

ACHIEVEMENTS IN ORGAN TRANSPLANTATION. WHY MEDICINE HAS CHANGED AND HOW

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Continuous success in transplantation have revolutionized the practice of medicine. This burgeoning success has acted upon both society and medicine itself.

Why has there been such an impact on medicine? Up to now, transplantation techniques have been expensive. Relatively few lives, probably less than 100,000 have been actually saved.

A CHANGE IN PHILOSOPHY

The reason is that transplantation has made possible a fundamental philosophic departure in the way that health care is delivered. Until 50 or 60 years ago, practitioners of medicine observed and presided over lethal diseases, powerless to provide much more than a priestly function. This began to change with increasingly specific drugs such as antibiotics, but for most organ specific chronic disorders, a rear guard strategy was all that could be offered. Patients with failing kidneys, livers or hearts could be treated with diet, medicines, or with operations which often were illogically designed. Suddenly, with the advent of transplantation, it became possible for the first time in human history to provide exactly what was needed: a completely new organ.

But immunosuppression was too poor to apply this thrilling concept widely until the 1980's. Then, with the introduction of cyclosporine, it became obvious that a great escape hatch had not only been formed but that future judgement in the care of organ specific diseases would have to be in the new perspective of possible eventual organ replacement. Nowhere was this more clear than in liver disease in which mutilating operations in the portal hilum such as portacaval shunts were virtually abandoned overnight since they jeopardized eventual candidacy for liver transplantation. Similar examples with renal and cardiac disease easily could be cited.

ADMINISTRATIVE AND EDUCATIONAL CHANGES

In addition, transplantation has forced a change in the way that medicine has been taught and organized.

The breadth and depth of expertise required to be at the State of the Art, much less progressive, in transplantation, have gone beyond the grasp of single individuals. Interdisciplinary teams have been formed within medical schools and hospitals that have cut across classical departmental and divisional lines. These new alliances have changed the face not only of practice but of research and have had wide-ranging influence on the development of other special fields.

RESEARCH POTENTIAL

A special note should be made about the extraordinary influence of transplantation on both basic and clinical research. Modern immunology has been in partnership with, not sponsorship of, transplantation. Our understanding of autoimmune diseases, and the appropriate treatment of these disorders owes much to observations after transplantation, an undertaking that first creates and then attempts to control the autoimmune disease known as rejection.

Thus, transplantation became the Pandora's box of 20th century science.

WHY AN IMPACT ON SOCIETY?

It is obvious that there is no more intimate human contact than with transplantation in which the objective is to transfer living tissue under the most perfect possible conditions. The corollary is that diseases including cancer, can be transplanted in the process. Most recently, AIDS carriers have been found in every major transplant program in which screening of the postoperative recipient population has been carried out systematically. Many of these patients already had been infected before transplantation in the course of their original illness by blood transfusions and other factors. A few obtained the AIDS virus from infected donors before donor testing was available. In almost half, the time and circumstances of infection never could be determined. The conclusion is clear, as it was with hepatitis, that precautions are crucial to prevent the transplant centers from being disease reser-

voirs from which other patients as well as health care personnel can be infected.

HOW SOCIETY HAS CHANGED

The impact has been seen everywhere; in the law, in government, in philosophy, and in the perception of ethics. The leaders of all of the world's great religions have had to consider the implications of transplantation in their beliefs.

The new issues began to emerge 25 years ago. Before then transplantation was not a practical therapeutic option. In 1962 and 1963, using the drug combination of azathioprine and prednisone, 'apparently' healthy recipients of kidneys began to emerge from clinics in increasing numbers.

In a meeting convened in London in 1965 to consider what the early successes in renal transplantation truly meant, many topics including living donation, human experimentation and brain death were discussed.

The Nuremberg code and the Helsinki declaration of 1964 were used as the frame work to judge what had already been done in transplantation and what might be considered next. The Helsinki declaration distinguished between non-therapeutic research designed solely for the objective of acquiring information as opposed to the use of unproven therapy in which the subjects who bore the risks were the same as those who stood to benefit.

Transplantation was a classical example of therapeutic investigation. The risks and benefits of so-called innovative procedures could be weighed without equivocation for the first recipients of kidneys, livers, hearts, and other organs.

Although stones could be thrown, there were no solid hits. What was done in transplantation in those days was sometimes foolish, but it was never ignoble.

In later times, there has been a tendency to construct formal and sometimes elaborate "human experiments" comparing different kinds of therapy. I once heard it seriously proposed that bonafide candidates for liver or heart transplantation should be randomized into those receiving therapy vs. untreated controls. I describe such suggestions as randomized "trialomania". This was a fair criticism. However, "trialomania" can present with

more subtle symptoms, such as insistence upon carrying on randomized trials before learning how to use new therapeutic tools. There is no better way to discredit promising new developments.

Even worse than premature randomization is randomization after the fact. For a randomized clinical trial to be carried out ethically, the necessary starting point is a null hypothesis of no treatment difference. A question that physicians must ask before assigning patients to a randomized trial is whether they would allow therapy to be decided by lot for themselves or their family members if they suffered from the same disease.

THE SIMPLE PAST

It is easier for me to talk about the past than to face the future. The work we did was once so simple. That has all changed. What was a crusade when it was not a reliable way of treatment became a business when it turned successful. The magical days were gone, not overnight but over a quarter of a century. This may have been just as well since victories easily won are lightly held.

I do not really have a grand vision of that happened in the last 25 years, only details. I can see a thousand air strips rolled into one, days turned into nights, flashing lights, mournful sirens, pale faces drained of hope in donor hospitals, faces grown beautiful with restored vitality and visions of the future in the transplant centers. Someone once told me that the greatest gift of God was to see something of yourself, if only once, in the face of another human being. Those working in transplantation have known this experience in the best of times and this experiences has made bearable the worst of times.

I have always been proud to be a surgeon. Sixty years ago another surgeon wrote. "To give courage to those who need it, to restore the desire for life to those who have abandoned it with our skill to heal disease or check its course, this is our great privilege. Ours are not the concerns of ordinary life. We who... are doomed to go in company with pain and fear and bloodshed have a higher mission than other men, and it is for us to see that we are not unworthy"⁽¹⁾.

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