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AMS RELEASE
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SAN FRANCISCO...What may prove to be a milestone on the road to ultimate control of transplant rejection was described here Monday by a Tulane School of Medicine surgeon at a meeting of transplantation specialists from throughout the world.

Speaking at an afternoon session of the Fourth International Congress of the Transplantation Society at the San Francisco Hilton, Dr. John C. McDonald revealed the discovery of a new system involved in kidney transplant rejection.

It is believed to be involved in most "acute" transplant rejections. This type of rejection represents an estimated 90 per cent of all rejections which lead to early failure of transplant.

The discovery by Dr. McDonald and his team of kidney transplant specialists at the Tulane Medical Center and Charity Hospital in New Orleans makes it possible for an earlier diagnosis of acute rejection.

The team, in research still going on, hopes now to be able to pinpoint the specific antigen responsible in organs before they are transplanted and thus avoid this type of rejection.

The McDonald team at the Tulane department of surgery has labeled its find the HTA system. Two other systems have been identified previously. One is the ABO blood group system; the other is known as the HLA system.

The HLA system previously had been thought largely responsible for unsolved rejection problems.

The HTA system involves the action of antibodies transmitted in blood;

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therefore rejection due to this system is what is known as a humoral process. In the HLA (Human Lymphocyte Antigen) system, the rejection process usually occurs through cell contact and therefore is primarily a cellular process.

For years,Dr. McDonald pointed out, it was believed that immunity to the HLA system was responsible for acute rejection. Thus, tissue matching for HLA would solve the problem.

Unfortunately, he said, "it has become clear that matching for HLA has not solved the problem in a large percentage of cases. Consequently, a number of people have become caught up with the idea that other systems are involved."

The first clue to a break in this scientific mystery came when the Tulane scientists studied several patients who had undergone acute rejection. They observed a consistent rise in the "titer", or strength of response, in a test to determine presence of the rejection antibody in blood taken from patients. In the test, serum from the patient is tested against rat red cells.

In the next study the researchers applied the same test to a selected group of patients following transplantation and noted that 15 of 16 with acute rejection showed a significant response while fluid from 20 of 28 who had no rejection showed no response.

It was during this phase of the research that the Tulane group also discovered that a rise in titer, or response, might also be caused by bacteria in certain infections previously suffered by the patient.

In a follow-up study of 40 patients with infections known as gram-negative infections, this finding was confirmed.

"We learned," Dr. McDonald explained, "that half these patients had the same type of immune response as patients undergoing rejection."

The team then noted that it was possible by observation to determine if the response in the serum test was being caused by infection or rejection in most instances.

At this stage the McDonald tests strongly indicated there was something going on in acute rejection, as shown by the serum tests, which had not been indicated through lymphocyte antigen matching tests, or the HLA system, and which was not due to infection.

Subsequent laboratory tests of serum from transplant patients against rat red cells and sheep cells showed the presence of antigens in human kidneys which were reacting with antibodies in patients' blood. Studies of 70 patients confirmed this relationship.

The picture which emerged, after further tests, was of antigens found in some human kidneys which produce an immune reaction, or rejection, when the kidney is introduced into a transplant patient sensitive to this antigen. This reaction shows up in the blood of the patient.

Dr. McDonald named this antigen the HT (Heterophile Transplantation) antigen and the system through which it is recognized the HTA system.

(Heterophile systems are antibody systems which react with antigens of diverse sources. This action stimulated by human tissues reacts with rat tissues, therefore the designation heterophile).

"We have also proved," Dr. McDonald stated, "that these antigens are not related to others which cause rejection. And we have shown that these HT antigens are not present in all kidneys and should act as a determinant of compatibility, i.e., whether or not the new kidney will take.

"The problem remaining," he continued, "is that we don't have a good technique to recognize the presence of HT antigens prior to transplant.

"To make the system useful in improving clinical results is to be able to predict the reaction beforehand."

However, the new system is proving useful in early recognition of acute rejection so it can be treated with immunosuppressive drugs.

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"For years we were convinced, " Dr. McDonald concluded, "that the HLA system was the major system involved in kidney transplant rejection. Now we believe that the HLA system is usually involved in hyperacute rejection, which occurs in the first or second day after transplant, and chronic rejection, which occurs weeks and months later.

"We believe that our research shows the HTA system is involved in the vast majority of acute rejection, which begins sometime between the third and fourth day following transplant and fifth or sixth week.

"The important thing is that we have recognized the system."