

DISCUSSION

DR. DAVID M. HUME (Richmond): It seems to me that it may be worth while to continue doing some experiments with heterografting in man, although I must say I was among those who thought it was pretty foolish at the start, because it did not seem likely that it was going to work clinically, and, of course, it still has not proved itself in this regard.

Nonetheless, there are some types of grafts which will have to come from a source other than man himself, and the heterograft, if it works, may provide this source.

I think Dr. Reemtsma and his group have done a careful study of renal heterografting in man and this is something which it might be well for them to continue doing. I do not think it is anything that can achieve general acceptance at the moment, even experimentally.

We did one chimpanzee transplant in man some time ago, and ran into one difficulty which I rise to mention at the present time: The patient had not been as well prepared for surgery as some of our subsequent or previous patients. He was still rather wet. He had 4+ ankle edema, 3,000 to 4,000 cc. of ascitic fluid, bilateral moist rales, and an extremely puffy face.

We transplanted him from a 130-pound chimp, using both kidneys, which probably we should not have done. The total kidney mass was greater than a single human kidney, about 340 Gm. The kidneys functioned at once. They began to produce urine extremely vigorously and put out 54,000 cc. in the first 24 hours.

This posed a massive problem in fluid-electrolyte balance. We began by holding back and giving the patient only half as much fluid intake as he put out, even though we fell far behind within a matter of six hours. The patient who had been extremely edematous, as I have described, lost all of his ankle edema completely. He lost all of his ascites, and his face, which had been swollen, became sunken, and by the next morning he was dehydrated. His sodium and potassium were extremely hard to manage. Chimps take a diet which is high in potassium, and they have kidneys which handle it much more easily than man. His potassium fell to 2.0 mEq./L, and we had to give him something like 600 mEq. of potassium to keep up.

The patient suffered a stroke the following morning, and lived for about three days, at which time he had a coronary and died.

There are some severe problems with this type of graft, apart from the immunological ones, and I certainly do not believe it is anything that should be widely applied to patients at this time. We do not plan any more in the future, but we will plan to watch Dr. Reemtsma carefully.

DR. T. E. STARZL (Denver): Dr. Waddell regrets being unable to attend this meeting, but

he asked me to speak of the six baboon heterografts which were done in Denver after considerable helpful guidance from the New Orleans group and in active collaboration with Dr. Claude Hitchcock of Minneapolis.

One of the basic objectives in this study was to compare the behavior of the baboon heterograft with that of the chimpanzee, because the baboon is far more plentiful, there being about 500 for every chimp, and far less expensive, the cost of a baboon being only about \$250.00.

Good renal excretion was obtained from all six heterografts. However, cross-comparison with Dr. Reemtsma's data suggests that the baboon does not provide as good immediate or sustained function as the chimpanzee. The pathologic specimens from our cases have been submitted to a referee. Dr. Reemtsma has submitted some of his autopsy material to the same referee, and it would appear that the pathologic changes in the baboon are also more severe than with the chimp.

The six patients who we operated upon were turned down for standard homotransplantation for various medical contra-indications. Four of the six patients are dead. Two of them are still living, but only by virtue of a secondarily performed homotransplantation, and it is of interest that the homografts functioned well despite the prior presence of the heterografts much like the experience which has been described with serial homografts.

(Slide) The first slide shows one of the heterografts. This one showed a very aggressive cellular reaction after about 25 days, although the heterograft had grossly not seemed to be severely damaged.

(Slide) The next slide shows a heterograft which was removed after 49 days, and this is the type of pathologic finding which characterized all of the other five. One can see the many infarcted areas on the surface of the kidney, and also the swollen appearance of these organs.

Because of our experience with this group, it is our opinion that baboon heterografts cannot work on a long-term basis at the present time. The results we have obtained are less encouraging in terms of function and pathologic tissue injury than have been found in Dr. Reemtsma's chimpanzees. We have, therefore, abandoned the use of the baboon heterografts.

DR. WILLARD E. GOODWIN (Los Angeles): At UCLA in Dr. Longmire's department we have been interested in heterotransplantation of the kidney for several years. However, we thought that it was a study for the laboratory up till now. We have done dog to sheep, sheep to dog, dog to monkey, human to dog three times, human to monkey once, monkey to monkey of a different species and human to chimpanzee transplants. All of these have been rejected, usually with an accelerated pattern. In the dog to sheep and

sheep to dog it happened while we were still watching it. The monkey to monkey of a different species was the most promising. This kidney survived for two months.

Human to chimpanzee heterotransplantation which we have done only once lasted a week, and the animal died probably not of rejection, but rejection was taking place in the kidney.

We have the greatest admiration for experiments of this sort and for the work that has been done and is being done in New Orleans and Denver. I would like to say that it may be that the most important observation that comes out of this is that transplanted kidney from a primate to man is capable of clearing vast quantities of fluid and acting as a crutch to the future in acute situations. Maybe this would be a cheaper and more appropriate way of handling this situation than an artificial kidney when you are dealing with a given limited time period in which you expect the patient to recover.

DR. KEITH REEMTSMA (Closing): I should like to acknowledge with gratitude the help we have received from the Boston, Richmond and Denver groups, particularly in the area of immunosuppression.

The other members of our group join me in expressing our appreciation to the Dean of our medical school, Dr. Charles C. Sprague, and to the director of anesthesiology at Charity Hospital, Dr. John Adriani, a member of this association. They have supported our work strongly from the outset.

Finally, I wish to thank the American Surgical Association for the privilege of presenting this work. Historically the field of heterotransplantation has garnered a rather unsavory reputation because of outright abuses and extravagant claims. The inclusion of this report on the program of the Association will aid immeasurably in restoring heterotransplantation to the position which we believe it deserves: an appropriate field for scientific investigation.