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## *How Medicine Has Impacted in Non-Medical Areas*

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I realized when I came here that this is predominantly an audience of non-physicians, so I thought maybe it might be more appropriate to talk about how medicine has impacted in non-medical areas. This may be especially important here because this is a liberal arts school. Some, and possibly much of what I say will be of direct interest to people who are not working in the field of medicine or even in science. There is a tremendous interface of interest between science and the humanities. What happens in medicine greatly influences practices in the humanistic specialties.

The role of modern medicine in society has been amplified by its almost unbelievable successes. The talks of this morning have emphasized how foreshortened is the history of science. Joe Holmes, whose name was mentioned as the father of ultra-sonography, worked at the University of Colorado. He also was one of the first people in the United States who realized the practical application of artificial kidneys. It was my good fortune 20 years ago to go to a university where a man like this was at work. You will be interested to know that Dr. Holmes is still extremely active. He would take immense pleasure in knowing, as Dr. Miller has told us, that there is a possibility that ultrasound techniques eventually may be found to be more discriminating and more valuable than the classical CAT scan (Computerized Axial Tomography).

The beginnings of other developments are also recent, and occurred under my eyes. I had the great pleasure a number of years ago, to go to the University of Minnesota to review the exciting developments there in cardiac surgery. I can only contrast what I saw there with the very modest statement made today by Dr. Warden that he played a minor role in the development of that program. Dr. Warden was the main person from whom Drs. Henry Bahnson, Merrill Brown, myself, and others from Johns Hopkins went to learn. Herb, I am sure that you remember our visit in 1953.

What I would like to do now is to tell you about developments in another field, transplantation, and to focus on how these developments

have influenced how we think in law, religion, philosophy and many other areas not excluding government. These events also have occurred in a relatively short time. Prior to 1960, it was thought that transplantation of any organ, including the kidney, but also including the heart and liver, was a biological impossibility. This pessimism was based on research in small animal models in which it was observed that rejection, once started and despite efforts at therapy, moved on to the destruction of the graft. The idea was ingrained that rejection was one of biology's most inexorable and strongest reactions. I remember reading an extremely pessimistic article in the *New England Journal of Medicine* in 1959 by Burnett, the Nobel laureate from Australia, assessing the prospects of successful transplantation as a fundamental impossibility.

Within 36 months of the appearance of that article, it became possible in our first series of kidney transplants, to reverse rejection, using relatively simple methods, and then later to observe in these patients a long term survival. Some of those first patients are still alive almost 20 years later. It was possible to later reduce the amount of immunosuppressive medication that the patients needed and so, in increasing numbers, the recipients returned to society. They came from the hospital wards, to be productive people who could go to restaurants, have babies, finish college, and even to go back into the practice of medicine, nursing or other areas in which they had systematic exposure to infectious diseases as they cared for other sick people. We realized at the outset that there were marvelous possibilities for a revolution in medicine.

The techniques that were developed with renal transplantations were applied directly with the transplantations of all organs. It is inconceivable that development of new immuno-repressive programs could really be done with the heart, liver, and lungs. Even today, the kidney transplants continue to be the model for which progress is based for transplantation of all other organs.

By 1963, successes in renal transplantation were being generated in Denver, Boston (at the Peter Bent Brigham Hospital) and the Medical College of Virginia where the late Dave Hume worked. There was little public understanding of what actually had been achieved. Early in 1964, there appeared an editorial in the "*Annals of Internal Medicine*" written by the editor of that august journal, Dr. J. Russell Elkinton, condemning these attempts at what he considered human experimentation.

I don't even remember the title of the article except that in it was contained the flash word "cannibalization," as well as references to possible violations of ethical codes. Dr. Elkinton was an extremely fine man who, I believe, almost immediately realized the potential harm that the editorial could do. He solicited responses from various people, including myself. These were published but by this time, the editorial was already out of date. It had become clear that a new chapter was at hand in medicine and in the treatment of end-stage renal disease. The ethical questions of transplantation were not thereby brushed away.

Seminars and meetings came as a result, of which I believe the most important was at the Ciba Foundation in London in 1965. It was a very

small meeting. There were only 25 members. Most were non-physicians. The U.S. medical contingent included Dr. Joseph Murray from Boston, George Schreiner of Washington, D.C. and myself. There were representatives from law, such as Lord High Justice Kilbrandon, who was the British counterpart of our Supreme Court Chief Justice. Other really interesting participants included David Daube, Regis Professor of Law at Oxford, who had spent and survived 4 years in a German concentration camp; the nephrologist, Professor Herbert de Wordener who had lived out a similar period of incarceration, and the surgeon Sir Michael Woodruff who had commanded a battalion of men imprisoned by the Japanese during the second World War. These last 3 men had a deep and abiding interest in the protection of human rights, which in their specific cases had been so totally violated.

The mere fact that transplantation had become a technological success didn't mitigate the somber tone of the meeting. Amongst other things considered was the appropriateness of donation of organs. In the early and mid 1960's, because of the legal and social situation at that time, the most convenient and usually the only donors for patients, were from within the family. The legal basis was examined of a process in which a completely healthy, but well motivated person, was physically assaulted by the removal of an organ which was used to save the life of another person. On the surface, it was a perfectly satisfactory chain of events in the context of Judeo-Christian theology being comparable, I suppose, to leaping into a lake to pull someone out who is drowning. But there were many concerns about the conditions under which these donations were taking place.

The legal basis for donation went back inevitably to a 1954 Massachusetts court ruling which had permitted an identical twin transplantation. With identical twins, there is no biological barrier and no rejection. It is a matter of transferring tissue from one person to another, doing a technically adequate job, and then having the organ function. The opinion of the judge reflected the probability that identical twins were so close, emotionally as well as in every other way, that the loss of a kidney by the donor would be less devastating in the holistic sense, than would be the loss of his identical twin. The same reasoning in subsequent court cases has been upheld and extended to other renal donations by parents to their offspring and so on down the list. It would take a great stretch of the imagination to extend this concept to transplantation from other living donors, as for example, using donors who were convicts.

I have been in the field long enough to have seen many examples of donor abuse, especially within families. The result could be the family power structure focusing on a donor within their midst on the basis of his or her presumed expendability in the eyes of the rest of the family. A mentally retarded person would often be singled out. I saw examples in which refusal of donation brought ostracism within the family, or alternatively a reluctant sacrifice being offered to someone for whom there was very little affection.

In connection with possible coercion, another issue went right straight back to the original Boston case of identical twins. The question was whether anyone could be a true volunteer if they don't have full possession of their civil rights. The original Boston twin donor was a minor, and subsequently, identical twins donors as young as 11 years of age have been used. Such donors must answer to their parents and thus are captive. The same captive concept applies to convicts, who could be induced by emoluments or other favors to step forward to give a kidney even though they have lost their full civil rights. To me, the concept of living donation remains a troubling one. Although I was one of the first to use that expediency, I have not, for a number of years, been willing to operate on well people in order to treat sick people.

Obtaining organs from dead people is the alternative solution. At the Ciba meeting in 1965, there surfaced for the first time from European centers, the concept of brain death, in which organs were removed from "heart-beating" cadavers. At first, the idea was appalling, at least to me, because I could envision an accident victim whose therapy would be jeopardized by virtue of his or her candidacy to be a donor.

The practice of cadaveric donation under these circumstances had been already in place in Belgium for some time. Subsequently I realized that with the collaboration of the neurosurgeons, neurologists and other specialists the chances of a brain-dead donor being properly cared for were actually greatly increased by virtue of the redefinition of death in accordance with brain function rather than by the old conventional criteria of cessation of heartbeat and respiration. Under the previous circumstances, when somebody with a serious brain injury was brought to an emergency room, it was often obligatory to try to make a decision on the spot whether the patient could survive. A negative decision precluded resuscitation. Under the new definitions of brain-death and their wide acceptance in the western world, all such patients have a fair trial at resuscitation. Then, in an orderly way, it can be determined whether they are merely heart/lung preparations or if they have some prospect of having brain function restored. The quality of care and the discriminate application of such care to terribly damaged people with central nervous system injury, was improved by the highly responsible actions of neurologists and neurosurgeons throughout the world.

In the meanwhile, to make all this legal, there was a subtle but definite change in the laws whereby state by state, and now involving all states, "brain death" is the definition of death, and not the cessation of respiration and heartbeat. If as I stood here, I had a heart attack and fell to the ground, there wouldn't be a doctor in the audience who would consider me dead even if my heart had stopped. Efforts would be made to resuscitate me. If this accident occurred while I was having a tonsilectomy, and my surgeon was incapable or untrained in resuscitation, he could be sued for not knowing what to do. Irreversible brain damage is now the definition of death and properly so.

People interested in these issues should examine and read carefully the basic documents upon which we must base our practices. These are

the Nuremberg Code, which is only six or seven pages long, and its predecessor the Helsinki Declaration which is only one page in length and simply stated. These documents divide what is human experimentation into two categories: One, the type of advanced therapy that can be, if it is successful, of direct and immediate benefit to the person who submits himself for care, and Two, the kind of human investigation which might benefit mankind, but which will not directly benefit the person upon whom experimentation is done. Those are important documents in everyone's surgical conscience which can easily be lost sight of if there is excessive zeal to obtain scientific information about human beings.

As we look at the Nuremberg Code and the Helsinki Declaration, it is important to realize that in caring for critically ill patients, pure experiments can sometimes not be done. At a recent American Surgical Association meeting, a paper was presented by a South African Surgeon describing a "controlled randomized trial" assessing how bleeding from vessels in the lower esophagus can be effectively controlled by a series of techniques. Bleeding could be stopped by a simple injection technique at the rate of 95%. In the discussion a group from one of the major U.S. universities talked about a similar randomized control study in which as a first step, they placed an instrument down the esophagus where they could see the bleeding coming across in spurts to the opposite wall. In spite of the fact that they knew that they could control the hemorrhaging immediately in 95% of the cases, they then went to a drawer, pulled a card, or in essence flipped a coin, to see whether they should do that now proven form of therapy, or take the instrument of salvation out and embark on a less effective plan of treatment.

I cannot simply understand that kind of a trial and yet, in all major universities, I am sad to say, even including the one where I now work, this practice is almost a reflex. We have to examine those practices because I do think they constitute a potential violation of those very documents upon which we base our medical practice.

Earlier today, we heard from Dr. Warden of the high cost of exploiting bona fide advances in medicine, with particular reference to coronary artery surgery. The same applies in the treatment of end stage renal disease in which there is, perhaps the best example, ever, of excessive costs. In 1973 there was passed a rider on the Social Security law which may have been the most noble act of medical legislation yet put into place. It socialized a disease since it paid for the care of all people with end-stage renal disease providing they had a Social Security number. Until then, the problems of keeping someone alive with end-stage renal disease were staggering. One couldn't obtain dialysis because it was too expensive. Transplantation was the only alternative but it was not widely available. Families bankrupted themselves in desperate efforts to keep one of their members alive.

With the passage of the 1973 law, it became not only feasible to put patients on end-stage renal disease programs, but in many parts of the country there developed competition for that Federal money which has grown to a total this year of \$2 billion. The bill in 1984 is projected to

be \$4 billion. I have sometimes been ashamed to see physicians or surgeons who are paid from this reservoir driving their custom made Mercedes Benz. That is not really why we are supposed to be here.

There is another bad side of the syndrome of excessive money which contributes to the fixation of therapeutic practices at an unsatisfactory level. I have seen violent resistance to change by members of end stage renal disease groups because change is going to affect the way the business is transacted. People who are not in medicine can do something about this.

I promised at the beginning not to talk about medicine, and yet what I have said has everything to do with medicine, its practice, and its responsibilities. In my field, as we look ahead and view the prospects of transplanting all major organs successfully, the ethical and other issues I touched on will become all the more pressing. There have been major recent developments in transplantation which will move this form of therapy from its present unreliable state onto a new plane. There is a new drug available now which is so powerful that it permits the chronic survival of kidney grafts at a near perfect rate. It is being applied to the transplantation of other organs. The drug is a fungus extract called cyclosporin A. It is being tested at the University of Pittsburgh.

One of the tragedies of life always has been that young people must die or suffer because of the malfunction or failure of a single organ but with all other organs viable and functioning. It is an electrifying thought to realize how effectively these patients will be treated in the years ahead. I think that the 1980's will be the time when transplantation, which didn't fully flower in spite of its marvelous promise in the early 1960's, will come to maturity. It will then have to come to terms with its own destiny in all of the other ways than its own successful technology.