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HORIZONS IN SURGERY

by

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Each generation contains its pessimists who regret having been born too late, at a time when the ultimate in discovery and progress has already been achieved. Surgery has been no exception. Advances in surgery have often been preceded by predictions of their impossibility, or followed by opinions that the last frontier has been breached, leaving only small details for future cultivation. In spite of such attitudes, the development of surgery has continued at an ever-accelerating rate.

Knowledge from virtually all the basic sciences has been applied to the practical problems of caring for the sick patient. Historically, the principal link with the laboratories was through anatomy and pathology. Now, the union has extended to physiology, bacteriology, physics and biochemistry. In the next few years, the application of genetics and immunology will become increasingly important. It has been necessary for the surgeon to become a Renaissance man in order to keep pace with his profession, and the diversification of his professional interests can only be expected to increase in the future.

Congenital Diseases. In the past 40 years, more progress has been made in the treatment of congenital malformations than in the entire preceding history of medicine. In particular, most cardiac lesions can now be effectively treated. Therapy has evolved for many formative defects of the face, central nervous and musculoskeletal systems, and the gastrointestinal and genitourinary tracts. Most of the advances have involved the development of surgical techniques for the restoration of normal structure.

Future surgeons can be expected to turn their attention to other aspects of congenital disease. These include investigation of the cause and prophylaxis of malformations. Considerable information has accrued on the development of congenital disease. Factors which can lead to congenital defects under controlled experimental conditions include anoxia, hypervitaminosis A, toxic drugs and irradiation. These agents act selectively upon the developing fetus, frequently causing no demonstrable or permanent injury to the mother. Except for irradiation, they act principally at the stage of most active organogenesis, and the time of injury can be extrapolated by identification of the organ system which is most severely altered. The induced anomaly is not carried to subsequent generations, except with the use of irradiation which may cause a transmittable genetic alteration.

One of the most important developments in recent years has been an increased understanding of the structure and function of the polynucleotides and the polypeptides in cell metabolism and division. Deoxyribonucleic acid (DNA) has two general functions. It provides information codes which direct the formation of enzymes, primarily from protein. In addition, DNA determines the replication of cells, the ability to pass on to daughter cells the same genetic potential present in the parents. Ribonucleic acid (RNA), another polynucleotide, serves as an intermediary substance. It is thought to carry information from the DNA-rich nucleus to the cytoplasm.

The first indication of the fundamental functions of DNA came from experiments using bacteria. It was found that the transfer of DNA from one bacterium to another of a different strain imparted characteristics of the first to the second organism. These characteristics were thereafter transmitted to subsequent generations, indicating the induction of a fundamental genetic alteration. Numerous observations have confirmed the role of the polynucleotides in determining cellular specificity.

The surgical implications of this information are numerous. It may become possible to control cellular structure and function in complex tissues by modifying the DNA and RNA. It is conceivable that various desirable characteristics could be induced in a controlled manner. Possibly, immune specificity could be altered, thereby making the wide use of homotransplantation feasible. The fundamental structure of malignant tissue could be transformed, with elimination of the feature of autonomous growth potential. All of these possibilities concerning the manipulation of polynucleotides are speculative at present, particularly in higher species, but there is reason to believe that they may come to fruition. Success, however, will raise a host of moral and social problems.

Special notice should be paid to projected research on some of the inborn errors of metabolism. Such metabolic disorders are currently being catalogued in terms of the defective enzyme systems, as well as the specific organs involved. With this dynamic approach, rapid strides will be made in the understanding and therapy of enzyme deficiencies. In some of these disorders, such as phenylketonuria and galactosemia, effective treatment consists of measures to prevent the accumulation of toxic substrates in the tissues. In galactosemia, the conversion of galactose to glucose is impaired, resulting in abnormal concentrations of galactose-1-phosphate. This can be avoided by ingestion of a galactose-free diet. Phenylketonuria can be similarly treated by a phenylalanine-free diet, since the specific deficiency is an enzyme which allows metabolic conversion of this essential amino acid.

From a surgical point of view, the enzyme deficiency states of greatest interest are those with organ selectivity. In some of the glycogen storage diseases, for example, low concentrations of glucose-6-phosphatase or phosphorylase in the liver may be the principal or the only abnormality. As a consequence, normal glycogen can be readily synthesized in the liver from glucose, but cannot be rapidly reconverted back to glucose, resulting in massive accumulation of glycogen within the liver. It is reasonable to expect that an operation which diverted the portal blood flow away from the liver might benefit such patients. In this way, the splanchnic drainage with its high postprandial concentration of glucose would reach the peripheral tissues first. The most obvious way to divert the portal blood is with a standard portacaval shunt, such as is used in the treatment of portal hypertension. Unfortunately, this operation produces ammonia intoxication in patients who do not have cirrhosis or portal hypertension, presumably as a result of reduction in total hepatic blood flow. A suitable alternative procedure might be portacaval transposition. In this operation, as yet not applied to patients, the splanchnic drainage is rerouted into the proximal inferior vena cava, and the inferior vena caval flow is redirected through the liver. Animals with portacaval transposition remain in good health, without the development of ammonia intoxication.

Trauma. Death, as defined 20 years ago, can now be reversed in almost all hospitals by cardiac massage. It is inevitable that techniques of resuscitation will be used increasingly in patients who are "dead on arrival." The greatest application should be in the young, critically injured but otherwise healthy patient. Several authorities have recommended resuscitation centers for this purpose, where immediate facilities would be available for cooling, extracorporeal support and other adjuvant measures.

Considerable investigative effort has been expended on the possibility of immediate refrigeration of the recently "dead" patient, in order to forestall irreversible tissue injury. Unfortunately, the protection thus afforded to the brain, heart and other organs is of short duration. The use of emergency extracorporeal support, possibly in conjunction with hypothermia, probably offers the greatest promise.

The surgical restoration of excised members has received great impetus recently as a result of the surgical reattachment of an amputated arm and an amputated foot, several hours after injury. A great deal of laboratory research and clinical observation will be required to assess the degree of functional restoration which can be expected from these autotransplants. The behavior of the anastomosed nerves will be of critical importance in this respect.

The local care of wounds may be influenced by future technical or biochemical research. Pioneer work on glues for peripheral nerve suture was done in the late 1940's. Recently, there has been interest in adhesive plastics for vascular anastomoses. The imperfections of these methods have discouraged their clinical use, but nonsuture techniques may soon become highly applicable. Finally, surgeons can be expected to continue a search for somatotrophic substances. Although no method has yet been found which will beneficially influence wound healing, this may not always be the case.

Inflammatory and Infectious Diseases. With the discovery of antibiotics, there was a brief illusory period in which it appeared that the problem of surgical infection would largely be eliminated. Instead, the emergence of resistant mutants has resulted in an antibiotic-resistant bacterial population in many hospitals. Such organisms, notably mutants of the Staphylococcus, can result in lethal superinfections which will probably be an increasingly difficult clinical problem. Pseudomembranous entercolitis and staphylococcal pneumonia are examples. New antibiotics, effective against resistant strains, will be developed. Techniques are also needed to increase the concentration of present-day antibiotics in regions which are relatively sequestered from the vascular compartment. The solution to this problem may be largely technical, or there may be physiologic means of obtaining access to the hidden and well-protected organisms.

One of the unsolved problems in infection concerns the treatment of burns. The survival of the burned patient has been prolonged by increased attention to the colloid, electrolyte and fluid requirements in the acute phase, but the overall survival rate has not materially improved. The chief cause of delayed death is infection. Effective therapy may eventually result from indirect means, in which the patient's immune defenses are artificially stimulated. Germ-free centers, which as yet have had little practical use, may have a role in the future treatment of burns.

Metabolic Problems. More precise information on the composition of body fluids is required. During the last 20 years, appreciation of the existence and importance of previously unstudied electrolytes in the serum and tissues has opened up new fields of investigation. The most recent clinically important "new" electrolyte has been magnesium. It is likely that there are other chemical constituents which have not yet been described. In addition to defining the composition of body fluids more extensively, disclosures of the shifts in fluids and electrolytes will continue to occupy the attention of surgeons. For example, the participation of the mineral-rich bones in the metabolic response to surgery has not yet been fully clarified. The biochemical knowledge which accumulates on these problems will eventually be applied on clinical wards.

In the future, more effective techniques of parenteral feeding will probably be developed. In the patient who has an uneventful convalescence, full maintenance of caloric requirements during the immediate postoperative period is not necessary. The situation is quite different in the patient who requires prolonged intravenous feeding. Calorie-rich infusates become a necessity to contravene the effects of starvation. In the past decade, the use of intravenous fat has been extensively investigated in animals and on a limited scale in humans. The toxicity of emulsified fat solutions has prohibited their widespread use despite the fact that fat has more than twice the caloric potenial of either carbohydrate or protein. It is inevitable that continued research will eventually provide safe and more effective parenteral solutions.

A somewhat more speculative solution to a prolonged postoperative catabolic phase might involve dialysis to place desired substances in the intravascular compartment. This technique has been widely used to remove materials from the blood in renal failure, in terminal liver disease and in acute poisoning, but it has not been exploited as a means of replacement. Eventually, further simplification of dialysis units may make this application practical.

Adequate tissue oxygenation is the most urgent single metabolic requirement. Future research will be directed toward methods of increasing the effectiveness of oxygenation. In recent years, there has been intensive evaluation of pressure chambers in which patients can be maintained for prolonged periods in an environment of high oxygen tension. Beneficial results have been reported in the treatment of tetanus, gas gangrene, myocardial infarction, carbon monoxide poisoning, peripheral vascular disease, pneumonia and congenital cardiac anomalies. Further experience is needed to assess the usefulness of this approach and to define its dangers and complications. The expense of building and operating high pressure oxygen chambers is great. If improved patient survival can be demonstrated, however, future hospital construction plans will include provisions for this kind of equipment.

Other means of increasing oxygenation will continue to be of developmental interest. During acute insufficiency of either the pulmonary or circulatory systems, the prolonged use of heart-lung equipment would seem to be direct and logical therapy. It would be expected that patients who might otherwise die from pneumonia, or massive myocardial infarction could be maintained until the underlying disease is improved or brought under control. Before such therapy is broadly applied, numerous problems will need to be solved. Long-term extracorporeal perfusion causes destruction of blood constituents, chiefly in the pump system but to a lesser degree in the oxygenators as well. The quality of the apparatus used will have to be improved, and the physiologic problems of long-term perfusion more clearly defined.

The application of hypothermia in various situations is based on the reverse principle, that of reducing the metabolic requirements rather than increasing the supply. At the moment, the limitations of hypothermia are sharp. Minimal total body cooling, to 33 or 34° C., is well tolerated for long periods. Below these temperatures, long-term hypothermia is unsafe. Cardiac instability develops, leading to ventricular fibrillation or cardiac standstill. Artificial respiration is necessary. Metabolic acidosis and fluid shifts quickly complicate the course.

The undesirable effects of long-term hypothermia are in contrast to the benign reaction to cooling in animals which hibernate by nature. Many hibernating animals have been noted to contain specialized subcutaneous fat deposits termed "brown fat." Removal of the brown fat results in loss of the hibernating ability, although the active substance in this tissue is unknown.

These findings suggest that a pharmacologically active substance may be present which, if isolated, would allow the induction of hibernation. The clinical applications of hibernation might then be far-reaching. Pulmonary and cardiac patients could be cooled to a state of minimum oxygen requirement. Prolonged severe cooling of cancer patients, therapy tried without success in the past, could be reassessed. The effectiveness of x-ray therapy might be enhanced, since it is already known that cooling reduces the toxicity and increases the permissible dose of total body irradiation. The use of such therapy will require proof that the hypothermic malignant cells are not protected to the same degree as normal tissue. Finally, the possible induction of an hibernative state for long-distance space travel has already received much attention. The advantages for space exploration are obvious if trips are to be made lasting months or years.

Neoplastic Disease. The extirpative approach to neoplastic disease has been extended to its virtual limits. Future research will focus on the physiologic and pharmacologic aspects of oncology. In planning investigation, the most fundamental defect is the lack of an explanation of the etiology of neoplasia. Furthermore, the precise nature of the alteration which renders the malignant cell autonomous is not known. As mentioned previously, the DNA and RNA complexes determine cell metabolism and replication. The fundamental disorder may be in these constituents.

There are many active programs designed to screen chemotherapeutic drugs. The most optimistic view is that drugs may be developed which are as specific for certain types of cancer as antibiotics are for bacterial infections. At present, only a few tumors such as choriocarcinomas can be effectively treated with specific drugs.

Immunology may play a significant role in future cancer therapy. At present, many laboratories are evaluating the antibody response to certain tumors and attempting to induce host antibodies which might slow or stop the growth of the malignancy. The potential application of this approach has yet to be defined. Although there is growing evidence that antibody titers rise in certain patients with cancer, the significance or specificity of this finding is not clear.

One unexplored approach may be to change the cancer victim's immunologic pattern by replacing it with the reticuloendothelial system of a donor. Since cancer cannot ordinarily be transplanted from one patient to another, there is reason to believe that complete alteration of the immune potential of the patient might cause the tumor to be rejected. Such an approach awaits perfection of techniques of homologous tissue transplantation. In simplified terms, it would be necessary to destroy the patient's reticuloendothelial system, and replace it with donated bone marrow or spleen, and perhaps other reticuloendothelial components.

Homografts and Heterografts. Many developments in surgery will depend upon the replacement of organs and tissues taken from another individual of the same or a different species. The principal deterrents to wide clinical use of homografts or heterografts are biologic rather than technical. The grafted tissue is recognized as foreign by the normal host and repudiated within a few days or weeks, presumably by an immunologic mechanism. Efforts to induce graft acceptance have been designed either to eliminate the antigenic properties of the transplanted tissue, or to paralyze the immune mechanism of the host so that it is incapable of reacting against the graft.

Inactivation of the host immunologic response has been exhaustively studied in the laboratory, and has been given a limited, and for the most part unsuccessful, clinical trial with renal homografting. Initially, whole-body ionizing irradiation was used to abolish or mitigate the rejection response of the host. Successes were uncommon. The irradiation was either excessive, causing agranulocytosis and death of the host, or inadequate, allowing rejection to proceed. Later, cytotoxic drugs were evaluated, with more encouraging results. It was found that the rejection response could be delayed or prevented without total suppression of white cell production, especially with the use of some of the purine analogues. The latter finding is of great significance since it suggests that agents may be available which selectively abrogate graft rejection without destroying the total immunologic capacity. Other procedures designed to alter the immunologic potential of the host have been shown to have a weak but definite effect when used alone. These include splenectomy, thymectomy and the administration of steroids.

In the past, immunologic suppression has usually been attempted with a single agent. It is possible that a combination of methods which are individually ineffective could allow consistent success when used together. Thymectomy, splenectomy, irradiation and cytotoxic drugs have been used together in experimental animals and in patients receiving renal homografts, with encouraging preliminary results. The primary disadvantage of all these methods, used singly or in combination, is that the capacity of the host to react to a variety of injurious influences is concomitantly impaired. The immunologic mechanism of rejection is a process of great force and perseverance, and is normally important to the survival of the host organism in a hostile environment. The patient who is conditioned to receive a homograft must also accept an increased susceptibility to infections, and a decreased ability to react normally to a variety of antigenic stimuli.

The relatively unexplored alternative approach to the induction of homograft tolerance is to weaken or eliminate the antigenic potential of the transplanted tissue. Thus, it would not be necessary to injure or alter the host to achieve graft survival. Attractive as this concept is, it would seem likely that uniform alteration of cellular DNA and RNA will be necessary before antigenicity is eliminated. This has been demonstrated by the fact that application of a variety of physical agents does not abolish antigenicity, even after cell death and disintegration.

Even after successful methods to avoid rejection have been perfected, technical problems will have to be met. Foremost among these is the necessity to protect grafts from ischemia during transfer and to allow their storage in tissue and organ banks. Although the sensitivity to anoxia varies with different tissues, the need for prompt restoration of an environment compatible with cell viability imposes sharp limitations on all graft procurement plans.

The simpler methods to preserve grafts will continue to involve reducing the metabolic requirements by cooling. However, such methods provide only short-term prolongation of viability. Freezing to temperatures of -10 to $-200°$ C. offers more promise of long-term tissue preservation. Simple tissues can be safely preserved for months or years in a frozen state, but until now the method has been ineffective for complex organs. It is likely that organs will be best preserved by perfusion through their vascular pedicles. It would then be possible to institute an artificial circulation to the organ immediately after removal from a cadaver or living donor. The advantages of hypothermia could be incorporated by controlling the temperature of the perfusate. With present methods, long-term perfusion has often resulted in edema and structural damage to the organs. Perfection of these techniques will occupy the efforts of surgeons in the next few years.

It would be inaccurate to leave the impression that homografting and heterografting of whole organs will be a simple matter when the problems of tissue rejection and preservation are solved. Implantation of organs or extremities will be difficult, and the physiologic problems of attaching a denervated bulk of tissue which has a completely severed lymphatic system will require intensive investigation. Whether an engrafted arm would ever be anything but a swollen and useless appendage is a matter for speculation. There has been recent evidence that whole-organ cardiac grafts never function in a normal manner. The question of graft versus host reactions must be answered with the use of organs such as the liver which contain reticuloendothelial tissue. The functional capacity of denervated lung grafts will have to be further studied. The present impression is that pulmonary transplants will not support respiration unless the contralateral lung remains to initiate coughing and respiratory reflexes.

Special techniques will have to be applied in the actual implantation. Cardiopulmonary by-pass will be needed for cardiac and probably for pulmonary transplants. Special shunts will be required to decompress the splanchnic and inferior vena caval venous beds during hepatic transplantation. The patients, who will all be critically ill from terminal organ failure, will be among the most difficult to care for before and after operation. Finally, the patients will have less than normal capacity to recover from a major operation if techniques of immunologic suppression have been used to prevent graft rejection.

Heterotransplantation can be expected to present immunologic problems similar to, but far greater than, those in homotransplantation. In the past, it was thought that the genetic differences between the host and donor would be so great that there could be no hope of obtaining prolonged functional survival. However, recent experiences with the transplantation of chimpanzee and baboon kidneys to humans have suggested the need for revision of this dogma. These simian grafts have functioned well for as long as two months, although the immunosuppressive regimens necessary for protection of the transplanted tissue are more stringent than those used with homografts. The real value of heterografts will, of course, be established only after further cautious evaluation of these and other patients. If renal heterografts prove successful, the employment of subhuman primate hearts, lungs, livers and other organs could become commonplace.

If heterotransplantation proves to have a role in clinical surgery, numerous areas of supporting research will have to be intensified. For example, more knowledge is necessary about the blood types of the various subhuman primates and the relationship of these groups to host-graft immunologic reactions. The baboon has blood types A, B, and AB, and the chimpanzee has blood types A and O, but the significance of these classifications in relation to transplantation problems is unknown. Controversies concerning the anthropologic classification of apes and monkeys will have to be clarified in order to arrive at a decision concerning which has the closest genetic kinship to man. Epidemiologic surveys of diseases in these potential donors will be necessary in order to avoid the infestation of man with incurable infections. The "B" virus, for example, which causes an invariably fatal disease in man, is endemic in rhesus monkeys. Latent schistosomiasis, malaria, and trypanosomiasis are common in both the baboon and chimpanzee—a favorite site of sequestration of the parasite being the liver, one of the organs which is of potential use. Finally, thought must be given to the preservation of species which could be of future use. Although the supply of baboons is still plentiful, chimpanzees, gorillas, orangutans and gibbons are rapidly becoming extinct.

Artificial Organs. Twenty-five years ago, the idea of employing artificial organs clinically was too remote to receive serious consideration. Today, every major medical center employs a variety of appliances which might be classified as artificial tissues or organs. Examples include vascular prostheses, plastic cardiac valves, artificial kidneys, heart-lung machines and internal cardiac pacemakers, to mention only a few. The design of the prostheses ranges from simple metal devices which provide mechanical support for fractures, to the complicated extracorporeal circuits in which problems of perfusion, gas exchange and biochemical control are each important.

For long-term use, the greatest success has been obtained with prostheses of simple design which provide a single function. The implantable cardiac pacemaker is an example. The sole purpose of this instrument is to deliver an intermittent electrical stimulus to the ventricular myocardium.

Plastic blood vessels, cardiac valves and hip prostheses are examples of tissue substitutes in which the only function is mechanical. The safety and durability of these types of prostheses will undoubtedly improve in the future as new materials are produced and tested in industrial research, and as more information accumulates on the behavior of substances now in use. Nevertheless, the feasibility of their long-term use has been clearly established.

The design and long-term implantation of more complex artificial organs will be of great research interest in the future. The heart-lung machines and the dialysis units, which are used in renal and hepatic failure, have shown that the function of vital organs can be performed at least partially by a mechanical apparatus. Until now, however, therapy has only been possible on a temporary basis, lasting for only a few hours. The function of the units is incomplete compared to that of the natural organ. For example, the major benefit from hepatic hemodialysis is removal of ammonia from the blood. The instruments used are bulky. Anticoagulation is necessary. All component parts are external to the body, the only connection being to the vascular system of the patient, thereby precluding mobility of the patient during treatment.

The ideal for the future is the manufacture of artificial organs of suitable size for internal implantation. The problems to be solved are enormous before satisfactory hearts, lungs, kidneys or livers can be used within the body. Substances will have to be developed which can be perfused without the production of clotting or other injury to the blood, which are durable and well tolerated by surrounding tissues, and which have the properties necessary to perform the function of the particular organ. Details of connection of the artificial organ with the blood supply will have to be solved. Power source, problems of heat dispersion and the types of pumps will all have to be considered for heart prostheses. Where exchange of gases or metabolites is concerned, highly efficient membranes will be essential.

Research in Technique. Alert surgeons will continue to develop new or improved mechanical solutions to old problems. It is inconceivable that technical innovations will not always have an important place in surgery. Although it has become fashionable to deprecate the science of anatomy, many technical advances will continue to come from new observations of gross structure or reinterpretation of previously known facts. For example, the segmental anatomy of the liver has been clearly described only in the past decade. The surgical applications of this knowledge will be exploited in the future for the development of methods of partial hepatectomy which will probably render the present crude techniques obsolete, just as newer concepts of segmental lung anatomy have already been used to devise methods of pulmonary resection.

Methods for obtaining hemostasis have been evolving for thousands of years. Clamping and tying blood vessels is an irreplaceable means of controlling hemorrhage. Nevertheless, new materials for ligatures and sutures, especially plastics, will be evaluated. Additional knowledge of coagulation mechanisms will make new purified agents available for the treatment of diffuse bleeding. Of interest are recent reports describing the use of low voltage negative currents in stopping otherwise uncontrollable capillary hemorrhage. The application and importance of the latter observation will await further investigation.

Surgical instrumentation has inevitably mirrored the development of new fields. Thousands of useful instruments have been designed, usually by surgeons, to meet the needs for new operations. In the immediate future, vascular and intestinal staplers and operating instruments which carry their own light supply will be further evaluated.

Reassessment of Established Methods. Self-criticism and a healthy skepticism have always occupied central roles in the evolution of surgical treatment. The surgeon is confronted with a seemingly inexhaustible supply of literature concerning established, as well as enthusiastically reported new methods of treatment. It is not only necessary for him to be conversant with these reports, but to evaluate them critically as they might apply to his individual patients. The treatment of common disorders such as duodenal ulcer, inguinal hernia and bronchiectasis have constantly been modified. The systemic-pulmonary arterial shunts, which definitively opened the field of cardiac surgery, were declared obsolete by some authorities after open heart surgery became available, only to be generally readopted a few years later as temporizing therapy for infants with tetralogy of Fallot. Numerous other examples could be cited supporting the admonishment of Alexander Pope's epigram: "Be not the first by whom the new is tried, nor yet the last to lay the old aside."

Surgical Specialties. Most of the potential developments mentioned will find application in one or more of the surgical specialties. A major breakthrough in the field of transplantation will be no less welcome to the urologist than to the thoracic surgeon. New methods of therapy for malignant tumors will be utilized by all surgeons. Nevertheless, each of the surgical subdivisions has problems which are of greatest interest within that specialty.

One of the newest fields is cardiovascular surgery. Despite the great strides of the past 15 years, many problems remain, some of which are related to the use of heart-lung machines. Investigations of the extracorporeal apparatus can be expected to continue along several lines. Efforts to improve the mechanical properties will allow longer perfusions with less blood destruction. The choice of priming solution will continue to be studied. During the last 2 or 3 years, there has been a growing interest in the use of substances other than blood to fill the extracorporeal circuit. The use of glucose or electrolyte solutions has reduced at least the cost and possibly the danger of open heart surgery. Efforts to minimize the priming volume will continue. With low volume circuits, it is possible that open heart surgery in infants can be accomplished without the present prohibitive risk. The areas of usefulness of hypothermia in conjunction with extracorporeal circulation will be more clearly defined.

Finally, the mechanical lung will probably differ from that in use today. Although the bubble, screen and disk oxygenators have enjoyed the greatest vogue until now, there is reason to believe that these may be replaced by lungs based on the membrane principle. The membrane oxygenators more closely simulate normal lung and cause less damage to blood, but the greatest deterrent to their use has been the inability to find a membrane substance with the proper diffusing properties to allow efficient gas exchange.

There are cardiac disorders which, because of the severity of the malformation or the irreversibility of cardiac damage, can receive only palliative treatment by presently available methods. These include tricuspid atresia, Ebstein's anomaly, truncus arteriosus, diffuse pulmonary artery atresia, endocardial fibroelastosis and advanced coronary artery disease. Effective treatment of these and other disorders will await solution of the problems of cardiac homotransplantation, and the development of artificial organs.

The treatment of peripheral vascular disease has also reached a temporary plateau, the present limiting factor being that vessels below a certain size cannot be effectively reopened. The opening of smaller arterial or capillary beds may have to await biochemical means, whereby occluding deposits can be returned to the blood in fluid form. Perhaps, greater hope might lie in the acquisition of increased knowledge of etiology, and the application of this information to prophylaxis.

Neurosurgery has been well established as a surgical specialty for almost half a century. The active investigation which has characterized this field shows no sign of diminishing. Techniques developed in animal laboratories have frequently been transferred to the clinical operating room, either for therapy or to learn more of the function of the human brain.

Stereotaxic instruments, previously used in neurophysiologic laboratories and more recently applied in clinical neurosurgery, will probably have an increasing role in the future. With stereotaxic techniques, electrical activity of the subcortical structures can be recorded with electrodes inserted into the deepest recesses of the brain. The results of stimulation can be recorded. Lesions in specific nuclei or tracts can be produced by electrocoagulation or by the insertion of chemical agents. The principal use of the stereotaxic instrument thus far has been the treatment of parkinsonism and the relief of intractable pain by localized destruction of subcortical areas. In the future, the method may be increasingly applied to the treatment of behavior disturbances, convulsive seizures and metabolic disorders. Further development of stereotaxic techniques will depend upon two types of investigative effort. Better means of localizing the tip of the probing needle must be developed. More importantly, increased information must be acquired about the function of discrete subcortical structures so the results of their ablation will become more predictable.

Neurosurgery is perhaps more closely allied to the field of electronics than any other specialty. To an extraordinary degree, present-day research on central nervous system function is dependent on electronic recording devices. In the concept of cybernetics, the brain is likened to a giant switchboard, the complex circuitry of which is theoretically reproducible. Indeed, electronic computers are in a sense artificial brains on which capacities of reasoning and even original thought have been conferred to a surprising degree. Further employment of electronic principles may become a reality in future neurosurgical practice. Purposeful alteration of the existing electrical activity of the brain might be possible with radiofrequency stimulation of short-wave receiving electrodes implanted into specific cortical or subcortical areas or by localized stimulation delivered through the calvarium. Behavior patterns might be altered in this way without causing obtundation of consciousness. Similar techniques may become available for production of controlled focal lesions, comparable to the methods using sound waves which are currently under investigation.

Other technical adjuncts will continue to be evolved in neurosurgery. Radioisotope methods for localizing brain tumors will prove invaluable if substances can be found that are more selectively localized in the neoplasm. Improvement of angiographic dyes is inevitable. Sonar techniques for localization of intracranial masses may become practical. Improved plastics may be developed for the reconstruction of defects in the bone and dura mater. Techniques of deep hypothermia to allow operations on the brain while the blood supply is occluded are already being intensively investigated, and will probably receive wider use in the future.

Progress in therapy of ear, nose and throat problems has been rapid, following the temporary atrophy of this specialty which resulted from the introduction of antibiotics. Impetus to the treatment of hearing defects was provided by the procedures for stapes mobilization which were developed for the treatment of otosclerosis. At first, the operations consisted of surgical manipulation of the ossicles to restore the mobility of the ankylosed anticular surfaces. Now, there is increased interest in total removal of the stapes with prosthetic replacement. Gelfoam, vein grafts, fat, wire and plastics have been used in various combinations. The suitability of these and other substituted materials will be the subject of studies in coming years.

Ophthalmology is also in a dynamic period of growth and reassessment. Although corneal transplantation is a widely used procedure, the failures which occur are not well understood. Unlike most other homografts, the cornea is not revascularized from the host. It receives nutrition by diffusion and, therefore, is not subject to cellular invasion and rejection. Nevertheless, an immunologic reaction is suspected in some of the cases in which the grafts become opaque. Clarification of this possibility may allow a more selective approach to corneal graft procurement as well as having wider application in the general field of tissue transplantation.

The operative treatment of cataracts may be simplified by improved zonulolytic agents. Recently, it was shown that alpha-chymotrypsin caused softening or dissolution of the anchoring lens zonules when introduced into the posterior chamber of the eye. Although this method facilitates removal of the lens, further studies will be necessary to establish that other ocular structures are not damaged. Other advances in the treatment of cataracts may follow increased understanding of the biochemistry of cataract transformation. Although altered protein metabolism of the lens is probably the responsible factor in cataract formation, the cause for this metabolic change is unknown. Effective prophylaxis might result from understanding of the pathophysiology.

A variety of unsolved genitourinary problems will occupy the attention of urologists and gynecologists. A continuation of past research on endocrine control of gonadal activity may result in the discovery of new hormones, or more precise information on the biochemistry and physiology of substances which are already known. Such fresh knowledge might have direct therapeutic application in the treatment of infertility. Conversely, advances in endocrinology may bear directly on the important social problems of birth control. The techniques of oral contraception, developed during the past few years, may be replaced by improved methods of endocrine control.

There are special problems in reconstructive surgery of the genitourinary tract. Although both the ureters and the bladder have been replaced with various parts of the gastrointestinal tract, these techniques of substitution are not completely satisfactory. Alternatively, the use of nonliving prostheses has had the inevitable complications of encrustation and stone formation. Methods for restoring patency of the uterine ducts have had a high incidence of reclosure. More satisfactory means of dealing with these common problems may become available.

Stone formation in the urinary tract has been the subject of much research in the past. This work has focused principally on the metabolism and bacteriology of urinary stones, but even this kind of information is still incomplete. In the future, there may be more interest in the physical composition of stones. Knowledge of the configuration of the crystals within stones, and the factors that influence their deposition, may allow development of measures for prophylaxis or for nonoperative dissolution of the stones.

Orthopedic surgery is another specialty in which considerations of biochemistry and physics will be of increasing importance. A vital avenue of research will continue to be the control of bone formation. If this could be achieved, the therapy of complicated fractures would be simplified as well as reconstitution of bone defects. The answer to the control of bone formation may lie in the increasing knowledge of the physicochemical factors of bone healing. Such information might also contribute to the innovation of methods for the early diagnosis of aseptic necrosis. At present, determination of this complication depends upon radiographic signs which are noted many months after bone necrosis. In animals, methods for the early operative detection of avascular necrosis have been developed based on the measurement of oxygen transport across the femoral head or upon the clearance rate of isotopes injected into the bone. The perfection and clinical application of these or other techniques would allow immediate and accurate diagnosis of aseptic necrosis. The devitalized bone could be removed at once and replaced with a prosthesis.

Short of finding a way to accelerate bone healing, the ideal method of treating acute fractures might be the introduction of an agent into the marrow cavity which would harden and impart rigidity and immobility to the fracture site. Casts and crutches would be made obsolete if the proper substance could be found. The most recent material to be tested is a rigid polyurethane foam termed Ostamer. Although this plastic is essentially nontoxic, there is increasing evidence that Ostamer evokes considerable inflammatory reaction, that it is not invaded by callus, and that it does not disappear from the body as bone formation proceeds. Although the use of Ostamer and other substances offers no advantages over accepted methods of fracture treatment at present, improved plastics may make possible the general application of this principle.

The operative treatment of arthritic deformities may become of increasing importance as a result of the availability of improved metal alloys and plastics. In the past, local reconstruction of the joints provided limited palliation. At present, cautious evaluation of prosthetic joints is in progress. Treatment of ankylosed elbows, fingers and knees may become commonplace if joints of suitable nonreactivity and fine design can be provided.

Surgical Education. The surgical education of medical students has changed markedly since the beginning of the twentieth century. The trend has been toward early practical exposure of students to patients on the clinical wards, in contrast to the older purely didactic approach. Electronic devices will permit ramification of such bedside teaching, particularly the audiovisual aids which are already in common use.

A few schools are now experimenting with drastically revised curricula, and there is reason to believe that others will follow their example. An essential feature of these programs is a shortening of the total time investment by a confluescence of the periods of premedical and medical education. A student committed to such a program might begin a course in human anatomy shortly after graduation from high school. Conversely, he might be studying calculus or history in his sixth or seventh year in a combined program in addition to his medical courses. Many medical educators have recommended that the period of education be further reduced by eliminating internships. The contention is that the internship is wasted time since the same skills or information could be acquired as a student or as a specialty resident.

Surgeons, among others, must evaluate critically the results of such innovations within the framework of medical school curricula. Practical experience in postgraduate surgical education has indicated the need for caution in reducing the time of training, and in promoting early specialization. The disappointing results of shortened or narrowly specialized residency programs have brought about a tendency to readopting postgraduate training methods which were in vogue several decades ago. Considerably more time is again being recommended to obtain basic training in the general principles of surgery before entering a surgical specialty. It would seem reasonable to expect that the specialist who operates within the abdomen should be able to deal with unexpected intestinal or vascular problems.

Broad education in surgery is also a necessity for the continued expansion of the horizons of surgery. In the past, new specialty fields have been opened, not by specialists with limited interests, but by surgeons whose training almost invariably included time spent in scientific laboratories. The progenitors of neurosurgery, cardiac and thoracic surgery, orthopedics, hand surgery, urology, gynecology and otolaryngology were all surgeons first and surgical specialists later. The discovery and utilization of new information will be by men who know surgery and its principles, not by those who know only a fraction of the total problem.