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The Changing Mores of Biomedical Research
A Colloquium on Ethical Dilemmas from Medical Advances

The Changing Mores of Biomedical Research

A Colloquium on Ethical Dilemmas from Medical Advances

Held at the Forty-eighth Annual Session of the American College of Physicians, San Francisco, April 12, 1967

Panelists

HON. WARREN E. BURGER, LL.D.
SIR PETER MEDAWAR, D.SC.
THOMAS E. STARZL, M.D., F.A.C.S.
DAVID KRECH, PH.D.
JOSHUA LEDERBERG, PH.D.
SAMUEL E. STUMPF, PH.D.

Challengers

CHAUNCEY D. LEAKE, PH.D.
RENÉ DUBOS, SC.D., M.D.

Co-chairmen

IRVING S. WRIGHT, M.D., F.A.C.P.
WALSH MCDERMOTT, M.D., F.A.C.P.

Editor

J. RUSSELL ELKINTON, M.D., F.A.C.P.

ANNALS OF INTERNAL MEDICINE
Vol. 67—September 1967 SUPPLEMENT 7 No. 3—Part II

The panelists: STARZL, MEDAWAR, LEDERBERG, KRECH, BURGER, STUMPF.

Editor and challengers: ELKINTON, LEAKE, DUBOS.

Opening Comments*

WALSH MCDERMOTT, M.D., F.A.C.P., *Co-chairman*

WHEN THE NEEDS of society come in head-on conflict with the rights of an individual, someone has to play God. We can avoid this responsibility so long as the power to decide the particular case-in-point is clearly vested in someone else, for example, a duly elected governmental official. But in clinical investigation, the power to determine this issue of "the individual versus society" is clearly vested in the physician. Both the power itself and, above all, *our awareness that we are wielding it* are increasing every day and can be expected to increase much further. It is this inescapable *awareness* that we are wielding power that has us so deeply troubled, for we are a generation nurtured on the slogan "the end does not justify the means" in matters concerning the individual and his society. Yet as a society we enforce the social good over the individual good across a whole spectrum of nonmedical activities every day, and many of these activities ultimately affect the health or the life of an individual.

Traditionally in our Judeo-Christian culture we have handled this issue by one of two mechanisms. When, as in our racial problem, for example, the conflict contains no built-in contradiction, we publicly and officially subscribe to a set of ideals. We can work privately and publicly toward the attainment of these ideals, and with their attainment would come the solution of the problem. This mechanism works when the forces in conflict are intrinsically reconcilable even though the reconciliation might take many decades or a century. But we use another mechanism when the conflict is head on, when the group interest and the individual interest are basically irreconcilable.

In circumstances like these, such as the decision to impose capital punishment or the selection of only a minority of our young men to become soldiers, the issue is decided by a judgment that is arbitrary as it affects the individual. In short, we play God. When we take away an individual's life or liberty by one of these arbitrary judgments we try to depersonalize the process by spreading responsibility for the decision throughout a framework of legal

* At the Colloquium the co-chairman elected to open by proceeding directly to the interchanges between the panel and the challengers and omitted the prepared introductory statement now presented here.

institutions. Thus, it is usually a jury, not a judge, that determines the death penalty; a local draft board, not a bureaucrat, that decides who goes to Vietnam. This second type of mechanism works only because there is widespread public acceptance that society has rights too and that it is preferable that the power to enforce these rights over the rights of the individual be institutionalized.

I submit that the core of this ethical issue as it arises in clinical investigation lies in this second category—the one wherein, to ensure the rights of society, an arbitrary judgment must be made against an individual.

This is not to say that all ethical problems in clinical investigation fall into the irreconcilable category. On the contrary, in numerical terms most of them probably do not.

Without question, a considerable portion of the lapses in fully protecting individual rights in clinical investigation can be avoided by more careful and open attention to the subject and by our ingenuity in developing new practices to attain some of the same old ends. This will prove quite costly in financial terms, but what is being accomplished in this way is very much to the good and is to be strongly encouraged. But there remains that hard core of the problem: the kind of situation in which it clearly seems to be in the best interests of society that the information be obtained. It can be obtained only from studies on certain already unlucky individuals, and no convincing case can be made that they can expect much in the way of benefits except those accruing to them as members of society.

Clearly there are three questions here: [1] From where does society get its rights or interest that makes it imperative to perform biomedical studies on an individual?; [2] how is the individual subject selected?; and [3] how are the social priorities decided?

The social priorities are easy; any small group of certified medical statesmen can settle them in an afternoon. As we all know, however, it is the other two questions that are so thorny.

Without too deep reflection it seems to me that society's actually having a right here is a relatively new phenomenon that is chiefly derived from the demonstration that knowledge gained by studies in a few humans can show us how to operate programs of great practical benefit to the group. Until the late nineteenth century, as I understand it, most human experimentation expanded knowledge but did not increase the power to control disease. The physicians of that day thus had no problem in maintaining the double ethical charge still preserved in the Helsinki Declaration: to "safeguard the health of the people," on the one hand, and to make the health of "my patient" the first consideration, on the other hand. But starting, I suppose, with the yellow fever studies in Havana, we have seen large social payoffs from certain experiments in humans, and there is no reason to doubt that the process could continue. It is by this demonstration, analogous to the great "invention of invention" of Newton's era, that medicine has given to society the case for its rights in the continuation of clinical investigation. Once this demonstration was made, we could no longer maintain, in strict honesty, that in the study of disease the interests of the individual are invariably paramount.

Yet we are temperamentally incapable of leaving it at that. Our reflex action here is to try to imitate what we do when the same conflict arises in irreconcilable form elsewhere in our society. That is to say, we are willing to concede that some judgments must be arbitrary, but we attempt to clothe them with institutional forms so that at least the judgments are not made solely by one person. We will play God, but we would like to do it by group effort.

I am deeply convinced that such efforts provide no real solution because our culture has not yet faced up to the irreconcilable nature of the conflict at the heart of this particular issue. And until it does so, there exists no recognized consenus or article in the "social contract," if you will, to provide that base on which any law or regulation must rest if it is to be viable.

Conventional juridical procedures including the traditional jury system are too slow to fit the urgent nature of many clinical decisions. Any peer group committee we might set up, let us say from law, theology, and medicine, would have credentials that are obviously suspect. It has been chosen neither by the society nor by the individual whose conflicting rights are to be arbitrated; more importantly, it lacks that widespread social consensus that supports trial by jury or your local draft board. Therefore, such a peer committee cannot, in fact, dilute and hence dissipate the ethical responsibility of the clinical investigator although it may give the superficial image of doing so. Thus, by the terms of our culture, as may be seen in the Declaration of Helsinki, no matter who the investigator takes into partnership when he acts, he acts alone.

What can we do to solve this agonizing dilemma? Obviously we cannot convene a constitutional convention of the Judeo-Christian culture and add a few amendments to it. Yet, in a figurative sense, until we can do something very much like that, I believe deeply that the problem, at its roots, is unsolvable and that we must continue to live with it.

To be sure, by careful attention we can cut down the number of instances in which the problem presents itself to us in its starkest form. But there is no escape from the fact that, if the future good of society is to be served, there will be times when the clinical investigator must make an arbitrary judgment with respect to an individual. The necessity for such arbitrary judgments has had *tacit* social recognition and approval for some time. Because the approval *was* tacit, however, there was an imbalance of actions and words, in effect, a hypocrisy, that marvelous human invention by which we are enabled to adapt to problems judged to be not yet ripe for solution. By this hypocrisy society had its future medical interests fully protected. At the same time the attitude could be maintained that in medical matters, *as contrasted with those in many other walks of life,* the sole public interest was in the inviolability of the individual.

Now, most unfortunately, these essentially harmless hypocrisies of our culture have been codified. For both the Helsinki Declaration and the new Food and Drug Administration regulations handed down this week are honest reflections of our culture complete with all its hypocrisies. As such, if they were followed to the letter, they would produce the curious situation in which the only stated public interest is that of the individual. The future interest of society and its sometime conflict with the interest of the individual, in effect, are ignored. I believe it has been most unwise to try to extend the principle of "a government of laws and not men" into areas of such great ethical subtlety as clinical investigation.

When in our cultural evolution it has not yet been possible to develop an institutional framework for a particular kind of arbitrary decision that may affect an individual, there is only one basis on which to proceed, and that is on the basis of trust. My position may sound paternalistic, as indeed it is. Making arbitrary decisions concerning an individual in conflicts as yet unsolved by our society is one of the major responsibilities of a parent.

Society may not have given us a clear blueprint for clinical investigation, but it has long given us immense trust to handle moral dilemmas of other sorts, including many in which, in effect, we have to play God. Thus, the moral dilemma of clinical

investigation is not something new; what is new about the problem is its rapid increase in size. This rapid increase in size is no help to us now, but it may hasten the day, still far off, when in medical investigations we can institutionalize this making of arbitrary decisions between an individual and his society.

In the meantime we can do no more than carry on under the mantle of the trust we now possess. To continue to receive that trust we must be ever conscious that the issue of the individual vis-à-vis society is always *there*, and we can try our best to create an environment of awareness of it on our clinical services. For once a moral dilemma has become clearly recognized; whenever each person *acts* within that dilemma, his act can be seen for what it is, and the extent to which he has seemed to act with acceptable propriety can be judged.

But the hard core of our moral dilemma will not yield to the approaches of "Declarations" or "Regulations": for as things stand today such statements must completely ignore the fact that society, too, has rights in human experimentation. Somehow, somewhere, in this question of human experimentation, as in so many other aspects of our society, we will have to learn how to institutionalize "playing God" while still maintaining the key elements of a free society.

* * *

Let us now start our consideration of the views set forth by our panelists with challenges from Drs. Leake and Dubos. Dr. Leake.

Technical Triumphs and Moral Muddles

CHAUNCEY D. LEAKE, PH.D.

IT WOULD BE presumptious of me to "challenge" the statements made by any of the distinguished participants in this important symposium on the ethical aspects of experimental studies on human subjects, arranged so well by my long-time friend Dr. Irving Wright. It is less aggressive and more relaxing to venture "comments" in amplification of what has been said so well.

Frequent now are discussions of the moral problems confronting us as a result of our amazing technical achievements. From the awful consequences of nuclear weaponry to the details of human experimentation, we are seeking vigorously to find ways of resolving the ethical confusion that so deeply troubles us. To our chagrin we are discovering that there are no comfortable absolutes on which to rely in our moral dilemma but rather that responsible choices have to be made by each of us as individuals as to an appropriate ethic or way of conduct in the ever-shifting confrontation with the realities of our tension-filled lives.

Recently I commented (1) on opinions already expressed by Drs. Joshua Lederberg (2) and Russell Elkinton (3) on the moral problems raised by organ transplantation and by Dr. Belding Scribner (4) on hemodialysis. At that time I collaborated with Dr. Thomas Starzl (5) in trying to analyze some aspects of these ethical matters. By then many newsmen and popular writers, such as Victor Cohn of the *Minneapolis Tribune,* Milton Silverman of the *Saturday Evening Post,* and Albert Rosenfeld and Shana Alexander of *Life,* were doing their best to call public attention to the moral problems caused by biomedical advances and were emphasizing that it is the responsibility of all people to aid in their solution.

A notable and recently published Ciba Foundation Symposium entitled *Ethics in Medical Progress* (6) has explored these ethical difficulties in depth. The problems are international. They involve people everywhere, as implied by the Helsinki Declaration of 1964 of the World Medical Association (see Appendix IV). The total human responsibility was previously emphasized by the Nuremberg Code of 1947 (see Appendix III). The specific responsibilities of members of the health profession were indicated in the Geneva form of the Hippocratic Oath adopted in 1948 (see Appendix II).

While the Ciba Foundation Symposium of 1966 was chiefly concerned with the

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Discussion (i)

Medical ethics and etiquette—experimentation on humans—Federal clearance of drugs—self-experimentation—informed consent and legal liability—stimulation of intelligence—"intellectual" drugs versus "mood" drugs—monstrous births and infanticide—genetic danger of nuclear testing—relaxation of natural selection—prisoners as experimental subjects.

DR. LEAKE: Now I come to the questions. I will try to keep one for each panelist as I go down the line unless we get into some kind of an argument, but I don't think we will.

DR. MCDERMOTT: I must say that in preparing for this Colloquium I had occasion to read all those Declarations as well as the Hippocratic Oath. I was vastly entertained to see that "first things are first" in the Hippocratic Oath in that the first part of it has nothing to do with the patient at all; it has to do entirely with the relationships of physicians to each other.

DR. LEAKE: It is important, I think, that we always make sure that we make the distinction between medical etiquette—the subject of the older principles of medical ethics—and the fundamental moral problems with which the public is concerned. We will turn, then, to Dr. Stumpf and his interesting discussion. The point that I'm raising here is in regard to the experimentation that he mentioned; he brought up the point that it is not possible to predict from animal experimentation what drugs will do in humans. Well, I've been working in this field for a long while, and my own feeling is that we can get a pretty good idea. But when it comes to experimentation on humans, I could ask, Isn't a therapeutic procedure of any sort undertaken by any physician on any patient a form of experimentation in the sense that we can never predict absolutely what the outcome of the therapeutic procedure may be?

PROF. STUMPF: I agree that there is a distinction between a patient and a subject, and I agree with your point that a physician almost always is experimenting with a drug in relation to the particular patient. But the difference is that a physician is experimenting on the *patient* with a drug that has been cleared, whereas (and this is the point that I have been raising) the *subject* is being subjected to a trial with something that has not been cleared. It may be that novel chemicals and drugs are used also in therapy, but the big distinction, I take it, is that, even in the case of using a drug that has not been thoroughly tested, the justification for it is the possible good it will do *this* patient in the context of a problem; whereas, when you give it to a *subject*, there is the question as to whether the possible side effects can justify its use.

DR. LEAKE: You have brought up a point, namely, whether the drug has been cleared. It is my opinion that judgment with regard to the use of any chemical agent for any purpose in medicine should be made by members of the qualified health professions and not by a group of bureaucrats. When we talk about clearance, I realize of course that it is necessary to have some consensus of judgment, but I believe that that consensus of judgment should be from the health professions.

PROF. STUMPF: I'm not aware that people who are unqualified are making judgments with respect to clearance. Now, I speak obviously as a philosopher who spends most

of his time in a very delightful ivory tower, but the logic of it is rather clear. Two things have to be said here, and I don't mean it to come out quite as abrasively as it will. In the first place, I'm not sure there would have had to be a bureaucracy if the issues hadn't provoked it; and, in the second place, I have a feeling that Dr. Goddard * is, in fact, a doctor.

DR. LEAKE: He is, and he is an excellent man. But he is attempting, in my opinion, to regulate what I believe is an unsatisfactory law or statute for this reason: that the law or statute implies that there is an absolute effectiveness or an absolute safety to every drug. There is no such thing.

PROF. STUMPF: No, but the implicit drift of your argument would be that there should be no controlling of any kind; and I don't think anyone in this room would want that.

DR. LEAKE: No, I didn't say that. I acknowledged the necessity for social control.

PROF. STUMPF: Well, then, the goodness or the badness of it is yet a different question, but I think the issue that you have raised is whether there really should be technical organized supervision of this very delicate matter.

DR. LEAKE: And that is what I have advocated that it be—through the members of the health professions. The AMA abrogated their rights in the matter.

PROF. STUMPF: Are you suggesting that the government, as the government, ought not to have anything to do with this even though the government bureaucracy is staffed by physicians?

DR. LEAKE: No.

PROF. STUMPF: Then what is the issue?

DR. LEAKE: I feel that there is a reasonable way in between where it can be worked out without the difficulties that are arising now, especially in experimentation. But let me go on, if I may. How about self-experimentation.

PROF. STUMPF: That's a rather interesting thing in that the only code that I know of that touches on this is, to the best of my recollection, the Helsinki Declaration in which it says—I think in Section 5—that certain very dangerous experiments ought not to be undertaken except in those cases where the experimenter himself is the subject.

DR. LEAKE: Remember, I tried to point out this is my own field, and, when one is dealing with chemicals for the first time, there is always a danger. I've had a lot of experience in this. In our laboratories out here we developed five useful drugs: divinyl ether for anesthesia, carbarsone for amebiasis, Vioform® (iodochlorhydroxyquinoline) for amebiasis and bacterial enteritis, the amphetamines, and nalorphine, the antagonist to morphine. In each case, no one of those drugs was ever used on anyone else first—on ourselves always. And I might say that in the experimentation in our laboratory we have kept from coming to any use on any other human being except ourselves those drugs that did show in ourselves undesirable effects. I think self-experimentation is pertinent for those who are going to develop a new drug. Now to go on with my questioning. Turning to Judge Burger, may I ask a question that I think is of importance to all of us. What is the real significance of consent—whether informed or not? My point is this: Does consent absolve the clinical experimenter from liability for malpractice or for injury to either his subject or his patient?

JUDGE BURGER: I know from talking to medical groups in the past and from long and intimate association with a great many members of the profession that it will never be possible for lawyers to explain really what informed consent means to doctors because it is a concept like that of the hypothetical "reasonable man." That makes it difficult. The consent problem in experimental medicine, I would think, is not fundamentally different from the consent problem that the astronauts have with the U. S. Government. They're engaged in an enormous experiment, and recent events have shown how dangerous; the recent three deaths were ones that apparently were unpredictable. Yet it's clear that these men knew the risk they were assuming, and that essentially settles the matter. If we could be clear on the disclosure, if the disclosure never holds back, and if it is articulated adequately, then the problem can be solved.

DR. LEAKE: Yes, but you haven't answered my question. Does the consent absolve the experimenter from liability?

JUDGE BURGER: Well, I think what you're really saying is, does it prevent someone from suing you? The answer is no; nothing ever prevents anybody from suing you.

DR. LEAKE: I just wanted to make that clear, because a lot of physicians and a lot of hospitals think that once they have a consent signed by a patient everything is in order and they are not going to be sued; and they are surprised when they are.

JUDGE BURGER: This is a common attitude in the medical profession. But let me emphasize that there is nothing to prevent some of the ladies in the audience from suing anyone of us for breach of promise if we've smiled at them during the course of this session. You can always sue, but the adequately obtained consent with informed judgment—with the disclosure factor—will generally be an adequate defense in most of those situations.

DR. LEAKE: The point is that we should do everything we can to promote mutual trust and mutual confidence.

JUDGE BURGER: Right.

DR. LEAKE: This, then, is a matter of extreme importance in interpersonal relations. I wish to turn now to Prof. Krech, if I may. He had a wonderful appeal to the hippy mystique, it seems to me. I think it's important to consider this enriched psychological environment. We are certainly in a tension-filled world. This does bring up plenty of problems. We all should get brains that will expand all over with this psychologically enriched environment that we're getting into. But I am interested in particular in some of the experiments that were quoted. I know something about experiments of this sort with rats and mice in maze learning. We did a lot of it when we were studying the amphetamines which are central nervous system stimulants, as are pentylenetetrazol and caffeine. The central nervous system-stimulating effects of many of these drugs have been studied quite exhaustively. I frequently used to tell my students, Certainly, caffeine is a central nervous system stimulant; it will promote association of ideas, but there is no guarantee that this association is ever more correct or accurate than that due to chance. One can say that coffee or caffeine tends to promote a diarrhea of words and a constipation of ideas. Now, when we were studying the amphetamines, we used pentylenetetrazol as controls, and we could find no significant increase in rate of maze learning either with pentylenetetrazol or with amphetamines or caffeine. All that I am pointing out is that one can use all sorts of experiments, but one must evaluate those experiments. As has been brought out very clearly in this discussion, what applies at an animal level can be carried over to the human level only with careful consideration.

DR. KRECH: I venture to take the risk. I agree that man—and his brain—is bigger and perhaps even better than a mouse. The experiments that I cited were just two of McGaugh's experiments—only two out of a whole series of about 10 years of experimentation over a whole range of drugs. But, despite his very positive and very exciting results (and, of the controls that you indicated should be taken, many have been taken), despite all the progress, I suspect that we are still in the Stone Age of this kind of experimentation. Add to that all

* Dr. James L. Goddard, Commissioner, Food and Drug Administration.

the experimentation on the deleterious effects of inhibitors of protein synthesis, the ribonucleic acid (RNA) experiments, and so on, and I think you can't avoid the feeling that we are close to the verge of an important breakthrough (awful word!). I just want to try to anticipate what we're going to do when the breakthrough comes. I know that already several of the pharmaceutical houses have on clinical trial a number of drugs intended to speed up or facilitate memory. These trials are being made on patients who are mentally retarded or senile. What the results will be, no one knows. But I would not bet against the project.

DR. LEAKE: This is all very important. In general, insofar as the central nervous system is concerned, it is much easier to find chemical agents that will inhibit in one way or another the activity of the central nervous system than ones that will improve or accelerate its activity. But very recently, as you know, magnesium pemoline was introduced by a former student of mine for the purpose of increasing RNA formation. It works, apparently, in experimental animals; it has been tried in humans, not too satisfactorily.

DR. KRECH: It doesn't work too satisfactorily in animals either. I might make just one point here. I find in general that physicians are familiar with mood drugs—they have been on the front pages. Physicians are not familiar with what might be termed "intellectual" drugs, and most of the exciting experimental work that is going on (as far as I am concerned) is with intellectual drugs. Now, it is important to understand that, to evaluate the significance of the current work with these drugs, one has to be sophisticated about psychology and behavioral measurement as well as about pharmacology. And I regret to say that most physicians and most pharmacologists are naive and ignorant about the sciences of behavior.

DR. LEAKE: Surely I will admit all this, but I also want to remind you that I did emphasize the distinction between mood and behavior; nothing exemplifies it more fully than the attitude or the way in which our hippies go about—their mood is exalted and wonderful; you can judge their behavior.

DR. MCDERMOTT: I gather that Dr. Krech has made the point that he likes it when the investigator is at least as smart as the drug.

DR. KRECH: By the way, we seem to be of the happy opinion that we can't do any self-experimentation on mental retardates!

DR. LEAKE: No. Speak for yourself, Dr. Krech; I can't.

DR. MCDERMOTT: Order!

DR. LEAKE: Now I'd like to ask Dr. Lederberg an important question. This has to do with the matter of voluntary abortion and the right to die. Let me ask, Is infanticide justified in the case of monstrous birth?

DR. LEDERBERG: What I spoke to was not a moral judgment about the consequences of reforms in our law or in our attitude but to plead that they be examined in terms other than so-called "absolutes" with respect to the objects in question. The question of whether infanticide is morally justified, I think, can only be answered by an inquiry as to the consequences of the introduction of this practice into contemporary society. I think it is possibly true—and this is the point that I believe should be debated—that to make it easier to kill a live-born infant may knock down other important barriers to misbehavior on the part of our population. I think that before I would advocate killing even monstrous births, I would want to inquire what the effect might be on the standards of care of other infants, on the attitude towards child beating, and so forth. I hope I did not leave the impression that I regarded our traditional attitudes or our traditions of care for human life in any casual fashion.

DR. LEAKE: No, not at all. I was not quite correct, perhaps, in emphasizing the positive aspect of infanticide. But how about letting the monstrous birth die? In other words, how about making no positive effort to keep it alive? That also is a moral problem.

DR. LEDERBERG: I can only express now a judgment that is personal and one that I would not advocate strongly but that might provide the point of departure for a discussion of the issue rather than a conclusive statement. This would be that I would very much prefer that we anticipate as many of these events as possible, that we improve our scientific technique for prenatal identification of monstrosities, that we do as much as we can to bring about the earliest possible detection of aberrations so that these genetic deaths can be made to occur at that period where they would have the least strenuous consequences for the other members of our society. That would still leave some monsters that are not detected before birth; my inclination with respect to them is that they may be such interesting objects for humane observation and experimentation that it may very well be worth making very great efforts to keep them alive once they have started to exist. But I think that one ought to do more than just lock them up in a warehouse or inflict them on an unfortunate family that doesn't know how to keep them or how to deal with them. They ought to be regarded as exactly what you've described—monsters—careful study and observation of whom under the most humane conditions could teach us more about human nature. We have not taken this approach.

DR. LEAKE: Could I ask you one more question? What actually is the genetic danger of nuclear energy? We've had a lot of conflicting statements recently.

DR. LEDERBERG: Well, I don't think there is much conflict about the facts despite the complexity of the subject. The issue that was raised 10 years ago was that, if nuclear testing into the atmosphere were to continue at the existing rate, there would be a gradual accumulation of radioactive effects on genetic material that would begin to match to a considerable percentage the already existing load. There is already an existing background of spontaneous mutation of essentially unavoidable exposure to cosmic rays and disintegration of potassium-40 in granite and so on, and this has been used as a commonsense measure of potential hazard. The existing pattern of fallout at that time, I believe, was calculated to be approximately 10% of the natural background of genetic effect. I believe it true that we would like to minimize this to the least possible value, and a 10% increase over the preexisting background would have begun to reach the level that I think we would not want to see continue and certainly not to increase. On the other hand, I would also point out that there are many, many measures that we could contemplate taking, or to which research could be directed, that might be expected to have the effect of reducing the background rate of mutation due to thermal and chemical mutagens. So, on the one hand, I would not be frantic about attempting to vary the background incidence of mutation within that realm of some few percent, but, on the other hand, I would be alarmed if there were any great increase—as indeed might have happened if atmospheric testing of nuclear weapons had continued to have increased.

DR. MCDERMOTT: Dr. Leake, I'm very anxious to get Dr. Dubos into the fray. I wonder if you could approach Prof. Medawar and Dr. Starzl at this time.

DR. LEAKE: Sir Peter, in connection with the relaxation of natural selection to which you referred, do you think that this will occur even in the face of the increased tensions of our overcrowded planet?

SIR PETER MEDAWAR: I don't quite understand that question. I referred to the relaxation of natural selection in the context of preserving the genetically unfit, those people who are genetically obliged to live in more restricted worlds than the majority of us. What I mean by the relaxation of natural selection is the preservation of life and the propagation of genes in people and by people who would otherwise have died. I think that this is a purely technical point; nothing very emotive turns on it.

DR. LEAKE: Finally, I will ask Dr. Starzl a question in connection with the matter of choice of subjects for human experimentation and the use of prisoners or soldiers or other people of that sort. Now, we don't want to coerce anyone to become a human subject for experimentation. But supposing the individual volunteers and honestly volunteers? Isn't he more or less in the same position as the medic at the battlefront who volunteers to go out after the wounded on the battlefield? I don't think that the prisoner who may volunteer honestly and fully should be denied the opportunity to serve the rest of us; he may be wishing to compensate. I remind you that in Walter Reed's studies on yellow fever death did occur—as it did later with Stokes and Noguchi. These were volunteers, but they also were self-experimenters. I've worked on prison volunteers—actual volunteers—at Ohio where the prisoners asked if they could be permitted to serve as subjects in testing new drugs. They came to us; we didn't go to them.

DR. STARZL: I didn't mean to suggest that we had ever used a penal donor who was not to our advance knowledge a legitimate volunteer. I think they were all strongly motivated, most for the very high-minded social reasons you have suggested. We know for certain that there were certain others or at least one other who was proved to be motivated by the thought that he would be able to more easily escape from the hospital than from the prison. This, in fact, he did. I think that the problem is not that there aren't legitimate volunteers in prisons but that in the absence of their civil liberties they might not be *really* free to make a choice. I think a 16-year-old minor who donates a kidney to his identical twin also probably wants to do so, but he does not have the requisite legal protection to be able to make his decision freely. I think we made a mistake in accepting prison volunteers, and I suspect that you probably did so also when you were in Ohio.

DR. LEAKE: No, I deny that; we did pretty well on it, and I think the prisoners enjoyed it. But, Mr. Chairman, might I take the opportunity here to thank the members of the panel for responding so directly and so clearly to these nasty questions that I have raised. The panel is an excellent one.

DR. MCDERMOTT: And may we thank you. We will now turn to Dr. Dubos for his challenge.

Individual Morality and Statistical Morality

RENÉ DUBOS, SC.D. (HON.), M.D. (HON.)

IN MOST HUMAN SITUATIONS we soon become involved in operations that we start without knowing too well what the consequences will be, operations that we do not know how to stop. Many of our ethical problems come from this inability to foresee the consequences of our actions. I am sure that our genial President, Dr. Wright, when he organized this conference, had no sense of what was going to come out of it. If he had had enough foresight, he would have recognized that there have been two entirely different issues before us throughout the morning; one I would summarize with the phrase "individual morality" and one I would express as "statistical morality." Now, the persons capable of discussing these two entirely different aspects of ethical problems should have come from entirely different backgrounds. I believe that for individual morality it might have been best to have had a practicing physician who is also a philosopher and a theologian. For statistical morality we should have had a sociologist concerned with the effects of any intervention on the community as a whole. Since here I stand, I shall act in both capacities.

Individual morality is the problem that is easiest to talk about and most difficult to say anything worthwhile about. Individual morality concerns all those ill-defined problems of the relation of the physician to his individual patient. Each and every one of you in this room meets this problem every day and knows far better than I do how to deal with it practically. I would only question the assumption that there are some permanent values involved here, that individual morality—a man-to-man relationship—is something that was determined many thousands of years ago on the basis of some kind of platonic values. In reality we all know, even with very little awareness of history, of differences in attitude in different parts of the world or even in different social groups within a given country. We know that our values in this regard are very different and that they change continually. I offer as an illustration one that was given by Dr. Lederberg, namely, how our attitudes towards contraception have changed and changed so profoundly and how unquestionably our attitudes towards abortion will change within a very short time. I am told by my friends who are physicians in practice that even our views towards euthanasia are changing; certainly they are changing in the general