Chapter II

WHAT IS MEDICAL TECHNOLOGY AND WHY SHOULD IT BE ASSESSED?

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New medical technologies have transformed medical practice in the past several decades by making effective preventive, diagnostic, and therapeutic tools available to the medical-care system (3). Some diseases can now be effectively prevented, and medical innovations such as antibiotics have provided effective therapies for a number of other diseases. New diagnostic techniques have frequently made it possible to detect disease in time to apply an appropriate therapy. Even in cases of diseases for which no effective preventive or therapeutic measures are available, relief of pain, amelioration of symptoms, and rehabilitation of individuals affected by chronic conditions have been increasingly feasible.

On the other hand, the accelerating pace of medical technology development has raised a number of troubling issues. Questions are being asked about whether current R&D efforts are directed at developing the most desirable technologies, whether adequate planning precedes the introduction of new technologies into the medical-care delivery system, and whether the introduction of some new medical technologies may have indirect or unanticipated social implications.

One way to address these issues might be to assess the social impacts of new medical technologies while they are still being developed. To begin the discussion of this possibility, this chapter describes the aims, nature, development, and clinical status of nine medical technologies.[1] These nine cases are designed to show what medical technologies are, how they are developed, and why it might be profitable to assess their social impacts. In addition, the cases and the overview that follows them point out some of the complexities that will have to be recognized if medical technologies are to be effectively assessed:

- Medical technologies are extraordinarily diverse in nature and are used for a wide variety of purposes.
- Medical technologies are devised in a great variety of ways and places.
- The development and use of medical technologies pose a large number of problems, including some that are purely technical (or medical) and others that involve wider social issues.
- Technical and social problems often cannot easily be separated; they are inextricably linked.

[1] The nine technologies described here were chosen by the Advisory Panel to this study because they illustrate a variety of technological solutions to medical problems and because they raise a broad array of important issues, These cases do not, however, purport to illustrate all of the important aspects of medical technology that must be considered in implementing programs of assessment, nor can the points illustrated here be generalized to all other cases.

1. The Continuous Flow-Blood Analyzer[2]

The primary function of the clinical laboratory is to analyze and provide data on samples of body tissues or fluids. After correlating these data with firsthand observations and results of other tests, physicians are better able to make accurate diagnoses and to determine the proper therapy for their patients. Reliable data from clinical laboratories is essential for current medical practice (143).

Clinical laboratories perform a wide variety of tests. Because some tests on blood are fairly simple, proceed according to a standard protocol, and yield easily quantified results, it has been possible to automate them. The advantages of automated testing include both increased precision and decreased unit cost (5, 154). A number of machines have been introduced to achieve automation of blood testing; perhaps the most widely adopted is the continuous flow-blood chemistry analyzer.

The continuous flow-blood analyzer was invented by Leonard Skeggs in 1950. His device removed protein from the serum, added test reagents to small amounts of the remaining sample, incubated the mixture, measured the rate of the test reaction, and drew a curve indicating the results. These curves could then be readily interpreted to indicate the amounts of certain chemicals (such as glucose or blood urea nitrogen) that were in the blood samples.

The tests are based on chemical and biochemical principles that have been derived from basic research and applied to clinical problems over a period of many years. Skeggs' contribution was to develop ingenious methods for automating the routine, iterative steps of the testing protocol.

Skeggs built a prototype machine in his basement for about $1,500, completing it in 1951. Between 1951 and 1954, he attempted to interest private companies in the machine. The Technicon Corp. signed a contract with Skeggs in 1954 and was assigned his patents. From 1954 to 1957, Technicon improved and modified the design at a cost of about $1 million and finally made a production model. By the end of 1957, Technicon had sold 50 systems for about $5,000 each. In 1961, Skeggs designed a new machine that performed multiple tests on a single sample of blood and reported the several results together. This new machine was tested in 1963, soon marketed, and readily accepted.

Subsequent models have improved the original design and permitted increasing numbers of tests to be done on a single sample. These new machines have been increasingly costly to develop and to manufacture. In 1973, for example, a machine that could perform up to 20 tests (the Sequential Multiple-Analyzer with Computer (SMAC)) was introduced. The cost of developing the SMAC was almost $7 million and each machine now sells for $250,000.

By adopting machines such as the continuous flow-blood chemistry analyzers, many hospitals and independent testing firms have automated their clinical laboratories during the past decade (5). Technicon sold about 18,000 analyzers by 1969, and by 1974 another 8,000 of a newer model, introduced in 1970, had been

[2]Most of the material in this case that is not otherwise referenced is drawn from ref. 117.

sold. By 1972, more than 50 percent of hospitals had automated their chemistry and/or hematology laboratories, and almost 50 percent of independent laboratories had automated one or both functions. Both operations had been automated in essentially all of the larger laboratories and hospital.

The fiscal impact of laboratory testing is profound. In 1971, an estimated 2.9 billion tests were done at a cost of $5.6 billion (218). The costs rose to over $11 billion by 1974 and were estimated to be $15 billion in 1975 (21), more than 10 percent of the total national health expenditure. The number of tests reached 5 billion in **1975** and is projected to rise at a rate of 11 percent per year for the foreseeable future (218).

Although large machines such as blood chemistry analyzers dramatically symbolize the huge expenses involved in clinical laboratory testing, the cost of the equipment itself is relatively small. Expenditures for laboratory instruments of all types in the United States reached $220 million in 1974 (115), but this was only 21/z percent of the clinical laboratory bill. The expense of clinical laboratory testing is made up primarily by investment in space, supplies, and maintenance; personnel costs for carrying out the procedures and collecting, recording, and reporting the results; and profits of the laboratories and the physician. Thus, relatively modest expenditures for equipment can lead to enormous costs for the medical-care system.

An additional cost, which is much more difficult to measure, stems from the increased use of laboratory testing that may have been stimulated by the ready availability of automated equipment (154). In particular, the multichannel analyzers described above make it possible to perform many "extra" tests on a single sample, at low unit but high aggregate cost. The growth of third-party payment mechanisms may also have provided some impetus for the increased use of clinical laboratories. Furthermore, as such testing has become increasingly used, fears of malpractice liability may have led to requests for even more tests, as part of the practice that has been called "defensive medicine." Some have suggested that many more clinical tests are now performed than are necessary for even the most rigorous medical practice *(176, 177),* and a study indicated that doctors frequently fail to use the results of tests that they have ordered (215).

This case illustrates two important points about the development and use of medical technologies. First, although the principles of clinical laboratory testing are based on knowledge derived from biochemical research, which is largely Government funded, the automated analyzers now used were developed almost entirely by private industry. Second, the bulk of high clinical laboratory costs are not due directly to the high cost of the machinery, but rather are due to the cost of supplies and personnel that the machines require, to substantial profits by laboratory owners and physicians, and to increased (possibly excessive) demand for testing that their availability has stimulated.

2. The Computerized Axial Tomography (CAT) Scanners

The computerized axial tomography (CAT) scanner, which combines sophisticated X-ray equipment with an on-line computer, has **been** hailed as the

[3] The historical material in this case is drawn from ref. 11, pp. K1–K8.

greatest advance in radiology since the field was created by the discovery of X-rays. The X-ray unit directs beams of X-rays through the human body from multiple directions, and the computer analyzes the information thus obtained to reconstruct images of cross-sectional planes that could not be visualized by conventional radiological techniques. The CAT scanner has revolutionized diagnosis of abnormalities within the skull, such as brain tumors, and is already being used widely.

The development of the scanner resulted from research in mathematics, radiology, and computer technology. Research at the beginning of this century provided a mathematical basis for image reconstruction, but the procedures were laborious and awaited the availability of computer methods for their complete development. Meanwhile, research in radiology provided sophisticated new techniques. Oldendorf and Cormack built crude scanning devices in the United States in the early 1960's, reporting their work primarily in the technical literature of applied physics. It was difficult to obtain funding for further work, because Government agencies such as NIH did not perceive its potential, and private companies felt that the costs of solving the engineering and computing problems that remained would exceed any potential profit.

Hounsfield, working in the research laboratories of a British electronics firm called EMI, Ltd., began to work on the same concept in 1967 and obtained a British patent in 1969. His company was also initially unwilling to assume the financial risk of developing a clinically useful device, but the British Government granted funds for developing four prototypes. A workable scanner was ready by 1971 and was first used clinically by Ambrose in England. The first unit in the United States was installed at the Mayo Clinic in 1973.

The scanner was immediately successful, and several firms quickly developed and marketed similar models. At present, there are more than 300 scanners in use in the United States, and several hundred more have been ordered. Each scanner costs from $350,000 to $700,000. These machines are used to detect abnormalities in the head; new scanners that extend tomographic capability to the whole body have recently been developed and are now being marketed.

The expenditure for CAT scanning is already enormous. Currently, more than $200 is charged Per scan, and a recent nationwide studv showed that each machine is used to scan "approximately 12 patients per day (100). Thus, with over 300 machines in use, the yearly bill for scanning may approach $200 million.

The CAT scanner is unquestionably a major technological advance, but its impact on the health of patients has not yet been carefully evaluated. Studies done so far indicate that CAT scanning does tend to replace pneumoencephalography, an invasive and painful diagnostic procedure (100). Many more scans are now done, however, than can be accounted for by substitution for previously available techniques. CAT scanning provides physicians with a wealth of diagnostic information that would not otherwise be available, but the extent to which this additional information can be used profitably to design programs of therapy is not known. Recent controversy has centered on the question of whether more scanners are being purchased and used than are necessary to insure an optimal level of medical care for neurologically disabled patients (214).

This case of the CAT scanner, a newly developed diagnostic device, raises three points that assessors of technology development must consider. First,

although much of the basis for the scanner was provided by research done in the United States, targeted development was not supported in this country, and the first clinically useful device was manufactured in England. Decisions made at the National Institutes of Health or other U.S. agencies may have a limited effect on the progress of R&D in other countries. Second, private companies were initially unwilling to invest in developing the scanner because they did not think it would be profitable. A (British) Government procurement program may have helped to overcome this barrier. Such collaborations between Government and industry may provide a mechanism for expediting the development of useful but costly technologies. Finally, although it was introduced only 3 years ago, the scanner has already been widely adopted and has had a profound effect on the medical economy. The scanner's technical advantages and value as a tool for diagnosis and clinical research are indisputable, but the effect of its use on the health of patients has not yet been carefully evaluated. Assessment of technologies like the CAT scanner might be directed at the patterns of their utilization as well as at their development or technical status.

3. Polio and Rubella Vaccines[4]

The objective of immunization is to prevent disease. Successful vaccines produce, without harm to the recipient, a degree of immunity which approaches that following a disabling attack of a natural infection. The human body has an immune system that can attack and destroy invading agents such as disease-causing bacteria or viruses. A vaccine is a preparation of inactivated or weakened bacterial or viral material that stimulates the immune system without itself causing serious disease. If infectious agents then invade the body, the immune system is prepared to attack; thus, the disease is prevented (163).

Jenner is considered to be the father of immunization. He observed that those infected naturally with cowpox did not subsequently contract smallpox. In 1796, he began using material from cows infected with cowpox as an agent for vaccinating people, thereby preventing smallpox. In the late 1800's, Pasteur discovered that infectious material (later shown to be viruses) from rabid animals could be treated to reduce its virulence. He used such treated material to vaccinate a boy who had been bitten by a rabid dog; the boy survived. Pasteur's use of a modified infectious agent to prepare a vaccine represents the beginning of modern preventive immunization (163). During the subsequent decades, vaccines were developed against a variety of diseases, including diphtheria, pertussis, and tetanus.

By *preventing* disease rather than treating its symptoms, vaccines have been able to avert much suffering and save many lives. Additionally, immunization programs have been quite cost saving for society. They not only save in the costs of medical care for the affected individual but also keep citizens productive for themselves, their families, and the entire society. Occasionally, vaccination may have undesirable side effects. Nevertheless, vaccines are the model preventive technique and are often used to illustrate the argument that knowledge gained from basic biomedical research can lead to conquest and nearly complete eradication of disease.

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[4] This case is adapted from material prepared for OTA by Dr. Joseph Melnick, a member of the Advisory Panel for this study.

POLIO

The prevention of poliomyelitis by immunization is a modern success story. Faced with poliomyelitis epidemics of great severity after World War I, the public regarded this disease with dread. Thousands died or were permanently crippled by extensive paralysis; even very costly and uncomfortable therapy often led only to partial rehabilitation. The specter of poliomyelitis gadgetry such as the "iron lung" still lingers in the public mind today.

This terrifying image of polio motivated the creation, in 1938, of the National Foundation for Infantile Paralysis. The Foundation sponsored the first large program of directed, interuniversity cooperative medical research and development in the United States. Under its auspices, diverse lines of exploratory research were pulled together toward the common goal of preventing or curing poliomyelitis. The public felt that the research effort was a legitimate path to this goal and gave its wholehearted support: contributions reached $20 million per year by the early 1940's and continued for two decades.

The development of successful polio vaccines followed a long history of research on immunization, viruses, and the nature of polio. Poliomyelitis was first recognized as a clinical entity in the late-18th century. In the early-20th century the. disease was successfully transmitted to laboratory animals and shown to be caused by a virus. These developments made possible experimental work on polio virus and an increased understanding of the disease. This research culminated in the cultivation of the virus in cell cultures by Enders, Weller, and Robbins in 1949 (62), providing a large-scale source of virus from which vaccines could be made. Based on the knowledge gained from immunization programs for other diseases, a polio vaccine was soon developed and tested in animals. Successful immunization of human subjects with killed virus was reported by Salk (174) in 1953 and nationwide field trials were carried out in 1954. The vaccine was licensed in 1955, and widespread administration began almost immediately. In the meantime, attenuated live virus vaccines were being developed, and the Sabin strains of such vaccines were licensed in 1961, following extensive field trials.

Results of large-scale immunization programs, using Salk and later Sabin vaccines, have been extraordinary: 18,000 cases of paralytic polio were reported in the United States in 1954, 2,500 cases in 1960, and only 6 cases in 1975 (79). The human, societal, and economic benefits have been enormous: a huge and costly program of rehabilitation has been dismantled, billions of dollars have been gained from increased productivity (210), thousands of lives have been saved, and incalculable suffering has been averted. Recently, however, the level of immunization among children has fallen off (118, 131), and there is some possibility of increased incidence of polio in the future.

RUBELLA

Rubella (German measles) briefly incapacitates its victims and occasionally leads to serious complications, but is rarely crippling or fatal. In 1941, however, Gregg discovered that pregnant women who contracted rubella had a greatly increased risk of giving birth to children with devastating congenital defects, including severe mental retardation. Other impacts of rubella are illustrated by the epidemic of 1964–65, which was estimated to have a direct cost (e.g., medical care for the ill and for congenitally damaged offspring) of more than $1 billion and indirect costs (e.g., lost productivity) of more than half a billion dollars (179). At least

20,000 congenitally infected "rubella babies" were born with abnormalities as a result of this epidemic, and there were as many as 30,000 fetal deaths due to maternal infection with the virus.

The technology gained in the development of poliovirus vaccines has been effectively applied to rubella. In 1961, rubella virus was grown in tissue culture and methods for measuring an immune response to the virus were developed (161, 21 1). Parkman, Meyer, and their colleagues at NIH developed an attenuated live rubella virus in 1966, and, in the same year, reported its experimental administration as a vaccine to children (132). After further trials, the vaccine was licensed in 1969. Another attenuated virus strain was developed in Belgium by Huygelen, Peetermans, and Prinzie (96) and was also licensed in 1969. A third vaccine strain developed in the United States without Federal funding was not licensed.

By 1974, 62 percent of the target population (children aged 1 to 12 years) had been vaccinated against rubella. In 1975, 16,343 cases were reported, a 66-percent decrease from a yearly average of 47,744 cases during the period preceding widespread use of the vaccine. Thus, an effective vaccine has been developed, but has not yet been adequately applied to provide optimal protection (175). There remains a risk to those not receiving the vaccine and a lack of overall protection that more widespread immunization could furnish.

The vaccine cases illustrate two interesting points. First, basic research has led to the rational development of technologies that can prevent disease and render less rationally designed, relatively ineffective, and costly treatments essentially obsolete. Second, even after such inexpensive and effective technologies are developed, they may not be universally used. The enormous human, social, and economic costs of this incomplete protection are due not to any failure in research or development, but to shortcomings in the medical-care delivery system.

4. Radical Mastectomy for Breast Cancer

Breast cancer (carcinoma of the breast) is the major fatal cancer among American women. It attacks 6 percent of women and kills half of its victims (38). In 1974 there were an estimated 89,000 new cases and 32,500 deaths from breast cancer in the United States. Epidemiological and biomedical studies have implicated genetic, environmental, hormonal, and viral factors in the etiology of breast cancer. No firm evidence is yet available, however, and the cause of the disease remains unknown.

Radical mastectomy was introduced as a treatment for breast cancer by Halsted, a pioneer of American surgery, in 1890. It involves removal of the breast, the underlying pectoral muscles, and the axillary (armpit) lymph nodes. The rationale for removing large amounts of tissue is that breast cancers spread rapidly and have often invaded nearby areas by the time of diagnosis and surgery. Radical mastectomy is a mutilating procedure and causes significant psychological and social as well as physical problems (170). Nevertheless, it was long the only form of therapy known and has remained the orthodox treatment for breast cancer since its introduction.

During the past few decades, several alternatives to radical mastectomy have been introduced. A surgical variant, simple mastectomy, entails removal of the

breast but not the underlying muscle and lymph nodes. Radiotherapy has been administered from external devices (25) and from implanted isotopic pellets, either alone or in conjunction with surgery. Similarly, a variety of anticancer drugs have been used in chemotherapy programs (18), either following mastectomy or as a primary treatment. Considerable success has been achieved with several of these procedures. No treatment devised so far, however, including radical mastectomy, is completely effective in preventing the recurrence of breast cancer or its spread to other parts of the body.

Despite the severity of radical mastectomy, its incomplete success, and the availability of other forms of treatment, few rigorous comparisons of alternate therapies have been attempted. Physicians have considered it unethical or inadvisable to withhold radical mastectomy, an accepted, partially effective procedure, from patients whose lives were threatened. Some studies were done, however, both in the United States and in Great Britain, and their results suggested that several forms of treatment are equally effective (22). In 1971, NIH initiated a controlled clinical trial under the direction of Dr. Bernard Fisher (66) at the University of Pittsburgh. Surgeons, radiotherapists, and pathologists in 34 institutions are attempting to compare the efficacy of alternate therapies for breast cancer. Patients have been divided into three groups and submitted to radical mastectomy, simple mastectomy, or simple mastectomy plus radiation therapy. The study involves 1,700 patients. The preliminary results indicate that the survival rates of patients in all three groups are essentially equivalent (153). These initial findings have already raised some doubt about the necessity for widespread use of radical mastectomy. However, firm conclusions cannot be drawn until the study is completed.

This case points out that a mutilating surgical procedure can be widely used without proof that it is more effective than alternatives that cause less physical and psychological damage. To seek this proof, an accepted procedure has been withheld from patients, and this is ethically troubling to many physicians. As new and potentially more effective therapies are developed, such ethical problems may again have to be confronted.

5. **Anticoagulants for Acute Myocardial Infarctions**

An "acute myocardial infarction," or heart attack, results from destruction of heart tissue following blockage of a coronary artery by atherosclerosis (deposition of fat in the arteries). Coronary heart disease leads all causes of death among the middle-aged and elderly, striking males two to five times as often as females (33).

A variety of therapies have been developed to deal with various clinical problems that follow acute myocardial infarction. One therapy that has been widely used is the administration of drugs called anticoagulants, which inhibit the reactions that cause blood to clot at the site of an injury. It was hoped that these drugs could prevent blood clots from forming on the damaged heart wall or in the partially blocked coronary arteries.

The potential value of anticoagulants in the treatment of myocardial infarction was demonstrated in research on dogs in 1939. Development of blood clots in an experimentally damaged heart was prevented by injection of the anticoagulant heparin. Because of high costs and problems of chronic administration, however, .

[5] The historical material in this case is drawn from ref. 60.

extensive human use was not feasible. In 1946, dicoumarol, an anticoagulant that could readily be administered orally, was discovered. This drug was administered to a number of patients, and the results of early experience were promising.

In 1948 a large-scale controlled clinical trial of long-term dicoumarol therapy was started in the United States. This was one of the first such clinical trials. A striking reduction in mortality was reported in the group receiving anticoagulants, and the treatment was rapidly and widely adopted.

During the subsequent several years, however, four smaller clinical trials of dicoumarol showed no significant difference in mortality between treated and control groups. It was belatedly realized that the method used in the first trial to assign patients to control and treated groups had been flawed. Patients admitted to cooperating hospitals on odd days were all given anticoagulants, while those entering on even days were assigned to the control group. Physicians, knowing this protocol, were aware of which patients were being treated. This knowledge could have affected their behavior, or even allowed them to admit "promising" patients on an appropriate day, thus affecting the results of the trial. To resolve the question, a new large-scale clinical trial was organized in Britain. Its results showed that there was no significant, long-term effect of dicoumarol on mortality following myocardial infarction.

In retrospect, it was realized that anticoagulants could be expected to prevent only some of the complications that follow acute myocardial infarction (in particular, "thromboembolic complications," involving clotting of the blood), and thus could lower mortality by only 2 or 3 percent even if completely effective. This recognition led to a large collaborative study in Veterans Administration hospitals focusing on thromboembolic complications, including strokes. The incidence of stroke in the untreated group was 3.8 percent compared with 0.8 percent in the treated groups (58). This difference was judged to be a benefit of anticoagulant therapy during a short period following infarction. However, long-term administration of anticoagulants was again found to have no discernible benefit (59).

Thus anticoagulation was rapidly accepted as a treatment based on what at the time seemed like rigorous evidence of efficacy. Many patients remained on the drug for years and were exposed to the real, albeit low, risk of harmful side effects. Only later were the inefficacy of long-term therapy and the possible usefulness of short-term therapy demonstrated (40).

This case points out that the results of evaluation, on which decisions must be based, may be misleading. Even with the best possible evaluation, based on the state of the art of the day, mistakes will be made. Because of this possibility for error, continuing surveillance of technology is necessary to identify ineffective or unsafe procedures after some period of use.

6. Renal Dialysis[6]

The kidneys filter or "dialyze" the blood to maintain the delicate chemical balance of the human body. If the kidneys are diseased and do not remove wastes from the blood, uremia—urea in the blood-develops.

[6]The historical material in this case is drawn from ref. 69, pp. 215–239.

The severity of uremia parallels the extent of kidney failure. The permanent loss of function of both kidneys, called chronic renal failure, is invariably fatal if untreated. In such cases, a dialysis machine, or "artificial kidney, " can remove the wastes from the blood, preventing death and often allowing the affected individual to function normally.

The first dialysis machine was built by Dr. Willem Kolff in Holland in the early 1940's from an old bathtub, spare automobile parts, and sausage casings. By 1950, several American medical centers were using experimental models. During this time, sustained therapy was limited by the fact that each time a patient was dialyzed, he or she had to undergo surgery to insert cannulas (tubes) into an artery and a vein. The main use of the early machines was to maintain patients during periods of acute short-term renal failure. As late as 1960, the longest reported maintenance of a patient on a machine was 181 days.

Long-term dialysis for chronic renal failure became possible in 1960 when Scribner and his colleagues developed a semipermanent apparatus that linked an artery to a vein. This device, the "Scribner shunt, " could be used to connect patient and machine, without surgery, for each session of dialysis. The shunt worked from the beginning: the first three patients treated by Dr. Scribner with the "Scribner shunt" were still alive for a reception in their honor in 1970.

The development of the shunt made dialysis possible for individuals with chronic renal failure. As an early analysis concluded, this was a sizable group:

> In considering the impact of kidney diseases we find that between July 1964 and June 1965 there were 58,788 deaths, a prevalence of 7,847,000 cases, 139,939,000 days of restricted activity . . . . Likewise in 1964 the total economic cost of kidney disease was $3,635,000,000. 'The indirect costs of morbidity and mortality accounted for $2,000, -412,000 of the total cost with the larger portion due to morbidity loss (81, p. 1).

It was not immediately possible to treat all eligible patients, however, because of shortages of dialysis machines and qualified facilities. A clinical center for hemodialysis was opened in Seattle with support from a 3-year grant of $250,000 from a private foundation. The center opened on January 1, 1962, and was immediately inundated with candidates for long-term hemodialysis. However, when the first grant ended, it was not renewed. NIH funds, which had supported research on dialysis, were not available for treatment. The center in Seattle, as well as others that were established, encountered serious financial problems.

Furthermore, dialysis is very expensive. The equipment itself is costly, but far more important is the fact that each patient must undergo two or three 6- to 8-hour sessions of dialysis each week in order to avoid uremia and its fatal outcome. Once a patient starts on hemodialysis, he or she may be able to return to normal functioning, but he or she cannot survive without dialysis unless kidney transplantation is possible and successful. The cost of dialysis ranges from about $30,000 per year for in-hospital dialysis to about $4,500 per year for dialysis carried out in the patient's home, after an initial expenditure of $3,000 for equipment and home alterations (106, p. 12). The need for sustained use of the "artificial kidney" imposes a tremendous financial burden on the patient.

These financial problems were addressed by Congress in the Social Security Amendments of 1973 (Public Law 92-603), which expands Medicare coverage to include all patients with endstage renal disease, whatever their age or financial status. This program provided care for 21,500 eligible patients in 1976, at a cost of $448 million. The cost of this program is expected to reach $1 billion by 1984 for the treatment of more than 50,000 patients. Some believe that the program will cost $1.7 billion by 1990, with up to 70,000 patients involved (205).

The early success of dialysis raised many difficult issues centering around the allocation of scarce medical resources. The cost of treatment was high, and machines were few. Very quickly, selection of patients for the limited number of machines available became the most difficult issue. The passage of Public Law 92-603 addressed some of these problems but created new ones. First, the Federal program unquestionably saves lives, but it is very expensive. Some have suggested that the money would be better spent on programs of preventive or community health that would benefit more people or on research, which holds the potential for leading to more definitive cures. Such programs of "catastrophic disease insurance" raise questions about national priorities (98). Second, now that Federal funds are available, dialysis is increasingly being used as part of a "life-support" system for terminally ill patients, raising questions about the provision of expensive care for patients who have little or no hope of recovery (48).

7. The Cardiac Pacemaker

The pathological condition ameliorated by the artificial pacemaker is heart block or Stokes-Adams syndrome. The electrical signal that triggers the heartbeat arises in a particular region of the heart and is transmitted through a cellular conduction pathway to stimulate the coordinated contraction of the heart. In heart block, signals are not properly conducted, resulting in abnormal heart function and circulatory insufficiency (188). The pacemaker provides a regular sequence of impulses to the heart, causing it to operate normally. The results are dramatic. The mortality rate in unpaced patients with severe heart block is about 50 percent over a l-year period, whereas the life expectancy of an artificially paced patient suffering from the disease is over 90 percent of that of the normal population of comparable age and sex. With an artificial pacemaker, those afflicted lead normal lives,

The pacemaker is an example of an advance that could not be made until knowledge in several related fields was ripe for it. As early as 1791 it was observed that the heart of a frog could be stimulated with electrical energy. Similar demonstrations were made on the human heart during the 18th and 19th centuries. In 1932, Hyman demonstrated that it was possible to stimulate the human heart by electrical impulses delivered by a needle electrode inserted through the chest wall into the heart. However, Hyman did not publish his resuIts at that time, possibIy because of opposition to his work in the medical and lay communities. Many people objected to his device as tampering with Divine Providence. Also, Hyman was

p The historical material in this case is drawn from refs. 11 (pp. J1–J11) and 12.

unable to find an American manufacturer who was willing to produce his device. World War II diverted his efforts, and, he did not pursue this research.

During the war, extraordinary technical advances in instrumentation and electronics occurred. Cardiac and thoracic surgery also developed rapidly. Bigelow and his associates in Canada experimented with pacing the heart after open-heart surgery. In 1952, Zoll reported that heart block could be treated by electrical impulses delivered to the chest wall. However, this mode of stimulation was too cumbersome and uncomfortable to the patient to be practical for sustained use. Lillehei and coworkers in the United States took a step toward solving these problems by developing a system with internal electrodes and a portable external power supply. Their pacemaker was first used in 1957.

Progress in electrode and battery technology soon made it clear that long-term pacing should be feasible. In 1958, Elmquist and Senning developed a totally implantable system with its own power source, a rechargeable nickel-cadmium battery. They implanted this pacemaker in a patient, but the electrodes did not work well. Finally, Chardack and Greatbatch, combining an improved lead devised by Hunter and Roth with new mercury cell batteries and a transistorized circuit, implanted a system in 1960. This device was very successful and, with a few modifications, was manufactured and marketed by Medtronic, Inc.

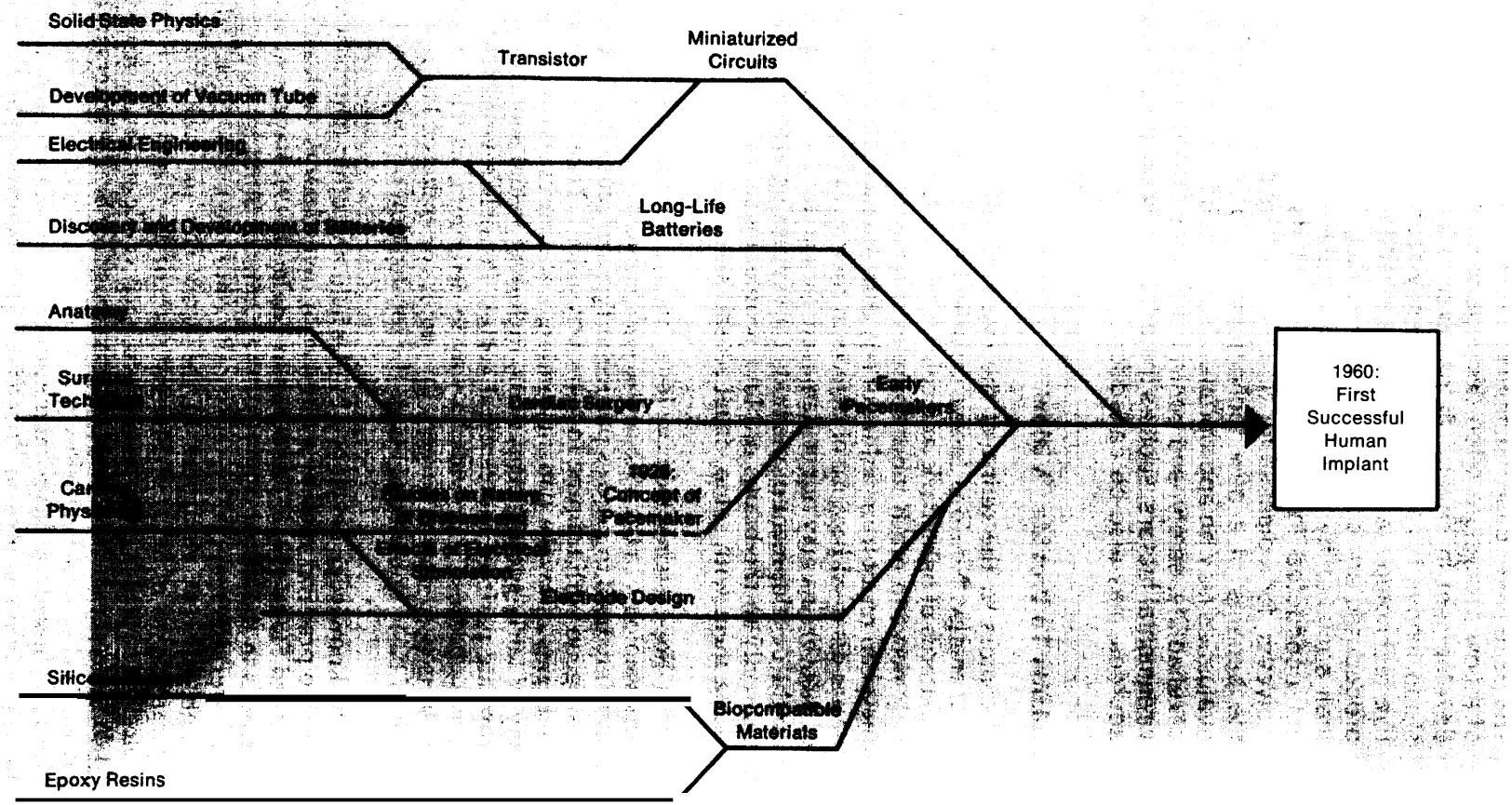
Thus, the totally implantable pacemaker required the development of basic knowledge about the physiology and electrical conduction system of the heart before it could be used. In addition, technological developments in batteries and electrodes were necessary. Materials to insulate the pacemaker and the body from each other were also necessary; epoxies and silicone rubber proved effective. Finally, innovative proven surgical techniques were required to enable implantation of the device. The confluence of these several lines of research and development to produce a clinically useful device is shown in figure 1.

Little Government funding for the research and development of the pacemaker **was** forthcoming until the latter stages. Zoll had Government help, and the practical work from that point was partially supported by Federal funds. Major development was carried on with private resources of Medtronic, Inc., and other companies that subsequently marketed models. The pacemaker is the result of a creative effort financed by both public and private sources,

Once developed, pacemakers were received as a genuine technological triumph and were widely accepted by the medical community. Use of pacemakers has increased each year since 1960 (see fig, 3D in app. A). About 75,000 units were sold in the United States during 1975, with worldwide sales estimated at 147,000 units. The world pacemaker business now grosses approximately $200 million a year.

CurrentIy, a principal limitation of pacemakers is the finite life of their batteries. Although unexpected failures are extremely rare, each patient requires periodic minor surgery for replacement of the unit. New power sources such as lithium cells might extend battery life to approximately 10 years. Nuclear-powered pacemakers may also alleviate this constraint and are presently undergoing clinical trials. Work on other types of energy sources, such as bioelectric fuel cells, is also proceeding, but at a relatively slow rate. Some are concerned that nuclear-powered pacemakers may expose the patient or others to radiation. The benefits and drawbacks of alternative power sources are currently being debated.

Figure 1—**Development the Cardiac Pacemaker**



The pacemaker case highlights several important points. First, development of a new procedure often depends upon a background of knowledge and development in several fields. Even if fundamental principles are understood, innovation and application may not be feasible until pertinent supportive technology is ready. Second, despite their complexity and cost, some procedures are so effective in restoring function that few would question their social utility. Third, a rigorous controlled clinical trial apparently was not conducted for the pacemaker in its early stages of development. However, for a disease for which the natural history is fairly well known and the benefits of a new technology are dramatic, alternative methods of evaluation may be appropriate. Such methods should include consideration of reliability, safety, and contraindications. Assessment of societal and environmental factors, such as the effects of widespread use of nuclear power sources, may also be called for.

8. Cortical Implants To Provide "Vision"

Receptors in the retina of the eye sense light and convert light energy to " electrical energy. Neurons (nerve cells) in the retina begin to analyze information about patterns of light, dark, and color, and then transmit electrical signals through the optic nerve to much more complex processing centers in the brain. Although blindness can result from failure of any component of the visual system, most blind people are disabled because of defects in their eyes or optic nerves, the visual centers of their brains may not be damaged. Research now in progress (19, 52, 53) may lead to the development of methods for connecting electronic light-sensing equipment directly to the brains of blind people, bypassing their failed eyes, and thus providing them with some visual sensation.

This hope stems from a long history of research in neuroanatomy and neurophysiology, In the 19th century, experiments showed that specific portions of the brain are used to process particular types of sensation. In the 1930's, Penfield, a neurosurgeon with training in neurophysiology, began using electrical stimulation of the brains of awake patients undergoing neurosurgery. He was able to elicit a variety of fairly specific sensations, including visual sensations, by stimulation of appropriate parts of the cerebral cortex. Penfield's work had immediate clinical usefulness because it provided a way to determine which areas of the brain could safely be excised during surgery for tumors or epilepsy. His results also provided a wealth of basic knowledge about the localization of function in the brain.

The knowledge developed by Penfield and other neuroscientist is now being applied to practical ends by a number of investigators. At least two groups, one in the United States (52, 53) and one in England (19), have now implanted arrays of electrodes in the visual centers of the brains of blind human subjects. Because the visual world is mapped systematically onto the brain, electrical stimuli delivered through different electrodes in the array can produce crude visual sensations (typically, spots of light) in different parts of the visual field. By stimulating groups of electrodes, it has been possible to elicit crude patterns of visual sensation (20, 54). A few subjects have been able to recognize Braille letters in this way and thus can read, although very slowly, "cortical Braille (53)." Very recently, Dobelle's group has linked the electrical output of a television camera to the electrode array, and one subject is able to "perceive" and identify rudimentary patterns—i.e,, a white stripe on a black background—that are actually "sensed" by the electronic circuitry of the television camera (53).

A number of problems must be overcome before cortical implants can be used to benefit blind or other neurologically disabled persons. For example, the brain may be damaged by implanted electrodes or by chronic electrical stimulation; electrodes may be degraded by the body; current methods for implanting electrodes are cumbersome; and presently used electrodes do not permit the stimulation of sufficiently small or delimited areas of the cortex. Some problems may require advances in neurophysiology for their solution; others await breakthroughs in bioengineering, electronics, or materials science. Work on new types of electrodes and on noninvasive methods of cortical stimulation, currently being sponsored by NIH, may lead investigators in entirely new directions if it is successful. Even the clinically oriented groups testing chronic implants in blind human subjects now claim to regard their research "primarily as a technique to begin investigation of dynamic pattern presentation rather than as a basis for clinically useful prostheses" (53). Nevertheless, recent promising results and current vigorous research on neural prostheses of various types, including cortical implants, make it possible to foresee development of clinically useful devices within the next few decades.

The development of cortical implant technology is being supported by several agencies. The American group doing cortical implants on human subjects has received NIH support in the past but is now supported by funds from several foundations, from industrial sources, and from their university (52–54). The British group is supported by the Medical Research Council, a Government agency (19-20). NIH, believing that a large number of technical problems must be solved before trials on human subjects will be profitable, is sponsoring work on biomaterials and electrode **design, animal** experiments on chronic electrode implantation and electrical stimulation, and basic research on the long-term effects of electrodes and brain tissue on each other. Some work is proceeding intramurally, but most is going on at universities, supported by NIH grants and contracts. NIH is also undertaking and supporting work on a variety of other neural prostheses, such as electrical control of bladder function in paraplegics. Some of these related technologies may be clinically useful well before cortical implants are fully developed and may provide useful information for developers of cortical implants.

This case raises two interesting questions. First, although clinically useful cortical implants are not yet available, ongoing research is targeted to a definite goal, and clinically useful devices may be developed within the next few decades. Is it possible to begin now to evaluate the social implications of such devices and to plan for their introduction? Second, NIH a Federal agency, is currently sponsoring research on animals, directed at solving fundamental technical problems. Meanwhile, foreign groups and privately supported researchers in the United States are already testing crude implants in human subjects. Might even rigorous efforts at technology assessment be futile if they are limited to the research programs sponsored by the Federal agency?

9. The Totally Implantable Artificial Hearts

The idea of substituting an artificial device for a damaged natural heart is an old one. The first real step in bringing this idea to fruition occurred in 1939 when John H. Gibbon, Jr., succeeded in keeping cats alive for nearly 3 hours with a

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This case is adapted from ref. 142,

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mechanical apparatus that substituted for both heart and lungs. After World War II, progress in the development of techniques for cardiovascular surgery was rapid. In 1953, Gibbon performed the first open-heart surgery on a human, using a heart-lung machine. This machine, which can temporarily bypass the heart, maintains blood circulation and also takes over the lungs' function of removing carbon dioxide from the blood and supplying it with oxygen. Gibbon's success helped to rekindle interest in a mechanical heart.

By the late 1950's progress in heart-assist devices encouraged medical investigators to consider the possibility of developing a totally implantable artificial heart with its own power supply. Proposals for further work were submitted to NIH at that time. Such proposals had to compete through the standard granting process, preventing a coordinated program effort. In the fall of 1963, the National Advisory Council of the National Heart Institute endorsed a suggestion that artificial heart research receive greater budget priority. In 1965 Congress responded by specifically designating funds for an artificial-heart program. NIH then established an Artificial Heart Program Office. The program has developed with an engineering orientation, targeted goals, and contract support, much of which went to profitmaking firms.

Several basic problems have beset the development of circulatory assist devices, including the artificial heart: materials used as pump linings have been consistently 'harmful to blood; reliable and compact pumps capable of operating for long periods have had to be developed; and efficient, unfailing energy sources are required. Strenuous attempts to cope with these problems have improved the situation, but completely satisfactory biomaterials and power sources have not yet been devised. Currently, three alternative types of power supply are being considered—biological fuel cells, conventional batteries, and a nuclear system-and developmental work on all three is being pursued.

The NIH staff was concerned that the availability of a totally implantable artificial heart might have serious implications for society. By the early 1970's, it felt that the technical feasibility of the device had been sufficiently demonstrated in animals to warrant formal consideration of social impacts. Therefore, in August 1972 the National Heart and Lung Institute (NHLI) convened an interdisciplinary panel to identify and evaluate the personal, social, and cultural implications of developing such a heart. The report (142) was published in June 1973 and constitutes the most comprehensive technology assessment done in the health field to date.

The assessment at NHLI was based on the "explicit assumption that the objectives of the NHLI artificial heart program [would] one day be realized in full" and that "certain issues connected with widespread availability" of a clinically useful device could be addressed while research program were . **still in progress (1 42). Material from that report will be used in chapter III of this report to illustrate the types of information that can be elicited when medical technologies are carefully assessed.**

AN OVERVIEW: THE COMPLEXITY OF MEDICAL TECHNOLOGY

Medical Technologies Are Diverse in Nature and Purpose

Actual medical practice often involves concurrent or sequential use of several different technologies. Nevertheless, some tentative classifications of medical tech-

nologies can be made. Such schemes might be useful in deciding whether or how to assess a particular new technology and in making prospective judgments about new technologies on the basis of previous experience or assessment.

For example, one might classify each technology in two different dimensions-according to its physical nature, and according to its purpose (122, 166):

By physical nature:

(a) A *technique* is an action of a health-care provider that does not require specialized equipment.

(b) A *drug* is a substance administered by a health-care provider to a patient. Drugs include chemicals that can be injected or ingested (such as anticoagulants, Case 5) as well as biological substances (such as vaccines, Case 3).

(c) *Equipment* includes both machines requiring large capital investments (such as the CAT scanner, Case 2; the continuous flow-blood analyzer, Case 1; or a renal dialysis unit, Case 6) and the many smaller medical devices and instruments used in medical practice.

(d) A *procedure* (such as implantation of a pacemaker, Case 7, or of a cortical prosthesis, Case 8) is a combination of technique with drugs and/or equipment.

By medical purpose:

(a) A *diagnostic* technology (such as the CAT scanner, Case 2, or the continuous flow-blood analyzer, Case 1) helps in determining what disease process is occurring in a patient.

(b) A *preventive* technology (such as a vaccine, Case 3) prevents disease.

(c) A *therapeutic, or rehabilitative,* technology is applied to an individual to give him or her relief from disease and its effects. Therapeutic technologies can be further divided into those few technologies (such as some antibiotics) that *cure* disease and those many technologies (such as renal dialysis, Case 6; cortical implants, Case 8; or the cardiac pacemaker, Case 7) that give *symptomatic* relief but do not change the underlying disease process.

(d) An *organizational* technology is used in management and administration to insure that medical practice is as effective as possible.

(e) A *supportive* technology is used to give needed services to patients, especially those ”in the hospital, such as hospital beds and food services.

Medical Technologies Are Developed in a Variety of Ways and Places

Knowledge gained from basic research may be applied to the development of clinically useful technologies quickly and directly or slowly and indirectly. In many cases, new technologies arise from the confluence of many lines of basic, applied, and clinical research, and the logic of the developmental pattern can be discerned only in retrospect (e.g., Case 7). Work leading to the development of new medical technologies may proceed in university, government, or industrial laboratories, in

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Organizational and supportive technologies are not discussed in this report.

medical centers, in clinical practice or, more often, in several of these settings, both concurrently and sequentially. The cost of technology development may be borne by philanthropic organizations (e.g., Case 3), private industry (e.g., Case 2), Government agencies (e.g., Case 9), or by combinations of funds from various sources (e.g., Cases 7 and 8). Because these developmental complexities pose special problems for the assessment of medical technologies, they will be discussed in detail in appendix A.

Medical Technologies Pose a Variety of Technical and Social Problems

Technical issues include concerns about safety and efficacy. *Social* impacts can result from special features of the technology itself or from the economic burden that its use imposes on society.

All invasive procedures, including administration of drugs as well as surgery and the use of equipment, involve some finite risk to the patient. Determination of the *safety* of new technologies is crucial because the risks that may be encountered in use must be weighed against the potential benefits in deciding how-or if-new technology is to be used. Belated discovery of toxicity, risk, or side effects can have tragic consequences for the patient. Even where the extent of risk is fairly well known, it is often difficult to weigh considerations of safety and efficacy, as illustrated in the case of radical mastectomy (Case 4).

Issues of *efficacy* are raised when proof of efficacy is lacking before introduction of a new technology, when a widely used technology is later shown to be inefficacious, or when the relative efficacy of alternative therapies is compared. The cases of oral anticoagulants (Case 5) and radical mastectomy (Case 4) illustrate some of these problems. Questions of efficacy have recently been raised about a variety of widely used medical technologies (6, 9, 37, 88, 99, 112, 130). Only 10 to 20 percent of all procedures used in present medical practice have been proven by clinical trial (213); many of these procedures may not be efficacious.

The *economic* burdens imposed by the use of medical technologies cause problems for the patient, for his family, and for society. Medical technologies contribute to rising medical care costs in various ways:

- Some new technologies require large capital investments. For example, a CAT scanner costs from $350,000 to $700,000 (Case 2) and a modern automated blood chemistry analyzer (the SMAC 60) costs $250,000 (Case 1).
- Costly supporting services are required to implement some new technologies. New personnel must be hired to operate equipment, and existing personnel must be retrained. A study of 15 Boston hospitals indicated that capital investment accounted for only about 5 percent of costs, but associated costs were much larger (47).
- Costly followup care is made possible-r even required—by some new technologies. For example, fetal monitoring during labor has led to intervention in the birth process by cesarean section (212).
- The need for continued use of technologies may lead to economic burdens. Chronic renal dialysis, for instance, requires lifetime use several times a week for most of those with end-stage kidney disease (Case 6). Each

session of dialysis is expensive, and use over a period of years results in an enormous overall cost.

- Initial proof of efficacy and reliability of new technologies may lead to overuse. Utilization rates for automated clinical laboratories (Case 1) and CAT scanners (Case 2) are rising rapidly without documented benefit to the health of either individuals or groups in society (88, 176). This problem is exacerbated by the malpractice situation, which fosters protective ordering of tests (defensive medicine).
- Technologies may be used for inappropriate purposes, thereby leading to economic as well as human costs. Variations in surgical rates between areas **(212),** systems of medical care (63), and countries (23) suggest that a certain amount of unnecessary surgery may be performed in the United States. Unnecessary surgery not only is costly in financial terms, but also causes pain, disability, and sometimes death (120, 199).

Although no definitive estimate can be made for the overall cost of medical technology, it has been estimated that 50 percent of the increase in costs of hospital care, from $13.2 billion in 1965 to $40.9 billion in 1974, was due directly or indirectly to medical technology (75, 207). The contribution of technology to costs for physician services is also substantial (217). The cost of certain technologically based activities can be estimated with more accuracy. As noted in the case of the continuous flow-blood analyzer, the costs in 1975 for clinical laboratory services were about $15 billion (21), more than 12 percent of the national health expenditure (133). X-ray services, both medical and dental, are estimated to have cost $4.7 billion in 1975 (67).

These economic burdens must be considered from the point of view of cost effectiveness. Undoubtedly, many if not most technologies in use have some effectiveness. One must then ask if society is prepared to pay for partially efficacious technologies that are very expensive. The use of Federal funds to pay for renal dialysis (Case 6) is the result of one such decision by society. New therapeutic regimens for cancer and rehabilitation devices such as voice-activated wheelchairs will pose similar problems in the future.

Medical technologies can also raise troubling *social* issues that are unrelated to economic considerations. For example, modern technology has challenged society's traditional view of death and dying. Although these issues are not new, they have been given added significance by new life-extending technologies such as artificial hearts (Case 9) and kidneys (Case 6). Modern technology can dehumanize the individual, affect the way people view themselves and others, and give awesome powers to physicians (104).

Current vigorous efforts in biomedical research seem certain to result in the development of new technologies that will pose important social problems. In the diagnostic area, use of new developments in imaging, including computed tomography (Case 2) and ultrasound, will add greatly to costs. New clinical laboratory equipment, such as centrifugal fast analyzers **(116),** may partially replace the continuous flow-blood analyzers described above (Case 1). In the therapeutic area, bone-marrow transplants are just beginning to be used for treatment of cancer patients, and their use could spread rapidly. Neural implants of electrodes to overcome neurological problems including blindness are now being developed (Case 8). Other cases, such as sex determination of unborn children,

genetic screening, and extrauterine fetal development, raise even more difficult issues concerning the future of mankind.

Although new medical technologies may cause concern, however, preoccupation with the issues that they raise must not overshadow recognition of the serious human and social problems posed by diseases for which no therapy is yet available. Modern medicine has developed a workable classification of disease and has developed sophisticated diagnostic procedures for determining what pathological condition is affecting the individual. However, basic understanding of the pathophysiology of these conditions is often inadequate, and effective medical interventions are few.

Technical and Social Issues Are Interrelated

This report will be limited to a discussion of ways to assess the social impacts of new medical technologies; methods for assessing technical concerns such as safety, reliability, and efficacy will be described in a subsequent report. Because of the separation imposed by this organization, it is necessary to state explicitly that the technical and social issues posed by new medical technologies are inextricably linked. For example, ethical considerations, seemingly remote from technical matters, can hamper the determination of medical efficacy, as noted in the case of radical mastectomy (Case 4). Unexpected toxicity or injurious side effects of new technologies can lead to social impacts that would not have arisen had the technology been safe, as shown by the well-publicized case of thalidomide. The degree of effectiveness of a new technology in combating disease determines its social impacts, and conversely, a whole variety of social and cultural factors determine the effectiveness, in practice, of a new technology. Although different methods are used to assess the technical and social impacts of new technologies, it must be recognized that problems (and their solutions) cannot, in reality, be separated.