

## Doctors

## Must Experiment

## On Humans

### But What Are

### The Patient's Rights?

By WALTER GOODMAN

W HEN, last winter, in the course of his persistent campaign against conditions and practices at New York's hospitals, State Senator Seymour R. Thaler charged that thousands of indigent patients were being used as guinea pigs, he struck at a peculiarly sensitive public nerve. Who in the past 20 years has been able to hear of medical experiments on humans without cringing again at the memory of the German doctors and their work on members of "lesser" races? Thaler did nothing in his emotional speech on the floor of the State Senate to spare us fresh horror. He told of 500 mentally retarded children between the ages of 3 and 9 being injected with a live hepatitis virus as part of a research program at Willowbrook State School on Staten Island; he charged that at Harlem Hospital children sometimes have their congenitally deformed limbs removed as a demonstration of surgical procedures to internes and residents, and that a 23-year-old woman was made to undergo a hysterectomy as part of a similar educational process; at Bellevue Hospital, said the Senator, five out of 1,000 alcoholics died after

doctors took liver biopsies for a research program.

Thaler's allegations were promptly disputed by hospital officials. The chief resident in surgery at Harlem Hospital indignantly denied both the hysterectomy charge and the assertion that deformed limbs had been amputated for demonstration purposes. A spokesman at Bellevue said that his records showed no case of a patient dying from a needle biopsy and that the biopsies were taken because liver damage is always suspected of alcoholics. (He did not pursue the question of using derelicts for experimental purposes.) As to the hepatitis tests, the State Commissioner of Mental Hygiene defended that program as having resulted in an 80- to 85-per-cent reduction in the incidence of the disease at Willowbrook.

So the particulars of the cases remain in controversy—and will no doubt continue to remain there, since doctors are famously loath to share medical records with outsiders. And even if the records were opened, we would have to be prepared for differences of interpretation among the experts. Whatever Thaler's failures as a reporter, however, the issue that he brought onto Page One is real. Medical experiments on human beings are being conducted in hospitals

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Chemists and doctors' offices, and not always under reassuring conditions.

**S**INCE World War II medical research has flourished in the sun of Federal largesse. In fiscal 1965, the National Institutes of Health spent \$1.1-billion on medical studies, \$1-billion more than the amount spent 10 years earlier. Most of us automatically cheer such evidence of Washington's concern for our health, without troubling to consider how all this money is spent. A good deal of it is spent on laboratory experiments with chemicals—and nobody objects to that. A good deal is spent on animal experiments—and not many people object to that. But in the end medical research requires that a new theory, a new drug, a new surgical technique be tried on human beings. There is no other way.

The benefits of such tests are immeasurable. Every surgical operation now in use is, obviously, a direct result of human experimentation. Both the Salk and Sabin polio vaccines required large-scale tests on children before final acceptance. A major complaint brought periodically against drug manufacturers is that in their haste to get profitable products on the market they have been remiss about subjecting new drugs to adequate tests—that is to say, tests on people. Dr. George E. Moore,

director of New York State's Roswell Park Memorial Institute, says that he is much less worried about the dangers of planned experiments on humans than about the drugs, surgical techniques and diagnostic methods that are commonly accepted for daily medical care, yet have never been proved worthwhile.

So the issue becomes not whether one is for or against experiments on humans (though that phrase alone is enough to set off shudders) but under what circumstances such experiments may properly be conducted.

**S**ENATOR THALER is not the first to raise this issue in recent years. Early in 1964, New York City's newspapers gave prominent coverage to the case of 22 elderly, seriously ill patients at the Jewish Chronic Disease Hospital in Brooklyn who had been injected with live cancer cells as part of a research project under the auspices of the Memorial Sloan-Kettering Cancer Center. Two doctors, Dr. Chester Southern of Sloan-Kettering and Dr. Emanuel Mandel, medical director of the Chronic Disease Hospital, were reprimanded by the Regents of the University of the State of New York—who are responsible for licensing doctors in this state—for "fraud and deceit in the practice of medicine" for

their part in the experiment, and were put on a year's probation.

A few months later, the New England Journal of Medicine carried an impressively documented article by Dr. Henry K. Beecher, Dorr Professor of Research in Anesthesia at the Harvard Medical School, titled "Ethics and Clinical Research." Dr. Beecher, who has directed the anesthesia laboratory at Massachusetts General Hospital for 31 years, is his professor's pre-eminent critic of human experimentation. Convinced that "what seem to be breaches of ethical conduct in experimentation are by no means rare but are almost, one fears, universal," he gathered from medical papers of the past decade 50 cases which seemed to him of doubtful propriety, and he was certain that he could have found hundreds more. Twenty-two of the cases were reviewed in the Journal—with the names of individuals and institutions omitted. Example No. 16 concerned the hepatitis experiment that became the most credible part of Senator Thaler's indictment.

On some basic points, there is little disagreement about experiments on humans. Everyone is agreed that such research ought to be motivated by a specific intent to benefit mankind and not by scientific curiosity

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*Continued*

Further, everyone is agreed that the research ought to be planned and carried out by skilled investigators under the most stringent safeguards. Finally, there is general agreement that a doctor treating his own patient must have ample leeway in prescribing new drugs or techniques, and that he should deal as honestly as possible with his patient, keeping him informed of the nature of his ailment and the methods of treatment (though most doctors hold that full and unadorned disclosure is not invariably in a patient's best interest).

So much for the areas of relative agreement. Controversy arises when tests are made on persons who have little or no prospect of direct benefit from what is done to them and, indeed, may suffer harm.

To return to the most publicized example, no one has questioned the integrity of Dr. Southam of Sloan-Kettering, or the significance of his experiment in Brooklyn. Researchers at Sloan-Kettering have been studying the body's ability to fight off cancer for years. In 1956 they began injecting live tissue-cultured cancer cells into prisoners at Ohio State Penitentiary. By the time this test was completed, some 300 volunteers had been injected and their bodies had thrown off the implanted cells. Carrying forward his tests on persons with cancer, Dr. Southam found that as the subject's condition worsened the body took longer to reject the cancer transplants. In approaching the Jewish Chronic Disease Hospital in 1963, he sought to learn whether the delay in rejecting the transplants was related specifically to the spreading cancer, as he hypothesized, or just to the body's general weakness. For this he needed a test group of severely debilitated patients who did not have cancer. He wished to inject them with cancer cells and compare the length of time it took their weakened bodies to throw off the foreign cells with the time it took cancer victims to do so.

What brought Dr. Southam and Dr. Mandel their reprimand from the Board of Regents was the way they went about obtaining—or failing to obtain—the consent of the patients, a group of old, very sick, somewhat confused people whose consent would have been questionable in the best of circumstances. They were told that the test was aimed at discovering their immunity or resistance to disease; that they would receive an injection, and that a lump

would form at the site within a few days and disappear within a few weeks. This was accurate as far as it went. But the patients were not told that the injections were not for the purpose of alleviating their own condition. Nineteen of the 22 patients suffered from ailments other than cancer—a word that was never whispered to them.

The experimenters later explained their avoidance of that fearsome word as an effort to spare the patients needless distress. Hundreds of previous tests had demonstrated to the satisfaction of experts that there was no danger in the procedure. "We are not doing something which is going to induce cancer," said Dr. Southam in his defense. "We are going to observe the growth and rejection of these transplanted cells. The fact then that they are cancer cells does not mean that there is any risk of cancer to this patient."

Had the patients been informed that they were being asked to receive cancer cells in their bodies, subjects for the experiment would probably have been lost. As it was, no written consent was obtained; no kin of even the most muddled patient were notified—which is the normal practice in ordinary surgery. The fact that the patients evidently did not suffer any ill effects from the transplants does not lay to rest the question of consent.

Dr. Mandel's role in the affair was especially delicate. One of his reasons for participating was the hope that a relationship with Sloan-Kettering might shed a bit of favorable light on his relatively obscure institution—not an unnatural nor an unworthy hope, but one that has no standing in the temple of medical ethics. As medical director of the hospital, his overriding responsibility was to his patients. Three staff doctors resigned in protest over the testing procedures and it was their complaint to the late William A. Hyman, a founder of the hospital and a member of its board of directors, that brought out the story.

If we think of this case in the terms that some writers have presented it, i.e., as 22 old and helpless people vs. science, it is cold-blooded not to come down on the side of the old and helpless. Dr. Beecher asks, "Whoever gave the investigator the godlike right of choosing martyrs?" But no one appears to have been martyred. And suppose that the Southam test, deceptively conducted though it indubitably was, moves us to-

ward a cancer virus? How many lives will such a virus have to save, how much suffering will it have to eliminate before the ethical balance is redressed and we can say that perhaps the doctors were right not to tell the whole truth?

**Y**ET, if we grant the Sloan-Kettering researchers the benefit of every doubt, the concept of a man's body being put to the service of a cause that is not his own remains to nag at us. To return to Dr. Beecher's study in the New England Journal of Medicine, several of the experiments he notes seem unnervingly gratuitous. One, involving 18 children about to undergo surgery for congenital heart disease, had to do with the effect of the thymus gland on skin grafts. While they were on the operating table, all 18 had skin grafts sutured to their chest walls. Eleven of the children also had their thymuses removed, while the seven others served as a control group. The eleven were thus subjected to an operation—removal of the thymus—whose long-term effects on the body are not known, in order to study a relatively uncommon phenomenon—skin transplants—which had nothing to do with their needs.

In another, quite different experiment which raises a similar question of judgment, 50 inmates of a children's center, none of whom was suffering from any ailment worse than acne, were given doses of a drug that was suspected—correctly, as it turned out—of causing abnormal functioning of the liver. Again, the test was, at best, unrelated to the immediate welfare of the subjects.

Still another type of troubling experiment was carried out in 1956 at the Francis E. Warren Air Force Base in Wyoming, on 585 Air Force men who were suffering from a bacterial infection of the food canal. One possible complication of their infection was rheumatic fever, which may cause permanent harm to the heart. According to Dr. Beecher, it was known that the rheumatic fever could be prevented with penicillin. Nonetheless, the doctors withheld penicillin from these men because they were interested in learning whether sulfa drugs, too, could do the job. Unfortunately, the sulfa failed. Twenty-five men—14 who had been given the sulfa and 11 in a control group who were deprived even of that ineffective substitute—developed rheumatic fever.

Medical officers involved in the experiment admit that

25 patients were given no real idea of the risks to which they were being subjected. They had a right to assume that they were receiving the best care available for their infections.\* In any case, even if the doctors had told the test group the whole story, even if each airman's consent had been asked, and given, the situation would have been suspect because of the military status of the patients. Soldiers, like prisoners hoping for parole, welfare cases hoping for attention, students hoping for good marks, are favorite subjects of experimentation. ("College students are particularly apt to believe that refusal to volunteer as subjects in an instructor's experiment will jeopardize their progress," notes a professor of medical psychology at the University of Nebraska College of Medicine, "and they are often right.")

Another group that cannot protest for themselves are children—popular subjects for all manner of tests, some of which have been hailed as medical achievements. In a celebrated experiment done after the war, researchers produced conclusive evidence that the oxygen-rich atmosphere customarily used for premature infants could cause blindness. They thereby saved countless babies from a life-long handicap—at the expense of six cases of blindness

\*The only circumstances in which alternative treatment of an ailment is permissible, according to the British Medical Research Council, is when doubt exists as to which of two approaches is better. If the doctors were certain of the benefits of penicillin, yet did not use it, their decision ran counter to the basic rule of the physician, *primum non nocere*—first of all, do no harm.

among the infants who happened to be placed in the high-oxygen group for purposes of the test. Although there are critics who charge that those six cases were unnecessary, that statistical evidence had already established the dangers of too much oxygen, this experiment caused little controversy. It was, after all, successful in a way that everyone can understand. But what would our response have been if babies in the low-oxygen group had been injured by being deprived of the needed and available oxygen? How many children saved from blindness would it have taken to make up for the loss of one infant's life, arbitrarily hazarded for the sake of an experiment?

What of the Willowbrook test criticized by Dr. Beecher and denounced by Senator Thaler, in which 500 mentally defective children were injected with a hepatitis virus? Their parents consented, but whether they fully understood the risks they were consenting to is hazy. Was this test (sponsored by the Army, which is interested in the possibility of developing an immunization to this highly contagious disease) justified by the fact that the incidence of hepatitis, heretofore endemic to the institution, has been dramatically reduced? Dr. Beecher replies with a ringing negative: "There is no right to risk an injury to one person for the benefit of others." Even a million others? Even an enormous benefit? Even an infinitesimal risk of an inconsequential injury?

One point on which all critics of human experimentation seem agreed is that no person should be used without his informed consent. "A patient has the right to know



**SCHOOL SHOT**—The Salk polio vaccine required large-scale tests before final acceptance. Here, a child is inoculated at a New York public school.



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berg rules, the Helsinki Declaration adopted by the World Medical Association in 1964, the A.M.A.'s Ethical Guidelines for Clinical Investigation put forth in 1966—all stress free, informed consent of subjects, careful assessment of risks, and certainty that the experiment is essential. These several codes are clearly necessary, and clearly not sufficient without some means of enforcement.

Last summer, the United States Public Health Service, which finances a large part of the medical research done in this country, ordered its grantees to give detailed assurances that they are maintaining strict procedures, supervised by review boards, to protect patients' rights. Although the United States Surgeon General has urged that "qualified individuals from outside the scientific area be involved in this review," as matters stand all of the commendable codes rely for enforcement on colleagues of the investigators. (Recently the reprimanded Dr. Southam was elected vice president of the American Association for Cancer Research.)

It has been suggested, too, that an independent physician be interposed between researcher and patient to serve as a sort of attorney for the latter, but such an idea is not likely to receive the informed consent of the medical profession. Doctors have no taste for independent supervision of any sort. In order to meet their objections, the Food and Drug Administration recently agreed to accept a waiver of written consent in clinical tests at the option of the physician. The new F.D.A. regulation was further modified before being published to eliminate the need to inform a patient that he is being used as a control. And instead of requiring that the investigator give the patient "all material information," the regulation was rewritten to require only "all pertinent information." A provision that would have called upon the physician to take into account the availability of other remedies before deciding to try an experimental drug was deleted.

Although the tone of some of the criticism constitutes a kind of esthetic inhumanity in itself, the present concern over experiments on humans is, at its best, part of a larger concern for the individual, set against the institution. Our doctors enjoy great prestige and power over individual lives; when they succumb to the casual callousness of the laboratory, to arrogance or ambition or indifference, we are all threatened. (Dr. Beecher's suggestion that the results obtained in unethical research be denied publication is aimed squarely at ambitious

young researchers out to make a quick name for themselves. "Every young man," says Dr. Beecher, "knows that he will never be promoted to a tenure post, to a professorship in a major medical school, unless he has proved himself as an investigator." Probe or perish.)

But critics have been known to be arrogant, too, to arrogate the finer sensibilities to themselves. The choices facing our medical investigators are hard, and those who compare these men to the Nazi doctors are taking a self-indulgent, cruelly self-righteous line. These critics suffer from the same defects of temperament and intellect as those who cannot speak out for civil rights without charging that all policemen are sadists and cannot be against the war in Vietnam without shrieking of genocide. It is possible that a researcher, in his craving for esteem or in his bemusement with some abstraction, will forget what he owes to flesh and blood, and he must not be allowed to forget. But it is also possible that easy sentimentalizing over babies and old people may so frighten patients that they will resist helpful treatment and bring unearned abuse and discouragement to decent men in whom our hopes for medical accomplishment are embodied. "All of us who do this kind of study put our careers on the line," says Dr. Moore. "And some of us have had dreams." That self-restraint that we demand of the scientist is also becoming in the critic.

**S**O we find ourselves in an uneasy position—reluctant to shackle the men who have done us so much good, yet unable to feel quite comfortable while they are entirely at liberty. The simplest code for the medical researcher remains that of Claude Bernard, the so-called founder of experimental medicine, who said that experiments "that can only harm are forbidden, those that are innocent are permissible, and those that may do good are obligatory." It says everything and settles nothing.

Today's more elaborate codes say some things, but cannot settle everything. Barring the unlikely introduction of effective Government supervision, the direction that a researcher's work takes, how fast and far he moves in that direction, and what rules he observes along the way will depend on his own sense of decency and compassion, on the spirit that emanates from his colleagues and superiors, and on the enforced regulations of the institution where he works. Finally, all of these can only reflect our national sense of what one man may and may not do to another. ■