1 Introduction

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This is the first of a series of five articles in which the whole field of organ transplantation is reviewed.

THE TRANSPLANTATION of tissues and organs is a new thing. In the Middle Ages, Fra Angelico painted a triptych showing St. Damien transplanting the leg of a black man onto a white man. The implication that such a transplant was unlikely to be successful without divine intervention did not deter him.

However, transplantation surgery was practised in India many years before the birth of Christ, where a sect of Brahmins, the Pootahs, had a flourishing trade in skin grafting, and had even elaborated the pedicle skin flap. In those days the punishment for adultery was to cut off the nose of the offender, so there was a thriving trade in nasal reconstruction using such a pedicle skin flap. Certainly the Pootahs knew that skin exchanged between unrelated donor and recipient was unlikely to be successful.

The techniques of the Indians were probably brought to Europe by traders, for in the 16th century, Tagliacozzi in Northern Italy was practising the art of the Pootahs with great success. Although he passed on his art, there was obviously place for fraud, and it was not long before the Church condemned all transplant surgery as fraudulent and interfering with the work of God. It lay condemned for two centuries until in the late 1700s some scattered observations started to be made.

John Hunter’s Interest

Thus, we have John Hunter interested in transplanting teeth, and others reporting the re-epithelialization of varicose ulcers by anointing them with scrapings of callouses. There were odd mixtures of fact, fancy, half-truth, and superstition in which the Renaissance observations of skin transfer between unrelated donor and recipient were soon forgotten. Tagliacozzi had written in 1597:

The singular character of the individual, entirely dissuades us from attempting this work on another person. For such is the force and power of individuality, that if any one should believe that he could accelerate and increase the beauty of union, nay more, achieve even the last part of the operation, we considered him plainly superstitions and badly grounded in physical sciences.

The early 19th century saw the first skin transplants of a more modern era, with sheepskin being transferred successfully from one part of a sheep to another part of the same sheep. This was followed in 1823 by the first recorded free skin graft when a part of patient’s nose was reconstructed using her own skin, but even in the first half of the 19th century it was often impossible to find out from the written accounts whether the surgeon was using skin from the patient’s own body or from another body—what we now call an allograft. Consequently, it is impossible to place much reliance on some of the successes recorded in these early accounts but tissue transplantation had arrived.

Early Corneal Transplants

Although the first successful series of corneal transplantations in man were not fully documented until 40 years ago, in fact the first successful corneal transplant was probably performed on a pet gazelle by Bigger in 1835. The biological significance of these and many other transplant operations were not fully appreciated until Bert, in 1878, showed that transplants of skin between unrelated animals (skin allografts) were not successful. He also did some research on the vascularization of these grafts but the significance of the corneal allograft remained hidden. Here was a successful allograft but it was only successful as long as it was not vascularized.

Meanwhile, the transplantation of tissues was a thriving practice in which the names of Reverdin and Thiersch (skin transplantation) and Oliver (bone transplantation) stand out spectacularly. Surgeons learned the hard way that disease, including tuberculosis and syphilis, could be transmitted with the graft. They learned that the host’s rejection of an allograft could sometimes be modified by freezing the graft. They learned that a bone transplant could die and still be successful; and this sort of observation confused the issue because if ignored the body’s ability to heal despite the transplant rather than because of it.

Thus we have Fenwick at the turn of this century using a sheep’s urethra to replace a human urethra. Then, two years later, there is the well-known case of the Honary Graft extraordinary’ record by Winston Churchill, in which a piece of his forearm skin was used to recover a ‘horrible gash’ on one of the troopers engaged in the Sudan War. Churchill, writing in 1930 recorded that the skin remained there ‘to this day’ but the body of scientific opinion even by 1930 was firm in its belief that such a graft was unlikely to succeed. It is probable that Churchill’s piece of skin died and was replaced by the trooper’s own skin, though the use of such an allograft as a temporary cover for the skin defect could certainly be defended.
Types of Transplants

As the subject of transplantation was investigated more fully, it became apparent that one of the critical factors concerned in the success or failure of a transplant was the relationship between the donor and recipient.

Thus tissues exchanged between identical twins usually behave in the same way as tissues transplanted from one part of an individual to another part of the same individual. Such tissues exchanged between identical twins are termed isografts. At the other end of the scale are tissues transplanted from non-identical members of the same species (sometimes called homografts). Transplants from one species to another (for example, from monkey to man) are called xenografts or heterografts. The allotransplant is almost invariably rejected by the recipient in about 10 to 14 days. While the xenograft is rejected more quickly, sometimes within hours.

The Body's Reaction

At a very early age the infant's body has learned to recognize 'self' from 'non-self'. This is part of the basic defence mechanisms of the body, and as a result of this immunological memory, the human body can react to many of the usual childhood infections, overcome them and, what is more important, learn by experience how to deal with that particular illness again. The body has reacted to 'non-self' and learned to recognize and reject it. Hence second attacks of certain diseases are rare.

The body reacts to a tissue transplant in a similar manner, for the allotransplant appears to function perfectly for a few days. The skin allotransplant initially takes, the kidney puts out urine, the bone transplant produces new bone, but during this period blood is circulating through the transplant and the blood's lymphocytes are helping the recipient's body to recognize a tissue which is different. The result of this information is that certain sites of the body produce antibodies. These build up in larger concentrations and as they recirculate through the transplant they react with the foreign tissue and cause an inflammatory reaction in the blood vessels of the transplant which thrombose. Rejection of the transplant through ischaemia then follows.

Rejection

This usually occurs about 10 days after transplantation; the skin transplant becomes purple and necrotic, the kidney puts out gradually less urine, becomes tender and swollen and dusky, the bone transplant's new bone shrivels up and dies. This process is called rejection.

There are, however, gradations of this rejection which will be considered in more detail later, but suffice it to mention two in passing.

First, it has been known for some time that skin transplants from one human to another, or between brothers and sisters, often take much longer to reject than unrelated allotransplants. At the other end of the scale is the condition of hyperacute rejection. If a recipient receives a second transplant from the same donor who gave the first transplant, then the second transplant is rejected very quickly by the recipient whose body has recognized the foreign proteins which it has met before. A second transplant from a different donor will usually be treated just as the first transplant.

If, therefore, transplantation is to be successful, the recipient's reaction to the transplant must be modified. The extent of this modification of the recipient's defence mechanisms will partly depend on the degree to which donor and recipient are matched; but there are many other factors in selecting donors which must be considered as these can pose technical and ethical questions which may be insurmountable.

There are, therefore, two main groups of problems to be overcome if organ transplantation is to be successful.

Demand Exceeds Supply

There is at the moment a far greater demand for organ replacement than can be met by the available supply. This problem can be overcome to some extent by collaboration between hospitals. This means that both kidneys from a cadaver may be used by different hospitals, and more compatible tissue matching can be used. There are problems here, though, in that the donor and recipient of an organ transplant may be in different hospitals.

Surgical Problems

The surgical problems are concerned with safe and speedy removal of organs, and their rapid cooling to a temperature at which they will not be irreparably damaged. Following this any surgical anastomosis must combine speed with meticulous technique as the immunosuppressed patient is not able to deal with minor leakages which would not trouble the normal patient.

Biological Problems

1. Immunological: Any treatment of the recipient which enables him to accept an organ transplant will usually weaken his resistance to foreign substances. The transplant patient is, therefore, particularly susceptible to infection and can easily develop septicaemia.

2. Non-immunological: These problems concern the transplant's functional ability despite interruption of its nerve supply or blood supply.

Cardiac transplants may respond differently to exercise than the normal heart. Large blood vessels leaving cardiac or lung transplants may not be able to change their calibre in response to normal physiological demands if their nerve supply has been damaged. The technique of suturing may produce a fixed calibre to blood vessel or bronchus which need to expand and contract.

(Courtesy Nursing Times)

Next: Kidney Transplantation -1

The Donor