Chapter One

AN OVERVIEW

Human experimentation began when the first doctors treated the first patients. Until recently, however, it was largely a trial-and-error process and, by today's standards, hardly scientific. For hundreds of years physicians made little effort to formally coordinate knowledge, relying instead on intuition from personal experience. It was not until the first medical journals appeared in the late seventeenth century that doctors began to systematically report cases. At first, these reports tended to be anecdotal accounts and isolated testimonials, not full-blown scientific studies.[1] Then, as the rudiments of the scientific process took hold, doctors began collaborative efforts. Many were simply marginal variations on standard therapies.

For most of history, medical research was passive, reflecting straightforward observation and description of the course of events in disease. Rarely did doctors intervene to influence nature's course in any other way than by giving herbs or applying poultices and other concoctions that were the forerunners of today's pharmaceuticals. Only in recent history have doctors tried to learn how to manipulate physiological processes in expectation of curing disease or improving the course of a patient's illness. This move to deliberate experimentation was an escape from the limitations of the methodology of observation. Purposeful tampering with the natural course of disease came late because it must be based on human experimentation, which exposes the patient to possible harm and which runs counter to the traditions of the medical profession. When it was first done, it was on criminals, not patients.[2]

The cardinal rule of medicine—to do no harm—has been taught from the time of Hippocrates in 460 B.C. "I will . . . abstain from

whatever is deleterious and mischievous," the Hippocratic Oath says.[3] Yet literal interpretation of this oath would wipe out a large part of research.

The ancient Greeks and Romans did not attempt serious experiments as we know them. For instance, while treating a boy whose brain had been exposed as the result of an injury, Hippocrates picked out the fragments of bone that had lodged in the brain and also "gently scratched the surface of the cortex with his fingernail."[4] Hippocrates observed the convulsions that occurred on the opposite side of the boy's body. Today, that act would be a teaching exercise. In Hippocrates' time, it amounted to an experiment because so little was known about the brain and the function of the central nervous system.

The ancient medical philosopher also warned in his famous First Aphorism that "life is short, the art long, opportunity fleeting, experience treacherous, judgment difficult."[5] Our interpretation of that aphorism depends on the translation. The words "experience treacherous" can also be translated from the Greek as "experiment perilous." This latter translation has been cited as a warning to doctors against experimenting with new and unknown therapeutic measures. It describes an attitude that undoubtedly contributed to the lack of progress in medicine for many centuries.

Those doctors who experimented did so at their own peril. The risks were emphasized in a British court decision in 1767: "Many men very skillful in their profession have frequently acted out of the common way for the sake of trying experiments . . . they have [acted] ignorantly and unskillfully, contrary to the known rule and usage of surgeons."[6] The warning was repeated as late as 1918 in a legal encyclopedia: "While it is the duty of a physician or surgeon to keep up with the advancement made by his profession, it is also his duty not to attempt to forge ahead of it by trying experiments on his regular patients."[7]

Nevertheless, movement developed toward a more liberated attitude about human experimentation. One of its proponents was the celebrated French physiologist, Claude Bernard (1813–1878), whose classic experiments demonstrated several functions of the liver, the digestive properties of the pancreas, and the nervous system's control of blood circulation. He stated his opinion on the subject in 1865: "Physicians make therapeutic experiments daily on their patients, and surgeons perform vivisections daily on their subjects. Experi-

ments, then, may be performed on man, but within what limits? It is our duty and our right to perform an experiment on man whenever it can save his life, cure him, or gain him some personal benefit. The principle of medical and surgical morality, therefore, consists in never performing on man an experiment which might be harmful to him to any extent, even though the result might be highly advantageous to science."[8]

But in recognizing the need to experiment on humans, Bernard emphasized the importance of self-experimentation: "Morals do not forbid making experiments on one's neighbor or on one's self. In everyday life men do nothing but experiments on one another. Christian morals forbid only one thing, doing ill to one's neighbor. So among the experiments that may be tried on man, those that can only harm are forbidden, and those that may do good are obligatory."[9]

By the end of World War II, such principles had been defiled by doctors in Nazi Germany, who invoked the name of science to justify atrocities labeled "experiments" that involved hundreds of thousands of victims, most of them Jewish. The Nazi doctors were not the first to betray their training as healers, but their experiments were the most horrible, at least in recent times. They were sadistic human torture under the guise of medical research. Among the twenty Nazi doctors who were tried at Nuremberg was an eminent malaria expert, Dr. Klaus Karl Schilling. A former member of the League of Nations Malaria Commission, Schilling infected more than one thousand prisoners at Dachau with the parasitic disease. More than four hundred died, many from complications of treatment with experimental antimalarial drugs, often given in excessively large doses. He was hanged.

Brigadier General Telford Taylor, the United States chief war crimes prosecutor at Nuremberg, testified that among the "experiments" Nazi doctors performed were:

> Locking prisoners into airtight chambers and then rapidly changing the pressures to duplicate the atmospheric conditions which an aviator might encounter in falling long distances without a parachute or oxygen.
>
> Infecting individuals with cholera, diphtheria, paratyphoid A and B, smallpox, typhus, and yellow fever and then testing experimental and mostly useless vaccines on them. Some inmates at Buchenwald and Natzweiler "were deliberately infected with

typhus with the sole purpose of keeping the typhus virus alive and generally available in the bloodstream of the inmates."

Injecting phenol or gasoline into the veins of prisoners, who died within sixty seconds.

Testing to determine how long humans could survive without water and after eating huge amounts of salt.

"These experiments revealed nothing which civilized medicine can use," and among the physicians who did them were leaders of German medicine, Taylor said.[10]

At the time of the Nuremberg Nazi war crimes trials, there was no formal code of ethics in medical research to which the judges could hold the accused Nazi doctors accountable. The Nuremberg trials forced doctors and scientists to consider openly for the first time the value, ethics, and limits of human experimentation, and made the medical profession realize that serious breaches of medical ethics had occurred in the past.

Out of the Nuremberg trials in 1947 came the Nuremberg Code, the first code to deal specifically with human experimentation. It created ethical guidelines for the conduct of medical research throughout the world. The Nuremberg Code recognized that human experimentation could yield results for the good of society unobtainable by other means. Although many researchers had customarily obtained consent from volunteers in the past, it was the Nuremberg Code that first established the practice formally. The code deals with self-experimentation in Article 5, which states: "No experiment should be conducted where there is an *a priori* reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects."[11]

Dr. Leo Alexander, an American psychiatrist serving as a consultant to General Taylor, prepared the memorandum on which the Nuremberg tribunal based the code. Alexander told me that in drafting the memorandum he had recalled several famous self-experiments from medical history, and, with them in mind, he wrote: "It is ethically permissible for an experimenter to perform experiments involving significant risks only if the solution, after thorough exploration along all the other lines of . . . scientific investigation, is not accessible by any other means, and if he considers the solution of the problem important enough to risk his own life along with those of his non-scientific colleagues . . ."[12]

Most people believed that unethical research could not happen in a democratic society. Yet, in the 1960s, only two decades after the adoption of the Nuremberg Code, there were shocking disclosures of glaring breaches of ethics that had been committed by a small number of American doctors just after World War II. These breaches came to attention largely through an article by Dr. Henry K. Beecher, an anesthesia and pain researcher at the Massachusetts General Hospital in Boston.[13] Beecher cited fifty unethical studies, among them:

> Deliberately withholding penicillin from 109 servicemen who suffered streptococcal infections, thereby exposing them to the risks of rheumatic fever.
>
> Administering several chemicals of no benefit to patients with advanced cirrhosis to determine their effect on the liver disease.
>
> Exposing twenty-six normal newborn infants to extensive X rays so their urinary bladder function could be studied.[14]

Most of this post–World War II criticism about breaches of scientific ethics involved civilian researchers working in private institutions. However, government researchers came under attack in 1972 when the public learned that United States Public Health Service officials had withheld antibiotic therapy from a group of syphilis patients whose medical histories they had carefully followed for more than forty years. The patients, who had acquired syphilis naturally, had been asked to volunteer for what came to be known as the Tuskegee Study.[15] Its aim was to observe the natural course of the infection and to further medical knowledge about the disease. In return for their cooperation, the volunteers—mostly poor and black—were to be given free medical care and free burials. The ethics of the study would not have been questioned except for a major development that occurred during its course. It was discovered that when penicillin was administered in the early—but not late—stages of the infection, syphilis could be cured. To be sure, most patients in the study were already in the late stages of the disease by this time, probably too late for them to have benefited from the discovery. Nevertheless, the researchers did not offer treatment to any volunteer.

Further erosion of the public's faith in the ethics of research came from revelations that Pentagon officials, in order to simulate a germ

warfare attack, had purposely spread microorganisms and other biological substances in eight areas of the United States, including a simulated poison through two New York City subway lines.[16] Only after the organisms were released did doctors learn that some of these bacteria could cause disease in humans. More recently it was disclosed that officials of another American government agency, the Central Intelligence Agency, secretly conducted experiments on Americans across the country, "slipping" LSD and other mind-affecting drugs to numbers of people without their knowledge or permission. At least one person committed suicide as a result.

News accounts of these experiments stimulated intense debate about the ethics of human experimentation. Scientists insisted that such examples of unethical behavior were rare exceptions, but the breaches made it clear that medical researchers did not always live up to their ethical pledges.

In the wake of the syphilis scandals, the federal government began to issue regulations in an attempt to legally enforce the principles set out in voluntary codes. Formal rules were adopted that drastically changed the role of human experimentation. Laws in the United States and some other countries now *require* human as well as animal experimentation. The Food and Drug Administration, a federal agency acting under a legal mandate, requires extensive experiments on humans to prove safety and efficacy before any drug or medical device can be marketed for general use. Additionally, the public endorses human experimentation via taxpayer funding for such research at medical centers throughout the country. Society clearly accepts, even encourages, ethical experimentation on humans toward gaining new knowledge against disease, but only within strict parameters and under clearly defined rules.

Since 1966, each medical center that receives federal funds for research has had to comply with federal regulations and to organize committees that go by various names such as Institutional Review Board or Ethics Committee. Before experimenting on humans, American research physicians must obtain prior approval from these groups, followed by written informed consent from each volunteer. These regulations were created to protect volunteers from participation in unethical research projects. There are about 550 review boards in the United States, and they have become the standard formal review mechanism at all American research institutions. Similar committees now exist in England and other countries.

These committees were conceived to address all ethical issues of human research, but, surprisingly, the question "Who goes first?" is not usually discussed. The review committee at the Johns Hopkins Hospital is an exception. In 1983 this committee sent a memorandum to the faculty of the medical school reminding members that proposed self-experiments must be submitted for review in the same way any investigation using human volunteers needed to be submitted. One stated purpose of this requirement was to protect an overenthusiastic self-experimenter from taking unwarranted risks. "Under these circumstances most of us are so excited about the prospect of new knowledge [that] the fact that there is any risk associated may be minimized or escape our attention," said Dr. Thomas R. Hendrix, the chairman of the Hopkins committee.[17]

Another regulation, issued in 1967 by the National Institutes of Health, specifically approves the practice of self-experimentation with the aim of providing "the same safeguards for the investigator-subject as for the normal volunteer." The regulation includes, among other things, a requirement that the self-experimenter undergo a complete medical examination beforehand.[18]

Nevertheless, in 1974, when Congress established a commission to review specific areas of human research, such as on prisoners and fetuses, no attention was directed to the subject of self-experimentation or to the question of who goes first. Still, the federal regulations that resulted from the congressionally mandated review were a recognition of the revolutionary changes in medical science that had occurred over recent decades, and they were to allow research and human experimentation to flourish on an unprecedented scale.

Earlier in this century, there were few researchers in the United States and they did their medical investigations in their spare time. Research was often a hobby for doctors with independent incomes or those who could support experiments through fees from private practice. These well-heeled individuals were members of an informal "gentlemen's club" that viewed research more as a luxury than a necessity. They would tend to visit their laboratories at leisure to solve puzzles that happened to intrigue them. Undoubtedly, there were many more doctors who had an interest in doing research but simply could not afford it.

The revolutionary change came in the latter part of the twentieth century, particularly after World War II, when Congress began to grant large sums of money to researchers in medical centers and universities.[19] Larger numbers of doctors were paid salaries to do

research full time in what became a respected, even coveted, career. Today, government grants support the salaries of most researchers as well as the costs of their experiments. The increased budgets led to the creation of new medical schools and to the vast expansion of research programs in most existing ones.

Today research is highly competitive, and the fierce competition for the shrinking research dollar has changed the gentlemen's club atmosphere. Research is often done by teams because, given the increased complexity of the nature of science, few medical investigators can truly work alone. A scientist cannot dream up an experiment in a few days and proceed with it. It can take years to acquire the basic information necessary to begin to comprehend the facts behind a research project, to plan the experiments, and to apply for funding to perform them.

Researchers, supported by public funds, are under constant pressure to produce results that justify taxpayer funding. Their careers are linked to getting new grants, and the applications for many of these grants are based on the ability to convince a sufficient number of volunteers to participate in a particular project.

This situation imposes new dangers. Researchers have become increasingly dependent on their ability to publish in the medical literature in order to win promotion and continued financial support. As Dr. Oscar D. Ratnoff, a leading blood researcher, and Marian F. Ratnoff have written: "Despite miles of verbiage about the need to recognize fine clinical teachers, the route to promotion is all too often dependent upon the production and publication of experimental results. Even disregarding promotion, the economic well-being of the member of a clinical department may be inextricably hitched to his ability to carry out experimental work. . . . Research, it would seem, must be conducted not only for its own sake but to gain both salary and advancement. No wonder the desire for short cuts to attractive answers blunts the investigator's judgment about what is and what is not appropriate."[20]

There are various motivations—sometimes hidden, sometimes overt—to entice other people to volunteer for research projects. Medical researchers may have much to gain personally in terms of career advancement and even monetary profit by doing something to someone else that they would not do to themselves or to family members. But in the midst of this situation, self-experimentation continues, a testimony to man's nobler instincts.

. . .

The earliest recorded self-experimenter I know of, Santorio Santorio, shared few of the concerns of his contemporary counterparts. He worked alone, without fanfare and with little reward, in Padua, Italy. Regarded as the father of the science of metabolism, Santorio Santorio (also called Sanctorius) lived from 1561 to 1636, the age of Shakespeare and of William Harvey's discovery of the circulation of the blood.[21] The great difficulty of scientists in Santorio's era was finding suitable instruments to measure changes in basic physiologic functions. Santorio was perhaps the first physician to use a thermometer to measure the temperature of the body. He also used a steelyard, a type of large portable balance, to discover what is called "insensible perspiration," the continual process by which the body loses large quantities of fluid that cannot be seen by the naked eye.

Santorio placed his worktable, his bed, and all his other daily necessities upon his steelyard balance. Over a thirty-year period, he experimented on himself to determine how his body responded to various physiological and pathological conditions. Each day he weighed himself and the amounts of food he ate and drank, as well as his bodily discharges. From these measurements he determined that there was always an appreciable difference between the weight of the food and drink he consumed and what his body lost as waste and sweat. This difference is insensible perspiration. Today, the knowledge gained from Santorio's self-experiments is applied in hospitals whenever doctors operate on patients or treat victims of burns, heart attacks, or other serious problems. Because the amounts of fluid lost through insensible perspiration can be critical in the care of such patients, doctors routinely prescribe extra amounts of intravenous fluids to compensate for what is lost.

It is said that Santorio's experiments were the first in which a physician thought of verifying theoretical statements by testing and retesting. Medical history books show a picture of the bearded physician seated in a chair facing a table, which is resting on balances hanging from the ceiling. On the table are several plates of food and some wine. Santorio's chair "was at a finger's height from the floor," according to a leading twentieth-century medical historian, Dr. Arturo Castiglioni.[22] When Santorio ate, Castiglioni said, "the chair lowered itself somewhat, and he was easily able to establish when he had taken the right quantity of food and drink. The elevation of the chair indicated the quantity of perspiration, since the sum of the excretions was deducted from the total amount of the loss of weight.

Assuming that the healthy adult body generally retains the same weight for twenty-four hours, the experimenter indicated with his balance the absorbed substances, the secretions and excretions, noting the rest of the loss until he obtained the actual weight effective on the next day."

More than two hundred years later another self-experimenter, Max Josef von Pettenkofer, was probably very much aware of Santorio's experiments and contribution to medical research.

Max von Pettenkofer is one of those scientists whose fame is based more on one mistake than on his several solid scientific triumphs. Pettenkofer was a public health pioneer who developed the first large city pure-water system, in Munich, Germany. He was one of the most influential scientists of his era and a man who at various times was a chemist, pharmacist, actor, and poet. As a scientist, he established basic facts and concepts about nutrition. He discovered a new amino acid, creatinine, that he detected in human urine; today doctors routinely test for it as a measure of kidney function. Pettenkofer also developed a color test for bile. In nonmedical areas, he created methods to retrieve precious metals used in minting coins and an industrial technique to make cement. Pettenkofer improved the illuminating power of wood gas, and his new method was used to light several German cities as well as the Munich railway station.

His famous mistake resulted in part from a self-experiment. In 1892, at the age of seventy-four, eight years after another German scientist, Dr. Robert Koch, had identified the bacterium that causes cholera, Pettenkofer swallowed a pure culture of the microorganism. For many years before Koch's discovery, Pettenkofer had believed that cholera was caused by a microorganism, but he was convinced that it took more than the cholera bacterium alone to cause the disease.[23]

Cholera kills by producing such severe diarrhea, quarts of it, that it dehydrates the body. It can strike suddenly, while the victim is in bed or walking the street. In the late nineteenth century, recurrent cholera epidemics were one of the grimmest challenges to public health. During one outbreak in Munich, Pettenkofer and his young daughter came down with the infection, and their cook died of it. This led Pettenkofer to begin an intensive study of ten cholera outbreaks, including the one that had affected his family. While investigating an epidemic in France in 1892, he noted that certain regions

escaped, despite the presence of cholera bacteria in the water. He developed a theory that a combination of four conditions was essential for an epidemic to occur: (1) a specific germ referred to as *X;* (2) certain local conditions, chiefly affecting the soil; (3) certain seasonal conditions; (4) certain individual conditions.

Pettenkofer became embroiled in a controversy that had been going on for decades. No one could agree whether cholera was spread directly from person to person or whether it struck many people at the same time due to a combination of atmospheric, climatic, hygienic, and other environmental factors. Only the waterborne nature of cholera had been clearly documented. In 1854, in one of the most dramatic applications of the principles of epidemiology, Dr. John Snow had traced an epidemic of cholera in London to drinking water obtained from a feces-contaminated well and particularly to a pump on Broad Street. Snow gained fame for his studies of the epidemic. The Soho parish councillors removed the pump handle. Thirty years before Koch's identification of the cholera-causing bacterium, Snow argued that cholera was caused by a specific waterborne microorganism, yet to be discovered.[24] However, Snow had many critics, and Pettenkofer was among them;[25] he pointed out that the epidemic had been on the wane by the time the pump handle was removed.

The controversy was fueled by Koch's discovery in 1884 of the bacterium that he described as "a little bent, comma-shaped" and that is called *Vibrio cholerae.* Koch saw it through the microscope and also grew it from samples of drinking water obtained from a pond in India during an epidemic. Koch believed the disease spread when cholera patients excreted the bacterium into the soil or when it came into contact with drinking water. Koch postulated the bacterium was the sole cause of cholera.

Pettenkofer accepted Koch's organism as the *X* factor. But Pettenkofer believed that subsoil water, not drinking water, played the principal role, and he held to his four conditions. According to Pettenkofer, the bacterium alone would not cause cholera. Pettenkofer was convinced the germ could be spread not just by patients but also by apparently healthy individuals traveling among cholera localities. We know today that Pettenkofer was describing the carrier state, which, because of the peculiarities of the body's immunologic defense system, allows some people to harbor the bacterium in their intestines without developing full-blown symptoms of the disease.

Instead of reasoning that the carrier state was due to an immunologic phenomenon, Pettenkofer attributed the carrier state to environmental factors. According to Edgar E. Hume, Pettenkofer's biographer: "So certain was Pettenkofer of his ground that the vibrio [the causative bacterium] cannot of itself cause cholera, that he resolved to perform what he termed the *experimentum crucis* on his own person, i.e., to swallow the comma bacillus. If this bacillus were the only cause of cholera, he could not escape the disease. Even the bacteriologists were willing to admit this and warned Pettenkofer that his experiment would prove fatal."[26]

On October 7, 1892, Pettenkofer swallowed one cubic centimeter of bouillon laced with cholera bacilli derived from a patient who had died of it. Koch had claimed that stomach acid might kill cholera bacteria. So, after neutralizing with sodium bicarbonate whatever acid might be present on an empty stomach, Pettenkofer took a swig of the contaminated water. He would allow no one to cast doubt on his challenge to Koch by saying the dose was weak; Pettenkofer emphasized the fact that the number of bacilli swallowed was of course far greater than the number ordinarily taken into the body under normal conditions of exposure. The next day he began to experience abdominal colic from extensive gas pains and diarrhea. The diarrhea lasted almost a week. He also had an enormous proliferation of the cholera bacteria in the stools, but he never became seriously ill.

The general conclusion of Pettenkofer's critics was that he had escaped cholera through luck, possibly coupled with some immunity from his earlier attack. Today, with a better appreciation of the spectrum of symptoms produced by cholera, most would agree he had contracted an extremely mild case of the disease.

Although Pettenkofer was confident of his theory, he said he was prepared to get a severe case: "Even if I had deceived myself and the experiment endangered my life, I would have looked Death quietly in the eye for mine would have been no foolish or cowardly suicide; I would have died in the service of science like a soldier on the field of honor. Health and life are, as I have so often said, very great earthly goods but not the highest for man. Man, if he will rise above the animals, must sacrifice both life and health for the higher ideals."[27]

Pettenkofer's cholera self-experiment was repeated by several other scientists with similar results. One was a Pettenkofer student,

Rudolph Emmerich. Another, Elie Metchnikoff, would later win a Nobel Prize for his studies on immunology. All three erred in the conclusions they drew from their experiments—not because they were done on themselves, but because parts of their theory that the bacterium was not the sole cause of cholera were wrong and because they did not accumulate enough data on a sufficient number of volunteers.[28] Even today the factors that allow one person to develop a full-blown case of cholera and others like Pettenkofer, Emmerich, and Metchnikoff to escape with trivial symptoms are poorly understood. Pettenkofer was correct in believing that cholera was due to the bacterium Koch discovered. He was wrong in his stubborn persistence that it was also caused by a factor in the subsoil, an error that, like John Hunter's, can be attributed in part to the scientific ignorance of his time.

The nineteenth-century tradition of self-experimentation embodied by Pettenkofer is as strong as ever. Self-experiments were not rare earlier in the twentieth century, and they have been anything but rare in recent years. Consider these several examples:

Acquired immune deficiency syndrome was first recognized in New York and California in 1981; no one knows whether it is a truly new disease or whether it has infected people in remote areas of the world for centuries. Clearly, infections with the AIDS virus have spread to almost every country, and it is now a scourge that threatens to kill millions of people.

In 1986, Dr. Daniel Zagury, a French physician, became the first to test a candidate AIDS vaccine on humans by injecting it into his own arm. That act quickened the pace of AIDS vaccine research. And in the scientific investigations to learn more about this fatal disorder that cripples the immune system and leaves the infected individual prey to a wide variety of opportunistic infections, researchers surely will continue to experiment on themselves.

Proof that AIDS is caused by a virus has led to an unparalleled worldwide effort to develop a vaccine to protect against it. The endeavor will take many years, even decades, with no guarantee that the research efforts will be successful. As scientists explore a wide variety of approaches, they are using molecular biology techniques to carve out selected proteins from different areas of the AIDS virus. The hope is that at least one of these small pieces of the virus will be harmless yet sufficient enough to stimulate protection against invasion of the body by the entire lethal virus.

In 1986, Dr. Zagury of the Pierre-et-Marie Curie University in Paris and his French and Zairian colleagues began the first reported human experiments with an AIDS vaccine in Kinshasa, Zaire. Zagury, whose blood tests showed no evidence that he was infected with the AIDS virus, injected himself with what he hopes will be an effective AIDS vaccine. The vaccine he used had been made by harnessing sophisticated modern genetic techniques to the oldest vaccine, the one that uses the harmless vaccinia (cowpox) virus to protect against smallpox. To create the experimental AIDS vaccine, the scientists inserted a protein called gp 160 that is located in the outer coat of the AIDS virus into live vaccinia virus.

After the injection of the experimental vaccine, Zagury tested his blood every week for nine weeks. Results showed that the experimental vaccine stimulated the production of the desired gp 160 antibody. Furthermore, since Zagury did not develop any toxic reaction or any symptoms of AIDS during the first several months after he took the injection, he felt his self-experiment indicated the safety of the vaccine for humans, at least in the short term. Zagury reported confirmatory results from injections of the experimental AIDS vaccine in "a few other" uninfected human volunteers. Nevertheless, because the incubation period of AIDS is so long—at least several years—dangerous reactions might show up in the future.

In fact, Zagury did not inject himself with the AIDS virus. His self-experiment was not designed to test the efficacy of the vaccine. Rather, its purpose was to test the vaccine's ability to produce an immune reaction in humans and to determine its safety. The experimental injection came after his team had tested a form of immunization known as immunotherapy on a small number of Zairians with AIDS and after the experimental vaccine had been tested on animals. Zagury said the results of these experiments led to his self-experiment.[29]

No one fully understands how the AIDS virus infects the body or how the body might protect itself against progression from infection to disease. No one even knows how many strains of the AIDS virus there are. Therefore, research into a number of different candidate vaccines is being conducted. Scientists often have looked to the envelope, or protective coat, of a virus as the most likely part of the infecting agent to stimulate production of protective antibodies. The gp 160 protein used in Zagury's experimental vaccine comes from this outer envelope. In the United States, Dr. Allan L. Goldstein of George Washington University in Washington, D.C., heads a team of

scientists who have developed another candidate AIDS vaccine that uses a synthetic protein which he hopes will protect by mimicking one in the inner shell of the AIDS virus. Because the core proteins of the AIDS virus are believed to be more stable than those on the surface, Goldstein theorizes that his experimental vaccine might protect against a wide variety of strains of the AIDS virus.

Goldstein's team has applied for permission from the Food and Drug Administration to test the vaccine on humans. If it is given, Goldstein says he will be the first to take the vaccine.

Dr. William Randolph Lovelace II, whose family founded the medical clinic that bears his name in Albuquerque, New Mexico, combined his interests in medicine and aviation by investigating the problems of high-altitude physiology and pilot fatigue. Early in his career he was a surgeon at the Mayo Clinic, and then, during World War II, he became head of the Aero-Medical Laboratory at Wright-Patterson Air Force Base in Dayton, Ohio.[30]

Flights above 35,000 feet in pressurized cabins are routine now. But when airplanes first reached those heights in World War II and an aviator was forced to jump, he would lose consciousness within a minute due to lack of oxygen. He could not pull the rip cord of his parachute. Even if he could pull it, another five to ten minutes would pass while he dropped to an altitude where he would have enough oxygen to survive, and then there would be little chance of regaining consciousness. There was an urgent need for special oxygen inhalation equipment. Lovelace became his own test subject to learn the problems of high-altitude escape and parachuting and to develop such a device. It contained about a fifteen-minute supply of oxygen, enough to keep an aviator who parachuted from 35,000 feet conscious until he reached the 15,000-foot level, at which height he would be safe.

On June 24, 1943, above Washington State, the thirty-five-year-old surgeon and army lieutenant colonel bailed out of a B-17 bomber at 40,200 feet. It was his first jump, and he wanted to convince himself and everybody else that the emergency oxygen unit he and his colleagues had devised worked in a real jump as well as it did under laboratory conditions. "We had believed that the shock of the opening parachute would put a force of less than eight *g*'s on the jumper at that high altitude, but we were wrong." Lovelace said. (The earth's forces of gravity act on humans to give them the weight to which

they are accustomed; under normal circumstances this is one *g*. But the effects of acceleration on the body are measured in weight. At two *g*, body weight doubles; at three *g*, it triples; and so on. Humans can easily withstand acceleration of up to ten *g* for several seconds because the physiologic effects are reversible. But acceleration of more than twenty *g*, even for only fractions of a second, may damage bone and tissues.) Computations later showed the force on Lovelace was thirty-two *g*. The shock of the opening parachute knocked him unconscious in forty-degree-below-zero temperatures, and his glove was torn away. His left hand was instantly frostbitten. Somewhere in his descent he regained consciousness, and at 8,000 feet he waved to a smaller plane that was following his path. Twenty-three minutes and fifty-one seconds after he dropped out of the bomber, Lovelace landed in a wheat field with a thump and a wrenched back. The test prompted development of delayed automatic opening devices for parachutes. Lovelace was awarded the Distinguished Flying Cross.

Automobiles, airplanes, and spacecraft are safer now because of the scores of deceleration experiments that Dr. John Paul Stapp, an Air Force physician, did on himself on fast track and rocket sled rides to determine the human tolerance limits to crash forces.[31]

Stapp became known as "the fastest man on earth" for having sped faster than a forty-five caliber bullet on a rocket sled that was mounted on heavy rails set in concrete at Holloman Air Force Base in New Mexico. There, on December 12, 1954, the forty-four-year-old Air Force colonel reached a peak velocity of 632 miles per hour in five seconds as the wind and sand stormed at his body. Then he slammed to a stop in one and a half seconds, withstanding pressure almost forty times his own weight. Bucket scoops underneath the sled allowed him to come to such an abrupt halt at such fantastic speeds. They dug into a trough of water, stopping the sled with about the same force as a car hitting a stone wall at fifty miles per hour. A web of straps locked Stapp in place, his head protected by a helmet and his teeth by a rubber bite. The five-foot-eight-inch Stapp suffered only a black eye and several bruises from the historic run. Stapp's contorted face became familiar to Americans in pictures in magazines, and his self-experiments became the basis of a 1956 movie, *On the Threshold of Space.*

John P. Stapp was born on July 11, 1910, the son of American Baptist missionaries, in Bahia, Brazil, where he spent the first twelve years