An Overview on Organ Transplantation

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Preconditions for Organ Transplantation

What are the conditions required for organ transplantation? First, it must be surgically possible to transfer the organ in its entirety from the body of one person to another. Second, a critical factor (and the one that even today causes the most problems) is rejection of the transplanted organ by the recipient. Third, and no less important, is the location of a suitable organ from a live or deceased donor in a state that will allow it to be transplanted. I emphasize, *in a state that will allow it to be transplanted*, for this point has given rise to much ethical debate and discussion. Organs obtained for transplant can be unsuitable for various reasons and can harm the patient receiving them.

Historical Background

In the Middle Ages the possibility of organ transplantation was considered, and evidence for it exists particularly in Christian texts which describe attempts by various monks to exchange organs. A famous illustration from the fifteenth century shows a patient undergoing "transplantation" of a leg in which decomposition has spread. But real organ transplantation began in 1902, when Karl, a French surgeon working in the United States, demonstrated a technique for connecting blood vessels. This represented the first basis for modern transplantation.

In 1936 a first attempt was made by Varonoy, a Russian surgeon, to transplant a kidney in a person dying of kidney failure. The transplant held for thirty-six hours, after which time the patient died. The concept of rejection was as yet unknown, as were other problems with which we are familiar today. It is important to note the breakthrough by Sir Peter Midber, who was the first to note the process of first and second set rejection, introducing the study and understanding of organ rejection.

In 1951 Kuss, a French surgeon, was the first to describe the

place where the kidney is transplanted, and in 1954 David Hume overcame the problem of rejection by transplanting a kidney between identical twins in Boston. Hume performed another nine kidney transplants, each of which were successful for a number of months. The patients' bodies eventually rejected the foreign kidneys and consequently the patients died. Although steroids were already in use, Hume considered them to be of no benefit in these transplants.

In 1959 Hamburge, at the Keer Hospital in Paris, applied total body radiation to patients to prevent organ rejection. Indeed, following his transplantation of a kidney his patients functioned very well as long as he kept them in total isolation. As soon as the patients were taken out of isolation, they contracted infections.

The first real move towards clinical transplantation took place in 1962 when Professor Tom Starzl began transplanting organs with the help of immunosuppressive agents using a method similar to that which we use today. In 1966 the HLA (Human Leukocyte Antigen) system was discovered, assisting in the determination of organ compatibility. In 1980 a new breakthrough was achieved by Borel, a Swiss researcher from the Sandoz company, who developed Cyclosporin A, a new immunosuppressive substance which is still widely used.

Dangers of Organ Transplants

What dangers are associated with organ transplants? First, there can be a technical failure with the connection of the actual organ. Whether it be obstruction of the veins or arteries or whether it involve connection of a kidney and ureter, there are problems related both to the surgical technique and to rejection of the transplanted organ.

Regularly transplanted organs can be divided into two types. The first type consists of organs which have no mechanical replacement, such as the liver or the heart. If transplant fails, a repeat transplant is immediately required. This poses a very serious problem as there is no "dialysis" for a liver or heart. Therefore, if someone undergoes a heart or liver transplant and the organ does not function, a new transplant is immediately required. Hence for every transplant of this type, one must plan for another heart or liver which may be required for a repeat transplant.

Transplantation of organs which do have mechanical replace-

ment, for example kidneys, is easier for if the new kidney is rejected, the possibility exists of returning to dialysis.

A second problem in organ transplantation is the risk of serious infections which attack patients receiving immunosupp- ressive treatment. The most important issue today is the selection of compatible organs which will not be damaged as a result of being removed from the donor's body. There are cases of serious infection following transplant, a phenomenon which occurs principally in patients receiving immunosuppressive therapy. Such infection is most likely to attack those patients who receive damaged organs with strong immunosuppressive treatment to suppress rejection.

A kidney removed from the body too long after death may be damaged and will not function following transplantation.

Which organs are transplanted today? Clinical transplants of the following have been carried out for many years: kidneys (since 1962), liver (since 1963), heart and lungs (1968), and pancreas and intestines in recent years. I have not mentioned skin transplants or corneal transplants since these do not require connection of blood vessels.

Kidney Transplants and Trade in Organs

Kidney transplants are routinely carried out almost worldwide. The kidney may come from a living relative, a live donor who is not related, or from a dead donor.

Let us concentrate on the second category: a live donor who is not related. Since he is not related to the recipient of the organ, such a donor is comparable to a dead donor. Owing to the shortage of organs, organ trade is flourishing, and it is well known that kidneys may be bought from live donors not related to the patient. People from all over the world travel to India to buy kidneys and even undergo the transplants there. Organ trade also exists in Egypt.

There are well-founded rumors from South America concerning the kidnapping of children, particularly from the poorer sectors. These children disappear, supposedly taken to resorts for treatment and support, but it is believed that their organs are removed and sold. With evidence of such worldwide trade, we are particularly careful in Israel. However we do treat Israeli patients who have undergone organ transplantation in India, particularly

kidney transplants, and who come back to us for continued treatment following the operation.

A review of the results of kidney transplants shows that there is 90% success during the first year for kidneys from live relatives, and 75% success during the first year from dead donors. Currently there are approximately one hundred kidney transplants carried out each year in Israel, with the demand reaching around two hundred and fifty. The organ-demand curve in recent years has been rising exponentially while the supply of organs has remained constant, giving rise to various phenomena which are entirely unethical.

Liver Transplants

In 1963 Prof. Starzl carried out the first liver transplant in Denver, Colorado. Thereafter he, with very few others (one surgeon in South Africa, and Prof. Kilna in Cambridge, for instance), continued transplanting livers. Since then, progress in surgical procedure has solved a number of problems which were encountered. In a liver transplant several blood vessels have to be connected as well as the bile ducts. There are also problems associated with the size-compatibility of the organ, particularly when an adult's liver is transplanted into a child.

In the event of definitive rejection of the organ which cannot be suppressed by immunosuppressive treatment, a new organ must immediately be transplanted, and any available source is approached for this purpose since without a liver the patient will die.

Owing to the shortage of organs from dead donors, attempts are being made to use live donors – a relative of the patient, most often parents to children – and to remove just a portion of the liver. In the case of dead donors, the liver is divided into two in order that one organ can be used for two patients, even though this is a much more complicated procedure and involves more danger to the recipients.

Liver transplants are carried out only in large medical centers, unlike kidney transplants which are much simpler and are routinely performed in most hospitals.

Cyclosporin A and Heart Transplants

Until 1980 transplants, especially of kidneys, were mostly taken for granted despite the fact that the success rate for transplantation of the heart, liver, pancreas and other organs was not high. The turning point occurred with the discovery of Cyclosporin A, a more potent immunosuppressive substance, which was put into use in 1980. Since then transplant results have dramatically improved.

Heart transplants began in 1968. This first was carried out in South Africa by Christiaan Barnard, although there are those who insist that the way was prepared for him by the laboratory work of Dr. Kantrowitz in California. In any event, many others subsequently attempted heart transplants, but owing to the high rate of failure, enthusiasm waned considerably. For a time few centers made further attempts at heart transplants until Cyclosporin came into use in the 1980's. Since then heart transplants have become routine and are carried out in many medical centers.

As mentioned, the problem with heart transplantation is that if we fail to control rejection using immunosuppressives, a repeat transplant needs to be immediately carried out.

Today life expectancy of a year after a heart transplant is about 50%-60%.

Lung Transplants

A lung transplant is required in the case of chronic lung failure. The number of patients requiring such a procedure is constantly rising. The transplant is complicated since the lung is very sensitive, and hence the failure rate is high. There are only a few medical centers in the world where lung transplants are carried out. At first the practice was to transplant the heart and lung as one unit, but today sufficient experience exists for the transplan- tation of a lung alone to be performed.

Pancreas Transplants

Pancreas transplants, too, are becoming increasingly common. The indication for a pancreas transplant is severe diabetes, especially juvenile diabetes, which affects the kidneys. (Hence some patients undergo transplant of both kidney and pancreas.) The organ can come from a dead donor or from a live relative. Experiments have been carried out at the University of Minnesota,

where a good procedure has been developed for transplantation of a portion of the pancreas from a living relative.

Some fairly serious technical problems continue to complicate the connection of the transplanted portion of the pancreas into the body of the recipient. The pancreas must also be connected to the bladder, into which its secretions must flow.

During the 1980's the revolution of Cyclosporin affected pancreas transplants, as well as other organs, and the number of transplants started rising exponentially as did the life expectancy figures for the organs transplanted. This improvement was due not only to the introduction of Cyclosporin, but also to the increased skill of the surgeons. With a growing number of such operations their experience in pancreas transplants increased, and the results improved accordingly.

Intestine Transplants

The transplant of intestines is also an important development. There are many patients whose intestines cease to function as a result of arterial or other damage. Such patients live permanently on intravenous nutrition, and we are therefore looking for ways to transplant intestines. This operation is still very complicated, the results are not yet satisfactory, and there are only a small number of centers which perform the procedure. Intestine transplantation can be said to be still in its experimental stages.

Life Expectancy and Future Aspirations

With regard to life expectancy at the end of the first year and after five years following transplantation, we see the best results from kidney transplants from live relative donors. Even after five years the results in these patients are excellent. Results of kidney transplants from dead donors are also excellent after a year, and after five years the survival figure remains higher than 75%. Liver transplants also yield excellent results today: five years following the operation the recipient's life-expectancy is the same as that of the transplanted organ, except for rare cases where repeat transplants are required. The success rate stands above 50%.

The figures for heart transplants are even better. In recent years we have also seen a considerable improvement in transplantation of heart and lungs, although the five-year prognosis is not as good as that of the first year. Here the results refer to the number

of transplanted organs which continue to function after one year and after five years. All in all the results are excellent signaling a positive forecast for future transplants.

One of the factors that will help to advance the success of transplants is the intensified fight against rejection using immunosuppressives. New substances are continuously being sought, and a long list of substances are being studied. 506FK, 61443RS, Refermicin and Cytocasein are among those being investigated today for their possible toxic effects, in order to ascertain whether they improve results.

Another important area, of course, is that of encouraging organ donation, which remains very cautious and slow both here in Israel and elsewhere.

A further possibility for advancing transplants is xenografting (gathering organs from animals). Professor Starzl has carried out some experiments, including some involving hearts. These experiments have yet to show signs of success, but there are those who attach considerable hope to them.

Attempts are today being made to increase the use of organs from live donors. Kidneys, liver, pancreas and large intestine are taken from live donors, relatives who are prepared to donate part of their organs to a loved one, most often parents to children or between siblings.

I have attempted to summarize the current situation of organ transplants. We hope that in the future, with the further development of immunosuppressive substances, and with increased support in the area of organ donation, we shall continue to progress.

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