CONGRESS REVIEW

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- Practice Applications
- Quality Improvement
- Multiprofessionalism

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This continuing medical education offering is intended to meet the needs of all physicians, nurses, pharmacists, respiratory therapists and other providers who care for critically ill patients.

Physicians

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Physicians should claim credit commensurate with the extent of their participation in the activity.

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For questions, please contact SCCM at congress@sccm.org or call +1 847-827-6888

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Faculty have reported the following disclosures. A copy of SCCM's policy on resolving conflicts of interest can be found online at: www.sccm.org/2010ConRev

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EVIDENCE-BASED NUTRITIONAL GUIDELINES IN 2010

Artificial nutrition support has come a long way since its introduction more than 50 years ago. Mounting evidence demonstrates that nutrition therapy impacts morbidity and mortality in the intensive care unit (ICU), underscoring the need for intensivists to institute changes in their practice and to implement guidelines.

The SCCM/A.S.P.E.N. Nutritional Guidelines: Examining the Evidence

Stephen A. McClave, MD

Representing a collaborative effort between the Society of Critical Care Medicine (SCCM) and the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.), guidelines for nutrition support in critically ill adults were published in May 2009 (Martindale RG, et al. *Crit Care Med*. 2009;37:1757). Development of this document was a five-year process involving about 50 expert reviewers and five rounds of review. The guidelines were targeted to adult critically ill medical and surgical patients with an expected ICU stay of at least two or three days.

"The guidelines are a basic list of recommendations and nothing more," stated Stephen A. McClave, MD, from the University of Louisville in Louisville, Kentucky, USA. "They are not absolute requirements. If your judgment at the bedside tells you one thing and the guidelines say something else, you are obligated to go with your clinical judgment. Nonetheless, some of these guidelines reflect the most rigorously defended and researched documents in the literature."

Although the guidelines committee focused on data from prospective randomized controlled trials (RCTs), they also considered national and international guidelines from other societies, expert opinion, and clinical practicality. In the absence of prospective RCTs, recommendations were based on expert opinion. When polarity existed among experts, the committee focused on providing total parenteral nutrition (TPN) recommendations that were most likely to result in outcome benefit.

One controversial area of the guidelines is the recommendation of permissive enteral nutrition (EN) underfeeding in obese ICU patients. "We recommended that these patients receive 60% to 70% of the caloric requirements of a target weight-based equation, along with significantly increased protein," said McClave. "However, around the time the guidelines were being published, review data emerged suggesting that obesity may be beneficial in ICU patients and that permissive underfeeding should not be practiced in this population." The data revealed that – although obesity in trauma/surgical and medical ICU patients was associated with increased infection, length of stay, organ failure, and mechanical ventilation duration – mortality results were mixed (Cave MC, et al. *Nutr Clin Pract*. 2008;23:16). Obese trauma/surgical ICU patients had a seven-fold increase in mortality, whereas obese medical ICU patients had reduced mortality. Another study found that mortality was reduced among ICU patients with a body mass index (BMI) of 35 or higher who had received an additional 1,000 calories (Alberda C, et al. *Intensive Care Med*. 2009;35:1728).

In addressing this matter, the committee considered the ways in which morbid obesity interferes with patient care, such as the need for special equipment, increased risks of pressure sores, atelectasis, pneumonia, and deep vein thrombosis as well as mechanical ventilation difficulties and challenges with diagnostic studies due to transport difficulty and inability to fit in imaging scanners. The committee also sought the opinion of an expert highly experienced in permissive underfeeding and obesity, who cited two physiologic studies supportive of permissive underfeeding (Elwyn DH. *Crit Care Med*. 1980;8:9; Hill GL, et al. *Br J Surg*. 1984;71:1). This research demonstrates that, if protein is increased to levels sufficient to stimulate protein synthesis to match degradation, the obese ICU patient can be fed 60% of required calories and maintain lean body mass while decreasing the fat mass (see Figure 1).

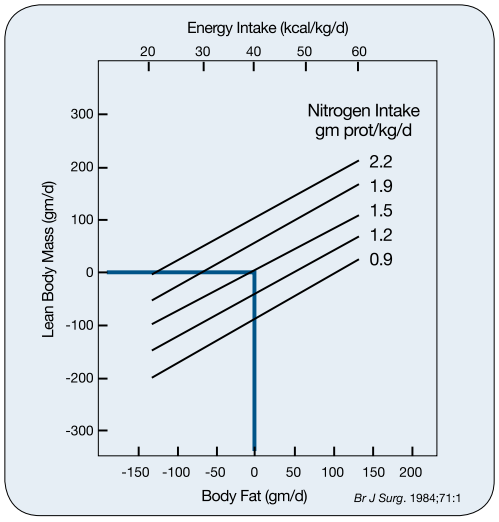

Figure 1. Effect of Low-Energy, High-Protein Intake on Fat and Lean Body Mass

Another debated recommendation pertains to tolerance of EN. The guidelines recommend that patients be monitored for tolerance and that clinicians: 1) avoid inappropriate cessation of EN; 2) avoid holding EN for gastric residual volumes (GRVs) of less than 500 mL in the absence of other signs of intolerance; and 3) minimize oral restrictive periods to promote EN delivery and avoid prolonged ileus. "Raising the GRV to the high level of 500 mL naturally prompted such questions as: Is 500 mL appropriate? What is the literature to support that? And do you agree with it as an individual practitioner?" noted McClave.

Clinicians may be concerned that raising the GRV to 500 mL in the critically ill patient increases the risk of aspiration pneumonia. "However, four prospective RCTs indicate that raising the GRV was associated with better, not worse, outcomes," stated McClave. In a British study, the incidence of complications significantly decreased when GRV was increased (Taylor SJ, et al. *Crit Care Med*.1999;27:2525). Two other studies revealed that the incidence of vomiting and overall intolerance remained the same when GRV was raised from 150 mL to 250 mL (Pinilla JC, et al. *JPEN J Parenter Enteral Nutr*. 2001;25:81) and from 200 mL to 400 mL (McClave SA, et al. *Crit Care Med*. 2005;33:320); no difference occurred in aspiration or regurgitation (McClave SA, et al. *Crit Care Med*. 2005;33:324). Supportive evidence also comes from a multicenter RCT in Spain, which reported a significant reduction in gastrointestinal complications with 500 mL GRV versus 200 mL GRV (Montejo, JC. Monitoring of gastric emptying. Presented at: The European Society of Intensive Care Medicine's 20th Annual Congress; October 2007; Berlin Germany).

"What would happen if we stopped measuring GRVs altogether? Would it be harmful? The answer is no," McClave said. A small nursing study showed no significant differences in incidence of aspirate pneumonia with routine GRVs compared with no GRVs, although tube clogging dramatically decreased (67% versus 8%) with no GRVs (Powell KS, et al. *JPEN J Parenter Enteral Nutr*. 1993;17:243). A more recent study found that intolerance improved, increased EN was delivered, and vomiting and pneumonia incidence rates remained the same when GRVs were stopped. (Poulard F, et al. *JPEN J Parenter Enteral Nutr*. 2010;34[2]:125). "It's ironic," McClave added. "Lowering the GRV to protect the patient may impede the delivery of enteral nutrition, and the risk of pneumonia might actually increase."

A third area of controversy in the guidelines relates to fish oil, specifically the recommendation that patients with acute respiratory distress syndrome (ARDS) or severe acute lung injury (ALI) receive EN characterized by an anti-inflammatory lipid profile formula (i.e., omega-3 fish oils, borage oil and antioxidants). "This was based on three prospective randomized trials," McClave explained. "Then, within two months of publishing the guidelines, we received news that the EDEN-Omega study from the ARDSNet group had been stopped for reasons of futility." The study, which compared trophic with full feeds and a fish oil/borage oil supplement versus placebo, was terminated early because, at the interim analysis, a difference in mortality emerged between the two groups. At question was whether this suggested potential harmful effects of fish oils.

In probing further, the committee learned there was no indication that fish oil was deleterious. Rather, of concern was an error of randomization, in which the control group was less sick than the study patients (specifically, an unexpected low mortality in controls). "Therefore, the therapy just couldn't be good enough for the study group to catch up," McClave said. "The message here is that we don't have a danger signal regarding fish oil."

In summary, McClave noted that "it's important to understand that with any controversy, there may not be a right answer, but controversy provides great opportunity to grow. The most important element in integrating guidelines is transparency: tracking the recommendation back to the evidence." He added that ICUs are obligated to review the supporting literature, decide how they stand on controversial issues, and determine whether that interpretation should alter their clinical practice.

Implementation of Nutrition Guidelines: Who Succeeds and Why?

Naomi Cahill, MSc, RD

"To be worthwhile, guideline recommendations need to represent best practice and should have a beneficial impact on clinical outcomes," stated Naomi Cahill, MSc, RD, from Queen's University in Kingston, Ontario, Canada. Cahill presented data from an international survey indicating that clinicians have mixed opinions about whether Canadian nutritional guidelines reflect best practice and would improve outcomes if implemented. "Some of this diversity of opinion or uncertainty might be because, to date, we have had little success in implementing guidelines. We haven't been able to demonstrate an impact of nutrition guidelines on clinical outcomes."

One theoretical model that can be used to demonstrate how clinical practice guidelines can be implemented successfully is the knowledge-to-action model by Graham and colleagues which links the creation of knowledge with implementation of that knowledge (Graham ID, et al. *J Contin Educ Health Prof.* 2006;26:13). In nutrition, the creation of knowledge has grown substantially over the past 30 years. "Since 1980, more than 200 randomized trials of nutrition intervention have been published, involving more than 2,000 critically ill patients," Cahill said. "However, many of these studies were small, of poor methodological quality, and included a heterogeneous patient population. That makes it difficult to make inferences from these studies and apply them to practice."

The next step in the Graham model after creating knowledge is synthesizing the evidence. Thus far, this has been achieved through systematic reviews and meta-analyses on 34 nutrition topics. Knowledge synthesis is followed by the creation of knowledge tools. "This involves packaging the synthesized evidence into a form (such as clinical practice guidelines) that makes it more useful to be applied in practice," explained Cahill. "The information becomes more succinct and easier to apply at the bedside."

Cahill discussed problem areas that reflect differences between nutrition guidelines and what is actually happening in the ICU. "In the three international nutrition practice audits we conducted to identify problem areas, we consistently observed large variations in practice in terms of percentage of calories received versus prescribed during the first 12 days of ICU stay," Cahill said. "If we think of this variation in nutritional adequacy as a surrogate marker for overall adherence to guidelines, we see there are gaps between guidelines and what's actually happening in practice. We need to bridge that knowledge-practice gap."

Three cluster RCTs addressing the implementation of critical care nutrition guidelines have produced mixed results. One Canadian study of 14 ICUs found that incorporation of guideline recommendations into a feeding algorithm resulted in shorter hospital stay and a trend toward reduced mortality (Martin CM, et al. *CMAJ.* 2004;170:197). Another Canadian study, which randomized 50 ICUs into either the passive arm (paper copy of guidelines) or the active arm (multifaceted interventions in which the dietitian, serving as the opinion leader, received Web-based tools and training toolkits), revealed overall improvement in enteral nutrition adequacy but no differences in clinical outcomes except glucose control (Jain MK, et al. *Crit Care Med.* 2006;34:2362). The most recent cluster study involved 27 ICUs in Australia and New Zealand (Doig GS, et al. *JAMA.* 2008;300:2731). In the intervention arm, ICU opinion leaders attended a two-day guideline development conference, where they helped develop the evidence-based guidelines and received in-service training on implementing 18 different change strategies, including an educational outreach session by the research team. The results showed small differences in nutrition practices, including the mean number of days that nutrition support was received, and no differences in clinical outcomes.

"What are the lessons learned from these studies?" asked Cahill. "First, we can acknowledge that delivery of nutrition therapy is complex and involves a multiprofessional team, which can be problematic when implementing change," she said. "Second, guideline implementation is time-consuming and underappreciated, so these trials show that more work needs to be done. Third, the 'one-size-fits-all' approach, where each ICU in the intervention arm received the same change strategies, may be flawed."

Guideline recommendations must be adapted to the local context and must be aligned with the values and practices at that site. To tailor guideline implementation strategies to local needs, barriers and enablers should be identified and addressed. "A barrier is any factor that may limit, hinder or restrict implementation of a guideline recommendation at the bedside," Cahill noted, "while an enabler is any factor that might promote or help implementation." To identify predictors of adherence to nutritional guidelines, Cahill and coworkers asked clinicians from four ICUs about the factors that helped or hindered guideline implementation. The results of these interviews were amalgamated into a framework for adherence to clinical practice guidelines in the ICU (see Figure 2).

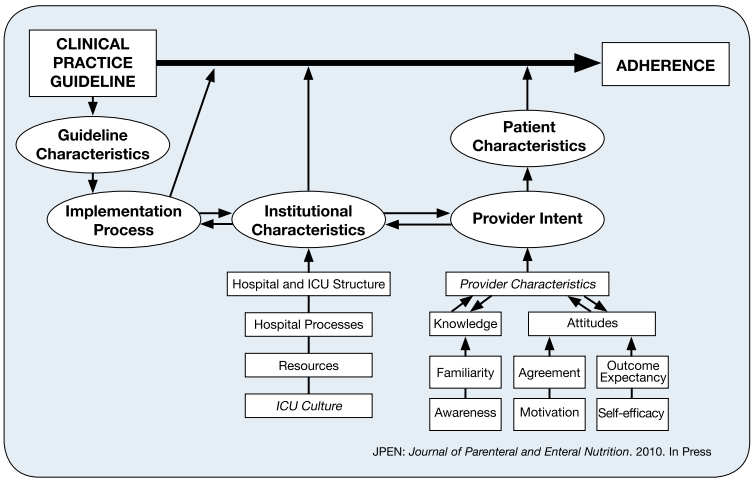

Figure 2. Framework for Adherence to Clinical Practice Guidelines in the ICU

The framework identifies five domains associated with guideline adherence: guideline characteristics, implementation process, institutional characteristics, intent of the intensivist to implement the recommendations, and patient characteristics.

Guideline characteristics. To enable implementation, guidelines must be up-to-date, evidence-based, user-friendly and developed by a respected team.

Implementation process. Multifaceted implementation strategies are needed to increase awareness in the ICU (e.g., posters), to increase knowledge of ICU clinicians through education (e.g., workshops, rounds, academic detailing), and to provide reminders/assistance for incorporating the recommendations into daily practice (e.g., preprinted orders, feeding algorithms, checklists).

Institutional characteristics. Large teaching hospitals with closed ICUs in urban locations were better able to adhere to guidelines than their smaller counterparts in rural locations. Long, slow hospital processes that dictate approval of multiple committees can hinder guideline implementation. Lack of resources (staff, equipment, nutritional products, specialist services) can also be barriers. A positive ICU culture (shared beliefs, attitudes, values, and behaviors) enables guideline implementation; this calls for multiprofessional teamwork, support from the ICU leadership, collaborative decision making, respect for the expertise of each team member, and informal, open communication.

Provider intent. Intent to follow guidelines is based on providers' knowledge and attitudes towards those guidelines. Knowledge is a function of familiarity with, and awareness of, the recommendations; attitude is a function of outcome expectancy, self-efficacy, motivation and agreement with the recommendations. Providers' intent also is influenced by their roles and experiences in the ICU, educational background and personality.

Patient characteristics. Guideline recommendations are made for the average critically ill patient. Therefore, when applying them in practice, patient characteristics must be considered. For example, surgical patients are more difficult to feed than medical patients.

"Clearly, we need to tailor interventions so that any change strategy is specifically chosen to address the barriers identified at a specific ICU

setting, at a specific time," urged Cahill. Current and future research projects are focusing on identifying the most effective methods of measuring barriers and tailoring guideline implementation strategies to overcome these barriers. In the meantime, Cahill suggested that clinicians wishing to optimize their nutrition practices can adopt an 'ABC' strategy:

- Automate – make feeding easy through checklists, verbal reminders, preprinted orders, and protocols
- Benchmark – participate in the 2011 international nutrition audit
- Communicate – make sure all ICU staff are educated and motivated about feeding their patients

The Future of Nutrition Therapy: Looking into the Crystal Ball

Paul Wischmeyer, MD

Before moving forward with nutrition in the ICU, clinicians need to look to the past. "We must identify what we need to unlearn and what we need to learn," said Paul Wischmeyer, MD, from the University of Colorado School of Medicine in Denver, USA. "The first thing we need to unlearn is that nutrition in the ICU is bad food that comes up from the kitchen that nobody eats. This is not nutrition therapy. The reality is that nutrition therapy saves lives and changes outcomes."

Nutrition science has advanced to the point where the mechanisms of nutrients are now understood. Nutrients can change gene expression at the most basic level and are vital to the functioning of cells under stress. Another clear advantage is that nutrition therapy is inexpensive and reduces hospital costs in comparison to most other drugs. "If we can achieve outcome changes from nutrients at a fraction of drug costs, that's a huge advance in the care of our patients," said Wischmeyer, "but the data are useless unless they are translated into practice. For instance, even though all medical society guidelines advocate use of glutamine in critically ill patients, we know this is not practiced in most ICUs."

One hindrance to guideline implementation has been a body of evidence limited to small clinical trials. Although this is now changing as data from larger trials emerge, mechanistic science to explain how nutrients works was previously lacking. "Therefore, nutrition therapy was always something clinicians didn't want to talk about on rounds," remarked Wischmeyer. "This attitude has to change, because we now have laboratory and clinical research supporting the value of nutrition therapy in critically ill patients."

Wischmeyer called for intensivists to actively change this attitude by keeping in mind and disseminating three positive insights gained through research: 1) nutrition can modulate the immune system; 2) nutrition can prevent infection; and 3) calories and protein may reduce mortality among critically ill patients.

Nutrients have been identified that can up-regulate and down-regulate the immune system, but they should be viewed as drugs that provide risks as well as benefits. Another crucial consideration: different patients have different nutrient needs. As an example, patients experiencing an inflammatory response to sepsis and infection require glutamine and omega-3 to intervene and attenuate the sepsis-associated hyperinflammation and immunosuppression. In contrast, patients undergoing an immunesuppressed response to surgery or trauma should receive arginine to reverse the immunosuppression caused by a deficiency of this nutrient.

Diets high in animal fat (omega-6 fatty acids) are linked to hyperinflammation and immune insufficiency, and such intake before hospitalization will affect the ICU patient's health status. "Many patients arrive at the ICU in this condition, and we may be able to reverse that and improve ICU outcomes with omega-3," stated Wischmeyer, noting that the omega-6 to omega-3 ratio of the American diet is 18:1 – a huge departure from the ideal "caveman" ratio of 1:1. Wischmeyer discussed the evolution of dietary intake as a means to understanding how omega-3 therapy can affect disease outcomes. Dietary fatty acids, inflammation and coronary artery disease (CAD) risk are known to exist in a linear relationship. Simply changing the ratio of dietary omega-6 to omega-3 fatty acids within the same population has been shown to reduce the mortality associated with CAD. (Simopoulos AP. *Exp Biol Med* [Maywood]. 2008;233:674).

Pharmacologic and clinical data provide evidence supporting the correction of the omega-6: omega-3 ratio in ICU patients. In 16 healthy volunteers, two doses of fish oil infused twice before an endotoxin bolus reduced the tumor necrosis factor (TNF)-α response, febrile response, and overall catechol response to endotoxin shock (Pluess TT, et al. *Intensive Care Med*. 2007;33:789). Favorable effects also were revealed in a meta-analysis of three clinical trials, each involving at least 100 patients with ARDS who predominantly also had sepsis (Pontes-Arruda A, et al. *JPEN J Parenter Enteral Nutr*. 2008;32:596). The results linked omega-3-based feeding with an 83% reduction in organ failure and a 60% reduction in mortality.

"All clinical practice guidelines agree that fish oil should be given to patients with ARDS, so in the future we need to look toward applying this to the right patients," Wischmeyer stated. "We need trials that focus on sepsis patients, because almost all of the data thus far involved sepsis-induced ARDS. We also need to begin looking at biomarkers and treating patients based on inflammatory markers."

Nutrition therapy has another crucial role in the ICU: prevention of infection. Up to 30% of major surgery patients develop infection, costing as much as $10,000 per patient. "This is an enormous burden that we can prevent because we know there is a nutritional mechanism for this problem," remarked Wischmeyer.

Surgery and trauma induce a deficiency of arginine, an amino acid required for T cells to divide and monitor the immune system. Arginine deficiency syndrome is a well-known condition correlated with increased infection among cancer and surgery/trauma patients. Surgery/trauma patients require different nutrition therapy than sepsis patients, as sepsis is a pro-inflammatory state mediated by different cytokines than those involved in the immunodepressed state that occurs following surgery or trauma. In fact, arginine deficiency is not present in sepsis.

A meta-analysis of 30 randomized controlled trials with more than 3,000 patients evaluated the effects of arginine therapy following surgery (Drover et al. *Annals of Surgery*. 2010. [In Press.]). The results showed that five to seven days of arginine-based nutrition reduced infectious complications by 40% and reduced length of stay by as much as one-third. None of the trials revealed harm in the arginine feedings. "Thus, we see enormous potential cost savings associated with arginine use in patients following surgery," said Wischmeyer. "I am not sure we need more research on this amino acid in surgery, but a definitive large-scale clinical trial would establish it as the standard of care."

As for caloric and protein intake among the critically ill, the needs vary from patient to patient. Surveys show that most ICU patients are underfed. "This may be safe for some, but harmful for others," Wischmeyer said. "If nutrition therapy is to save lives and improve outcomes, we have to actually feed the patients so they can receive the nutrients. Also, we must realize that our patients have different nutrition goals."

Determining caloric and protein amounts is challenging. According to one hypothesis, BMI defines chronic nutritional risk. ICU data show that patients with a low (<25) or very high (>35) BMI and low caloric intake have increased mortality rates; however, caloric intake does not have as great an impact in the patients with BMIs of 25 to 35. Protein intake also affects outcomes. For every additional 30 g/day of protein given to critically ill patients, the odds ratio of mortality significantly decreases. As with caloric intake, this effect of protein is BMI-dependent.

"Because we're unsuccessful in getting calories into our high-risk patients, should we start total parental nutrition sooner in malnourished and very obese patients?" asked Wischmeyer. "That is probably something the Europeans have right and that constitutes a topic in need of future study." It is worth noting that nutrition products have varied availability in different parts of the world.

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Continuing Education Self-Assessment

EVIDENCE-BASED NUTRITIONAL GUIDELINES IN 2010

1. Which of the following was observed in a prospective randomized controlled trial regarding gastric residual volumes (GRVs)?
   a. Higher GRVs were associated with a decreased incidence of gastrointestinal complications.
   b. Higher GRVs were associated with an increased incidence of aspiration.
   c. Stopping GRVs was associated with an increased incidence of pneumonia.
   d. Stopping GRVs was associated with an increased incidence of vomiting.

2. Arginine therapy is recommended in patients with sepsis-induced ARDS.
   a. True
   b. False