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YEAR BOOK OF
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The Year Book of SURGERY®

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SURGERY®**

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Journals Represented

Year Book Medical Publishers subscribes to and surveys nearly 700 U.S. and foreign medical and allied health journals. From these journals, the Editors select the articles to be abstracted. Journals represented in this YEAR BOOK are listed below.

Acta Chirurgica Scandinavica
Acta Medica Scandinavica
Acta Physiologica Scandinavica
American Journal of Cardiology
American Journal of Medicine
American Journal of Pathology
American Journal of Physiology
American Journal of Surgery
American Surgeon
Annales Chirurgiae et Gynaecologiae
Annals of Internal Medicine
Annals of Plastic Surgery
Annals of Surgery
Archives of Disease in Childhood
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British Medical Journal
Burns
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Cell
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Cleft Palate Journal
Clinical Nephrology
Clinical Radiology
Contemporary Orthopedics
Critical Care Medicine
Digestive Disease and Sciences
European Journal of Plastic Surgery
Gastroenterology
Head and Neck Surgery
Infections in Surgery
Injury
International Journal of Cancer
Journal of the American Medical Association
Journal of Bone and Joint Surgery (British volume)
Journal of Clinical Microbiology
Journal of Experimental Medicine
Journal of Hand Surgery (American)
Journal of Immunology
Journal of Infectious Diseases
Journal of the National Cancer Institute

Journal of Pathology
Journal of Pediatric Gastroenterology and Nutrition
Journal of Pediatric Surgery
Journal of Pediatrics
Journal of Pharmacology and Experimental Therapeutics
Journal of Surgical Research
Journal of Thoracic and Cardiovascular Surgery
Journal of Trauma
Journal of Urology
Journal of Vascular Surgery
Lancet
New England Journal of Medicine
Plastic and Reconstructive Surgery
Postgraduate Medical Journal
Radiology
Reviews of Infectious Diseases
Science
Southern Medical Journal
Surgery
Surgery, Gynecology and Obstetrics
Topics in Emergency Medicine
Transplantation
World Journal of Surgery

Annual Overview

General Considerations

Vascular surgical strategies for patients with heparin-associated thrombocytopenia are described. The suggestion is made that in order to achieve optimum results, the extent of anterior mediastinal dissection should be increased when performing thymectomy for myasthenia gravis.

Fluid, Electrolytes, and Nutrition

Several reports related to the nutritional support of patients sustaining significant operative or nonoperative trauma have shown changes in granulocyte function in response to trauma, including burn injury. Reduced chemotactic potency and loss of recruitment of phagocytes at sites of injury appear to be real and might well lead to uncontrolled bacterial invasion.

It is clearer that starvation alone produces multiple specific cell defects. Simple maintenance of nitrogen balance is inadequate to reverse a cellular injury following injury and starvation. Studies have been designed to evaluate the addition of branched-chain amino acids to parenteral nutrition in a variety of settings, but despite the setting, their addition has not been shown to improve malnutrition or reduce the phagocyte dysfunction that occurs with severe injury. Phagocyte dysfunction can be reversed by a normal diet, and the preoperative time for optimal reversal appears to be about 2 weeks. One study showed that even with optimal total parenteral nutrition, there is usually no increase in the body protein. This was partially corrected by adding human growth factor in patients requiring parenteral nutrition for 2 or more weeks. When growth hormone was added, the levels of urinary nitrogen, urea, phosphorus, potassium, and sodium excretion all declined significantly, whereas the nitrogen balance rose and was maintained. Consequently, it becomes clearer that starvation, with or without concomitant injury, has a striking effect on skeletal muscle amino acid metabolism and membrane function, and that standard total parenteral nutrition only partially reverses these changes. Other manipulations of the protein content of parenteral nutrition solutions are being pursued.

Severely burned, obese, or edematous patients with life-threatening complications such as cardiac arrest or severe volume depletion can be accessed by a 16-gauge bone marrow needle inserted into any long bone but generally in the tibia. Apparently, this intraosseous access approach provides a route for a large volume of fluid and even medications under these special emergency circumstances. One article reported that autotransfusion blood, even when contaminated by enteric contents, is perfectly safe to use in a massively hemorrhaging traumatized patient. The autotransfused blood was processed through a cell-washing recovery system. All patients received parenteral broad-spectrum antibiotics perioperatively and were closely monitored. No significant adverse effects were seen.

Most investigators would agree now that the bowel is the source of organisms that trigger endogenous mediators in response to a number of stimuli including sepsis, remote sepsis in the body, hemorrhage, and even prolonged bowel disuse, resulting in atrophy. As a consequence, a number of specific solutions are being tried to reduce bowel atrophy, in addition to sterilizing the bowel. One such solution is monoacetoacetin, the glycerol ester of acetoacetate. This substance is a preferred oxidative fuel for enterocytes and appears to be more mucosa specific as a fuel than does glucose in general. This may well become a useful adjunct in patients given parenteral nutrition.

Shock

Interest continues to run highest in the most commonly seen forms of shock, i.e., septic shock and hemorrhagic shock. Generally speaking, the major efforts during the past year have focused on the pathogenesis and treatment of septic shock, involving an intensive study of mediators, as well as continuing efforts at improving resuscitation for patients in shock.

There is continuing interest in the use of smaller-volume hypertonic solutions for resuscitation in hypovolemic shock. Several experimental articles indicate that hypertonic solutions can be given in very small volumes initially without producing phlebitis at the injection site in peripheral veins. With moderate degrees of hemorrhage there were no acute changes in renal or cerebral dysfunction despite significant hypernatremia and hyperosmolality that occurred with the use of hypertonic solutions. These studies do not examine the question of preexisting disease or even deleterious effects on altered renal function in response to this form of non-physiologic resuscitation. One controlled study examined the tendency to continue to bleed where major branches of the ileocolic artery were severed but not controlled. It was interesting that the mortality rate was much higher in the group given hypertonic saline, because the hypertonic saline increased the blood loss, probably through vasodilation, and this led inevitably to a fall in arterial pressure and early death. These investigators warned against the use of hypertonic saline as initial resuscitation in the acutely injured, because the solution might increase the amount of uncontrolled blood loss through its central vasodilatory action such as in an intra-abdominal injury.

With the continuing need for oxygen-carrying solutions in resuscitation of hypovolemic shock, there is an intense effort being made to develop stroma-free hemoglobin solutions of practical value. This work is of critical importance because of risks involved with transfusion, particularly transmission of the causing acquired immunodeficiency syndrome. One study pointed out that the bovine polymerized hemoglobin solution is complicated by toxic impurities in the preparation, preventing a clinical trial at the present time. It appears that the toxic impurities are largely phosphates in the broken-down hemoglobin solution, and these impurities are the most difficult of the toxic factors to remove from what otherwise is a very good oxygen-carrying hemoglobin solution. Models have

been designed and columns devised to absorb the impurities from the stroma-free hemoglobin solution. This unique fluid is stable at room temperature, providing a hemoglobin equivalent of approximately a half normal hematocrit.

One of the most interesting studies of endotoxin or hemorrhagic shock is that concerning the importance of bacterial translocation from the gut. Experiments have shown that hemorrhagic shock alone promotes translocation of bacteria from the gut to visceral organ in experimental animals. Furthermore, the duration of shock correlated directly with the 24-hour mortality in such studies. The bacteria most often seen translocating were *Escherichia coli* and enterococcus, and this obviously led to the suggestion that antibiotic decontamination of the gut would lower the incidence of bacteremia in the face of hemorrhagic shock. Previous studies from the same investigators have shown a similar increase in translocation from the systemic administration of endotoxin.

Many studies examine the role of the mediators that emanate from endotoxin-stimulated endogenous macrophage-secreting cytokines. It appears that cachectin is a prime mediator that, when released into circulation in response to invasive infection, causes profound shock and multiple organ injury. Further studies have also shown that, in experimental animals, cachectin antibodies, now available as monoclonal specific antibodies, exert a protective effect from endotoxin sepsis.

Attempts to investigate resuscitative fluid include a recent study on hydroxyethyl starch. This study has shown that all serum protein, including albumin, globulin, and coagulant proteins, is significantly decreased when resuscitation is supplemented with hydroxyethyl starch. The findings further demonstrate that hydroxyethyl starch induces an oncologically controlled extravascular protein relocation.

Since it has been shown that hypothermia critically interferes with platelet function, attempts are increasing to prevent a reverse to the hypothermia that occurs with shock. By adding washed red blood cells to saline, preheated to 70 C, the red blood cells can be given in warmed solution without hemolysis or a change in plasma hemoglobin from increased osmotic fragility. This newer blood-warming process looks promising for infusing red blood cells and fluids at body temperature without harming them.

Trauma

A large volume of good clinical research concerns the detailed technical improvement in care of the severely injured patient. The use of ultrasound to evaluate abdominal trauma is reported this year. There were no false negative studies in patients who sustained abdominal trauma. Several positive findings, including renal injury, in patients with free intra-abdominal fluid that proved to be blood led to laparotomy. The authors point out that the presence of fluid in the hepatorenal pouch is a good indicator of the presence or absence of free intraperitoneal fluid. Because this is a quick, relatively inexpensive, noninvasive procedure, the technique bears further study in patients with blunt abdominal injury. Many

articles reassess the use of diagnostic peritoneal lavage in blunt trauma. As the years pass, the relative contraindications for diagnostic peritoneal lavage have begun to fade, even including a gravid uterus and a history of multiple abdominal operations. Now there are relatively few contraindications to the use of open, small incision peritoneal lavage as a safe, rapid, and accurate method of identifying intraperitoneal injury. Subclavian catheterization in the emergency room is rarely, if ever, justified. There seems to be little doubt that the complication rate is much higher when the procedure is carried out in the emergency setting; this is true whether the same individuals place the catheter or rotating personnel in the emergency department do so. Consequently, the use of invasive monitoring via the subclavian drain should probably be done as an elective procedure, either in the stable setting of an intensive care unit or in the operating room.

Controversy continues over the efficacy of observation of penetrating wounds of the neck. More studies indicate that arteriography and observation are inadequate, particularly for stab wounds that penetrate the platysma muscle or zone 2 of the neck. More authors believe that these patients should be explored promptly. Similarly, immediate exploration of the abdomen in patients identified with splenic injury reduces the mortality rate and increases the splenic salvage rate.

Sepsis is the leading cause of death after initial care of the hepatic injury, thus efforts are directed toward its control. Many correlates have been examined, including mode of injury, whether or not resection was done, gastrointestinal tract perforation, and even the number of associated injuries. The development of sepsis correlates only with the severity of the injury. Many authors advocate closed suction drainage to reduce sepsis after hepatic injury, but no firm, comparable data are available. Blunt trauma produces a higher mortality rate than most penetrating traumatic injuries. Reexamination reveals that resection procedures are generally the only method of control for severe, shattering, deep hepatic injuries. One of the most devastating injuries is that of the juxtahepatic veins. Hemorrhage is controlled quickly with an atrial caval shunt. Salvage of some of these patients with any other method was simply not possible. Although these are severe injuries with a high mortality rate, there are times when a shunting procedure will allow temporary control while retrohepatic caval injuries or hepatic venous injuries are repaired.

In past reports, less severe injuries to the pancreas and liver were treated by simple control of bleeding and drainage, but current reviews indicate that with severe injury (e.g., transection of the pancreas), the Roux-en-Y anastomosis, for control of bleeding and salvage of pancreatic tissue, is a useful and safe procedure. Similarly, pancreaticoduodenectomy, to manage combined injury to the pancreas, duodenum, and common bile duct, is a useful procedure.

An interesting article reports reduction in the cost of diagnostic tests for renal injury in patients sustaining trauma. These authors used the dip stick to test urine and reported that with more than 10 red blood cells per high power field in urine, the dip stick test will be positive. These pa-

tients should be presumed to have renal injury and should be hospitalized. For the patient with multiple injuries, complex operative procedures, and significant blood loss, the superior mesenteric vein may be ligated safely.

Helicopters are used in conjunction with level I trauma centers, and articles have now documented improved survival with this form of transportation. Even when the transport time was similar, with and without air transport, the critical therapeutic interventions enhanced survival in the air-transported group because of the availability of well-equipped medical helicopters.

Wound Healing

A study of the natural history of midline sternotomy scars in children reveals that only about one third of the scars classified as hypertrophic remain so for longer than 1 year. Girls are more likely to have long-term hypertrophic scars, and wounds closed with absorbable deep sutures leave hypertrophic scars more often than wounds closed with nonabsorbable deep sutures. Experimental débridement of soft tissue wounds with ultrasound-radiated energy appeared promising in 1988, particularly in wounds of the hand where vital structures in the depth of the wound prevent wide excision of all involved tissues. Failure to appreciate the presence and extent of osteomyelitis in trophic ulceration was shown to be responsible for most failures of soft tissue closure. Plain pelvic roentgenography, white blood cell count, and sedimentation rate make the diagnosis most of the time. Jamshidi needle biopsy was helpful in making the diagnosis when standard x-ray studies and blood test results were normal. Deep pelvic ulcerations in paraplegic patients are best treated by amputation and thigh rotation pedicle flaps. If all of the osteomyelitis is removed, the long-term results of thigh rotation flaps are excellent at follow-up, even when prolonged sitting cannot be avoided. The circulation in dangerously ischemic musculocutaneous flaps can be improved by electrical stimulation with a transcutaneous electrical nerve stimulation unit. In one of the most refreshingly simple demonstrations in wound healing biology, it was shown that skin expansion can be obtained within a few hours and without expensive expansion devices. Presuturing a lesion under tension the evening before extirpative surgery produced expansion sufficient to close most wounds that could not be closed otherwise without a graft. Skin expansion preoperatively before separating conjoined twins also was shown to be effective in closure of the skin defects. New expansion devices to stretch an infant's skin are probably superior to the older technique of inducing pneumoperitoneum. The midabdominal rectus myocutaneous flap continues to enjoy popularity, but the complication of abdominal wall hernia attests to the lack of skill of many surgeons in rebuilding the abdominal wall after taking a rectus myocutaneous flap. The donor defect after removal of such flaps is substantial, and expert use of local tissue or the addition of a prosthesis is necessary if postoperative hernia is to be eliminated. Growth factors continue to dominate research in wound healing biology. Macrophage-

derived protein, growth hormone, and platelet-derived growth factor appear to be the most promising substances in stimulating repair. Studies concerning the ability of such agents to prepare a tissue for healing and thus eliminate the lag phase as in a secondary wound have not been reported yet.

Infections

As one organism appears to be eradicated, two others seem to arise to plague surgeons. In 1988, *Scedosporium inflatum* emerged as a pathogen with more sinister possibilities than previously recognized. On the other side of the scale, new therapeutic alternatives to immunoglycosides for treating gram-negative infections in surgical patients also appeared. Comparative trials of aztreonam and imipenem-cilastatin against conventional therapy with aminoglycosides revealed superior penetration of tissue and excellent clinical control of infection. These new agents are not as dependent on renal excretion as aminoglycosides are. Because they require less intensive pharmacokinetic monitoring, they appear to be less expensive than tobramycin or aminoglycosides. Similar comparative studies against clindamycin and gentamycin produced similar data. Moreover, imipenem-cilastatin can be used as a single agent as effectively as treatment of mixed aerobic and anaerobic infections as any combination therapy now available.

Although it was shown that *Candida*-caused esophagitis can usually be treated successfully with amphotericin B administered intravenously, most patients receiving such therapy are so immunologically depressed from systemic disease that death is not far away. The value of hyperbaric oxygen in treating gas gangrene was reported again in 1988. The major problem, however, continues to be transportation of desperately ill patients to a center where hyperbaric oxygen can be administered expertly and with safety. The results of a study published in 1988 evaluating immunocapacity in malnourished patients showed that more than four immunologic tests often are needed. Some malnourished patients can be correctly identified by only three antigens, but such a small battery misclassified well-nourished patients twice as often as a seven-test battery. Misclassification of nutritional immunologic defects can lead to unwarranted use of total parenteral nutrition. In some patients, oxygen requirements for normal metabolism are $1\frac{1}{2}$ times greater during sepsis.

Arterial lactate still appears to be the most valid measure of perfusion failure and, therefore, shock. Pharmacotherapy can improve cardiac output and systemic oxygen delivery in selected patients, but there are pitifully few data to support the routine use of inotropic, vasopressor, or vasodilator drugs in septic shock. In a prospective study, the influence of the surgeon's maturity and experience turned out to be significant in the outcome of postoperative sepsis; the difference between level I trainees and senior surgeons' results was impressive. The importance of administering antibiotics when urinary tract infections develop in a hospital setting was reported in 1988. These data leave little doubt that excessive postoperative prophylactic antibiotic therapy compounds the problem of

nosocomial infection. The role of viruses in making surgical patients more susceptible to systemic and local infection also was demonstrated in 1988.

Burns

Basic investigation into the vascular changes produced by thermal injury showed in 1988 that heat may depolarize smooth muscle membranes, thereby altering voltage-dependent calcium channels. Interestingly, pulmonary vessels do not appear selectively to be affected. Suppression of vasoactive responses appear to prevent significant pulmonary arterial hypertension. These data help to explain why, even after adequate fluid replacement, some burned patients cannot be resuscitated. It was also shown in 1988 that hypermetabolism in burned rats is driven by a corresponding increase in evaporative heat loss through the burn wound. Neither the method nor the timing of feeding could be shown to affect the relationship between hypermetabolism and evaporative heat loss through burned skin. Only patients with classic risk factors such as obesity or lower extremity burns appeared to benefit from routine heparinization. Embolic events in burned patients apparently are relatively rare. Topical treatment of burned skin with povidone-iodine was shown to induce hyperthyroidism in some patients and thus increase hypermetabolism.

Reports of the successful utilization of scalp as a skin donor site suggest that this structure has been overlooked in the past as a potential source of life-saving skin. The thickness of the scalp apparently makes it especially valuable, because more grafts can be taken successively from it than from areas of thin skin. The search continues for some way to produce autogenous skin in the laboratory. The present status of this work can be summarized succinctly by stating that cells can be grown in tissue culture, and all manner of collagen substances can be synthesized in a test tube. The frontier, however, is combining the two methods. Rete pegs have not been produced yet, and the problem persists of how to attach cultured epithelial cells to an artificial collagen substrate or dermis. Until this problem can be solved, temporary membranes such as biobrane or allografts must suffice.

Multiple tiny skin grafts (micrografts) can be used to close large burn wounds, but no evidence was presented in such recommendations to show that any new skin develops from seeding a burn wound in this manner. The interstices between micrografts still heal by epithelialization and wound contraction. A review of various methods to resurface the anterior neck after release of a burn scar contracture confirms earlier studies showing that there really is not a completely satisfactory technique for releasing the contracture and reestablishing the neck line and chin profile. Eradication of *Candida* in burned patients is not as simple as "swish and swallow," as may be used in other patients. Some degree of immunologic competence must be reestablished before *Candida* can be eradicated. When severe immunologic deficiencies are present it may be necessary to

replace the entire immunoglobulin class specifically, whereas in other patients replacement of a single subclass may be all that is required.

Transplantation

The national network for organ procurement and sharing is off and running. Logistical factors of size, blood type, ischemia time, and distance have been predominant in the protocols for nonrenal organs and will continue to be so until considerably more flexibility in terms of organ preservation is achieved. The perfusion solution devised by Belzer's group after years of careful and cautious development has already been found to be a marked improvement over previous cold storage methods for the liver and has been applied to preservation of the pancreas as well. Evidence that much organ injury in the early hours of ischemic preservation is not irreversible but is mediated by oxygen-derived free radicals generated by reperfusion injury may extend the pool of cadaver donors by treatments designed to ablate these free radicals. The heart has been found to be the most limiting organ, tolerating *ex vivo* cold storage for less than 4 hours. No new or improved heart preservation methods have been reported.

The distribution of kidneys, however, remains controversial. The benefits or lack thereof of HLA matching of donor and recipient are still being debated. Some progress is being made in better definition of the HLA system and in definition of the elements of matching that appear to be important. The most notable contributions to this controversy have come from Terasaki's group and from the Collaborative Transplant Study headed by Opelz. In long-term follow-up studies a clear-cut survival advantage is had by patients receiving HLA-matched kidneys. This translates to an increase in mean survival time of kidneys from 7 years to 14 years. This survival advantage pertains even when the kidneys are transported for long distances. These data should prove to be powerful in reinforcing and extending the mandate to share kidneys on the basis of matching.

Pancreas transplantation has become considerably safer since most surgeons have reverted to transplantation of the entire gland together with a segment of duodenum, implanted into the urinary bladder for exocrine drainage. Patient mortality and morbidity are now approaching acceptable levels, and a successful transplant is said to contribute substantially to the patient's well-being, although no studies to this point have been published. It has come as a great disappointment, therefore, that retinopathy has been observed to progress essentially unhindered in patients having successful transplantation. Although it is rumored that the outcome after longer follow-up has been somewhat more encouraging, it is really no surprise that progression occurs, because the ischemic changes in the retina that precede diabetic retinopathy are essentially irreversible. Again, it seems obvious that pancreas transplantation is undertaken too late in the course of the disease to be of any but symptomatic benefit to the patient with end-stage diabetic microvascular disease.

The mysteries of the blood transfusion effect in enhancing allograft

survival have been explored by several groups. Wood and her co-workers have postulated, on the basis of experiments in mice, that transfusion induces the appearance of activated macrophages that secrete inhibitory prostaglandins, resulting in failure of transfused mice to produce interleukin-2 (IL-2). Soluble and cell-mediated suppression both seem to be induced by transfusion.

Progress has been achieved in transplantation of the heart in neonates, of single lungs in patients with pulmonary fibrosis, and of the liver in children, using adult organs reduced in size for the pediatric patient.

Oncology and Tumor Immunology

That an immune response occurs in the development of malignancy is now quite clear. Interest is high in defining the regulatory mechanisms of this response, because suppression seems to be a prominent factor. Studies of tumor-infiltrating lymphocytes and of lymphocytes in involved and noninvolved lymph nodes draining a tumor, have demonstrated that cells with high specific cytotoxic potential in vitro exist side by side in vivo with healthy tumor cells. In interesting experiments, a soluble suppressive factor has been identified and blocked and the nonsuppressor cells amplified with a lymphokine, IL-2; metastases were dramatically reduced. The balance between immunoregulation and surveillance, cytotoxicity, or containment of the tumor is the topic of many investigations.

As industrial-size quantities of lymphokines have become available through genetic engineering, it has been possible to conduct experiments to define the roles of these soluble factors released by macrophages and other mononuclear cells. Interleukin-2, known to expand lymphocyte populations indiscriminately, has been used for several years in experimental protocols to produce lymphokine-activated killer (LAK) cells. Both IL-2 and LAK cells are then infused into patients with disseminated malignancy, and a few good responses have been obtained. The severe toxicity of these agents, however, almost precludes the clinical development of these techniques. This also seems to be the case in the initial studies of tumor necrosis factor or cachectin, an interesting soluble substance thought to mediate, at least in part, the physiologic events in endotoxic shock. An old observation that experimental sarcomas in mice underwent hemorrhagic necrosis when exposed to endotoxin has been reproduced with tumor necrosis factor, but only when an immune response against the tumor was present. This potentially useful agent with activity against the endothelial surfaces of the tumor blood supply has been combined in low, tolerable dose levels with other lymphokines such as γ -interferon, α -interferon, and IL-2. Clinical trials of combination lymphokine therapy are planned.

Clinical trials, and who should bear their costs, was the subject of a 1988 "Sounding Board" article in the *New England Journal of Medicine* (Antman K, Schnipper LE, Frei E: *N Engl J Med* 319:46-48, 1988). Although the costs of phase III randomized clinical trials are often reimbursed through usual third-party sources, funding for the costs of phase I (toxicity, dose) and phase II (therapeutic effect) has become limited by