

## The New Biology: What Price Relieving Man's Estate?

Efforts to eradicate human suffering raise difficult  
and profound questions of theory and practice.

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Recent advances in biology and medicine suggest that we may be rapidly acquiring the power to modify and control the capacities and activities of men by direct intervention and manipulation of their bodies and minds. Certain means are already in use or at hand, others await the solution of relatively minor technical problems, while yet others, those offering perhaps the most precise kind of control, depend upon further basic research. Biologists who have considered these matters disagree on the question of how much how soon, but all agree that the power for "human engineering," to borrow from the jargon, is coming and that it will probably have profound social consequences.

These developments have been viewed both with enthusiasm and with alarm; they are only just beginning to receive serious attention. Several biologists have undertaken to inform the public about the technical possibilities, present and future. Practitioners of social science "futurology" are attempting to predict and describe the likely social conse-

quences of and public responses to the new technologies. Lawyers and legislators are exploring institutional innovations for assessing new technologies. All of these activities are based upon the hope that we can harness the new technology of man for the betterment of mankind.

Yet this commendable aspiration points to another set of questions, which are, in my view, sorely neglected—questions that inquire into the meaning of phrases such as the "betterment of mankind." A full understanding of the new technology of man requires an exploration of ends, values, standards. What ends will or should the new techniques serve? What values should guide society's adjustments? By what standards should the assessment agencies assess? Behind these questions lie others: what is a good man, what is a good life for man, what is a good community? This article is an attempt to provoke discussion of these neglected and important questions.

While these questions about ends and ultimate ends are never unimportant or irrelevant, they have rarely been more important or more relevant. That this is so can be seen once we recognize that we are dealing here with a group of technologies that are in a decisive respect unique: the object upon which they operate is man himself. The technologies of energy or food production,

of communication, of manufacture, and of motion greatly alter the implements available to man and the conditions in which he uses them. In contrast, the biomedical technology works to change the user himself. To be sure, the printing press, the automobile, the television, and the jet airplane have greatly altered the conditions under which and the way in which men live; but men as biological beings have remained largely unchanged. They have been, and remain, able to accept or reject, to use and abuse these technologies; they choose, whether wisely or foolishly, the ends to which these technologies are means. Biomedical technology may make it possible to change the inherent capacity for choice itself. Indeed, both those who welcome and those who fear the advent of "human engineering" ground their hopes and fears in the same prospect: *that man can for the first time recreate himself.*

Engineering the engineer seems to differ in kind from engineering his engine. Some have argued, however, that biomedical engineering does not differ qualitatively from toilet training, education, and moral teachings—all of which are forms of so-called "social engineering," which has man as its object, and is used by one generation to mold the next. In reply, it must at least be said that the techniques which have hitherto been employed are feeble and inefficient when compared to those on the horizon. This quantitative difference rests in part on a qualitative difference in the means of intervention. The traditional influences operate by speech or by symbolic deeds. They pay tribute to man as the animal who lives by speech and who understands the meanings of actions. Also, their effects are, in general, reversible, or at least subject to attempts at reversal. Each person has greater or lesser power to accept or reject or abandon them. In contrast, biomedical engineering circumvents the human context of speech and meaning, bypasses choice, and goes directly to work to modify the human material itself. Moreover, the changes wrought may be irreversible.

In addition, there is an important

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practical reason for considering the biomedical technology apart from other technologies. The advances we shall examine are fruits of a large, humane project dedicated to the conquest of disease and the relief of human suffering. The biologist and physician, regardless of their private motives, are seen, with justification, to be the well-wishers and benefactors of mankind. Thus, in a time in which technological advance is more carefully scrutinized and increasingly criticized, biomedical developments are still viewed by most people as benefits largely without qualification. The price we pay for these developments is thus more likely to go unrecognized. For this reason, I shall consider only the dangers and costs of biomedical advance. As the benefits are well known, there is no need to dwell upon them here. My discussion is deliberately partial.

I begin with a survey of the pertinent technologies. Next, I will consider some of the basic ethical and social problems in the use of these technologies. Then, I will briefly raise some fundamental questions to which these problems point. Finally, I shall offer some very general reflections on what is to be done.

### The Biomedical Technologies

The biomedical technologies can be usefully organized into three groups, according to their major purpose: (i) control of death and life, (ii) control of human potentialities, and (iii) control of human achievement. The corresponding technologies are (i) medicine, especially the arts of prolonging life and of controlling reproduction, (ii) genetic engineering, and (iii) neurological and psychological manipulation. I shall briefly summarize each group of techniques.

1) *Control of death and life.* Previous medical triumphs have greatly increased average life expectancy. Yet other developments, such as organ transplantation or replacement and research into aging, hold forth the promise of increasing not just the average, but also the maximum life expectancy. Indeed, medicine seems to be sharpening its tools to do battle with death itself, as if death were just one more disease.

More immediately and concretely, available techniques of prolonging life—respirators, cardiac pacemakers, artificial kidneys—are already in the lists

against death. Ironically, the success of these devices in forestalling death has introduced confusion in determining that death has, in fact, occurred. The traditional signs of life—heartbeat and respiration—can now be maintained entirely by machines. Some physicians are now busily trying to devise so-called “new definitions of death,” while others maintain that the technical advances show that death is not a concrete event at all, but rather a gradual process, like twilight, incapable of precise temporal localization.

The real challenge to death will come from research into aging and senescence, a field just entering puberty. Recent studies suggest that aging is a genetically controlled process, distinct from disease, but one that can be manipulated and altered by diet or drugs. Extrapolating from animal studies, some scientists have suggested that a decrease in the rate of aging might also be achieved simply by effecting a very small decrease in human body temperature. According to some estimates, by the year 2000 it may be technically possible to add from 20 to 40 useful years to the period of middle life.

Medicine's success in extending life is already a major cause of excessive population growth: death control points to birth control. Although we are already technically competent, new techniques for lowering fertility and chemical agents for inducing abortion will greatly enhance our powers over conception and gestation. Problems of definition have been raised here as well. The need to determine when individuals acquire enforceable legal rights gives society an interest in the definition of human life and of the time when it begins. These matters are too familiar to need elaboration.

Technologies to conquer infertility proceed alongside those to promote it. The first successful laboratory fertilization of human egg by human sperm was reported in 1969 (1). In 1970, British scientists learned how to grow human embryos in the laboratory up to at least the blastocyst stage [that is, to the age of 1 week (2)]. We may soon hear about the next stage, the successful reimplantation of such an embryo into a woman previously infertile because of oviduct disease. The development of an artificial placenta, now under investigation, will make possible full laboratory control of fertilization and gestation. In addition, sophisticated biochemical and cytological techniques of monitoring the “quality” of the fetus have been and are

being developed and used. These developments not only give us more power over the generation of human life, but make it possible to manipulate and to modify the quality of the human material.

2) *Control of human potentialities.* Genetic engineering, when fully developed, will wield two powers not shared by ordinary medical practice. Medicine treats existing individuals and seeks to correct deviations from a norm of health. Genetic engineering, in contrast, will be able to make changes that can be transmitted to succeeding generations and will be able to create new capacities, and hence to establish new norms of health and fitness.

Nevertheless, one of the major interests in genetic manipulation is strictly medical: to develop treatments for individuals with inherited diseases. Genetic disease is prevalent and increasing, thanks partly to medical advances that enable those affected to survive and perpetuate their mutant genes. The hope is that normal copies of the appropriate gene, obtained biologically or synthesized chemically, can be introduced into defective individuals to correct their deficiencies. This *therapeutic* use of genetic technology appears to be far in the future. Moreover, there is some doubt that it will ever be practical, since the same end could be more easily achieved by transplanting cells or organs that could compensate for the missing or defective gene product.

Far less remote are technologies that could serve *eugenic* ends. Their development has been endorsed by those concerned about a general deterioration of the human gene pool and by others who believe that even an undeteriorated human gene pool needs upgrading. Artificial insemination with selected donors, the eugenic proposal of Herman Muller (3), has been possible for several years because of the perfection of methods for long-term storage of human spermatozoa. The successful maturation of human oocytes in the laboratory and their subsequent fertilization now make it possible to select donors of ova as well. But a far more suitable technique for eugenic purposes will soon be upon us—namely, nuclear transplantation, or cloning. Bypassing the lottery of sexual recombination, nuclear transplantation permits the asexual reproduction or copying of an already developed individual. The nucleus of a mature but unfertilized egg is replaced by a nucleus obtained from a specialized cell of an adult organism or embryo (for

example, a cell from the intestines or the skin). The egg with its transplanted nucleus develops as if it had been fertilized and, barring complications, will give rise to a normal adult organism. Since almost all the hereditary material (DNA) of a cell is contained within its nucleus, the renucleated egg and the individual into which it develops are genetically identical to the adult organism that was the source of the donor nucleus. Cloning could be used to produce sets of unlimited numbers of genetically identical individuals, each set derived from a single parent. Cloning has been successful in amphibians and is now being tried in mice; its extension to man merely requires the solution of certain technical problems.

Production of man-animal chimeras by the introduction of selected nonhuman material into developing human embryos is also expected. Fusion of human and nonhuman cells in tissue culture has already been achieved.

Other, less direct means for influencing the gene pool are already available, thanks to our increasing ability to identify and diagnose genetic diseases. Genetic counselors can now detect biochemically and cytologically a variety of severe genetic defects (for example, Mongolism, Tay-Sachs disease) while the fetus is still in utero. Since treatments are at present largely unavailable, diagnosis is often followed by abortion of the affected fetus. In the future, more sensitive tests will also permit the detection of heterozygote carriers, the unaffected individuals who carry but a single dose of a given deleterious gene. The eradication of a given genetic disease might then be attempted by aborting all such carriers. In fact, it was recently suggested that the fairly common disease cystic fibrosis could be completely eliminated over the next 40 years by screening all pregnancies and aborting the 17,000,000 unaffected fetuses that will carry a single gene for this disease. Such zealots need to be reminded of the consequences should each geneticist be allowed an equal assault on his favorite genetic disorder, given that each human being is a carrier for some four to eight such recessive, lethal genetic diseases.

3) *Control of human achievement.* Although human achievement depends at least in part upon genetic endowment, heredity determines only the material upon which experience and education impose the form. The limits of many capacities and powers of an individual are indeed genetically deter-

mined, but the nurturing and perfection of these capacities depend upon other influences. Neurological and psychological manipulation hold forth the promise of controlling the development of human capacities, particularly those long considered most distinctively human: speech, thought, choice, emotion, memory, and imagination.

These techniques are now in a rather primitive state because we understand so little about the brain and mind. Nevertheless, we have already seen the use of electrical stimulation of the human brain to produce sensations of intense pleasure and to control rage, the use of brain surgery (for example, frontal lobotomy) for the relief of severe anxiety, and the use of aversive conditioning with electric shock to treat sexual perversion. Operant-conditioning techniques are widely used, apparently with success, in schools and mental hospitals. The use of so-called consciousness-expanding and hallucinogenic drugs is widespread, to say nothing of tranquilizers and stimulants. We are promised drugs to modify memory, intelligence, libido, and aggressiveness.

The following passages from a recent book by Yale neurophysiologist José Delgado—a book instructively entitled *Physical Control of the Mind: Toward a Psychocivilized Society*—should serve to make this discussion more concrete. In the early 1950's, it was discovered that, with electrodes placed in certain discrete regions of their brains, animals would repeatedly and indefatigably press levers to stimulate their own brains, with obvious resultant enjoyment. Even starving animals preferred stimulating these so-called pleasure centers to eating. Delgado comments on the electrical stimulation of a similar center in a human subject (4, p. 185).

[T]he patient reported a pleasant tingling sensation in the left side of her body 'from my face down to the bottom of my legs.' She started giggling and making funny comments, stating that she enjoyed the sensation 'very much.' Repetition of these stimulations made the patient more communicative and flirtatious, and she ended by openly expressing her desire to marry the therapist.

And one further quotation from Delgado (4, p. 88).

Leaving wires inside of a thinking brain may appear unpleasant or dangerous, but actually the many patients who have undergone this experience have not been concerned about the fact of being wired, nor have they felt any discomfort due to the presence of conductors in their heads. Some women have shown their feminine

adaptability to circumstances by wearing attractive hats or wigs to conceal their electrical headgear, and many people have been able to enjoy a normal life as outpatients, returning to the clinic periodically for examination and stimulation. In a few cases in which contacts were located in pleasurable areas, patients have had the opportunity to stimulate their own brains by pressing the button of a portable instrument, and this procedure is reported to have therapeutic benefits.

It bears repeating that the sciences of neurophysiology and psychopharmacology are in their infancy. The techniques that are now available are crude, imprecise, weak, and unpredictable, compared to those that may flow from a more mature neurobiology.

### Basic Ethical and Social Problems in the Use of Biomedical Technology

After this cursory review of the powers now and soon to be at our disposal, I turn to the questions concerning the use of these powers. First, we must recognize that questions of use of science and technology are always moral and political questions, never simply technical ones. All private or public decisions to develop or to use biomedical technology—and decisions *not* to do so—inevitably contain judgments about value. This is true even if the values guiding those decisions are not articulated or made clear, as indeed they often are not. Secondly, the value judgments cannot be derived from biomedical science. This is true even if scientists themselves make the decisions.

These important points are often overlooked for at least three reasons.

1) They are obscured by those who like to speak of "the control of nature by science." It is men who control, not that abstraction "science." Science may provide the means, but men choose the ends; the choice of ends comes from beyond science.

2) Introduction of new technologies often appears to be the result of no decision whatsoever, or of the culmination of decisions too small or unconscious to be recognized as such. What can be done is done. However, someone is deciding on the basis of some notions of desirability, no matter how self-serving or altruistic.

3) Desires to gain or keep money and power no doubt influence much of what happens, but these desires can also be formulated as reasons and then discussed and debated.

Insofar as our society has tried to deliberate about questions of use, how

has it done so? Pragmatists that we are, we prefer a utilitarian calculus: we weigh "benefits" against "risks," and we weigh them for both the individual and "society." We often ignore the fact that the very definitions of "a benefit" and "a risk" are themselves based upon judgments about value. In the biomedical areas just reviewed, the benefits are considered to be self-evident: prolongation of life, control of fertility and of population size, treatment and prevention of genetic disease, the reduction of anxiety and aggressiveness, and the enhancement of memory, intelligence, and pleasure. The assessment of risk is, in general, simply pragmatic—will the technique work effectively and reliably, how much will it cost, will it do detectable bodily harm, and who will complain if we proceed with development? As these questions are familiar and congenial, there is no need to belabor them.

The very pragmatism that makes us sensitive to considerations of economic cost often blinds us to the larger social costs exacted by biomedical advances. For one thing, we seem to be unaware that we may not be able to maximize all the benefits, that several of the goals we are promoting conflict with each other. On the one hand, we seek to control population growth by lowering fertility; on the other hand, we develop techniques to enable every infertile woman to bear a child. On the one hand, we try to extend the lives of individuals with genetic disease; on the other, we wish to eliminate deleterious genes from the human population. I am not urging that we resolve these conflicts in favor of one side or the other, but simply that we recognize that such conflicts exist. Once we do, we are more likely to appreciate that most "progress" is heavily paid for in terms not generally included in the simple utilitarian calculus.

To become sensitive to the larger costs of biomedical progress, we must attend to several serious ethical and social questions. I will briefly discuss three of them: (i) questions of distributive justice, (ii) questions of the use and abuse of power, and (iii) questions of self-degradation and dehumanization.

### Distributive Justice

The introduction of any biomedical technology presents a new instance of an old problem—how to distribute scarce resources justly. We should as-

sume that demand will usually exceed supply. Which people should receive a kidney transplant or an artificial heart? Who should get the benefits of genetic therapy or of brain stimulation? Is "first-come, first-served" the fairest principle? Or are certain people "more worthy," and if so, on what grounds?

It is unlikely that we will arrive at answers to these questions in the form of deliberate decisions. More likely, the problem of distribution will continue to be decided ad hoc and locally. If so, the consequence will probably be a sharp increase in the already far too great inequality of medical care. The extreme case will be longevity, which will probably be, at first, obtainable only at great expense. Who is likely to be able to buy it? Do conscience and prudence permit us to enlarge the gap between rich and poor, especially with respect to something as fundamental as life itself?

Questions of distributive justice also arise in the earlier decisions to acquire new knowledge and to develop new techniques. Personnel and facilities for medical research and treatment are scarce resources. Is the development of a new technology the best use of the limited resources, given current circumstances? How should we balance efforts aimed at prevention against those aimed at cure, or either of these against efforts to redesign the species? How should we balance the delivery of available levels of care against further basic research? More fundamentally, how should we balance efforts in biology and medicine against efforts to eliminate poverty, pollution, urban decay, discrimination, and poor education? This last question about distribution is perhaps the most profound. We should reflect upon the social consequences of seducing many of our brightest young people to spend their lives locating the biochemical defects in rare genetic diseases, while our more serious problems go begging. The current squeeze on money for research provides us with an opportunity to re-think and reorder our priorities.

Problems of distributive justice are frequently mentioned and discussed, but they are hard to resolve in a rational manner. We find them especially difficult because of the enormous range of conflicting values and interests that characterizes our pluralistic society. We cannot agree—unfortunately, we often do not even try to agree—on standards for just distribution. Rather, decisions tend to be made largely out of a clash of competing interests. Thus, regret-

tably, the question of how to distribute justly often gets reduced to who shall decide how to distribute. The question about justice has led us to the question about power.

### Use and Abuse of Power

We have difficulty recognizing the problems of the exercise of power in the biomedical enterprise because of our delight with the wondrous fruits it has yielded. This is ironic because the notion of power is absolutely central to the modern conception of science. The ancients conceived of science as the *understanding* of nature, pursued for its own sake. We moderns view science as power, as *control* over nature; the conquest of nature "for the relief of man's estate" was the charge issued by Francis Bacon, one of the leading architects of the modern scientific project (5).

Another source of difficulty is our fondness for speaking of the abstraction "Man." I suspect that we prefer to speak figuratively about "Man's power over Nature" because it obscures an unpleasant reality about human affairs. It is in fact particular men who wield power, not Man. What we really mean by "Man's power over Nature" is a power exercised by some men over other men, with a knowledge of nature as their instrument.

While applicable to technology in general, these reflections are especially pertinent to the technologies of human engineering, with which men deliberately exercise power over future generations. An excellent discussion of this question is found in *The Abolition of Man*, by C. S. Lewis (6).

It is, of course, a commonplace to complain that men have hitherto used badly, and against their fellows, the powers that science has given them. But that is not the point I am trying to make. I am not speaking of particular corruptions and abuses which an increase of moral virtue would cure: I am considering what the thing called "Man's power over Nature" must always and essentially be. . . .

In reality, of course, if any one age really attains, by eugenics and scientific education, the power to make its descendants what it pleases, all men who live after it are the patients of that power. They are weaker, not stronger: for though we may have put wonderful machines in their hands, we have pre-ordained how they are to use them. . . . The real picture is that of one dominant age . . . which resists all previous ages most successfully and dominates all subsequent ages most irresistibly, and thus is the real master of

the human species. But even within this master generation (itself an infinitesimal minority of the species) the power will be exercised by a minority smaller still. Man's conquest of Nature, if the dreams of some scientific planners are realized, means the rule of a few hundreds of men over billions upon billions of men. There neither is nor can be any simple increase of power on Man's side. Each new power won by man is a power *over* man as well. Each advance leaves him weaker as well as stronger. In every victory, besides being the general who triumphs, he is also the prisoner who follows the triumphal car.

Please note that I am not yet speaking about the problem of the misuse or abuse of power. The point is rather that the power which grows is unavoidably the power of only some men, and that the number of powerful men decreases as power increases.

Specific problems of abuse and misuse of specific powers must not, however, be overlooked. Some have voiced the fear that the technologies of genetic engineering and behavior control, though developed for good purposes, will be put to evil uses. These fears are perhaps somewhat exaggerated, if only because biomedical technologies would add very little to our highly developed arsenal for mischief, destruction, and stultification. Nevertheless, any proposal for large-scale human engineering should make us wary. Consider a program of positive eugenics based upon the widespread practice of asexual reproduction. Who shall decide what constitutes a superior individual worthy of replication? Who shall decide which individuals may or must reproduce, and by which method? These are questions easily answered only for a tyrannical regime.

Concern about the use of power is equally necessary in the selection of means for desirable or agreed-upon ends. Consider the desired end of limiting population growth. An effective program of fertility control is likely to be coercive. Who should decide the choice of means? Will the program penalize "conscientious objectors"?

Serious problems arise simply from obtaining and disseminating information, as in the mass screening programs now being proposed for detection of genetic disease. For what kinds of disorders is compulsory screening justified? Who shall have access to the data obtained, and for what purposes? To whom does information about a person's genotype belong? In ordinary medical practice, the patient's privacy is protected by the doctor's adherence to the principle of confidentiality. What

will protect his privacy under conditions of mass screening?

More than privacy is at stake if screening is undertaken to detect psychological or behavioral abnormalities. A recent proposal, tendered and supported high in government, called for the psychological testing of all 6-year-olds to detect future criminals and misfits. The proposal was rejected; current tests lack the requisite predictive powers. But will such a proposal be rejected if reliable tests become available? What if certain genetic disorders, diagnosable in childhood, can be shown to correlate with subsequent antisocial behavior? For what degree of correlation and for what kinds of behavior can mandatory screening be justified? What use should be made of the data? Might not the dissemination of the information itself undermine the individual's chance for a worthy life and contribute to his so-called antisocial tendencies?

Consider the seemingly harmless effort to redefine clinical death. If the need for organs for transplantation is the stimulus for redefining death, might not this concern influence the definition at the expense of the dying? One physician, in fact, refers in writing to the revised criteria for declaring a patient dead as a "new definition of heart donor eligibility" (7, p. 526).

Problems of abuse of power arise even in the acquisition of basic knowledge. The securing of a voluntary and informed consent is an abiding problem in the use of human subjects in experimentation. Gross coercion and deception are now rarely a problem; the pressures are generally subtle, often related to an intrinsic power imbalance in favor of the experimentalist.

A special problem arises in experiments on or manipulations of the unborn. Here it is impossible to obtain the consent of the human subject. If the purpose of the intervention is therapeutic—to correct a known genetic abnormality, for example—consent can reasonably be implied. But can anyone ethically consent to nontherapeutic interventions in which parents or scientists work their wills or their eugenic visions on the child-to-be? Would not such manipulation represent in itself an abuse of power, independent of consequences?

There are many clinical situations which already permit, if not invite, the manipulative or arbitrary use of powers provided by biomedical technology: obtaining organs for transplantation, refusing to let a person die with dignity, giving genetic counselling to a frightened

couple, recommending eugenic sterilization for a mental retardate, ordering electric shock for a homosexual. In each situation, there is an opportunity to violate the will of the patient or subject. Such opportunities have generally existed in medical practice, but the dangers are becoming increasingly serious. With the growing complexity of the technologies, the technician gains in authority, since he alone can understand what he is doing. The patient's lack of knowledge makes him deferential and often inhibits him from speaking up when he feels threatened. Physicians *are* sometimes troubled by their increasing power, yet they feel they cannot avoid its exercise. "Reluctantly," one commented to me, "we shall have to play God." With what guidance and to what ends I shall consider later. For the moment, I merely ask: "By whose authority?"

While these questions about power are pertinent and important, they are in one sense misleading. They imply an inherent conflict of purpose between physician and patient, between scientist and citizen. The discussion conjures up images of master and slave, of oppressor and oppressed. Yet it must be remembered that conflict of purpose is largely absent, especially with regard to general goals. To be sure, the purposes of medical scientists are not always the same as those of the subjects experimented on. Nevertheless, basic sponsors and partisans of biomedical technology are precisely those upon whom the technology will operate. The will of the scientist and physician is happily married to (rather, is the offspring of) the desire of all of us for better health, longer life, and peace of mind.

Most future biomedical technologies will probably be welcomed, as have those of the past. Their use will require little or no coercion. Some developments, such as pills to improve memory, control mood, or induce pleasure, are likely to need no promotion. Thus, even if we should escape from the dangers of coercive manipulation, we shall still face large problems posed by the voluntary use of biomedical technology, problems to which I now turn.

#### **Voluntary Self-Degradation and Dehumanization**

Modern opinion is sensitive to problems of restriction of freedom and abuse of power. Indeed, many hold that



a man can be injured only by violating his will. But this view is much too narrow. It fails to recognize the great dangers we shall face in the use of biomedical technology, dangers that stem from an excess of freedom, from the uninhibited exercises of will. In my view, our greatest problem will increasingly be one of voluntary self-degradation, or willing dehumanization.

Certain desired and perfected medical technologies have already had some dehumanizing consequences. Improved methods of resuscitation have made possible heroic efforts to "save" the severely ill and injured. Yet these efforts are sometimes only partly successful; they may succeed in salvaging individuals with severe brain damage, capable of only a less-than-human, vegetating existence. Such patients, increasingly found in the intensive care units of university hospitals, have been denied a death with dignity. Families are forced to suffer seeing their loved ones so reduced, and are made to bear the burdens of a protracted death watch.

Even the ordinary methods of treating disease and prolonging life have impoverished the context in which men die. Fewer and fewer people die in the familiar surroundings of home or in the company of family and friends. At that time of life when there is perhaps the greatest need for human warmth and comfort, the dying patient is kept company by cardiac pacemakers and defibrillators, respirators, aspirators, oxygenators, catheters, and his intravenous drip.

But the loneliness is not confined to the dying patient in the hospital bed. Consider the increasing number of old people who are still alive, thanks to medical progress. As a group, the elderly are the most alienated members of our society. Not yet ready for the world of the dead, not deemed fit for the world of the living, they are shunted aside. More and more of them spend the extra years medicine has given them in "homes for senior citizens," in chronic hospitals, in nursing homes—waiting for the end. We have learned how to increase their years, but we have not learned how to help them enjoy their days. And yet, we bravely and relentlessly push back the frontiers against death.

Paradoxically, even the young and vigorous may be suffering because of medicine's success in removing death from their personal experience. Those born since penicillin represent the first

generation ever to grow up without the experience or fear of probable unexpected death at an early age. They look around and see that virtually all of their friends are alive. A thoughtful physician, Eric Cassell, has remarked on this in "Death and the physician" (8, p. 76):

[W]hile the gift of time must surely be marked as a great blessing, the *perception* of time, as stretching out endlessly before us, is somewhat threatening. Many of us function best under deadlines, and tend to procrastinate when time limits are not set. . . . Thus, this unquestioned boon, the extension of life, and the removal of the threat of premature death, carries with it an unexpected anxiety: the anxiety of an unlimited future.

In the young, the sense of limitless time has apparently imparted not a feeling of limitless opportunity, but increased stress and anxiety, in addition to the anxiety which results from other modern freedoms: personal mobility, a wide range of occupational choice, and independence from the limitations of class and familial patterns of work. . . . A certain aimlessness (often ringed around with great social consciousness) characterizes discussions about their own aspirations. The future is endless, and their inner demands seem minimal. Although it may appear uncharitable to say so, they seem to be acting in a way best described as "childish"—particularly in their lack of a time sense. They behave as though there were no tomorrow, or as though the time limits imposed by the biological facts of life had become so vague for them as to be nonexistent.

Consider next the coming power over reproduction and genotype. We endorse the project that will enable us to control numbers and to treat individuals with genetic disease. But our desires outrun these defensible goals. Many would welcome the chance to become parents without the inconvenience of pregnancy; others would wish to know in advance the characteristics of their offspring (sex, height, eye color, intelligence); still others would wish to design these characteristics to suit their tastes. Some scientists have called for the use of the new technologies to assure the "quality" of all new babies (9). As one obstetrician put it: "The business of obstetrics is to produce *optimum* babies." But the price to be paid for the "optimum baby" is the transfer of procreation from the home to the laboratory and its coincident transformation into manufacture. Increasing control over the product is purchased by the increasing depersonalization of the process. The complete depersonalization of procreation (possible with the development of an artificial placenta) shall be,

in itself, seriously dehumanizing, no matter how optimum the product. It should not be forgotten that human procreation not only issues new human beings, but is itself a human activity.

Procreation is not simply an activity of the rational will. It is a more complete human activity precisely because it engages us bodily and spiritually, as well as rationally. Is there perhaps some wisdom in that mystery of nature which joins the pleasure of sex, the communication of love, and the desire for children in the very activity by which we continue the chain of human existence? Is not biological parenthood a built-in "mechanism," selected because it fosters and supports in parents an adequate concern for and commitment to their children? Would not the laboratory production of human beings no longer be *human* procreation? Could it keep human parenthood human?

The dehumanizing consequences of programmed reproduction extend beyond the mere acts and processes of life-giving. Transfer of procreation to the laboratory will no doubt weaken what is presently for many people the best remaining justification and support for the existence of marriage and the family. Sex is now comfortably at home outside of marriage; child-rearing is progressively being given over to the state, the schools, the mass media, and the child-care centers. Some have argued that the family, long the nursery of humanity, has outlived its usefulness. To be sure, laboratory and governmental alternatives might be designed for procreation and child-rearing, but at what cost?

This is not the place to conduct a full evaluation of the biological family. Nevertheless, some of its important virtues are, nowadays, too often overlooked. The family is rapidly becoming the only institution in an increasingly impersonal world where each person is loved not for what he does or makes, but simply because he is. The family is also the institution where most of us, both as children and as parents, acquire a sense of continuity with the past and a sense of commitment to the future. Without the family, we would have little incentive to take an interest in anything after our own deaths. These observations suggest that the elimination of the family would weaken ties to past and future, and would throw us, even more than we are now, to the mercy of an impersonal, lonely present.

Neurobiology and psychobiology

probe most directly into the distinctively human. The technological fruit of these sciences is likely to be both more tempting than Eve's apple and more "catastrophic" in its result (10). One need only consider contemporary drug use to see what people are willing to risk or sacrifice for novel experiences, heightened perceptions, or just "kicks." The possibility of drug-induced, instant, and effortless gratification will be welcomed. Recall the possibilities of voluntary self-stimulation of the brain to reduce anxiety, to heighten pleasure, or to create visual and auditory sensations unavailable through the peripheral sense organs. Once these techniques are perfected and safe, is there much doubt that they will be desired, demanded, and used?

What ends will these techniques serve? Most likely, only the most elemental, those most tied to the bodily pleasures. What will happen to thought, to love, to friendship, to art, to judgment, to public-spiritedness in a society with a perfected technology of pleasure? What kinds of creatures will we become if we obtain our pleasure by drug or electrical stimulation without the usual kind of human efforts and frustrations? What kind of society will we have?

We need only consult Aldous Huxley's prophetic novel *Brave New World* for a likely answer to these questions. There we encounter a society dedicated to homogeneity and stability, administered by means of instant gratifications and peopled by creatures of human shape but of stunted humanity. They consume, fornicate, take "soma," and operate the machinery that makes it all possible. They do not read, write, think, love, or govern themselves. Creativity and curiosity, reason and passion, exist only in a rudimentary and mutilated form. In short, they are not men at all.

True, our techniques, like theirs, may in fact enable us to treat schizophrenia, to alleviate anxiety, to curb aggressiveness. We, like they, may indeed be able to save mankind from itself, but probably only at the cost of its humanness. In the end, the price of relieving man's estate might well be the abolition of man (11).

There are, of course, many other routes leading to the abolition of man. There are many other and better known causes of dehumanization. Disease, starvation, mental retardation, slavery, and brutality—to name just a few—have long prevented many, if not most,

people from living a fully human life. We should work to reduce and eventually to eliminate these evils. But the existence of these evils should not prevent us from appreciating that the use of the technology of man, uninformed by wisdom concerning proper human ends, and untempered by an appropriate humility and awe, can unwittingly render us all irreversibly less than human. For, unlike the man reduced by disease or slavery, the people dehumanized à la *Brave New World* are not miserable, do not know that they are dehumanized, and, what is worse, would not care if they knew. They are, indeed, happy slaves, with a slavish happiness.

### Some Fundamental Questions

The practical problems of distributing scarce resources, of curbing the abuses of power, and of preventing voluntary dehumanization point beyond themselves to some large, enduring, and most difficult questions: the nature of justice and the good community, the nature of man and the good for man. My appreciation of the profundity of these questions and my own ignorance before them makes me hesitant to say any more about them. Nevertheless, previous failures to find a shortcut around them have led me to believe that these questions must be faced if we are to have any hope of understanding where biology is taking us. Therefore, I shall try to show in outline how I think some of the larger questions arise from my discussion of dehumanization and self-degradation.

My remarks on dehumanization can hardly fail to arouse argument. It might be said, correctly, that to speak about dehumanization presupposes a concept of "the distinctively human." It might also be said, correctly, that to speak about wisdom concerning proper human ends presupposes that such ends do in fact exist and that they may be more or less accessible to human understanding, or at least to rational inquiry. It is true that neither presupposition is at home in modern thought.

The notion of the "distinctively human" has been seriously challenged by modern scientists. Darwinists hold that man is, at least in origin, tied to the subhuman; his seeming distinctiveness is an illusion or, at most, not very important. Biochemists and molecular biologists extend the challenge by blur-

ring the distinction between the living and the nonliving. The laws of physics and chemistry are found to be valid and are held to be sufficient for explaining biological systems. Man is a collection of molecules, an accident on the stage of evolution, endowed by chance with the power to change himself, but only along determined lines.

Psychoanalysts have also debunked the "distinctively human." The essence of man is seen to be located in those drives he shares with other animals—pursuit of pleasure and avoidance of pain. The so-called "higher functions" are understood to be servants of the more elementary, the more base. Any distinctiveness or "dignity" that man has consists of his superior capacity for gratifying his animal needs.

The idea of "human good" fares no better. In the social sciences, historicists and existentialists have helped drive this question underground. The former hold all notions of human good to be culturally and historically bound, and hence mutable. The latter hold that values are subjective: each man makes his own, and ethics becomes simply the cataloging of personal tastes.

Such appear to be the prevailing opinions. Yet there is nothing novel about reductionism, hedonism, and relativism; these are doctrines with which Socrates contended. What is new is that these doctrines seem to be vindicated by scientific advance. Not only do the scientific notions of nature and of man flower into verifiable predictions, but they yield marvelous fruit. The technological triumphs are held to validate their scientific foundations. Here, perhaps, is the most pernicious result of technological progress—more dehumanizing than any actual manipulation or technique, present or future. We are witnessing the erosion, perhaps the final erosion, of the idea of man as something splendid or divine, and its replacement with a view that sees man, no less than nature, as simply more raw material for manipulation and homogenization. Hence, our peculiar moral crisis. We are in turbulent seas without a landmark precisely because we adhere more and more to a view of nature and of man which both gives us enormous power and, at the same time, denies all possibility of standards to guide its use. Though well-equipped, we know not who we are nor where we are going. We are left to the accidents of our hasty, biased, and ephemeral judgments.

Let us not fail to note a painful irony: our conquest of nature has made us the slaves of blind chance. We triumph over nature's unpredictabilities only to subject ourselves to the still greater unpredictability of our capricious wills and our fickle opinions. That we have a method is no proof against our madness. Thus, engineering the engineer as well as the engine, we race our train we know not where (12).

While the disastrous consequences of ethical nihilism are insufficient to refute it, they invite and make urgent a re-investigation of the ancient and enduring questions of what is a proper life for a human being, what is a good community, and how are they achieved (13). We must not be deterred from these questions simply because the best minds in human history have failed to settle them. Should we not rather be encouraged by the fact that they considered them to be the most important questions?

As I have hinted before, our ethical dilemma is caused by the victory of modern natural science with its non-teleological view of man. We ought therefore to reexamine with great care the modern notions of nature and of man, which undermine those earlier notions that provide a basis for ethics. If we consult our common experience, we are likely to discover some grounds for believing that the questions about man and human good are far from closed. Our common experience suggests many difficulties for the modern "scientific view of man." For example, this view fails to account for the concern for justice and freedom that appears to be characteristic of all human societies (14). It also fails to account for or to explain the fact that men have speech and not merely voice, that men can choose and act and not merely move or react. It fails to explain why men engage in moral discourse, or, for that matter, why they speak at all. Finally, the "scientific view of man" cannot account for scientific inquiry itself, for why men seek to know. Might there not be something the matter with a knowledge of man that does not explain or take account of his most distinctive activities, aspirations, and concerns (15)?

Having gone this far, let me offer one suggestion as to where the difficulty might lie: in the modern understanding of knowledge. Since Bacon, as I have mentioned earlier, technology has in-

creasingly come to be the basic justification for scientific inquiry. The end is power, not knowledge for its own sake. But power is not only the end. It is also an important *validation* of knowledge. One definitely knows that one knows only if one can make. Synthesis is held to be the ultimate proof of understanding (16). A more radical formulation holds that one knows only what one makes: knowing *equals* making.

Yet therein lies a difficulty. If truth be the power to change or to make the object studied, then of what do we have knowledge? If there are no fixed realities, but only material upon which we may work our wills, will not "science" be merely the "knowledge" of the transient and the manipulatable? We might indeed have knowledge of the laws by which things change and the rules for their manipulation, but no knowledge of the things themselves. Can such a view of "science" yield any knowledge about the nature of man, or indeed, about the nature of anything? Our questions appear to lead back to the most basic of questions: What does it mean to know? What is it that is knowable (17)?

We have seen that the practical problems point toward and make urgent certain enduring, fundamental questions. Yet while pursuing these questions, we cannot afford to neglect the practical problems as such. Let us not forget Delgado and the "psychocivilized society." The philosophical inquiry could be rendered moot by our blind, confident efforts to dissect and redesign ourselves. While awaiting a reconstruction of theory, we must act as best we can.

### What Is To Be Done?

First, we sorely need to recover some humility in the face of our awesome powers. The arguments I have presented should make apparent the folly of arrogance, of the presumption that we are wise enough to remake ourselves. Because we lack wisdom, caution is our urgent need. Or to put it another way, in the absence of that "ultimate wisdom," we can be wise enough to know that we are not wise enough. When we lack sufficient wisdom to do, wisdom consists in not doing. Caution, restraint, delay, abstention are what this second-best (and, perhaps, only) wisdom dictates with

respect to the technology for human engineering.

If we can recognize that biomedical advances carry significant social costs, we may be willing to adopt a less permissive, more critical stance toward new developments. We need to reexamine our prejudice not only that all biomedical innovation is progress, but also that it is inevitable. Precedent certainly favors the view that what can be done will be done, but is this necessarily so? Ought we not to be suspicious when technologists speak of coming developments as automatic, not subject to human control? Is there not something contradictory in the notion that we have the power to control all the untoward consequences of a technology, but lack the power to determine whether it should be developed in the first place?

What will be the likely consequences of the perpetuation of our permissive and fatalistic attitude toward human engineering? How will the large decisions be made? Technocratically and self-servingly, if our experience with previous technologies is any guide. Under conditions of *laissez-faire*, most technologists will pursue techniques, and most private industries will pursue profits. We are fortunate that, apart from the drug manufacturers, there are at present in the biomedical area few large industries that influence public policy. Once these appear, the voice of "the public interest" will have to shout very loudly to be heard above their whisperings in the halls of Congress. These reflections point to the need for institutional controls.

Scientists understandably balk at the notion of the regulation of science and technology. Censorship is ugly and often based upon ignorant fear; bureaucratic regulation is often stupid and inefficient. Yet there is something disingenuous about a scientist who professes concern about the social consequences of science, but who responds to every suggestion of regulation with one or both of the following: "No restrictions on scientific research," and "Technological progress should not be curtailed." Surely, to suggest that *certain* technologies ought to be regulated or forestalled is not to call for the halt of *all* technological progress (and says nothing at all about basic research). Each development should be considered on its own merits. Although the dangers of regulation cannot be dismissed, who, for example, would still object to



efforts to obtain an effective, complete, global prohibition on the development, testing, and use of biological and nuclear weapons?

The proponents of laissez-faire ignore two fundamental points. They ignore the fact that not to regulate is as much a policy decision as the opposite, and that it merely postpones the time of regulation. Controls will eventually be called for—as they are now being demanded to end environmental pollution. If attempts are not made early to detect and diminish the social costs of biomedical advances by intelligent institutional regulation, the society is likely to react later with more sweeping, immoderate, and throttling controls.

The proponents of laissez-faire also ignore the fact that much of technology is already regulated. The federal government is already deep in research and development (for example, space, electronics, and weapons) and is the principal sponsor of biomedical research. One may well question the wisdom of the direction given, but one would be wrong in arguing that technology cannot survive social control. Clearly, the question is not control versus no control, but rather what kind of control, when, by whom, and for what purpose.

Means for achieving international regulation and control need to be devised. Biomedical technology can be no nation's monopoly. The need for international agreements and supervision can readily be understood if we consider the likely American response to the successful asexual reproduction of 10,000 Mao Tse-tungs.

To repeat, the basic short-term need is caution. Practically, this means that we should shift the burden of proof to the *proponents* of a new biomedical technology. Concepts of "risk" and "cost" need to be broadened to include some of the social and ethical consequences discussed earlier. The probable or possible harmful effects of the widespread use of a new technique should be anticipated and introduced as "costs" to be weighed in deciding about the first use. The regulatory institutions should be encouraged to exercise restraint and to formulate the grounds for saying "no." We must all get used to the idea that biomedical technology makes possible many things we should never do.

But caution is not enough. Nor are clever institutional arrangements. Institutions can be little better than the people who make them work. However

worthy our intentions, we are deficient in understanding. In the *long* run, our hope can only lie in education: in a public educated about the meanings and limits of science and enlightened in its use of technology; in scientists better educated to understand the relationships between science and technology on the one hand, and ethics and politics on the other; in human beings who are as wise in the latter as they are clever in the former.

#### References and Notes

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10. It is, of course, a long-debated question as to whether the fall of Adam and Eve ought to be considered "catastrophic," or more precisely, whether the Hebrew tradition considered it so. I do not mean here to be taking sides in this quarrel by my use of the term "catastrophic," and, in fact, tend to line up on the negative side of the questions, as put above. Curiously, as Aldous Huxley's *Brave New World* (Harper & Row, New York, 1969) suggests, the implicit goal of the biomedical technology could well be said to be the reversal of the Fall and a return of man to the hedonic and immortal existence of the Garden of Eden. Yet I can point to at least two problems. First, the new Garden of Eden will probably have no gardens; the received, splendid world of nature will be buried beneath asphalt, concrete, and other human fabrications, a transformation that is already far along. (Recall that in *Brave New World* elaborate consumption-oriented, mechanical amusement parks—featuring, for example, centrifugal bumble-puppy—had supplanted wilderness and even ordinary gardens.) Second, the new inhabitant of the new "Garden" will have to be a creature for whom we have no precedent, a creature as difficult to imagine as to bring into existence. He will have to be simultaneously an innocent like Adam and a technological wizard who keeps the "Garden" running. (I am indebted to Dean Robert Goldwin, St. John's College, for this last insight.)
11. Some scientists naively believe that an engineered increase in human intelligence will steer us in the right direction. Surely we have learned by now that intelligence, whatever it is and however measured, is not synonymous with wisdom and that, if harnessed to the wrong ends, it can cleverly perpetrate great folly and evil. Given the activities in which many, if not most, of our best minds are now engaged, we should not simply rejoice in the prospect of enhancing IQ. On what would this increased intelligence operate? At best, the programming of further increases in IQ. It would design and operate techniques for prolonging life, for engineering reproduction, for delivering gratifications. With no gain in wisdom, our gain in intelligence can only enhance the rate of our dehumanization.
12. The philosopher Hans Jonas has made the identical point: "Thus the slow-working accidents of nature, which by the very patience of their small increments, large numbers, and gradual decisions, may well cease to be 'accident' in outcome, are to be replaced by the fast-working accidents of man's hasty and biased decisions, not exposed to the long test of the ages. His uncertain ideas are to set the goals of generations, with a certainty borrowed from the presumptive certainty of the means. The latter presumption is doubtful enough, but this doubtfulness becomes secondary to the prime question that arises when man indeed undertakes to 'make himself': in what image of his own devising shall he do so, even granted that he can be sure of the means? In fact, of course, he can be sure of neither, not of the end, nor of the means, once he enters the realm where he plays with the roots of life. Of one thing only can he be sure: of his power to move the foundations and to cause incalculable and irreversible consequences. Never was so much power coupled with so little guidance for its use." [J. Cent. Conf. Amer. Rabbis (January 1968), p. 27.] These remarks demonstrate that, contrary to popular belief, we are not even on the right road toward a rational understanding of and rational control over human nature and human life. It is indeed the height of irrationality triumphantly to pursue rationalized technique, while at the same time insisting that questions of ends, values, and purposes lie beyond rational discourse.
13. It is encouraging to note that these questions are seriously being raised in other quarters—for example, by persons concerned with the decay of cities or the pollution of nature. There is a growing dissatisfaction with ethical nihilism. In fact, its tenets are unwittingly abandoned, by even its staunchest adherents, in any discussion of "what to do." For example, in the biomedical area, everyone, including the most unreconstructed and technocratic reductionist, finds himself speaking about the use of powers for "human betterment." He has wandered unawares onto ethical ground. One cannot speak of "human betterment" without considering what is meant by *the human* and by the related notion of *the good for man*. These questions can be avoided only by asserting that practical matters reduce to tastes and power, and by confessing that the use of the phrase "human betterment" is a deception to cloak one's own will to power. In other words, these questions can be avoided only by ceasing to discuss.
14. Consider, for example, the widespread acceptance, in the legal systems of very different societies and cultures, of the principle and the practice of third-party adjudication of disputes. And consider why, although many societies have practiced slavery, no slaveholder has preferred his own enslavement to his own freedom. It would seem that some notions of justice and freedom, as well as right and truthfulness, are constitutive for any society, and that a concern for these values may be a fundamental characteristic of "human nature."
15. Scientists may, of course, continue to believe in righteousness or justice or truth, but these beliefs are not grounded in their "scientific knowledge" of man. They rest instead upon the receding wisdom of an earlier age.
16. This belief, silently shared by many contemporary biologists, has recently been given the following clear expression: "One of the acid tests of understanding an object is the ability to put it together from its component parts. Ultimately, molecular biologists will attempt to subject their understanding of all structure and function to this sort of test by trying to synthesize a cell. It is of some interest to see how close we are to this goal." [P. Handler, Ed, *Biology and the Future of Man* (Oxford Univ. Press, New York, 1970), p. 55.]
17. When an earlier version of this article was presented publicly, it was criticized by one questioner as being "antiscientific." He suggested that my remarks "were the kind that gave science a bad name." He went on to argue that, far from being the enemy of morality, the pursuit of truth was itself a highly moral activity, perhaps the highest. The relation of science and morals is a long and difficult question with an illustrious history, and it deserves a more extensive discussion than space permits. However, because some readers may share the questioner's response, I offer a brief reply. First, on the matter of reputation, we should recall that the

pursuit of truth may be in tension with keeping a good name (witness Oedipus, Socrates, Galileo, Spinoza, Solzhenitsyn). For most of human history, the pursuit of truth (including "science") was not a reputable activity among the many, and was, in fact, highly suspect. Even today, it is doubtful whether more than a few appreciate knowledge as an end in itself. Science has acquired a "good name" in recent times largely because of its technological fruit; it is therefore to be expected that a disenchantment with technology will reflect

badly upon science. Second, my own attack has not been directed against science, but against the use of *some* technologies and, even more, against the unexamined belief—indeed, I would say, superstition—that all biomedical technology is an unmixed blessing. I share the questioner's belief that the pursuit of truth is a highly moral activity. In fact, I am inviting him and others to join in a pursuit of the truth about whether all these new technologies are really good for us. This is a question that merits and is susceptible of seri-

ous intellectual inquiry. Finally, we must ask whether what we call "science" has a monopoly on the pursuit of truth. What is "truth"? What is knowable, and what does it mean to know? Surely, these are also questions that can be examined. Unless we do so, we shall remain ignorant about what "science" is and about what it discovers. Yet "science"—that is, modern natural science—cannot begin to answer them; they are philosophical questions, the very ones I am trying to raise at this point in the text.

## The Cholinergic Synapse and the Site of Memory

J. Anthony Deutsch

That learning and memory are due to some form of change of synaptic conductance is a very old idea, having been suggested by Tanzi in 1893 (1). It is a simple idea and in many ways an obvious one. However, the evidence that learning is due to changes at the synapse has been meager (2). Although changes occur at a spinal synapse as a result of stimulation, there is no evidence that the changes are those utilized in the nervous system for information storage. To use an analogy, if we pass large amounts of current across resistors in a computer, temporary increases in temperature and perhaps even permanent increases in resistance occur. However, such an experiment shows only that the computer could store information by using "post-stimulation" alterations in its resistors, but it does not show that this is the actual way in which the computer stores information. Sharpless (3) has pointed out that learning is not due to simple use of stimulation of a pathway. He therefore questions whether the phenomena studied by Eccles (2) have anything to do with learning as observed in the intact organism. Nevertheless, this does not mean that learning is not due to synaptic changes of some sort. It means only that a different experimental test of the possibility must be devised.

In designing our experimental ap-

proach to this problem, clues from human clinical evidence were used. After an individual receives blows to the head, as might be sustained in accidents, he cannot recall events that occurred closest in time prior to the accident (retrograde amnesia). Such patches of amnesia may cover days or even weeks. The lost memories tend to return, with those most distant in time from the accident becoming available first (4). In the Korsakoff syndrome (5), retrograde amnesia may gradually increase until it covers a span of many years. An elderly patient may end up remembering only his youth, whereas there is no useful memory of the more recent intervening years. From such evidence concerning human retrograde amnesia we may conclude that the changes in the substrate of memory take a relatively long time and are measurable in hours, days, and even months. If we suppose from this that the substrate of memory is synaptic and that it is slowly changing, then it may be possible to follow such synaptic changes by pharmacological methods. If the same dose of a synaptically acting drug has different effects on remembering that depend on the age of the memory (and this can be shown for a number of synaptically acting drugs), then we may assume that there has been a synaptic alteration as a function of time after learning, and we may infer that such a synaptic change underlies memory.

### Pharmacological Tools to Investigate Hypothesis

Pharmacological agents are available that can either increase or decrease the effectiveness of neural transmitters (6). For instance, anticholinesterase and anticholinergic drugs affect transmission at synapses which utilize acetylcholine as the transmitter. During normal transmission, acetylcholine is rapidly destroyed by the enzyme cholinesterase. Anticholinesterase drugs, such as physostigmine and diisopropyl fluorophosphate (DFP), inactivate cholinesterase. Therefore they indirectly prevent the destruction of acetylcholine. Because submaximum doses of these drugs inactivate not all but only a part of the cholinesterase present, they slow down but do not stop the destruction of acetylcholine. The overall effect at such submaximum levels of anticholinesterase is to increase by some constant the lifetime of any acetylcholine emitted into the synapse, which increases the concentrations of acetylcholine in the synapse which result from a given rate of emission. Within certain limits the greater this concentration the greater is the efficiency of transmission, that is, the conduction across the synapse. Above that limit, which is set by the sensitivity of the postsynaptic membrane, any further increase in acetylcholine concentration produces a synaptic block (6, 7). Thus, the application of a given dosage of anticholinesterase will (by protecting acetylcholine from destruction) have different effects on the efficiency of synaptic conduction that depend on the rate of acetylcholine emission during transmission and on the sensitivity of the postsynaptic membrane. When emission of acetylcholine is small, or when the sensitivity of the postsynaptic membrane is low, an application of anticholinesterase will render transmission more efficient, a property used to good effect in the treatment of myasthenia gravis. In the treatment of this disorder, anticholinesterase is

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