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Ethical Problems in Organ Transplantation

A Clinician's Point of View

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IT COULD BE CONCLUDED from the existence of this colloquium and from others like it in the recent past that there is a tide of dissatisfaction against the way in which medicine has developed in the twentieth century. Articulate critics can be found, both within and outside the profession, who find fault with the rapidity, or alternatively the sluggishness, with which new knowledge of potential therapeutic values has been applied. Still others have deplored the way in which the transition has been made from animal experimentation to human trial. It has been suggested that an

immutable philosophical, moral, and ethical code be defined within the limits of which scientific advances could be exploited effectively and humanely in man.

It seems to me that the most vexing and profound questions with which we will ultimately be confronted are those concerning measures that could control both the numbers and the genetic constitution of great masses of people in a deliberate effort to improve the quality and the comfort of the human race. Fortunately, it is not my responsibility today to discuss these matters beyond drawing attention to the distinction between the noble aims of these society-oriented programs and the humbler but by no means ignoble objectives of the vast majority of practicing physicians and surgeons whose efforts sometimes seem almost to be in the opposite direction.

It is doubtful if many doctors who actually care for the sick and the infirm plan their actions on the basis of the predicted effect upon society. Instead, the dominant tradition is for the physician to provide the best care of which he is capable for those who either seek his services or are assigned to his responsibility; by and large this is done without regard for the conceivably broader issue of whether treatment is justifiable on social grounds. His reasons may include pride, altruism, compassion, curiosity, a spirit of competition, even avarice, or a combination of all these things. Whatever the motives, the reflexes that follow are sure and respond similarly to the needs of the productive members of the

community, the insane and feeble-minded, children with incurable birth defects, condemned criminals, or even soldiers who moments before were members of a hostile army.

The foregoing viewpoint is a narrow one, but there is no reason to believe that it should be abandoned in the face of advancing technocracy. It has shielded the ill from the caprices and the moral judgments of other men through centuries of evolving philosophical, religious, and legal doctrines. It has placed the concept of the sanctity of human life on a practical foundation, since the responsibility of one person for another could not be more clearly defined than through the doctor-patient relationship, irrespective of the reasons for the contract entered into between the two involved parties.

Has this ancient creed of medicine been ravaged by the scientific explosion in which we are now involved? Examination of this question as it applies to organ transplantation is inevitable, first, because of the widespread lay publicity that has accompanied such efforts and, second, because the harsh term "purely experimental" has consistently been applied to these procedures by virtually all workers in the field as well as by interested observers.

The designation of *experimental* is perfectly correct. Few endeavors have ever yielded such a rich and diversified harvest of both fundamental and practical information, have so united basic and clinical scientists in the pursuit of a common goal, and have defined and stimulated such large areas of potentially fruitful new research. Nevertheless, the primary purpose in these human cases was therapeutic, and it is important to realize that this objective has been met to a degree that may not be generally appreciated.

Excluding identical twins, four of the first six patients treated with renal homo-transplantation at our institutions are well 4 to 4½ years later. Half of the recipients

who were operated upon 1 to 4½ years ago are still alive. In these older cases, survival to date is 62% (44 of 71), 31.4% (11 of 35), and 22.2% (2 of 9) for those who received their kidneys from familial donors, non-related volunteers, and cadavers, respectively.

During the time when these cases were being accumulated, it was hoped that the results could be improved by the acquisition of increased experience, by adjustments in the timing and doses of immunosuppressive drugs, and by attempts to identify biologically suitable donors in advance of operation by tissue typing. This objective was met only to a minor degree. It appeared that an impasse had been reached beyond which further reductions in mortality and morbidity could not be expected without new immunosuppressive techniques.

This conclusion raised two related new issues that are relevant to the general topic of this symposium. The first concerned the advisability of continuing to provide a "standard" form of therapy that carried a high and by now relatively predictable failure rate. The corollary question was whether new, clinically untried, and potentially dangerous immunosuppressive measures should be incorporated in the therapeutic regimen for fresh cases. The gain might be a substantial improvement in patient care. The loss in the event of unexpected complications could be the injury or death of patients who might otherwise have had an untroubled postoperative convalescence had it been realized in advance that they were unusually favorable candidates.

Eventually, a change in therapy was instituted with the addition of a heterologous antilymphocyte serum derivative to reduced doses of the commonly used immunosuppressive agents. The first patient was treated with adjuvant antilymphocyte globulin in June 1966, and 19 more patients were so treated up to mid-December. Only one

death has occurred, that resulting from an operative accident. Now, after 4 to 10 postoperative months, survival is 95%. Since the predominant mortality after transplantation has always been in the early postoperative months and inasmuch as the first eight consecutive cases have already been followed for 9 to 10 months without evidence of late homograft deterioration, it seems likely that 90% or more of these patients will live at least through the first year.

I refer to the foregoing statistics and to similarly encouraging results from other centers with some fear of seeming to use them to justify the means by which they were obtained. This is not my purpose, a position I can make most clear by alluding to eight consecutive attempts at orthotopic or auxiliary homotransplantation of the liver made at the University of Colorado; all eight patients died within 5 weeks.

Instead, the growing field of transplantation can be used to illustrate some principles to which most involved investigators have adhered. First, the clinical trial of new therapeutic methods is based more firmly than ever on prior animal experimentation. Virtually all practices in cardiac as well as in transplantation surgery have been transferred, almost without change, from the laboratory to the clinical ward or operating room.

Not infrequently the transition has been made with haste and with an air of urgency that, the generous may concede, was fed by the needs and wishes of desperate patients who had the misfortune of not becoming ill at a later and more convenient time. Historically, the decisions to proceed have often been wrong. Nevertheless, they have almost invariably been based on the hope, however fleeting or erroneously conceived, of potential benefit to the individual patient.

Right or wrong, the actions are eventually subjected to implacable scrutiny, principally by other members of the scientific community but also by intelligent and in-

formed outsiders. Inaccuracies in reporting, claims that cannot be reproduced, and procedures that neither relieve suffering nor prolong life are rapidly identified. Harmful practices are snuffed out quickly; homeopathic ones may suffer a lingering death, but they also ultimately disappear from the scene. The system is ruthless and without pity and demands a policy of non-concealment from those who would innovate in medicine. It is not sufficient to report only successes. Failures must also be fully documented, no matter how painful and humiliating these may be, in order to prevent repetition by others of the same mistakes. In general, such openness has characterized efforts in the field of transplantation.

Until now I have discussed some problems of transplantation only as they apply to the recipients of potentially life-sustaining organs. The thoughtful trial of a variety of therapeutic variables, in which the risk of adverse effects was borne by the persons who had the most to gain, seems highly defensible in both prospect and retrospect. The involvement in such ventures of persons who may be harmed or who do not stand to derive any direct benefit is not such a simple matter. This practice, as epitomized by the testing of new drugs or procedures in human volunteers, is defined in the Helsinki Declaration (1964) as "clinical research, the essential object of which is purely scientific and without therapeutic value to the person subjected to the research." It adds that the subject must "be in such a mental, physical, and legal state as to be able to exercise fully his power of choice." Since the propriety or even the legality of such experimentation has been questioned, it may now be well to examine, in this context, the problem of organ donation.

No easy answers are available. When intrafamilial homotransplantation is performed under the proper circumstances, it cannot be reasonably said that there is no

value to the donor, who the first to suggest this poingness may be based on which the fullness of his involved with and depends the recipient or because other acceptable reasons; the objective is never the scientific data. Progress confronts him with a decision difficult but (as Prof. D. Dau it (1)) "is consonant with responsibility of free life."

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value to the donor, who usually has been the first to suggest this possibility. His willingness may be based on the extent to which the fullness of his inner life is involved with and dependent upon that of the recipient or because of a variety of other acceptable reasons; to my knowledge, the objective is never the acquisition of scientific data. Progress in medicine confronts him with a decision that may be difficult but (as Prof. D. Daube has expressed it (1)) "is consonant with the dignity and responsibility of free life."

Quite another situation exists, of course, with the reluctant donor who by arbitration has been selected by the family on the basis of his or her presumed expendability. It is ordinarily not difficult to detect this kind of coercion, particularly if the trouble is taken to make the appropriate specific inquiries. The potential victim is excused from further work-up on the grounds of some medical diagnosis that will protect him from guilt feelings and from the ostracism of those who were so anxious to volunteer his services.

In a recent symposium on ethics in medical progress (1), the above-cited matter of free choice as it affected all kinds of clinical investigation became one of the dominant themes of the conference. The ability of minors, prisoners, and even medical students to "fully exercise their power of choice" was seriously questioned and discussed at some length since transplantation donors had already been used from the first two of these classes of "captive" populations.

The transplantations from minors had been done in other institutions under exceptionally favorable psychological and medical circumstances involving identical twins. Nevertheless, it was challenged that these accidents of birth should have set the well twins apart, in the eyes of the law, from other minors who would automatically have been disqualified.

The penal volunteers had been accepted

in our Colorado hospitals under conditions that it was thought would fully insure the protection of their individual rights and permit their complete freedom of choice, objectives that in principle may have been less realistic than with the identical twin minors. In any event, there is every reason to believe that this practice, however equitably handled in a local situation, would inevitably lead to abuse if accepted as a reasonable precedent and applied broadly. For these reasons, and because the donor motivation that characterizes proper intrafamilial transplantation could not be said to exist except in the most idealized and universal sense, the acceptance of criminal volunteers was permanently discontinued at the University of Colorado 1½ years ago.

I have dwelt at some length on the question of organ procurement from living volunteers because it is perhaps the most sensitive and limiting issue in clinical transplantation. Today, the best prognosis can be offered to the recipient only with the use of such donors, particularly when these are from within the family. In the future it is hoped that the need for living donors will be made obsolete by improvements in immunosuppression, antigen typing, and tissue preservation. Then, organs obtained solely from cadavers could be used with a high expectation of long-term survival.

Unfortunately, success will not imply that an ethical panacea will have been found, primarily because the terminal events in a prospective cadaveric donor are of such importance in determining the quality of a subsequently transplanted organ. It is conceivable that this fact could lead to subtle or even major adjustments in care that would be designed for the protection of the organ to be removed rather than for the benefit of its donor.

Examples can be cited. In several centers outside the United States conventional death has been redefined, in some cases in the presence of a continuing heart beat, in

terms of objective evidence of irreversible injury to the central nervous system. The judgment that death was imminent and unavoidable was made by a panel of expert referees who were not members of the transplantation team, although the need for their mediation was clearly the consequence of the requirement for fresh and uninjured organs. One or both kidneys were then removed from these "living cadavers," with apparent benefit to the recipients; the incidence of immediate urine excretion was very high. That a high degree of social conscience dictated these actions is beyond dispute. What could be questioned is the concept of imposing further trauma upon a dying patient, however apparently hopeless his condition, at a moment when he is the epitome of mental incompetence. The act itself could be construed as an erosion of the historic medical creed of responsibility to the individual patient to which I referred in my opening remarks, at least as this applies to the donor, and the timing as a violation of the principle of free choice mentioned later.

In the course of this discussion perhaps

I have emphasized unduly certain details of the selection and management of homograft recipients or their donors, but this has been only to illustrate some problems of day-to-day ethics that apply in principle to other forms of clinical investigation and in fact to traditional medical practice. No effort has been made to say that errors have not been made in the development of clinical transplantation nor to imply that new mistakes can be completely prevented from this day forward. I have, however, suggested that progress in this and other new fields of medicine has been made in a sturdy framework that is ethical, practical, and efficiently policed. I do not believe that the traditional responsibility of the physician for the welfare of his patient has been, or that it should be, lessened by the emergence of new forms of therapy that of necessity must at some time be tried for the first time in man.

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