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Paul E. Wischmeyer

The Future of Critical Care Nutrition Therapy **433**

Paul E. Wischmeyer and Daren K. Heyland

At present, we are in a “revival” period in clinical nutrition in critical care, especially in the area of “pharmaco-nutrition.” Adequate nutrition may hinge not only on how many calories are provided but also on the ability to provide key pharmacologically acting nutrients. Traditionally, nutrition has been viewed as vital for metabolism, growth, and repair. But, it is now known that some nutrients, when given in therapeutic doses, appear to serve as pharmacologic agents to improve clinically relevant outcomes. Thus, larger therapeutic doses of specific nutrients may be required to replace acute deficiencies brought on by specific injury or disease states. Recent data also imply that the number of calories and protein delivered early in the intensive care unit (ICU) stay has a significant effect on outcome in at-risk patients. It is thought that the future of ICU nutrition will involve administering early nutrition preferentially via the enteral route. Supplementation by parenteral route may be used in at-risk patients when adequate enteral calories cannot be provided. Specific pharmaco-nutrients can also be administered as separate components, much like a drug is given. Large multicenter trials are planned or are underway to test these hypotheses. The use of basic clinical pharmacology, molecular biology, and clinical research principles in the study of nutritional therapy will lead to answers on how to administer the right nutrients, in the right amounts, at the right time to critically ill patients.

The Evolutionary Role of Nutrition and Metabolic Support in Critical Illness **443**

Nicolas Mongardon and Mervyn Singer

Maintenance of nutritional status is particularly challenging during critical illness. There is a common perception of a race against the clock to adequately feed the patient to prevent or minimize the sometimes catastrophic muscle wasting and general catabolic state that can result in the patient’s deterioration. However, the course of critical illness may be separated into 3 phases, each with highly differing metabolic needs. The initial phase, in which the body attempts to fight the acute insult, is generally hypermetabolic. When the body fails to overcome the insult, it enters into a second phase, which is akin to hibernation. This stage is characterized by a functional metabolic shutdown triggered either by a lack of adequate energy supply or perhaps by the direct switching off of metabolism to spare excess use of a dwindling substrate and energy resource. Those strong enough to survive this phase enter into a period of recovery during which appetite returns, anabolism recommences, and organ function is restored. Nutrition should perhaps closely follow these nonlinear requirements, so as to avoid deleterious under- or overnutrition during the appropriate phase. This approach fits a teleologic argument that enabled many sick

people to survive well before the advent of modern medicine and explains why catabolism still occurs despite adequate feeding.

Clinical Guidelines and Nutrition Therapy: Better Understanding and Greater Application to Patient Care

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Stephen A. McClave and Ryan T. Hurt

The volume of clinical guidelines produced by national and international societies has virtually exploded in the literature over the past decade. The most important aspect of guidelines is transparency, that is, the connection between the recommendation or guideline statement and the underlying supportive studies from the literature should be transparent. Clinical guidelines should help organize the literature, identify key areas of patient management, and provide a framework with which the clinician may operate. The reader of a guideline should embrace controversy, trace back and review the underlying literature, and then determine whether practice should be altered as a result of the guideline recommendations. The purpose of this article is to understand the derivation of clinical guidelines, to learn how to resolve controversy or differences between guidelines and clinical practice, and to learn steps to apply the guidelines to an individual institution or clinical practice.

Parenteral Nutrition in Critical Illness: Can it Safely Improve Outcomes?

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Ronan Thibault and Claude Pichard

Total parenteral nutrition was developed in the 1960s and has since been implemented commonly in the intensive care unit (ICU). Studies published in the 1980s and early 1990s indicate that the use of total parenteral nutrition is associated with increased mortality and infectious morbidity. These detrimental effects were related to hyperglycemia and overnutrition at a period when parenteral nutrition was not administered according to the all-in-one principle. Because of its beneficial effects on the gastrointestinal tract, enteral nutrition alone replaced parenteral nutrition as the gold standard of nutritional care in the ICU in the 1980s. However, enteral nutrition alone is frequently associated with insufficient coverage of the energy requirements, and subsequent protein–energy deficit is correlated with a worse clinical outcome. Recent evidence suggests that all-in-one parenteral nutrition has no significant effect on mortality and infectious morbidity in patients in the ICU if a glycemic control is obtained and hyperalimentation avoided. Thus, the time has come to reconsider the use of parenteral nutrition in the ICU. Supplemental parenteral nutrition could prevent onset of nutritional deficiencies when enteral nutrition is insufficient in meeting energy requirements. Clinical studies are warranted to show that the combination of parenteral and enteral nutrition could improve the clinical outcome of patients in the ICU.

Gastric Residual Volumes in Critical Illness: What Do They Really Mean?

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Ryan T. Hurt and Stephen A. McClave

The practice of measuring gastric residual volumes (GRVs) has become a routine part of enteral feeding protocols in the critical care setting. However, little scientific evidence indicates that their use improves patient outcomes. The use of GRVs is more of a tradition, which unfortunately guides

the delivery of enteral nutrition (EN). The practice of GRVs is predicated on several flawed assumptions. Using GRVs in hospitalized patients assumes that the practice is well standardized, that GRVs reliably and accurately measure gastric contents, and that they sufficiently distinguish normal from abnormal emptying. The practice also assumes that GRVs are easy to interpret, that a tight correlation exists between GRVs and aspiration, and that continuing EN after a high value for GRV is obtained leads to pneumonia and adverse patient outcomes. And finally, clinicians assume that GRVs are an inexpensive “poor man’s test” for determining tolerance of EN. This article reviews studies showing the fallacies of these assumptions. Although clinicians are unlikely to stop using GRVs, interpretation of these must be modified so as not to interrupt the delivery of EN. Using a protocol that directs appropriate responses to elevated GRVs should promote the delivery of EN and improve patient outcome.

Immunosuppression and Infection After Major Surgery: A Nutritional Deficiency 491

Xinmei Zhu, Gabriel Herrera, and Juan B. Ochoa

T cell dysfunction significantly increases susceptibility to infections and organ failure after trauma or surgery (physical injury). This coincides with a persistent drop in arginine availability, a necessary amino acid for normal T cell function. Recent data led to the identification of a novel mechanism of T cell suppression caused by the depletion of arginine through the induction of arginase 1 (ARG1) in a specialized group of immature myeloid cells, now named myeloid-derived suppressor cells (MDSC). In addition to T cell dysfunction, arginine depletion leads to the decrease in nitric oxide (NO) production. Dietary therapy containing arginine at supraphysiologic concentrations along with other components such as omega-3 fat acids, antioxidants, nucleotides, and vitamin A is associated with improvement in T cell function, NO production, and a significant decrease in infection rates. The authors propose that a pathologic decrease in arginine availability is an identifiable nutrition deficiency syndrome that worsens outcomes if left untreated.

Fish Oil in Critical Illness: Mechanisms and Clinical Applications 501

Renee D. Stapleton, Julie M. Martin, and Konstantin Mayer

Fish oil is rich in omega-3 fatty acids, which have been shown to be beneficial in multiple disease states that involve an inflammatory process. It is now hypothesized that omega-3 fatty acids may decrease the inflammatory response and be beneficial in critical illness. After a review of the mechanisms of omega-3 fatty acids in inflammation, research using enteral nutrition formulas and parenteral nutrition lipid emulsions fortified with fish oil were examined. The results of this research to date are inconclusive for both enteral and parenteral omega-3 fatty acid administration. More research is required before definitive recommendations can be made on fish oil supplementation in critical illness.

Glutamine in Critical Illness: The Time Has Come, The Time Is Now 515

Lindsay-Rae B. Weitzel and Paul E. Wischmeyer

Glutamine (GLN) has been shown to be a key pharmacnutrient in the body’s response to stress and injury. It exerts its protective effects via

multiple mechanisms, including direct protection of cells and tissue from injury, attenuation inflammation, and preservation of metabolic function. Data support GLN as an ideal pharmacologic intervention to prevent or treat multiple organ dysfunction syndrome after sepsis or other injuries in the intensive care unit population. A large and growing body of clinical data shows that in well-defined critically ill patient groups GLN can be a life-saving intervention.

Enhanced Recovery After Surgery: The Future of Improving Surgical Care

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Krishna K. Varadhan, Dileep N. Lobo, and Olle Ljungqvist

Enhanced recovery after surgery (ERAS) is a multimodal perioperative care pathway designed to attenuate the stress response during the patients' journey through a surgical procedure to facilitate the maintenance of pre-operative bodily compositions and organ function and in doing so achieve early recovery. The key factors that keep patients in hospital after uncomplicated major abdominal surgery include the need for parenteral analgesia, intravenous fluids secondary to persistent gut dysfunction, and bed rest caused by lack of mobility. The elements of the ERAS pathways are aimed to address these issues and the interventions that facilitate early recovery cover all three phases of the perioperative period during the patients' journey. They also provide clear guidance to all members of the clinical team.

Can We Protect the Gut in Critical Illness? The Role of Growth Factors and Other Novel Approaches

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Jessica A. Dominguez and Craig M. Coopersmith

The intestine plays a central role in the pathophysiology of critical illness and is frequently called the "motor" of the systemic inflammatory response. Perturbations to the intestinal barrier can lead to distant organ damage and multiple organ failure. Therefore, identifying ways to preserve intestinal integrity may be of paramount importance. Growth factors and other peptides have emerged as potential tools for modulation of intestinal inflammation and repair due to their roles in cellular proliferation, differentiation, migration, and survival. This review examines the involvement of growth factors and other peptides in intestinal epithelial repair during critical illness and their potential use as therapeutic targets.

Mitochondrial Dysfunction and Resuscitation in Sepsis

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Albert J. Ruggieri, Richard J. Levy, and Clifford S. Deutschman

Sepsis is among the most common causes of death in patients in intensive care units in North America and Europe. In the United States, it accounts for upwards of 250,000 deaths each year. Investigations into the pathobiology of sepsis have most recently focused on common cellular and sub-cellular processes. One possibility would be a defect in the production of energy, which translates to an abnormality in the production of adenosine

triphosphate and therefore in the function of mitochondria. This article presents a clear role for mitochondrial dysfunction in the pathogenesis and pathophysiology of sepsis. What is less clear is the teleology underlying this response. Prolonged mitochondrial dysfunction and impaired biogenesis clearly are detrimental. However, early inhibition of mitochondrial function may be adaptive.