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Nutritional Support of the Critically Ill

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To the men and women who have devoted their careers to the care of critically ill patients

Foreword

Dr. Schlichtig and Dr. Ayres have written an excellent book on the nutritional support of critically ill patients. Oftentimes, a book or review on the nutritional aspects of patient care emerges that, although important, usually is quite sterile and presents a series of poorly integrated topics. To wit, reading such a book is a necessity and not a pleasure. After reviewing the contents of this book, I find that it can be read by choice and not by necessity. Even with my bias, I enjoyed reading it because of the coverage of the literature, the contradictory nature of some findings, and the clear summary or ''take-home'' message (so aptly coined by our recent chief surgical resident) all of which are presented in an easy-to-read style of writing.

I shall not comment on the content in detail, but I will note that the book reviews the metabolic sequelae important in understanding the use of current modalities of nutritional support in the critically ill patient. This in-depth discussion of metabolic changes and therapeutic use of various support systems will educate the clinician, allowing him or her to practice the science of nutrition and not simply prescribe what is presumed correct based on stored memory.

The authors have made recommendations for nutritional support based on their experiences and on the available evidence. They have accepted, as I have, that the current evidence is sufficiently compelling to strongly support the routine use of enteral and parenteral feeding in those patients with catabolic disease processes as soon as possible after admission. Such actions will improve the morbidity and/or mortality of the critically ill patient.

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Preface

Critically ill patients slip precariously close to the precipice of death because of damage to or dysfunction of one or another life-sustaining bodily function. Physicians and other health care providers have learned to artificially support many of these functions using mechanical ventilation, intra-aortic balloon counterpulsation, continuous hemofiltration, and a host of other mechanical and pharmacologic devices. These devices are intended to preserve patients' lives until such time that the damage or dysfunction is repaired. Included among the life-support technologies is hyperalimentation, the ability to infuse nutrients into the veins or into the gastrointestinal tract. Although the role of hyperalimentation as a life-support modality remains controversial in many instances, none can doubt that nutritional supplementation has saved the lives of those patients who have remained critically ill and unable to eat for months on end, but who have subsequently recovered to leave the hospital.

"Critical illness" obviously encompasses a large number of different disease states. However, critically ill patients are increasingly cared for by groups of physicians, nurses and other health care professionals whose activities are confined largely or exclusively to the intensive care unit. In addition to location within the hospital, many critically ill patients share similarities in intermediary metabolism and in the appropriate approach to nutritional management.

In this book, we attempt to integrate nutritional concepts with other physiologic concepts used by intensivists to understand and treat critical illness. Indeed, all organ systems are ultimately derived from ingested lipids, carbohydrates, electrolytes, trace elements, and vitamins, and each organ system involutes to a greater or lesser degree during acute illness when the patient is allowed to starve. Our goal is to summarize theoretical issues, and to make recommendations for treatment based both on our experience and on available evidence.

An important question — which we felt compelled to answer before proceeding with the main text — is whether or not stress-induced hypercatabolism significantly alters host defense, and whether hyperalimentation improves morbidity and/or mortality of critically ill patients. We address this issue in Chapter 1. Although literature is far from conclusive, current evidence is sufficiently compelling that we believe hyperalimentation should be routinely administered within several days of intensive care unit admission to those patients with catabolic disease processes.

Metabolism of protein, carbohydrate, lipid, and oxygen is often profoundly altered by many acute illnesses. Although all critical disease states are not identical, sufficient similarities exist to draw some generalizations. Critically ill patients consume considerably more of their endogenous protein than do healthy people, but lipid remains the primary fuel during fasting. In Chapters 2 and 3 we briefly review pathophysiology of disturbed intermediary metabolism and the influence of exogenous nutrients.

Nutritional assessment of critically ill patients differs considerably from that of patients who are less ill. The majority of parameters commonly used are unreliable in this population. Nutritional assessment of critically ill patients is addressed in Chapter 4.

"Autocannibalism" of critically ill patients is treated by infusing nutrient mixtures containing carbohydrates, protein, lipids, electrolytes, trace elements, and vitamins. Each of these nutrients influences the efficacy of the nutritional formula in a qualitatively and quantitatively different manner. The mechanism of action and dose required of each of these classes of nutrients is examined in Chapters 5 and 6.

Either the enteral or intravenous mode of nutrient infusion can be used for many patients. However, one or the other is usually preferable under

different circumstances. In Chapter 7 we explore differences in risk, metabolism, and nutrient balance that have been observed when these modes of delivery have been compared. In addition, we describe methods of implementation and management of complications.

Hyperalimentation often produces metabolic complications in critically ill patients because of disturbed intermediary metabolism. Management of these complications is addressed in Chapter 8. Nutritional approaches to patients with failure of various organ systems are outlined in Chapter 9.

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Stephen M. Ayres, M.D.

CONTENTS

CHAPTER 1

Nutritional Status, Nutritional Therapy, and Survival of Critical Illness

Most clinicians are well aware, both from personal observations and from published literature, that starved critically ill patients become rapidly malnourished. An almost unbelievably rapid erosion of endogenous protein is well documented (see p. 36). Consequently, many believe that untreated "hypercatabolism" independently increases morbidity and mortality because protein depletion weakens host defense. An increasing number are further convinced that modern nutritional therapy can prevent and even reverse the malnutrition and deterioration of these host defenses that would otherwise occur. They believe, therefore, that administration of appropriate quantities of fuel and protein increases the probability of survival.

We believe that these hypotheses are largely correct. However, they have not been rigorously proved. This is important because the risk-benefit ratio for nutritional support increases for the most unstable patients. Volume overload, hyperglycemia, electrolyte imbalance, diarrhea, and sepsis are all too familiar (Chapters 7 and 8). In addition, some evidence suggests that nutritional therapy may overburden oxygen transport and carbon dioxide elimination mechanisms of patients whose conditions are particularly marginal (Chapter 3).

Our goal in this chapter, therefore, is to determine whether nutritional therapy is, in fact, a life-support measure, and whether the proposed benefit justifies the risks. Data from a small number of investigations suggest that nutritional supplementation can alter morbidity and/or mortality of selected groups of patients. However, these data are limited. Therefore, we must approach the question indirectly. We begin in the following section by considering (1) host defenses required for survival of various critical illnesses, and (2) the strain routinely placed on them during a typical stay in the intensive care unit (ICU). These data support the hypothesis that intact host defense is required for the best chance of survival. In the next section, we examine (1) the effect of malnutrition on these host defenses and (2) evidence that supports or contradicts the hypothesis that nutritional therapy may prevent or reverse a deterioration in these host defenses. These data support the hypothesis that nutritional supplementation may, in some instances, improve probability of survival by preserving or enhancing important host defenses. In the last section, we briefly review the few investigations that have related the effect of nutritional support to outcome of several critical disease states.

We believe that current evidence, viewed as a whole, justifies the use of nutritional therapy as an adjunct to other life-support measures in many critically ill patients. However, more prospective, randomized studies are badly needed.

THE OPTIMAL STRESS RESPONSE: HOST DEFENSE OF THE WELL-NOURISHED

Insults sufficiently catastrophic to force a patient to the brink of death activate a multitude of host defenses. The vigor of these defensive reflexes, re-

gardless of the rapidity and appropriateness of medical intervention, is often the most important determinant of survival or length of ICU stay. In this section we review several vital host defenses and the stresses commonly placed on them during critical illness. If malnutrition significantly impairs any of these host defenses—assuming that they are stressed during the course of critical illness—then it very likely reduces probability of survival and/or lengthens ICU stay. If nutritional supplementation enhances any of these host defenses or prevents their deterioration, then it may reduce morbidity or mortality of patients for whom these host defenses are stressed.

The Myocardium

All living tissues require a continuous supply of oxygenated erythrocytes to maintain vital metabolic functions. For this reason, patients with severe cardiac failure rarely survive insults that significantly stress myocardial reserve. Many conditions stress myocardial reserve during a typical ICU stay. For example, increased myocardial work may be required when arterial oxygen content is reduced. If serum hemoglobin concentration of a patient with critically low oxygen transport falls by one half, he or she must increase cardiac output twofold to meet tissue demands. If the patient is unable to do so ischemia and damage in one or more peripheral vascular beds may develop.

Many critical illnesses impose sizable mechanical or metabolic workloads that also stress myocardial reserve. Failure of the cardiovascular system to support this increased work will also result in rapid demise. For example, Aubier et al. showed that the work of breathing may exhaust the systemic supply of oxygen during pulmonary edema when myocardial reserve is deficient. They injected sufficient saline into the pericardium of dogs to reduce cardiac output by 70%. Animals who were allowed to breathe spontaneously developed lactic acidosis and died much sooner than animals whose work of breathing was reduced by mechanical ventilation. Thus, these animals had sufficient myocardial function to support nonrespiratory muscle work, but died rapidly when forced to assume the additional work of inflating stiff, noncompliant lungs.[1] The defensive response to many human disease states demands an increased oxygen supply. For example, total body oxygen consumption may increase by as much as 50% above the resting value as a result of severe respiratory distress. Increased uptake of oxygen by the respiratory muscles effectively reduces the quantity of oxygen available

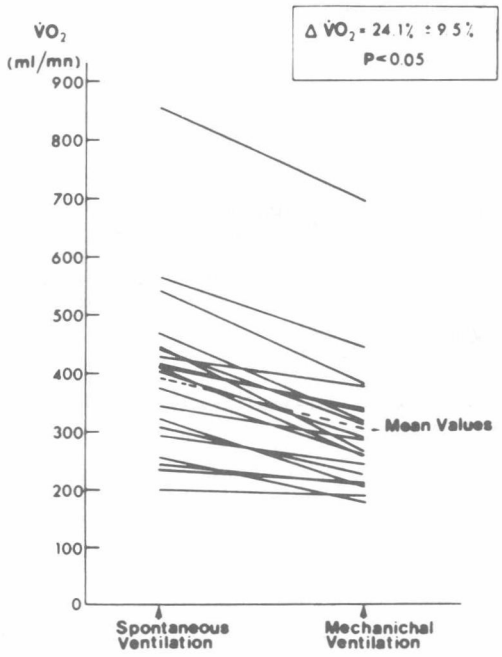

FIG 1–1.

Changes in oxygen consumption ($\dot{V}O_2$) observed when mechanically ventilated patients inspiring 21% oxygen were allowed to breathe spontaneously. These changes suggest increased demands on the respiratory musculature. (From Bursztein S, Taitelman U, DeMyttenaere S, et al: Reduced Oxygen consumption in catabolic states with mechanical ventilation. *Crit Care Med* 1978; 6:162–164. Used by permission.)

to other tissues by an identical amount unless the circulation can compensate[2, 3] (Fig 1–1). Similarly, oxygen consumption following a large body surface area burn may increase by as much as 200%. Patients who develop pathologically diminished peripheral vasomotor tone, particularly during profound sepsis, require the most extraordinary increase in cardiac performance (Fig 1–2). During "high-flow" phases of sepsis, myocardial stroke work approaches levels observed during maximal exercise.[4]

During any of the above conditions a cardiac output considerably higher than the normal resting 2.5 L/minute is clearly necessary to deliver the quantity of oxygen to the tissues required for survival. Myocardial "rest" is obviously not permissible during these periods of stress; the heart must sustain its high level of performance continuously, often for days or weeks. Failure to do so even transiently quickly results in anaerobic metabolism and end-organ damage.[5, 6]

Respiratory System

The respiratory system is solely responsible for disposing of the entire body's burden of carbon dioxide. During critical illness, respiratory muscle reserve is often heavily taxed. During pulmonary edema or severe bronchoconstriction, for example, respiratory muscles must generate markedly negative intrathoracic pressure to expand the lungs. Patients with elevated dead space–to–tidal volume ratios must move proportionately greater volumes of air in order to dispose of the CO_2 burden because of decreased alveolar ventilation (see p. 70). The respiratory burden is also greater when carbon dioxide generation by the tissues increases, either because of increased oxygen consumption or because of nutritional supplementation with carbohydrate (see p. 69). Finally, work of breathing increases during metabolic acidosis, as the patient attempts to compensate for reduced blood pH. During severe diabetic ketoacidosis, for example, pre-hospital survival depends on the patient's ability to increase minute ventilation sufficiently to maintain a viable pH. In each of these conditions, inadequate respiratory muscle strength or endurance results in life-threatening hypercarbic acidosis. Although mechanical ventilation may salvage patients with respiratory failure when provided in a timely manner, this intervention is costly, unpleasant, and associated with multiple complications and an increased probability of death.

Oxygen Extraction Mechanisms

A patient's ability to enhance extraction of oxygen from the arterial blood may allow him to survive periods when systemic oxygen transport is critically

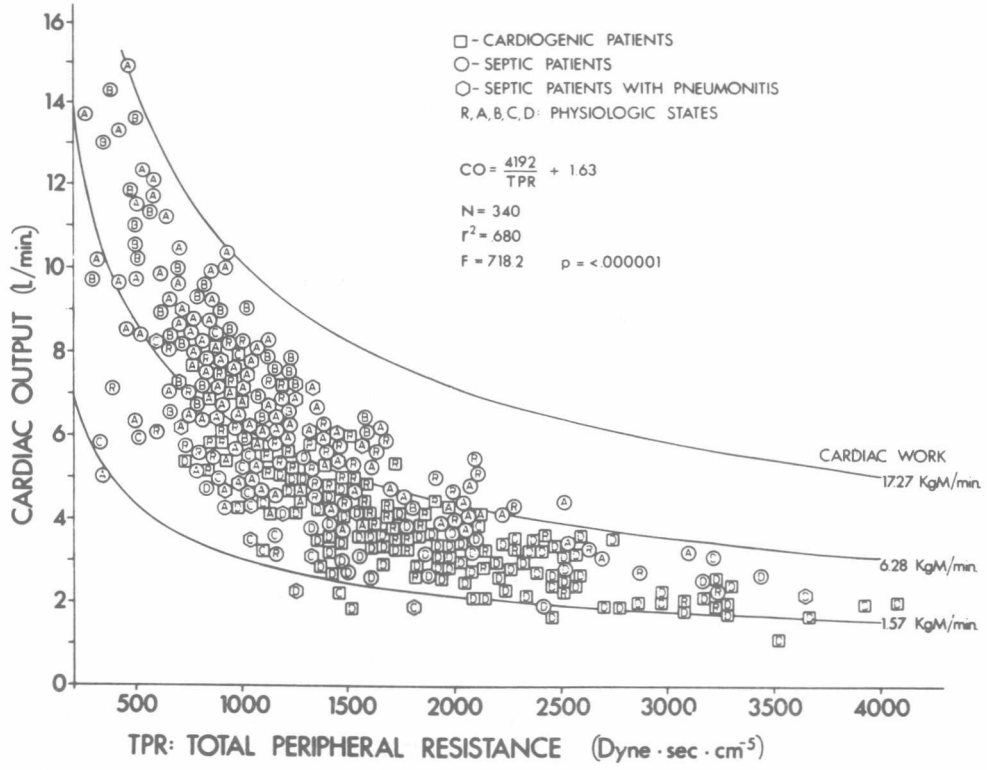

FIG 1–2.
Cardiac output plotted against total peripheral resistance in septic patients. Myocardial work is normally 6 (kg.m/minute) at rest. During sepsis, the heart often performs considerably more work. Patients in early to middle phases of septic decompensation perform primarily volume work due to peripheral vasomotor paralysis. Increased pressure work is characteristic of later stages, when total peripheral resistance rises. Myocardial work near 17 kg.m/minute similar to myocardial work during heavy exercise, was calculated for some of these patients. (From Siegel JH: Physiological and metabolic correlations in human sepsis. *Surgery* 1979; 86:163–193. Used by permission.)

reduced. Enhanced oxygen extracting ability therefore is often crucial for survival.[5, 6] Increased total body oxygen extraction occurs at two levels. During hypoxia, hypovolemia, left ventricular failure, or heavy exercise, blood flow diminishes to vascular beds that normally receive considerably more blood flow than they need to survive (skin, gastrointestinal tract, kidneys). This redistribution of flow occurs because of selective vasoconstriction and is mediated by sympathetic nervous system activity and angiotensin; these phenomena are manifested clinically as diminished urine output and/or skin pallor. In this manner the relatively scarce supply of oxygenated erythrocytes is diverted from relatively low-priority areas and is directed to the heart and central nervous system. Diminished blood flow to deprived organs does not necessarily cause damage, since they are capable of extracting more oxygen from the blood that reaches their capillaries. This increased oxygen extraction is accomplished at the cell-capillary interface, by relaxation of precapillary sphincters that thereby increase perfused capillary density. This process is facilitated by factors that minimize interstitial water at strategic sites.[7–9] Thus plasma oncotic pressure maintained by adequate levels of serum albumin and other proteins helps prevent peripheral and pulmonary interstitial flooding and thereby preserves oxygen diffusion in these areas. Tissue fibronectin, necessary for cellular adhesion, may also play a role. Circumstantial evidence suggests that deficiency may predispose to the capillary leak syndrome in the lung or other tissues.[10–14]

The Immune System

Sepsis complicates many critical illnesses and is often the immediate cause of death. Consequently, critically ill patients with intact immune function enjoy a distinct survival advantage (see p. 10). An optimal immune response depends on adequate function of several organ systems. An intact T-lymphocyte population is required to recognize infectious agents, generate lymphokines, and stimulate immunoglobulin synthesis by B lymphocytes.[15, 16] Rapid synthesis and release of granulocytes and macrophages from lymphopoietic organs is required for phagocytosis of bacteria and cellular debris. Adequate levels of fibronectin synthesized in the liver may be required for opsonization of gram-positive and possibly gram-negative organisms. Complement components, also synthesized in the liver, are required both for chemotaxis and for bacterial killing. Not surprisingly, intact delayed hypersensitivity, a reflection of a large number of immune components, is associated with low infection rates, whereas anergy correlates with high rates of septic morbidity and mortality in both the surgical and medical patient populations.[17–23]

Host-Defense Protein Synthesis

Rapid synthesis of host-defense protein is vital for survival of many insults. For example, patients with severe liver impairment frequently cannot synthesize coagulation factors fast enough to prevent exsanguination. Patients who have received chemotherapy are at very high risk for life-threatening sepsis until the pool of granulocytes is repleted. Traumatized patients who have exhausted their supplies of haptoglobin expose their kidneys to free hemoglobin and myoglobin and are at increased risk of acute renal failure.

Available evidence suggests that the body does indeed increase the rate of protein synthesis during acute, life-threatening insults. Total body protein synthetic rate has been reported to increase by 20% to 100% in humans during infection,[24–26] trauma,[27, 28] or burns.[26, 29] Although it is not clear whether this is a regional or total body phenomenon, it appears that a large proportion of new protein synthesized consists of acute phase reactants and other proteins required for defense and/or repair. Rosenblatt et al. found that protein synthesis was three times greater in liver biopsy specimens of septic patients than in uninfected controls, and suggested that increased visceral protein synthesis is a phenomenon of high biologic importance during infection.[30] This suspicion was further strengthened by Clowes et al., who found that protein synthesis was twice normal in incubated liver specimens of septic patients who subsequently survived, but only slightly higher than normal in septic patients who subsequently died.[31] They also found a correlation between hepatic protein synthesis and the rate of clearance of amino acids from the plasma, and between both of these parameters and survival.[31, 32] These findings suggest that both peripheral mobilization of amino acids and new protein synthesis may be important determinants of survival.

A number of other experts have also emphasized the crucial importance of increased hepatic secretory and other "stress protein" synthesis during critical illness.[33–37] Markedly increased "acute-phase reactant" production by the liver is common to such diverse and seemingly dissimilar illnesses as myocardial infarction,[38, 39] sepsis,[39, 40] or surgical trauma.[39] Included in these acute phase proteins are

fibrinogen, required for hemostasis; haptoglobin, required to detoxify hemoglobin; and alpha$_1$-antitrypsin, needed to inhibit proteases.[34] In addition to acute phase proteins, accelerated synthesis of other proteinaceous substances is required to supply protein lost in pulmonary, wound, and fistula secretions of many patients. Accelerated production of fibroblasts, granulocytes, lymphocytes, immunoglobulins, platelets, mucus, fibrous connective tissue, complement components, and a multitude of other proteinaceous substances is also necessary for survival. These substances are generally not stored by the body but rather must be synthesized immediately from endogenous protein, a process that exacts a heavy cost from protein stores as cardiac, diaphragmatic, other skeletal and possibly gastrointestinal (GI) smooth-muscle stores are sacrificed. Despite the harmful effect on muscular strength, this translocation of amino acids from existing protein to stress protein synthesis appears to be adaptive, allowing the injured patient to undergo partial metamorphosis in a desperate attempt to ward off noxious stimuli (see pp. 37–38).

Endogenous Amino Acid Release

In order to synthesize host-defense protein during starvation, protein from other organs must be released, preferably from the least essential source. While data are not conclusive, the primary source of endogenous amino acids appears to be skeletal muscle (see pp. 36–37). Thus, coincident with the increased "stress protein" synthesis discussed above is a massively increased outpouring of amino acids from skeletal muscle during trauma,[41] sepsis,[30, 41] acute GI tract bleeding with hepatic cirrhosis,[42] and other disease states. Associated with this rapid amino acid mobilization is loss of considerable quantities of urea in the urine, suggesting that much of the protein released from endogenous stores is utilized as fuel. Consequently, many have speculated that accelerated muscle proteolysis may be stimulated by an increased requirement of the body for glucose or for amino acid fuel. However, while total body protein catabolism increases 20% to 100% relative to normal, total body protein synthesis measured simultaneously has been nearly equal, suggesting that only a small proportion of liquified protein appears in the urine.[24, 25, 28, 29] Furthermore, infusion of glucose alone into stressed patients fails to reduce nitrogen loss significantly. Taken together, these findings suggest that a primary requirement of the body for amino acid fuel may not be the primary stimulus for release of amino acids from endogenous tissues (see pp. 36–42).

Viewed teleologically, recent evidence suggests that the stimulus for amino acid mobilization may instead arise from a "need" to synthesize new protein. Recently discovered macrophage-derived mediators including interleukin-1 and cachectin may be primarily responsible for stimulating skeletal muscle proteolysis. These substances also cause increased hepatic synthesis of acute phase reactants, fever, granulopoiesis, B-cell proliferation, and T-cell activation, and may thereby be responsible not only for endogenous proteolysis, but also for directing the catabolized amino acids toward vital areas of synthesis[35–36, 43–48] (Fig 1–3). Serum levels of "proteolysis-inducing factor" correlated strongly with hepatic protein synthetic rate, peripheral release of amino acids, and central clearance of amino acids in septic patients.[31, 49] Glucagon, cortisol, epinephrine, and, possibly, relative insulin levels may also be important in determining the rate of amino acid release from muscle (see pp. 38–40). Thus both stimulatory and permissive mechanisms may lead to release of amino acid substrate from endogenous stores for synthesis of the vast array of proteinaceous substances that are not ordinarily produced at high rates but that may be necessary for survival of stressful conditions.[30–32, 40, 42, 50]

Mobilization of Fuel Reserves

Survival of critical illness depends not only on synthesis of defensive proteins but also on the patient's ability to mobilize and burn sufficient quantities and species of fuel. Fuel availability should not be taken for granted; caloric substrate is equally as important as oxygen availability for oxidative phosphorylation and therefore may potentially be equally rate-limiting when deficient. During normal starvation, fuel derives primarily from adipose reserves that release free fatty acids under the influence of hormone-sensitive lipase. In addition, amino acids are released and serve as gluconeogenic precursors for supply of glucose-dependent organs. Both processes are facilitated by low circulating levels of insulin (see pp. 31 and 53).

During critical illnesses, maintenance of the fuel supply may require a more vigorous response than during unstressed states. Serum insulin levels of starved critically ill patients, unlike those of unstressed patients, are often normal or high, presumably as a consequence of elevated levels of serum glucose, glucagon, cortisol, epinephrine, and growth hormone. Consequently, lipid mobilization may require increased sympathetic nervous system activity,

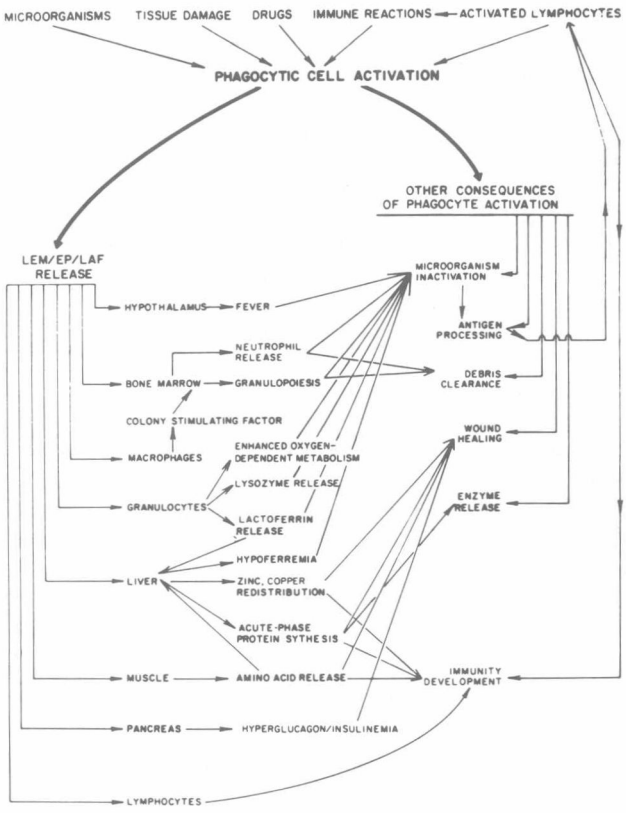

FIG 1–3.
Postulated scheme for activation of the stress response. Multiple stimuli may activate phagocytic cells to release lymphocyte endogenous mediator/endogenous pyrogen/lymphocyte-activating factor (LEM/EP/LAF), now referred to as interleukin-1. Included in the integrated response are fever, activation of stress protein synthesis, and muscular proteolysis. (From Powanda MC, Beisel WR: Hypothesis: Leukocyte endogenous mediator/endogenous pyrogen/lymphocyte-activating factor modulates the development of nonspecific and specific immunity and affects nutritional status. *Am J Clin Nutr* 1982; 35:762–767. Used by permission.)

since catecholamines are required to overcome the lipid-trapping effect of insulin on adipose tissue (see Fig 3–4). Tissues that are inadequately perfused may maintain a fraction of metabolism anaerobically if supplied with glucose; some believe that enhanced gluconeogenesis during critical illness may represent a response to tissue anaerobiasis.[51] Lactate and pyruvate are consequently released, to be resynthesized in the liver to complete the Cori cycle.[52–54] Amino acids and glycerol remnants of lipolysis are similarly cleared by hepatic parenchyma. These are burned directly or disposed of via gluconeogenic pathways. Glucagon levels rise, providing an adequate glucagon-to-insulin ratio for gluconeogenesis to ensure that these waste products are cleared.[4]

Summary

A myriad of reflex responses is activated by various critical illnesses, any one of which may be crucial for survival. Myocardial, respiratory, immune, oxygen extraction, and protein synthetic defenses may be stressed to the limit of endurance. In addition, critically ill patients must maintain fuel availability despite an adverse serum hormonal milieu. Intact host defenses are essential not only for recovery from the initial insult but also to defend against a continuous onslaught of iatrogenic insults that are necessary for life support. A consequence of a prolonged stress response is decimation of protein stores due to accelerated nitrogen loss. Whether malnutrition adversely affects any of these defenses, and whether nutritional supplementation may protect or repair these defenses are subjects that we will explore next.

MAXIMUM STRESS RESPONSE OF MALNOURISHED PATIENTS

In the previous section, we reviewed the role of several host defenses in determining survival of life-threatening insults. Significant impairment of any of these defenses—when they are acutely challenged—should prolong ICU stay and/or reduce probability of survival. In the present section we attempt to determine whether malnutrition impairs these host defenses to a degree that is clinically relevant, and

whether nutritional supplementation may prevent or reverse defective host defense.

Cardiovascular System

Since the heart beats continuously, we might expect it to maintain its cellular mass during progressive emaciation by virtue of continuous exercise. Surprisingly, available evidence indicates that the mass of the myocardium is not spared. Radiographic[67] and postmortem[68–70] examinations of malnourished individuals have consistently demonstrated reductions in cardiac size and mass. Echocardiographic measurements of left ventricular wall thickness and left ventricular mass are reduced, although the rate of loss of myocardial mass is only half the rate of reduction of total body weight.[71, 72] At the microscopic level, markedly diminished size of myocardial fibers with fragmentation of myofibrils,[73] myocardial edema, patchy necrosis, and round cell infiltration[68, 74] have been observed in severely malnourished individuals. Cardiac arrhythmias are often the terminal event of prolonged ''dieting'' despite normal electrolyte patterns.[68, 73, 75] Sudden death is not uncommon in extremely malnourished patients suffering from anorexia nervosa and may be related to QT prolongation or focal inflammation of the cardiac conduction system.[75] Diminished myocardial mass also occurs as a result of malnutrition during acute catabolic states; individuals who died after one to several weeks of hospitalization and whose average weight was 30% less than ideal were found to have myocardial weight that was significantly (13%) less than that of a similar group of individuals with normal body weight.[69]

The implications of diminished myocardial mass for myocardial function are difficult to interpret. Myocardial function of severely malnourished women with anorexia nervosa has been assessed at rest by echocardiography. Ejection fraction, ventricular circumferential fiber shortening, percent thickening of the posterior left ventricular wall, and left ventricular posterior wall excursion were normal in these patients with 25% or greater weight loss.[72, 73] Anorectic patients generally go about activities of daily living without apparent difficulty. However, these observations may not be relevant to the question of maximum cardiac performance, which may be required to deal with stress. It is important to recognize that starvation is associated with reduced left ventricular afterload due to diminished blood pressure, heart rate, and systemic vascular resistance. Therefore, assessment of myocardial function of malnourished individuals at rest may obscure abnormalities that may occur when myocardial reserve is taxed.

An important question for the malnourished critically ill patient is whether cardiac output may increase sufficiently to survive conditions that demand increased systemic oxygen transport. Several groups of investigators have employed animal models to study this question. In 1979, Abel et al. reported a study of myocardial performance in malnourished dogs. They fed a hypocaloric, hyponitrogenous diet to 11 dogs until 42% of body weight had been lost. Following this period, left ventricular (LV) compliance, contractility, and peak pressure were studied in an isovolumic left-sided heart preparation at multiple levels of preload in control and malnourished animals. The most striking change observed was impaired ventricular compliance. Peak LV pressure and dp/dt were also diminished but were not significantly different from control animals; however, these investigators thought that the methodology used may have obscured real differences.[74] Freund and Holroyde subsequently studied developed force (F) and velocity of the developed force (dF/dt) of malnourished isolated rat hearts with a strain gauge; significant differences in systolic and diastolic performance were noted. These differences were greater at 60 minutes than at the beginning of the experiment.[76] Finally, Alden et al. found reduced myocardial contractility in an intact chronic canine model using pressure and ultrasonic dimension transducers; contractility did not improve with beta-agonists.[77] These investigators have studied animals who are extremely emaciated, and have found significant, but not striking, reduction in myocardial function. Relevance of these findings to critically ill patients is not clear.

Human data are sparse, but suggest that maximum myocardial performance of malnourished hearts may be limited. During early refeeding of severely malnourished individuals, pulmonary edema has been reported, suggesting that myocardial reserve is reduced. However, it is not clear whether the pulmonary edema reported represents a nutritional myocardial defect, volume overload, or transient abnormalities of sodium-potassium ATPase activity (see Chapter 8). In the late 1940s, Keyes et al. studied maximal exercise tolerance in conscientious objectors who voluntarily submitted to a diet that caused a 25% decrease in body weight; although maximal exercise tolerance diminished markedly, the extent to which myocardial (as opposed to skeletal muscle) performance was a limiting factor was not clear.[78] Recently, Marcotte et al. measured maximum work capacity, cardiac output, and stroke volume in 22 adults with cystic fibrosis who had varying nutritional status.