

CONGRESS REVIEW



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Continuing Education Information

Learning Objectives

- At the conclusion of this activity, participants should be able to:
- Evaluate the implications of developing delirium in the ICU
 - Assess the risk factors and prevention techniques for various ICU patient populations
 - Describe the new pharmacological options for management of delirium in the ICU
 - Assess the benefits of pre-mix total parenteral nutrition solutions in the ICU
 - Discuss the risks of caloric deficit in ICU patients and the benefits of supplemental parenteral nutrition
 - Discuss results of a 2008 international nutrition survey, with a focus on success or failure in nutrition delivery
 - Identify the clinical problems presented by thromboembolic disease in the ICU
 - Assess the therapeutic options for deep vein thrombosis and pulmonary embolism in the ICU with emphasis on the newer agents
 - Evaluate the controversial areas of management

Target Audience

This continuing medical education offering is intended to meet the needs of any healthcare provider involved in the care of critically ill patients, including advanced practice nurses, critical care nurses, intensivists, critical care fellows, anesthesiologists, internists, surgeons, cardiologists, pulmonologists, emergency medicine practitioners, neurologists and respiratory therapists.

Type of Activity

This activity will focus on increasing knowledge-based content. It is presented as summaries of live activities, followed up with a few questions for self-assessment.

Competencies

SCCM supports recommendations that will promote lifelong learning through continuing education. SCCM promotes activities that encourage the highest quality in education that will enhance knowledge, competence or performance in critical care practice. This activity will meet the following:

- Practice Applications
- Communication
- Quality Improvement

Evaluations and CE/CME Applications

To apply for credit and evaluate the course, visit www.sccm.org/2009ConRev. For additional information, please call SCCM at +1 847 827-6869 or email education@sccm.org

Physicians/Physician Assistants

SCCM designates this educational activity for a maximum of 1.5 *AMA PRA Category 1 Credits*[™]. Physicians should claim credit commensurate with the extent of their participation in the activity.

Nurses

SCCM is approved by the California Board of Registered Nursing, Provider No. 8181, and approves this activity for 1.5 contact hours.

Pharmacists

SCCM is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmaceutical education. This activity will provide 1.5 continuing education hours (236-000-09-230-H01-P).

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INITIATING SAFE PRACTICES: CAN PARENTERAL NUTRITION BE USED SAFELY TO PREVENT CALORIC DEBT AND IMPROVE OUTCOMES?

Can total parental nutrition (TPN) be used safely to prevent caloric debt and improve outcomes? How many calories do critically ill patients really need? Many intensivists today may think their intensive care unit (ICU) is providing adequate nutritional support, but studies – including an international survey that provides benchmarks for performance – suggest that great improvement is needed.

Standardized TPN in the ICU: Safe or Sorry? Jane M. Gervasio, PharmD

In discussing whether standardized parenteral nutrition (SPN) is safe to use in critically ill patients, Jane M. Gervasio, PharmD, from Butler University and Methodist Hospital in Indianapolis, Indiana, examined the rationale for administering SPN to ICU patients and explored its advantages and challenges.

“Parenteral nutrition is a complex drug – and it *is* a drug – and we have to follow the guidelines appropriately,” said Gervasio. In addition to containing lipids, fats, dextrose, multivitamins, and trace elements, TPN provides pharmacologic agents and electrolytes. These can cause complications to both the patient and the compounding procedure.

In fact, TPN is the second most reported drug class associated with medication errors, totaling 22% of all medication reports.¹

The complications of TPN have been associated with morbidity and mortality. They can arise from a full spectrum of problems: inadequate education and knowledge of the prescriber, transcribing errors, compounding errors, mistakes made in the administration, and monitoring errors.

In 2007, The Joint Commission released its National Patient Safety Goals for Hospitals and Critical Access Hospitals, recommending that institutions standardize and limit the number of drug concentrations they use.² The Joint Commission worked with the American Society of Parenteral and Enteral Nutrition (A.S.P.E.N.), realizing that when considering TPN, it is critical to provide patient-specific nutrition, while also looking toward standardization. A.S.P.E.N. stated that SPN goes beyond a premixed bag to also include ordering, labeling, screening patients, and administration. While agreeing on the need to standardize parenteral nutrition, A.S.P.E.N. also recognized that not all patients would benefit from the one-size-fits-all theory. Instead, hospitals should select candidates for SPN.

In discussing how ordering processes can be standardized, Gervasio explained how the forms used at her hospital allow the prescriber to select a standard peripheral formulation, a standard central formulation or a standardized electrolyte profile. Prescribers also may customize a formula. While these standardized formulations are compounded by the hospital's pharmacy, premix solutions are also available. Premix solutions are manufacturer-compounded and are available in various concentrations for both peripheral and central formulations.

The rationale for using SPN is multifold. “SPN improves safety to the patients and reduces costs,” Gervasio said. Safety is improved by minimizing ordering error by the prescriber and misinterpretations of orders by the pharmacist. “The specifics for each solution have already been preloaded into the computer, and the pharmacist simply enters the volume,” she explained. SPN also promotes enhanced patient safety by minimizing calculation and compounding errors, and decreasing contamination risk. Labor costs also are reduced, as less time is required to prepare bags, clarify unclear orders, and correct incomplete or unsafe orders. Standardization reduces inventory, supply needs and waste.

In addition, SPN is designed to meet standard nutrient requirements. While an understanding of the patient's uniqueness is important, identifying which patient's nutritional needs may be met with SPN is advantageous. As an added benefit, standardization provides decision guidance to the prescriber while promoting ease and convenience in the prescribing.

Premix solutions offer several advantages and a few disadvantages. They are sterile, accurate, meet strict quality assurance standards and reduce compounding errors. Contamination risks are decreased, as the bag can be opened only once (when spiked by the nurse). Premix solutions do not need refrigeration, have a two-year shelf life, are readily available, and require less preparation time. However, only the dextrose plus amino acid solution is available in the United States; triple-mix solutions, which contain the fat com-

ponent of TPN, are not available. Fat concentration must be provided via a separate bag. Additionally, if premix solutions are utilized alone, vitamins or minerals must also be added. Errors can occur in administering the solution, as this is a new technology that requires nurses and pharmacists to be properly trained in its implementation.

Is it advisable to use standardized or premix solutions in ICU patients? “Different areas are being investigated to see if we can use these in critically ill patients,” said Gervasio. In some studies, ICU patients receiving enteral nutrition have been given supplemental trophic feeds of SPN. Also being evaluated are dual feedings in ICU patients, in which enteral and parenteral nutrition are started at the same time. The aim of these approaches is to help patients reach nutritional goals earlier.

SPN may be especially advantageous if parenteral nutrition must be initiated over weekends and in the evenings. “The standard formulations are a safety net for our physicians,” remarked Gervasio. “Some of our young practitioners who may not know how to start parenteral nutrition feel more comfortable if they start a liter or 1,500 mL of an SPN. We haven't had a problem when they start with that amount and then get the standard electrolytes going. It provides a starting point from which we can adjust accordingly.”

The limited formula selections can be problematic when managing ICU patients. Standardized formulas have been criticized for failing to meet the high protein needs of critically ill patients. “In reality, with some of the newer triple mixes and high-concentration premixes, as well as with our own standard formulation, we can meet the protein needs of many patients,” Gervasio remarked. “However, the obese population is very challenging because they require a hypocaloric formula and, therefore, less dextrose. It's difficult to meet their protein needs when the amount of dextrose is reduced.”

The greatest challenge in parenteral nutrition is electrolyte management. Parenteral nutrition should be used for maintenance electrolyte management; it should never be used to correct an acute deficiency. Electrolytes have a wide range of normal values, but it is important to identify trends. “For example, even if the patient's potassium values are within the normal range, going from 3.5 to 4 to 4.5 over a three-day period, that's a trend, and it's telling you something,” Gervasio said. “Look for those trends before you make a change.” On the other hand, practitioners should resist reacting to single, nonsignificant abnormal values. Gervasio also advised using electrolytes with intermittent infusions if possible. She noted that electrolytes could be added to premixed solutions, but compatibility issues must be considered.

The use of SPN versus customized parenteral nutrition (CPN) was studied in a 496-bed, tertiary care trauma center with 103 ICU beds in various settings.³ “This was the only study I could find, and it was not robust,” said Gervasio. During 1,298 patient days of parenteral nutrition over a four-month period, 992 patients received SPN and 306 received CPN. More than 3,600 laboratory determinations were made throughout that period. Results showed that laboratory values stayed within the normal range for 73% of patients receiving SPN and 67% of patients receiving CPN. The authors concluded that patients receiving standardized formulations of electrolytes in the parenteral nutrition solutions are more likely to have laboratory serum electrolyte levels within normal levels.

“Where are we headed?” asked Gervasio. “More research is absolutely necessary. An ICU premix formulation may be forthcoming. I would not be surprised to see a variety of premix TPN solutions tailored to different patient populations in the future, similar to what we see now with enteral nutrition.”

Advantages and Disadvantages of Premix Solutions

Advantages

- Provide sterility and accuracy.
- Meet strict quality assurance standards.
- Reduce compounding errors.
- Reduce contamination risks.
- Do not need refrigeration.
- Require less preparation time.
- Offer a two-year shelf life.

Disadvantages

- Premixed TNA (triple mix) solutions are not available in the United States.
- Fat concentration must be provided separately.
- Vitamins or minerals must be added.
- Errors can occur during administration.

Calorie Deficit and Outcome in the ICU: Can We Narrow the Gap? Paul Wischmeyer, MD

"ICU patients are not created equal, so we shouldn't expect the impact or requirements of nutrition therapy to be the same for all patients," said Paul Wischmeyer, MD, from the University of Colorado Health Sciences Center in Denver. "Not only are our patients different, but their illnesses are different – sometimes the disease is hypermetabolic, sometimes it's not. Regardless, muscle wasting is inevitable, and early overfeeding won't fix this. Continued lean body mass loss and calorie deficit have been shown to be lethal. So in some patients, we probably do need to learn how to narrow the gap."

In discussing the metabolism of critical illness, Wischmeyer explained the differences between the stress response and starvation. The stress response leads to increased metabolic rates, increased glucose production, protein catabolism, hyperglycemia, increased catecholamines, increased glucocorticoids and hyperinsulemia. In contrast, starvation leads to decreases in metabolism, calorie use and endocrine function. "Exceeding goal calories during stress reduction will not improve nitrogen balance or decrease catabolic rate as compared with starvation," Wischmeyer said.

During illness, the body must degrade protein to generate the amino acids and other key nutrients to survive. "This protein breakdown is evolutionarily protective," remarked Wischmeyer. He hypothesized that a patient with a larger body mass index (BMI) and increased lean mass would have a better chance for survival because there is more muscle and protein to break down. According to this theory, moderate obesity would be highly protective in heart failure, cancer and other diseases.

Are trauma and sepsis hypermetabolic conditions? Early in their care, patients with trauma and sepsis are not particularly hypermetabolic.

In fact, the more severe their condition, the less hypermetabolic they are. However, as the condition progresses patients become very hypermetabolic. "That's the key time when we cannot fail our patients in their nutritional therapy," he explained.

Patients become hypermetabolic because of the release of tumor necrosis factor (TNF)-alpha and other cytokines during the acute inflammation stage. "Interestingly, when it was first discovered, TNF-alpha was called *cachexin*," Wischmeyer remarked. "It tells the body not to take in much. This raises the question: Why does early, acute inflammation tell us not to eat, and is this relevant to modern medicine? This is what is driving the concept of permissive underfeeding," said Wischmeyer.

In the era of the caveman (prior to ICUs, ambulances, and emergency rooms) hypocaloric feeding made sense because survival in the face of critical illness for more than 24 to 72 hours was not evolutionarily advantageous. Injured organisms were a drain on the primitive community. Thus, early loss of lean mass and the breakdown of amino acids and protein were self-limited.

However, in the modern era of intensive care and emergency medicine, patients are kept alive, and those who are underfed accumulate a caloric debt and continue to lose lean body mass. This is problematic, as research indicates that calorie deficit is lethal. Calorie deficit appears to be highly predictive of mortality, with

a 76% mortality rate reported for ICU patients who developed a 10,000 calorie deficit.⁴

Other studies also have linked poor outcomes with poor caloric balance and insufficient enteral feeding. Gatt and colleagues found that gut failure (defined as enteral/oral tolerance of $\geq 80\%$ of nutritional requirements for ≥ 48 hours at any time during a patient's hospital stay) was more predictive of death than sepsis or renal failure.⁵ In another investigation, which examined caloric debt and complications, Villet observed that caloric deficit was associated with longer ICU stay, more days on mechanical ventilation and more complications.⁶

Most of the data related to the beneficial effects of hypocaloric feeding emanate from permissive underfeeding studies performed several years ago. These investigations evaluated the impact of hypocaloric feeding on short-term outcomes, such as length of stay and infection rates. "However, just because patients leave the ICU doesn't mean they go on to have a good quality of life or even survive two months," said Wischmeyer. "After all, what do we know about our patients after they leave the ICU?"

Research on the continued effect of sepsis on survival indicates that patients treated for sepsis who leave the ICU have a significantly lower survival rate over the next several years compared to a control population.⁷ This finding is true across all age groups, even among younger patients (ages 18 to 44 years).

"One reason for this poor survival rate might be the dramatic loss in lean body mass in our patients," stated Wischmeyer. He related a hypothetical case, in which a major trauma patient becomes septic and develops acute respiratory distress syndrome (ARDS). The patient has a long ICU stay, during which he becomes hypoxic and receives corticosteroids. After he leaves the ICU, he goes into rehabilitation but continues to be weak. He has lost much of his muscle mass and cannot get out of bed. The patient eventually develops a pulmonary embolism and dies.

Survey data has revealed ICUs in the United States do a poor job of delivering adequate calories to patients receiving nutritional therapy, Wischmeyer said. "In comparison with other countries, we also take the longest – on average 60 hours – to start our feeds," he said. "This is likely the major cause of ileus both postoperatively and in the ICU. It is not the surgeon or the disease that cause the ileus. It is the lack of enteral feeding (even for 24 hours) that leads to gastroparesis and gastric intolerance. We must be better at preventing this iatrogenic complication."

Results from the 2007 International Critical Care Nutrition Practice Survey found that patients on average received 1,034 kcal and 47 g of protein.⁸ This resulted in an average caloric deficit of 7,500 kcal and 12,000 kcal over 10 days in lean and obese patients, respectively. In looking at these data, a statistically significant relationship was found between the number of calories delivered and survival in patients with a BMI of <25 or >35 . This relationship indicated that for every additional 1,000 calories fed (up to 2,000 total calories), there was a statistically significant reduction in 60-day mortality in the patient with a BMI of <25 and ≥ 35 . No relationship between calories delivered and mortality was observed in the patients with BMI between 25 and 35. Thus, the decision to aggressively narrow a patient's caloric gap may be very dependent on the patient's admission BMI. We hope to have the opportunity to evaluate this in a future trial, entitled the "TOP-UP" trial.

New Nutrition Support Therapy Guideline Highlights

The Society of Critical Care Medicine and A.S.P.E.N. recently jointly published "Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient."¹¹ Highlights include:

- Prior to initiating TPN, early enteral nutrition should be started to prevent ileus.
- Enteral nutrition, supplemented with omega-3 fats, is a clear recommendation for patients with ARDS.
- For burn or trauma patients, consider enteral glutamine and switch to a small bowel tube, if gastric feeding fails.
- Consider parenteral nutrition if a promotility agent and small bowel feeding does not work or if the nutrition goal is not reached after seven days in well-nourished patients (although perhaps it should be started earlier in malnourished patients).

Visit www.learnICU.org to access the complete guideline.

Are We Still Failing to Deliver What Our Patients Need?

Daren K. Heyland, MD

Daren K. Heyland, MD, from Queen's University in Kingston, Ontario, Canada, addressed results of the International Critical Care Nutrition Survey. Conducted in 2001, 2003, 2004, 2007 and 2008, this survey yields important data that help define targets for quality improvement in ICUs. "It enables us to benchmark our performance and see what actually is feasible and reasonable to accomplish," said Heyland.

During its earliest years, the survey collected data from approximately 50 ICUs in Canada. In 2007, the survey extended its reach to include 165 ICUs worldwide, primarily from North America. In 2008, it was expanded further to include Australia, New Zealand and Southeast Asia.⁹

Designed as a prospective, observational cohort study, this international survey seeks to determine current nutrition practice

in the adult ICU setting, illuminate gaps between best practice and current practice, and identify interventions to target for quality improvement initiatives. "It's also designed to enable statistical analyses, so we can identify factors associated with best practice or optimal provision of nutrition," Heyland said.

The 2008 cohort involved 20 consecutive mechanically ventilated patients. Data were collected on hospital and ICU demographics, patient baseline information (e.g., age and admission diagnosis), baseline nutritional assessment and daily nutritional intake for up to 12 days. Researchers followed patients for 60 days, documenting ICU and hospital outcomes.

Participating ICUs were required to have at least eight beds as well as an individual with clinical nutrition knowledge available to collect data. Patients had to be in the ICU for at least 72 hours and mechanically ventilated within 48 hours. A Web-based data capture system was created to enable worldwide participation. A total of 157 ICUs participated in the 2008 survey, with the strongest representation coming from the United States (44 sites). The total number of finalized patients was 2,850. Days of observation averaged 9.4 per patient, providing nearly 24,000 total number of ICU patient days.

More than three-quarters of the participating ICUs resided in teaching or academic hospitals. The average hospital and ICU sizes were approximately 600 and 17 beds, respectively. Patient cases varied; median patient age was 62, and approximately 60% were medical patients. The average Acute Physiology and Chronic Health Evaluation (APACHE) II score was 22, and ARDS was present in 11% of patients within the first 72 hours. The admissions diagnoses spanned a wide range.

"The 60-day patient outcomes data showed that, on average, the patients in this study were on a ventilator for seven days, in the ICU for 10 days, in the hospital for 20 days, and 26% of them died," reported Heyland. "We were dealing with a very sick, ventilated population of ICU patients."

In presenting the nutrition practices results from the 2008 study, Heyland noted that 66% of patients received enteral nutrition, while 9% received parenteral nutrition. These results uphold the recommendation, set forth by the Canadian Clinical Practice Guidelines for Nutrition Support in Mechanically Ventilated, Critically Ill Adult Patients, that enteral nutrition be used over parenteral nutrition.¹⁰ "Wide geographic differences were seen regarding the combined use of enteral nutrition and parenteral nutrition, which averaged 9%," said Heyland.

"For patients prescribed parenteral nutrition, we wanted to know if there was a contraindication to enteral nutrition," Heyland explained. "Survey participants provided a variety of reasons for prescribing parenteral nutrition, although about 50% of them offered no rationale. Others indicated specific contraindications to enteral nutrition, such as small bowel anastomosis, fistula and perforation."

The Canadian clinical practice guidelines also recommend that enteral nutrition be started within 24 to 48 hours of ICU admission. Great variation across geographic regions was documented in the 2008 survey (see Figure 1), with the average site initiating enteral nutrition just before the benchmark of 48 hours. "The value of benchmarking is being able to see how others are performing and what is achievable in other ICUs," remarked Heyland. He noted that in the United States, enteral nutrition typically is started in critically ill patients within the first 50 to 60 hours of admission.

Among suggested strategies to optimize enteral nutrition delivery, the Canadian clinical practice guidelines recommend a feeding protocol that includes consideration of using motility agents and small bowel feeding tubes. According to the 2008 survey, 80% of ICUs have a feeding protocol. Of these, 72% incorporate use of a motility agent and 53% include small bowel feeding. Among all patients involved in the survey, only 16% received motility agents. The most common drug used was metoclopramide. Very few patients in the database (10%) received the combination of erythromycin and metoclopramide. Small bowel feeding is recommended by the Canadian clinical practice guidelines in patients

with gastrointestinal intolerance or risk of aspiration. Overall, use of small bowel feedings was low – instituted by an average 20% of ICUs – and showed wide regional differences. Another strategy to minimize the risks of enteral nutrition delivery – head of bed elevation – was implemented by approximately 30% of ICUs.

The 2008 survey also evaluated the use of intensive insulin therapy in ICUs. The Canadian guidelines recommends that hyperglycemia (blood glucose >180 mg/dL) be avoided in all critically ill patients, and 89% of ICUs said they have a protocol in place to control blood glucose, with most of these protocols targeted between 79.2 to 144 mg/dL.

Finally, the survey assessed the overall performance of ICUs in providing nutrition support. Nutritional adequacy was defined as the number of calories received (from enteral nutrition, appropriate parenteral nutrition, and propofol) divided by the number of calories prescribed. "The results showed that, on average, patients are getting about 50% to 60% of goal calories," reported Heyland. "However, there was one site where patients received 80% of goal calories. If they can do it, why can't the rest of us?" Similar overall performance results were obtained in provision of adequate protein.

Heyland went on to explain the detailed benchmark report sent to survey participants. "Benchmarking lets you identify your strengths and weaknesses as they relate to other ICUs," he said. To create a culture of excellence, the 2008 survey held a "Best of the Best" campaign and recognized 10 ICUs for high nutritional adequacy and adherence to the Canadian guidelines. "Which hospital and ICU characteristics are associated with the best of the best?" asked Heyland. "We found that the presence of a dietitian was by far the strongest predictor of a high ranking," he said. "Being in the United States or China was equally as strong in denoting you as the worst performer," he added.

"Clearly there are opportunities for improvement," Heyland concluded. "We need to close the gap between what we're prescribing and what our patients are getting. Using better feeding protocols will help, particularly those that use motility agents and small bowel feeding. There is also a huge gap in optimizing the use of pharmacutrients." Other areas of improvement include assuring tighter glycemic control and withholding soybean emulsion lipids.

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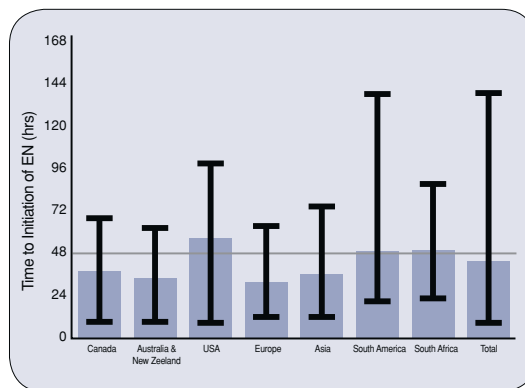


Figure 1. Early vs Delayed Enteral Nutrition (EN).

Continuing Education Self-Assessment

INITIATING SAFE PRACTICES: CAN PARENTERAL NUTRITION BE USED SAFELY TO PREVENT CALORIC DEBT AND IMPROVE OUTCOMES?

- Which of the following statements is true regarding electrolyte management in parenteral nutrition?
 - Electrolytes should not be used with intermittent infusions.
 - Trends in electrolyte levels that appear in the normal range are important to consider.
 - The addition of electrolytes to premix solutions is not recommended.
 - Electrolyte management can be used in parenteral nutrition to correct an acute deficiency.
- Negative calorie balance during a hospital stay is as predictive of mortality as sepsis and renal failure.
 - True
 - False