or more antigens in the entire group tested) average survival was 8·3 days.
In division E (no antigens not common to recipient and donor) average survival was 10·2 days.

Thus, in terms of either the donor or the recipient, the greater the number of leucocyte antigens not common to both, the shorter the survival period. In addition, on the basis of the differences in survival periods, it appears that when no leucocyte antigens are detected in the donor it may be of less significance than if the antigens are totally absent in the recipient. When the donor possesses leucocyte antigens not possessed by the recipient, it seems as if those in division B are more harmful to survival, regardless of the treatment. No such differentiation was observed in terms of the recipient.

This system of grouping the various antiserum factors does, however, prevent the estimation of the relative importance of a single antiserum or of small groups of anti-

TABLE II. LEUCOCYTE TYPING RESULTS

Donor to recipient differences

No.	Treatment	Human antisera groups 1–5	6–10	11–15	16–21	22–26	PO days survival
1	Control	+	+	+	+	+	17
2	Control	0	0	0	0	0	6
3	Control	+	+	+	0	0	15
4	Control	0	0	0	0	0	11
5	Thalidomide	+	0	0	0	0	12
6	Thalidomide	+	0	0	0	0	6
7	Chloroquine	0	0	+	0	0	15
8	Chloroquine	+	+	+	+	+	5
9	Chloroquine	+	0	0	+	+	8
10	Imuran	0	0	0	0	0	7
11	RNA-ase	0	0	0	0	0	9
12	RNA-ase	0	0	0	0	0	6
13	RNA-ase	0	0	0	0	0	4
14	Goat γ-globulin	+	+	+	+	+	11
15	Kidney-cell fraction	0	0	0	0	0	7
16	Kidney-cell fraction	0	+	+	0	+	6
17	Kidney-cell fraction	+	0	0	0	+	6
18	Kidney-cell fraction	0	+	0	+	+	7
19	Kidney-cell fraction	0	0	0	0	0	8
20	Kidney-cell fraction	0	0	0	+	0	5
21	Cortisone	+	0	0	+	0	5
22	Cortisone	0	+	0	+	0	7
	Average survival	+9/22 (41%) 9·4 days	+7/22 (31·8%) 9·7 days	+6/22 (27·2%) 11·5 days	+8/22 (36·4%) 8·1 days	+7/22 (31·8%) 8·9 days	8·3 days

sera among the 26 types tested. It also makes no allowance for the total number of antigenic differences between specific donor or recipient pairs, or vice versa, in terms of leucocyte antigens.

Tables II and III further elucidate these differences. Table II presents more detailed findings in leucocyte antigen differences in terms of those possessed by the donor, and not by the recipient. As shown in Table II, a similar frequency of antigens was detected in all the groups. The difference varied from 27·2 to 41%. The presence of leucocyte antigens in antisera-groups 16 - 21 or 22 - 26 again were associated with a shorter survival rate when compared with antisera-groups 1 - 5, 6 - 10, or 11 - 15. This suggested that, when the donor possessed leucocyte antigens not present in the recipient (especially those in groups 16 - 26), decreased survival rates were noted irrespective of the various forms of treatment employed.

Comparison of the distribution of leucocyte antigens, seen in the recipient but not in the donor, are shown in Table III. Within the various subgroups of antisera tested, no particular benefit in terms of survival rate could be appreciated when any specific antigen was absent. The frequency of antigens of any subgroup present in the recipient but not in the donor was again similar (41 - 54·5%). There were, however, more leucocyte antigens present in each group. Thus no particular antigen, as tested by a particular antiserum, could be identified as being associated with a poorer graft survival. However, as seen in Tables II and III, in this particular series of animals, the recipients more frequently possessed leucocyte antigens not seen in the donor rather than conversely. Thus, in 20 of the 26 human antisera tested, the recipients possessed solitary leucocyte antigens more frequently than the donors. In only 2 of the antisera tested (numbers 2 and 25) did the donor more frequently possess a leucocyte antigen not seen in the recipient. This difference between donor and recipient in terms of leucocyte antigen specificity is a likely explanation for the differences in survival periods noted when the donor possessed antigens not also seen in the recipient. In other words, the leucocyte antigens were more evenly distributed in the recipients.

Exchange of Renal Grafts

In 5 instances grafts were simultaneously exchanged between donor and recipient pairs, both with and without antirejection treatment (Table I, cases 1 - 4, 10, 16 - 19, 21). Thus the differences in leucocyte antigens between donor and recipient were exchanged in every instance. From 2 to 10 leucocyte antigens were different between donor and recipient. In 3 of the 5 pairs of renal allografts a shorter survival was observed when the recipient possessed leucocyte antigens not present in the donor, irrespective of whether antirejection treatment was given or not. Of the 26 human antisera tested, significant blood leucocytes (antigen serotypes) were: 1, 5, 7, 8, 9, 10, 11, 17, 18, 20, 21 and 25. It is interesting to note that of these 12 antigens, as determined by the various tests, only one (21) was commonly, or more frequently, observed in the 100 animals tested (Figs. 1 and 2). When these antigens were present in the recipient or donor, a shorter survival time was noted.

It is at present unknown how similar or different these various numbered human antisera are, both in terms of antisera prepared by others, and in terms of their own inherent differences.[1,2,5] Antisera from transplanted animals were also retested postoperatively for the possible presence of antibodies against the donor. The results were variable. In three instances no alterations were observed for as long as 18 days after allotransplantation. Further studies on animals surviving for longer periods are in progress. A larger number of transplantations are required before definite conclusions can be reached on the basis of postoperative serological alterations.

TABLE III. LEUCOCYTE TYPING RESULTS

Recipeint to donor differences

No.	*Treatment*	*Human antisera groups* 1–5	6–10	11–15	16–21	22–26	*PO days survival*
1	Control	0	0	0	0	0	17
2	Control	+	+	+	+	+	6
3	Control	0	0	0	0	0	15
4	Control	+	+	+	0	0	11
5	Thalidomide	+	+	+	+	0	12
6	Thalidomide	+	+	0	+	0	6
7	Chloroquine	+	0	+	+	0	15
8	Chloroquine	+	0	+	+	0	5
9	Chloroquine	+	+	+	+	0	8
10	Imuran	+	0	0	+	0	7
11	RNA-ase	0	+	0	+	0	9
12	RNA-ase	+	+	+	+	+	6
13	RNA-ase	+	0	+	+	+	4
14	Goat γ-globulin	0	0	0	0	+	11
15	Kidney-cell fraction	0	0	0	0	0	7
16	Kidney-cell fraction	+	0	0	0	+	6
17	Kidney-cell fraction	0	+	+	0	+	6
18	Kidney-cell fraction	0	0	0	0	0	7
19	Kidney-cell fraction	0	+	0	+	+	8
20	Kidney-cell fraction	0	+	+	0	+	5
21	Cortisone	0	0	0	0	0	5
22	Cortisone	+	+	+	+	+	7
	Average survival	12/22 (54·5%) 7·8 days	11/22 (50%) 7·6 days	11/22 (50%) 7·7 days	12/22 (51·5%) 7·8 days	9/22 (41%) 6·6 days	8·4 days

Human and Baboon Leucocyte Antigens

Blood was obtained for testing from a baboon (P-13) who was compatible in terms of human ABO and MN blood-groups with an anephric human awaiting renal allotransplantation. The leucocyte antigens tested in the manner of Van Rood and associates[5] gave the results shown in Table IV. The patient possessed 1 leucocyte antigenic

TABLE IV. COMPARISON OF HUMAN AND BABOON LEUCOCYTE ANTIGENS

	*Human antisera types**											
	4a	*4b*	*5a*	*5b*	*6a*	*6b*	*7a*	*7b*	*7c*	*7d*	*8a*	*9a*
Patient	−	+++	++	++	++	++	−	++	++	−	+	−
Baboon P-13	+	++	+	++	++	+	+	++	−	+	−	−

*After Van Rood *et al.*[5]

group (7c), not seen in the animal. Conversely the animal possessed 2 known leucocyte antigens (7a and 7d) not seen in the human. These results were interpreted as showing a good tissue match.[3,4] Another baboon (Q-19) with similar erythrocyte and leucocyte antigenic groups was used in a modified third-man test.[1] Skin from the patient and P-13 were grafted onto Q-19 and an autograft of Q-19 was performed as a control. All grafts were viable for several days. No treatment was given. The animal was killed on the 15th day after skin grafting. Serial blood specimens obtained before and after grafting showed no increase in total complement titre. No heterohaemolysins or humoral antibodies were detected, while these can be observed within this time period in untreated baboon renal allografts.[6] Histological examination of the human skin graft showed a dense mononuclear infiltration with many eosinophils underlying the dermis. A similar infiltrate, but less marked, was seen underlying the dermis of the baboon skin graft from P-13, but no such reaction was observed in the autograft. The observed infiltrate is similar to that described in baboon renal allografts and human heterografts, and is associated with the rejection process.[6] Thus, although similarity may be observed between human and baboon leucocytes, rejection will still occur without therapy. Other animal species, in addition to man, have been tested and found to possess similar leucocyte antigenic groups.[2] In fact, common human erythrocyte antigens have also been demonstrated in cell cultures of rhesus monkey kidneys.[8] These results notwithstanding, further characterization of heterospecific antigens must be completed before grafts between man and other primates can be safely attempted.

These findings confirm the previous observation that skin grafts may be more difficult to match immunologically than kidney or tumour allografts.[9]

Organ-Specificity Studies

The 20 preserved kidneys, stored for 24 hours with constantly circulated perfusate, gave no reactions when tested against the 26 human antiserum types. The perfusate also gave no reaction when tested against the antisera. These results indicate that the antigens present in baboon leucocytes, as tested by the antisera, are not freely elutable in the baboon kidney. As would be expected, similar antigens, when present in the organs, are fixed to the tissue and not attached in a more soluble fashion.[3,4]

Homogenates of fresh baboon organs were tested, as in the manner recently described in human studies.[4] The material reacted only with the 4a antiserum of Van Rood[5] as judged by absorption studies. Similar studies performed with the baboon leucocytes against the battery of 26 human antisera[3,4] produced weak-positive reactions with antisera 11, 16 and 25. Freeze-dried preparations were made of the organs of the animal after death.[3,4] When these were tested against the battery of human antisera in the same manner as the leucocytes[3,4] the renal tissue from the same animal was found to react against the same antisera (numbers 11, 16 and 25).

This baboon renal tissue reacts against the battery of human antisera in a manner similar to baboon leucocytes. Multiple tests with other organs prepared in a similar fashion are in progress. The present results, however, suggest that tissue typing of baboon organs, such as the kidney, may be feasible with the presently available human antisera.

DISCUSSION

The present report describes the frequency of occurrence of baboon leucocyte antigens as tested with 26 human leucocyte antisera and the alterations in survival rate of baboon renal allografts matched for compatibility in terms of human ABO erythrocyte groups, but differing in various leucocyte antigens. These antigens were detected in baboon leucocytes tested against a battery of 26 human antisera prepared from pregnant human donors.[3,4] The results have been interpreted to show that, regardless of the absence or presence of antirejection treatment, the greater the number of differences in leucocyte groups between donor and recipient, the shorter the survival periods. This observation further assists in current experimental attempts to characterize the significant determinants of renal antigenicity in the Chacma baboon.

These results also adequately demonstrate that certain erythrocyte and leucocyte antigens are shared by both baboon and man (Tables I - IV). This similarity has provided us with a non-human renal transplant model whose reactions are applicable to current clinical transplant problems.[3,4]

The frequency distribution of the various leucocyte antigens has been determined on 100 baboons, and will be helpful in further histocompatibility testing in this and other projects.

There are 3 or 4 major groups of antigens as tested with the 26 antisera. This population distribution, observed in a large number of animals, is similar in some respects to human population studies.[3-5] However, the present antisera have yet to be further characterized in terms of those isolated by other investigators.[1,2,5]

A marked difference in the distribution of different leucocyte antigens was noted in more recipients than donors in this experimental group (Tables II and III).

When renal grafts were simultaneously exchanged between donor and recipient, 12 of the 26 human leucocyte types tested appeared to have a deleterious effect on graft survival period.

Skin tests between human and baboon kidney donors (Table IV) have confirmed that, although good erythrocyte

and leucocyte matching can be achieved, histological evidence of rejection is still observed. Further studies on primate xenografts are currently in progress and may further characterize the important antigenic differences.

In the present studies attempts were also made to relate the observed leucocyte agglutinating antigens to other antigens in the kidney and other organs. The studies indicate that organ specific antigens fixed to renal tissue cannot be eluted. On the other hand, the results obtained with organ homogenates in humans,[4] and in the present studies, indicate that the leucocyte agglutinating antigen testing is in part relatable to other organ antigenic responses. Thus, this method of leucocyte agglutination is a true test of tissue compatibility. Further refinement in antigen-antiserum responses will therefore greatly assist organ transplantation.

SUMMARY

Renal allografts were exchanged between adult male and female baboons, both with and without antirejection treatment. In 5 pairs of animals renal grafts were simultaneously exchanged between donor and recipient. A total of 22 renal allografts were completed and matched in terms of their major human ABO erythrocyte blood-groups. All were dead within 3 weeks after allotransplantation.

Before transplantation, the animals were tested for the presence of leucocyte antigens against a battery of 26 human antiserum types.

Differences between donor and recipient leucocyte antigens were identified and related to the observed graft survival periods. Twelve of the 26 leucocyte antigenic types least commonly found in baboons, were more frequently associated with shortened graft survival.

The greater the number of differences in leucocyte antigens between donor and recipients, the shorter the graft survival, irrespective of whether immunosuppressive treatment was employed or not.

Further tests in over 100 baboons have confirmed that this species shares leucocyte antigens with humans. The frequency distribution of these results is described. There are 3 or 4 commonly-occurring leucocyte antigen reactions as observed with the battery of 26 human antisera tested.

Skin grafts, as part of a modified third-man test between an anephric human and two baboons, all well matched in terms of erythrocyte and leucocyte antigens, were performed. Serological and histological tests demonstrated the similarity in the rejection process between man and baboon.

Organ perfusion studies of preserved kidneys demonstrated that renal antigens, similar to those detected in baboon leucocytes, are not elutable. Homogenates of baboon kidney reacted with similar antisera as the leucocytes and thus demonstrated that the antigens as tested are similar. Leucocyte antigenic responses may thus be true tissue-typing criteria.

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