# CARE OF THE CRITICALLY ILL

STEPHEN M. AYRES
ROBERT SCHLICHTIG
MICHAEL J. STERLING

**Third Edition** 

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### STEPHEN M. AYRES, M.D.

Dean, School of Medicine
Professor, Internal Medicine
Professor of Medicine
Virginia Commonwealth University
Medical College of Virginia
Richmond, Virginia

### **ROBERT SCHLICHTIG, M.D.**

Assistant Professor, Anesthesiology and Critical Care Medicine Director, Surgical ICU Medical Director, Respiratory Therapy Oakland Veterans Administration Medical Center Pittsburgh, Pennsylvania

### MICHAEL J. STERLING, M.D.

Director, Medical-Surgical ICU Medical Director, Respiratory Therapy North County Hospital Newport, Vermont

Illustrated by and with the assistance of META E. BUEHLER, R.N., B.S.





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### To My Family

Dolores Kobrick Ayres Stephen Elizabeth Ann Margaret Louise

### PREFACE TO THE FIRST EDITION

This book evolved from our experience in caring for cardiac surgical patients. The lessons learned from these patients were applied to other critically ill individuals who shared the common problem of cardiorespiratory collapse. It soon became apparent that although certain well-established concepts provided the basis for treatment of such patients, they could not be applied unless continuous quantitative observations were made. We have emphasized circulatory and respiratory derangements because they are usually present in the critically ill. Hence, we have presented basic physiologic concepts together with methods of measurement and have discussed plans of therapy which seem reasonable in light of present knowledge. Our goal has been to present a workable framework enabling the physician to reevaluate continually his treatment by constant observation of his own efforts and critical assessment of the growing literature in this area.

The modern care of the critically ill patient is a team effort. Many dedicated individuals were responsible for the development and execution of the concepts presented in this book. The authors gratefully acknowledge the assistance of:

Sister Anthony Marie, Administrator of Saint Vincent's Hospital and Medical Center, Dr. William J. Grace, Director of Medicine, and Dr. Louis M. Rousselot, Director of Surgery, who have provided a hospital environment fostering the aggressive care of the sick patient. We thank Dr. Grace, a pioneer in the field of cardiac monitoring, for contributing his chapter on the electrical management of heart disease.

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The editorial and art staffs of the Medical Department of Appleton-Century-Crofts for their direction and guidance.

STEPHEN M. AYRES, M.D. STANLEY GIANNELLI, JR., M.D.

### PREFACE TO THE THIRD EDITION

The number of hospital beds specifically reserved for the care of critically ill patients has multiplied many times over since we began preparing material for the first edition of this book in 1965. Prior to 1960, almost all hospitalized patients received the same type of medical care regardless of the complexity of their illness. The stratification of patients by intensity of nursing and medical care requirements is a relatively recent practice. Governmental decisions to control cost rather than quality has led to a dramatic shift in the types of patients admitted to hospitals. Only the sickest patients are eligible for admission, and their care is compressed into the shortest possible time because of the need to reduce length of stay and make the predetermined flat-rate reimbursement profitable to the hospital. Incredibly, the diagnosis-related grouping system was embraced by the Federal Government without considering the severity of illness within each grouping. Careful evaluation of physiologic status of patients within specific diagnostic groupings have demonstrated wide variation in the severity and expected mortality of individual patients. The need for early detection and prevention of potentially lethal situations is more urgent at this moment than ever before.

Recent studies have shown that the quality of critical care varies widely from

hospital to hospital. Unfortunately, practice too often lags behind theory, and inappropriate use of high technology too often becomes a substitute for careful diagnostic and treatment planning. More than fifteen years ago, Senator Abraham Ribicoff, in an important essay entitled "The American Medical Machine," told of patients dying in intensive care units because of clogged tracheostomy tubes or accidentally disconnected respirators. The key to better performance in the treatment of such patients lies in the development of an organized system for the delivery of intensive care. Important as well-engineered hardware is, the success of a system for the care of the critically ill depends upon the availability of an experienced team of physicians, nurses, and other health professionals, interacting and growing together, and continuously evaluating their performance as they attempt to translate basic physiologic information into better patient care. Here more than anywhere else in the hospital, patient survival depends upon nurses who have been educated to observe, question, diagnose, and initiate independent action; and upon physicians who have been educated to function as team members-not as infallible despots.

This book has been written for all concerned with the care of extremely sick people, for practicing physicians, house officers, medical students, intensive care nurses, general staff nurses, and allied health personnel. These individuals share a common-knowledge base, and the authors believe that the concepts presented here are as useful to a nurse preparing for certification in critical care nursing as to a physician preparing for subspecialty certification in medicine, surgery, or anesthesiology.

One of the authors (S.M.A.) has been actively involved in the practice of critical care medicine since 1961, and most of the material presented in this third edition has resulted from personal observation and almost continuous communication with colleagues throughout the world. An incomplete list of those whose own ideas have contributed to this book

include: Diane C. Adler, Roger C. Bone, Frank Cerra, Jacqueline Coalson, Foster Conklin, John B. Downs, Alpha Fowler, Frank Gafford, Stanley Giannelli, Thomas Hyers, Robert Kirby, William Knaus, Joanne Lagerson, Ian Ledingham, Sally Millar, Hiltrud Mueller, Joseph Parrillo, Norma Shoemaker, William Shoemaker, Peter Safar, William Sibbald, Harvey Sugerman, Joan Stoklosa, Max Weil, Robert Wilson, Harold Young, and Jack Zimmerman.

The third edition could not have been written without the editorial expertise of Meta Buehler, who illustrated and edited most of the text, and Ann Ramey, who typed and supervised the final preparation of the manuscript.

STEPHEN M. AYRES, M.D. ROBERT SCHLICHTIG, M.D. MICHAEL J. STERLING, M.D.

### INTRODUCTION

### THE EMERGENCE OF THE CRITICAL CARE CONCEPT

The life of an individual experiencing critical injury or illness hangs in a delicate balance between the forces promoting life and those leading to death. Not so long ago the physician stood helpless as the balance shifted away from life, and death became inevitable. Step by labored step an understanding of the life-promoting forces evolved, and, at some moment in the very recent past, an extremely ill individual could be said to profit more by medical action than by medical inaction.

The newest health care specialties, critical care medicine and critical care nursing, practiced informally for many years, have rapidly acquired theoretical foundation, state-of-the-art expectations, and organizational structure. Like almost all new socioscientific enterprises, they have also become focal points of significant controversy. Arriving on the American scene at a time when there was public concern over the high cost of medical technology, ethical questions over the initiation and termination of life-support measures, and increasing pressure for improved accountability of health professionals, these specialties now provide the health care system with important opportunities and vexing problems.

A historical paradigm summarizes how

critical care medicine began and how it could mature or even disappear. For many years, poliomyelitis was frequently fatal because the failure to breathe was considered synonomous with the failure to survive. The introduction of the negative-pressure whole body ventilator or "iron lung" in the years following World War II saved many lives as communities acquired hardware and professional expertise. The very first acute care units arose in Scandinavia in the early 1950s1 to centralize the use of these respirators, and similar respirator clusters arose in the United States. The number of respirators necessary was illustrated in a recent edition of the Journal of the American Medical Association. It republished as a Landmark Article the 1929 description by Drinker and McKhann of the first tank respiratory or iron lung.2 Accompanying the actual article was a startling photograph showing more than 50 iron lungs in a Los Angeles County Hospital during a poliomyelitis epidemic in the 1950s. The economic problems of long-term care for ventilator-dependent patients were frequently solved by sideshow techniques. Vans carrying a "man in the iron lung" traveled from town to town and charged admission to wide-eyed youngsters and adults. Parallel progress in immunology and microbiology ended the need for iron lungs as widespread immunization prevented poliomyelitis.

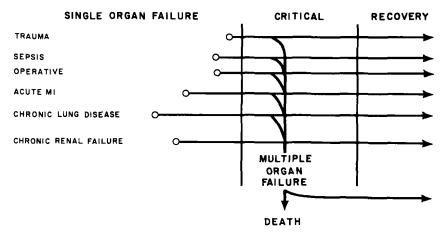
Much of the present practice of critical care is rooted in experiences gained from the two World Wars, the Korean War, and Vietnam War. Wiggers et al.,3 in a series of papers published between 1942 and 1945, showed that experimental bleeding of 4% of an animal's body weight produced irreversible shock if restoration of blood volume was delayed. Reinfusion during the first one to two hours of hemorrhagic hypotension could lead to complete restoration of health, but reinfusion after that time led to a syndrome of vascular collapse and death. The balance point between reversibility and irreversibility was named the "critical stage" and focused attention on the importance of prompt restoration of volume and flow to prevent death (Fig I-1).

At about the same time, Cournand et al.<sup>4</sup> studied human traumatic shock at Bellevue Hospital. They used right atrial catheterization to obtain mixed venous blood, and they calculated cardiac out-

put from the arterial-venous oxygen content difference and calculated oxygen consumption using the Fick equation. They concluded that traumatic shock in humans was a "rapid or precipitate failure of the circulation, usually associated with inadequate return flow of blood to the heart. The chief findings were decreased cardiac output, low pressure in the right auricle, low arterial pressure, and decreased blood volume." They found that oxygen delivery was markedly reduced and that oxygen consumption was maintained at a lower-than-normal level by increased oxygen extraction at the expense of a reduction in mixed venous oxyhemoglobin saturation.

In the beginning, anesthesiologists played a leading role in the application of advanced technology to seriously ill patients. They were in the hospital for much of each day, were skilled at intubation, and were accustomed to dealing with seriously ill patients after surgery. Peter

#### THE MOMENT OF CRITICAL ILLNESS



#### FIG I-1.

The forces leading to life or death hang in critical balance during the moments of critical illness. A variety of morbific (etiologic) processes can lead to single organ failure. Many patients rapidly recover from single organ failure, but others develop multiple organ failure and require highly organized specialized care in critical care units. A large number of these patients die, but early identification and treatment allow some to recover.

Safar, an anesthesiologist, organized the first special care unit in the United States at the Baltimore City Hospital in 1958 and called it an "intensive care" unit.5 Internists soon became involved when it was discovered that apparent death from myocardial infarction could be successfully treated by electrical defibrillation. The observation that resuscitation was possible only if a trained team of health professionals armed with endotracheal tube and defibrillator arrived on the scene within several minutes led to the emergence of the coronary care unit and institutionalized the involvement of internists in critical care units.

The coronary care units introduced in the 1960s revolutionized the care of hospitalized patients.6 Special observational techniques, the availability of skilled nursing care, and the regular assignments of physicians knowledgeable about the care of the extremely ill patient were necessary to reduce complications and improve survival. Technology forced the stratification of patients by severity and type of illness because expensive equipment could not be widely dispersed throughout the hospital. Such equipment was frequently too costly for general use and required special training. The direct current defibrillator was an important addition to patient care but was of little use unless immediately available. When the diagnostic value of ventricular premature contractions in patients with acute myocardial infarction was identified, the coronary care unit, with continuous electrocardiographic monitoring, resuscitation equipment including defibrillators. and specially trained personnel, became necessary. Amazing as the new technology seemed to be, the changes in utilization of health personnel were even more earth shattering. Registered nurses were suddenly propelled into the forefront of coronary care, since physicians were frequently not available on a 24hour basis in many hospitals. They made electrocardiographic observations, diagnosed the specific types of cardiac arrhythmias, and prescribed electrical therapy, frequently in the total absence of physician support. A new era arrived as physicians delegated major diagnostic and decision-making responsibility to well-trained nurses.

Coronary care units have markedly improved the care of patients with acute myocardial infarction and reduced the mortality from cardiac arrhythmias. They became a prototype of intensive care limited to a specific problem. While patients rarely died from electrical problems associated with equipment, many continued to die from ventricular failure, forcing the cardiologist to acquire new skills as limited cardiac care became more generalized and included care of other failing physiologic systems. Patients with acute pulmonary edema were intubated, and hemodynamic measurements with bedside catheterization techniques were made in patients suffering from shock.7 Perhaps the most significant change was the routine use and interpretation of arterial blood respiratory gas analysis to determine the level of pulmonary venoarterial shunting and the adequacy of alveolar ventilation. The acute respiratory care unit was born, and chest physicians joined cardiologists in the application of new techniques to old clinical problems.

In 1967, Ayres, Giannelli, and Mueller<sup>8</sup> published the first edition of *Care of the Critically Ill* based on their experiences caring for cardiac surgical patients at Saint Vincent's Hospital in New York City. "The lessons learned from these patients were applied to other critically ill patients who shared the common problem of cardio-respiratory collapse," they wrote in the preface. "It soon became apparent that although certain well-established concepts provided

the basis for treatment of such patients, they could not be applied unless continuous quantitative observations were made....The modern care of the critically ill patient is a team effort." The publication of that text and an article published the same year by Max Harry Weil<sup>9</sup> entitled "A New Look at the Critically Ill" provided a new name for the organized care of such individuals. Safar<sup>10</sup> had called the science of emergency life-support "resuscitation" or "reanimation" and used "intensive care" to mean long-term resuscitation in special units. The term "critical care" is now used to describe the entire continuum from emergency treatment at the scene of illness or accident to the special care provided in the hospital.

The first coronary care and medicalsurgical intensive care units were located in large nonuniversity hospitals and arose because of obvious patient need. A new literature was created, and organizations to educate and motivate health professionals working in critical care units became necessary. The American Association of Cardiovascular Nurses, first incorporated in 1969, changed their name to the American Association of Critical Care Nurses (both organization abbreviated AACN) in 1971. They had 2,800 members at the time of the name change and grew to 58,000 in 1987. In 1971, 26 individual physicians representing medicine, anesthesiology, pediatrics, and surgery founded the Society of Critical Care Medicine. The society journal, Critical Care Medicine, skillfully edited by William Shoemaker, has become an important focus for scientific communication in the field. Another journal, Heart and Lung, reaches thousands of nurses and other health professionals, including physicians, and is a major educational source for high standards in critical care.

Critical care medicine was at one time focused on the heart and the lungs. The once secure belief, however, that the

problems experienced by the patient of an organ specialist would remain conveniently limited to that organ was shaken by the growing realization that multiple organ failure frequently followed critical illness. A multi-institutional study organized by the Division of Lung Diseases of the National Institutes of Health<sup>11</sup> to study extracorporeal membrane oxygenation for acute respiratory failure found that two-thirds of the 490 patients studied had failure of other organ systems besides the lung. Mortality rates were 40% when only the lung was involved; however, rates rose to 85% in the 162 patients with renal failure, to 79% in the 143 patients with central nervous system involvement, and to 77% in the 116 patients with sepsis. The number of additional organs involved, not the nature of the organ system itself, appeared to determine mortality, so that involvement of one additional organ led to 55% mortality, three additional to 85%, and four additional to 100%. Had traditional deployment of medical specialists been followed, many patients would have required at least five subspecialists in addition to their primary physician.

A group of subsequent studies, most of them in the surgical literature, emphasized the need for comprehensively trained generalists ("intensivists") able to deal with the simultaneous or sequential malfunction of multiple organ systems. It was soon recognized that a rising creatinine, bilirubin, or fibrin split products in apparently stable patients might herald disaster even though they were frequently ignored. While precise knowledge of etiology permitted early application of corrective action, an expanding experience suggested that analysis of physiologic abnormalities provided a parallel and sometimes more predictive indicator of ultimate outcome. Cumulative scoring of physiologic abnormalities in the first few hours of care generated a predictive index that could be used to determine optimal treatment and allocation of scarce resources. 12

The long-held clinical belief that a relatively stable "golden" period is often interposed between the inciting event and subsequent deterioration probably began with the important work of Wiggers et al.<sup>3</sup> The importance of early intervention has been buttressed by the gradual understanding that a group of primary etiologic factors seem to produce diffuse vascular injury with sluggish regional blood flow and leakage of plasma contents into interstitial spaces. 13 Animal models of all sorts suggest that early treatment may prevent multiple organ failure and may help expand the concept of critical care medicine to include on-site stabilization. safe transport to a hospital, and immediate care in emergency room and intensive care units.

Early recognition of life-threatening illness has become a major challenge for the medical community. At the moment, the advance of technology appears to have outdistanced the available human resources; better ways must be found for the recruitment, training, and organization of the people necessary to master this new technology. Medical care is traditionally delivered by office-based, primary care physicians or organ-focused specialists who spend a relatively small portion of their time in the hospital. While organ-oriented medical or surgical specialists perform superbly in situations involving their own areas of expertise, bedside care frequently becomes suboptimal when an unmanageable group of consultants attempt to forge a cohesive plan of action. Training and continued experience in the comprehensive care of critically ill patients, with emphasis on total function rather than a more parochial concern for organ protectionism, are essential.

The American Board of Medical Specialties recently attempted to define the boundaries of critical care medicine by

examination and prescribed training. In 1980, the American Boards of Internal Medicine, Anesthesiology, Surgery, and Pediatrics joined together to offer a certificate of special competence in critical care medicine. Of novel design, an identical examination was proposed for all applicants-internists, surgeons, anesthesiologists, and pediatricians. The vision of the 26 founders of the Society of Critical Care Medicine seemed imminent. However, after several years of discussion, the Joint committee for Critical Care Medicine (JCCCM) fell apart. The proximate cause of dissolution was disagreement over training standards, but more important concerns actually undergirded the ultimate decision. The concept of critical care had simply become too important and too vital to allow transfer to a new, transdisciplinary, certifying authority. Within months after conversations ended, the American Boards of Anesthesiology and Internal Medicine announced their own plans for independent examination and certification. The anesthesiologists and surgeons gave their first examination in 1986, and the internists gave theirs in the fall of 1987. Critical care had entered the mainstream of American medicine.

A systematic assessment of the role of critical care medicine was undertaken by the Office of Medical Applications of Research (OMAR) of the National Institutes of Health. A Consensus Development Conference was held in Washington. D.C. in March 1983; the official Consensus Development Report was written by a panel that included biomedical investigators, critical care physicians, other medical specialists, nurses, a biostatistician, and a jurist. The panel report was published widely, and the entire proceedings were later presented in book form.14 The panel concluded that modern therapeutic interventions benefit many patients admitted to critical care units but

that the evidence of benefit was equivocal in another larger group of patients. The weight of clinical opinion supported the belief that intensive care was useful for this larger population, but the risk of iatrogenic illnesses and complications could outweigh any potential benefit. Many patients, the report emphasized, were admitted to intensive care units because they were at risk of becoming critically ill. In these patients, mortality might well be decreased if the likelihood of critical illness was strong and the benefits of treatment substantial. The panel emphasized that limited resources should not be devoted to patients "without reasonable prospects of significant recovery when patients who need those services, and who have significant prospect of recovery from acutely life-threatening disease or injury, are being turned away due to lack of capacity."

The Consensus Development Conference identified a number of perplexing systems problems that demand early solutions. Highly trained experts in critical care are of little use to the critically ill patient unless these people are available almost immediately. The staffing of emergency rooms and critical care units in the thousands of small hospitals that provide first-contact care in the United States is of great concern. At the very least, a physician with broad training, that is, who is able to intubate and initiate vascular monitoring, should be on the premises in any hospital receiving ambulance patients.

The sociopolitical uncertainties that have hindered the optimal organization of human resources for the care of the critically ill have also had an impact on other aspects of the health care system. Philosophers, politicians, ethicists, and other designers of public policy have had great difficulty deciding whether health care is a right or a luxury. Many shrink from orderly consideration of the alloca-

tion of scarce and expensive resources, but certain vexing questions must be faced.

The quality of critical care becomes an important issue. Recently published studies have emphasized the complications and errors of medical practice. Knaus. Draper, and Wagner<sup>15</sup> have recently published an important study evaluating outcome following admission to critical care units in 14 American hospitals. The severity of illness has determined by their APACHE scoring system, and expected mortality was derived from the overall experience of the involved hospital centers. Several of the hospitals had mortality rates significantly lower than predicted, while others had mortality rates significantly greater than the other hospitals. The hospital with the best mortality rate was characterized by the use of standard protocols, the presence of a medical director with considerable authority. a high level of educational achievement for staff nurses, and a collegial relationship among physicians and nurses. Interestingly, in the hospital with the best mortality rate, nursing personnel rather than physicians made the decisions to cancel elective surgery when the unit became crowded.

Consider the following the questions: Should all individuals have access to highquality critical care medicine? How can seriously ill and sometimes unconscious patients reach appropriately staffed units within minutes of the onset of illness? How can those patients who appear too sick to benefit from treatment in a fullservice intensive care unit receive sensitive and appropriate care in alternate settings? How can family members of a critically ill individual learn more about serious illness, prognosis, cost, and subsequent rehabilitative care. The Foundation for Critical Care was recently founded to explore these complex social issues. Members of the foundation board include representatives from the Society of Critical

Care Medicine and the American Association for Critical Care Nurses, as well as public-minded citizens without health care backgrounds.

This text deals with the science and art of critical care. Reliance on hightechnology life-support systems should soon be replaced by techniques that can prevent or lessen the impact of serious illness at an early stage. The promise of cell and molecular biological research, demonstrated perhaps best in the eradication of poliomyelitis, may soon prevent the vascular damage that is a common pathogenic pathway for most serious illness. The fruits of molecular biology have rapidly influenced almost every area of medical science. Prestitious journals regularly publish important studies on the nature of critical illness, studies that were impossible even to contemplate when experimental design was limited to physiologic study. The endothelial cell and the capillary-interstitial interface have moved to center stage. Endothelial cells secrete proteins such as (1) the von Willebrand factor, which promotes platelet adhesion and aggregation. (2) prostacyclin, and (3) protein S and thrombomodulin, which amplify the anticoagulant activity of protein C. These cells also secrete both plasminogen activators and activator inhibitors. Ribes, Francis, and Wagner<sup>16</sup> recently demonstrated that the fibrin produced by vascular injury modulated endothelial cell behavior and promoted the release of the von Willebrand factor. This amplification of the coagulation cascade-platelet-endothelial cell interaction takes on special importance since thrombin increase lung vascular permeability. Another newly explored group of molecules-the reactive oxygen species, or free radicals-appears to mediate granulocyte-dependent, thrombin-induced lung injury. Johnson et al. 17 have shown that the protective enzyme. superoxide dysmutase, reduces the permeability response to thrombin. The endothelium is normally thrombo-resistant, but in certain pathologic states, such as gramnegative sepsis, the balance may shift to thrombosis. Moore et al., <sup>18</sup> for example, have demonstrated that sepsis stimulates a tissue factor that profoundly decreases the thrombomodulin activity on endothelial cell surfaces, promoting coagulation.

The evolution of new methods permitting the scientist to examine the inner workings of the cell itself has led to the discovery of a specific macrophage product that appears to have a powerful tumor necrosis effect. This substance, which is called tumor necrosis factor or cachectin, has been analyzed and found to be a peptide that normally exists as an innocuous prohormone until it is activated. The activation process appears closely controlled so that inadvertent release is minimized. Beutler and Cerami<sup>19</sup> recently reviewed the properties of this cell destroyer and concluded that

Thus it would seem possible that neutralizing monoclonal antibodies directed against human cachectin may prove useful in the treatment of sepsis, particularly in its early stages. It remains to be seen whether such antibodies (or other cachectin antagonists) will also prove useful in the treatment of other pathologic states in which inflammation has a role. However, it is anticipated that specific neutralization of cachectin and of related cytokines may offer new therapeutic directives with which to treat a broad spectrum of diseases.

None of these studies could have been performed until quite recently. While it is likely that continued study of the cell and its organelles will provide the intensivist with agents that will dramatically interrupt the pathogenetic cascade leading to multiple organ failure, problems of access and skilled care will remain. The immunization against poliomyelitis led to the virtual disappearance of that disease

from the United States, but reduction in mortality from critical illness will require the skillful application of precise pharmacological remedies by skilled health care professionals.

The acquired immune deficiency syndrome (AIDS) has replaced poliomyelitis as a paradigm for critical care medicine. Admissions for AIDS and its associated infections have increased geometrically, and it is likely that there will be 150,000 patients per year admitted with Pneumocystis carinii pneumonia by 1990.20 The use of scarce and expensive resources for patients with fatal illnesses will come under increased national scrutiny. Already, for example, physicians in areas of high prevalence have decided not to admit seriously ill patients with Pneumocystic pneumonia to intensive care units. The number of admissions to the ICU at San Francisco General Hospital<sup>21</sup> actually decreased from 17 during the second quarter of 1984 to 5 per quarter in 1985, even though hospital admissions for that condition were increasing. The need for better understanding of cell function, the development of vaccines, attempts to augment natural immunity, an understanding of a group of infectious agents once considered rare, the allocation of scare resources, and the possibility of recommending the termination of life support systems in relatively young individuals are important issues that place AIDS in the center of any discussion of critical illness. As iron lungs and then vaccines conquered poliomyelitis, so must highly organized critical care and modern cell biology learn to control the consequences of infection with the human immunodeficiency virus (HIV) and any of the newer infectious agents certain to follow.

It is probably fortunate that HIV did not emerge from its murky cradle any sooner. Biomedical science and health care professionals are almost ready for the challenge. Organized hospital care is an important part of the solution to this and other human maladies that will almost certainly follow the containment of AIDS. Comprehensive critical care is an idea that was born in the high technology that emerged following World War II. Its maturation reflects the important shifts from medical art to medical science that have marked the latter part of this century. It represents the concentration of sustaining resources gathered together where they can be most useful, and it is a concept rather than a specialty. Many can understand the value of early and rapid correction of disordered physiology; only those with training, continuing experience, and availability should attempt to practice those concepts at the bedside.

### REFERENCES

- 1. Ibsen B: The anesthetist's viewpoint on treatment of respiratory complications in poliomyelitis during the epidemic in Copenhagen, 1954. *Proc R Soc Med* 1954; 47:72–74.
- 2. Drinker P, McKhann CF: The use of a new apparatus for the prolonged administration of artificial respiration. I. A fatal case of poliomyelitis. *JAMA* 1929; 92:1658. Reprinted *JAMA* 1986; 255:1473.
- 3. Wiggers CA: Physiology of Shock. New York, The Commonwealth Fund, 1950.
- 4. Cournand A, Riley RL, Bradley SE, et al: Studies of the circulation in clinical shock. Surgery 1943; 13:964-995.
- 5. Safar P, De Kornfeld T, Pearson J, et al: Intensive care unit. *Anaesthesia* 1961; 16:275–284.
- 6. Day HW: An intensive coronary care area. Dis Chest 1963; 44:423.
- 7. Mueller H, Ayres SM, Gregory JJ, et al: Hemodynamics, coronary blood flow, and myocardial metabolism in coronary shock. J Clin Invest 1970; 49:1885.
- 8. Ayres SM, Giannelli S Jr, Mueller HS. Care of the Critically Ill, ed 1. New York, Appleton-Century-Crofts, 1967.

- 9. Weil MH: A new look at the critically ill. Hosp Pract 1967; 2:27-37.
- 10. Safar P: Reanimatology—the science of resuscitation. Crit Care Med 1982; 10:134-136.
- 11. Extracorporeal Support for Respiratory Insufficiency. A Collaborative Study in Response to RFP-NHLI-7320. National Heart, Lung and Blood Institute, 1979.
- 12. Knaus WA, Zimmerman JE, Wagner DP, et al: APACHE: acute physiology and chronic health evaluation: a physiologically based classification system. *Crit Care Med* 1981; 9:591.
- 13. Shasby DM, Shasby SS, Peach MJ: Granulocytes and phorbol myristate acetate increase permeability to albumin of cultured endothelial monolayers and isolated perfused lungs. *Am Rev Resp Dis* 1984; 127:72.
- 14. Parrillo JE, Ayres SM (eds): Major issues in Critical Care Medicine Consensus Conference. Baltimore, Williams & Wilkins Co, 1984.
- 15. Knaus WA, Draper EA, Wagner DP: An evaluation of outcome from intensive care in major medical centers. *Ann Intern Med* 1986; 104:410.

- 16. Ribes JA, Francis CW, Wagner DD: Fibrin induces release of von Willebrand factor from endothelial cells. *J Clin Invest* 1987; 79:117–123.
- 17. Johnson A, Perlman MB, Blumenstock FA, et al: Superoxide dismutase prevents the thrombin-induced increase in lung vascular permeability: role of superoxide in mediating the alterations in lung fluid balance. *Circ Res* 1986; 59:404.
- 18. Moore KL, Andreoli SP, Esmon NL, et al: Endotoxin enhances tissue factor and suppresses thrombomodulin expression of human vascular endothelium in vitro. *J Clin Invest* 1987; 79:124–130.
- 19. Beutler B, Cerami A: Cachectin: More than a tumor necrosis factor. N Engl J Med 1987; 316:379.
- 20. Centers for Disease Control Update: Acquired Immunodeficiency Syndrome—United States. MMWR 1986; 35:757.
- 21. Wachter RM, Luce JM, Turner J, et al: Intensive care of patients with the acquired immunodeficiency syndrome, outcome and changing patterns of utilization. *Am Rev Resp Dis* 1986; 134:891–896.