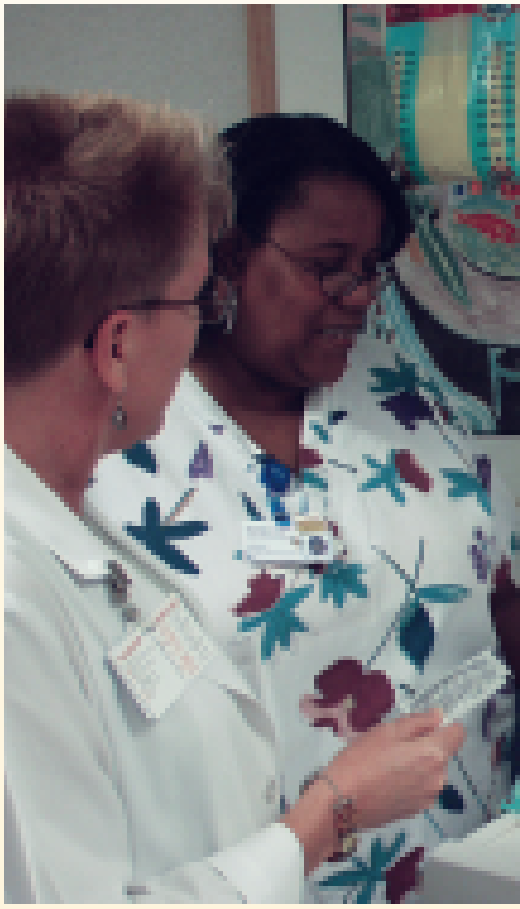
Peptide-Based Formulas:
The Nutraceuticals of Enteral Feedings?

Peptide-based formulas help mitigate the consequences of tube-feeding intolerance, preserve or restore gut integrity, and improve patient outcomes.

EVELYN M. PHILLIPS, MS, RD, LDN, NICOLE SHORT, MA, RD, LDN, CHERI TURNER, RPH, MBA, AND JULIANNE RECE, RN, MSN, CRRN, CWOCN



Many clinicians hesitate when it comes to justifying the cost (around $20–$25/day) of specialized elemental enteral formulas. True, standard enteral formulas are less expensive (around $5–$7/day) and well tolerated by many patients, especially if nutritional intervention is started early. There are, however, numerous circumstances that delay nutrition therapy, and subsequently the incidence of hospital acquired malnutrition remains high.[1]

Loss of gut integrity from metabolic stress and illness goes hand in hand with malnutrition by causing loss of appetite, diarrhea, decreased absorption of nutrients, and increased intestinal gut permeability. Increased intestinal gut permeability allows for microbial translocation and may lead to sepsis.[2] Those at risk for malnutrition are also at risk for compromised gut function. It should be of no surprise that in patients with impaired gut function, standard enteral formulas are not well tolerated. In a study[3] by Meredith et al. comparing the incidence of tube feeding related diarrhea in 2 groups of ICU patients, the researchers found that 44% of the group on a standard, intact protein formula had diarrhea versus 0% in the group on a therapeutic, peptide-based formula.

The total cost of tube feeding-related diarrhea is almost impossible to determine.[4] At a minimum, it contributes to the etiology of malnutrition, dehydration, and skin breakdown as well as increased nursing time and length of stay. When indicated, peptide-based formulas can be cost-effective. Similar to medications, peptide-based enteral formulas have specific indications, dosages, and duration of therapy and, therefore, meet the definition of a nutraceutical. The term nutraceutical, coined in 1989 by Dr. Stephen DeFelice, refers to "any substance that may be considered a food or part of a food and provides medical or health benefits, including the prevention and treatment of disease."[5] According to Joint Commission on Accreditation of Healthcare Organizations (JCAHO) standards, nutraceuticals are considered drugs to be managed by pharmacy, not food service. As a result, their costs are more fittingly included in the budget analysis of medical and nursing care.

As a nutraceutical, a peptide-based formula has its place. These specialized formulas are indicated to preserve and/or restore gut integrity during periods of illness and help prevent the consequences of tube-feeding intolerance to improve outcomes.[6-9] The dose or amount of formula varies according to individual nutrient needs as assessed by the registered dietitian. The duration of therapy depends on the individual's response to treatment, which is influenced by factors including, but not limited to, the timeliness of enteral feeding and the severity of illness and malnutrition. In most cases, the sooner appropri-

ate treatment is initiated, the quicker the transition to standard feeding. Therefore, a suitable transitional formula needs to be part of the nutritional care plan—a key point in controlling costs.

Traditional nutrition support protocols often require demonstrated intolerance to a less expensive feeding to justify a change in treatment to a specialized

or more expensive formula. This can be an expensive method of treatment in critical illness or in cases of less severe illnesses with pre-existing malnutrition. To reduce the incidence of tube feeding-related diarrhea, the likelihood of intolerance should be considered in the initial formula selection process. Clinicians should not make the assumption that tube feeding-related diarrhea is an acceptable or unavoidable consequence. It is doubtful that any parent would find it acceptable if his or her infant developed diarrhea associated with the baby formula. Yet, in reviewing transfer charts of patients admitted to our facility receiving enteral feeds, it is not uncommon to see the notation, "tolerating tube feeding with diarrhea."

While medications and *Clostridium difficile* (*C. difficile*) infections can also be contributing factors, in patients with compromised gut function, it should be anticipated that standard enteral feedings will be poorly tolerated. The effect of acute illness or trauma characteristically includes stress-induced catabolism in conjunction with lower anabolic activity, resulting in the loss of essential structural and functional proteins required for restoring and maintaining physiologic homeostasis.[10] The ensuing hypoalbuminemia is associated with loss of gut integrity, including reduced enzyme availability and activity, resulting in decreased nutrient absorption and increased nutrient losses through diarrhea/malabsorption.[11-14] The Malabsorption Index[15] is a validated tool that can help the clinician in identifying individuals with malabsorption, and it facilitates the selection of an appropriate type of enteral formula.

DEFINING THE TERMS

Standard enteral formulas contain whole (intact) proteins, the same as those found in orally consumed diets. During normal digestion, protein is enzymatically broken down (ie, hydrolysis) in the intestinal lumen to a mixture of peptides (small strands of amino acids) and free amino acids with peptides as the predominant component.[16]

This enzymatic protein hydrolysis is not a random process; peptides are produced in specific lengths to facilitate absorption. Commercially prepared peptides can be manufactured using digestive enzymes that mimic normal digestion or by bacterial hydrolysis that produces a random mixture of peptides. When selecting a peptide-based formula, it seems most logical to choose a product that employs enzymatic hydrolysis in order to provide peptide chains that can be readily recognized by luminal transport systems.

Immune-enhancing formulas contain specific immune modulating nutrients, such as arginine, glutamine, omega 3 fatty acids, and/or dietary nucleotides.[17,18] However, the protein composition can vary from whole proteins plus free amino acids (FAA) to a combination of whole proteins, peptides, and FAA, all the way to products with FAA and 99% of the protein as peptides. Oddly, all of these products are similarly priced, regardless of their protein composition. The gastrointestinal (GI) tract is one of the largest immune systems in the body. It stands to reason that those with suppressed immunity would also be at risk for compromised gut function. Therefore, when selecting an immune-

Table 1. Enteral Formula Protein Composition

Manufacturer	Product	% Protein of Total Kcals	Protein Composition
Standard Formulas: Intact or Whole-Protein Based			
Nestlé Nutrition	Nutren® products	16	Whole/Intact Protein, Calcium-Potassium Caseinate
	ProBalance®	18	
Novartis Nutrition	FiberSource™ Isosource®	14	Whole/Intact Protein Soy Protein Isolate
	FiberSource™ HN, Isosource® HN and 1.5	18	
Ross Products	Osmolite® and JEVITY® products	14 –18.5	Whole/Intact Protein Sodium and Calcium Caseinate
Standard High Protein Formulas: Intact or Whole-Protein Based			
Nestlé	Replete®	25	Whole/Intact Protein Calcium-Potassium Caseinate
Novartis	Protain XL® TraumaCal®	22	Whole/Intact Protein Sodium and Calcium Caseinate
	Isosource® VHN	25	
Ross	Promote®	25	
Peptide-Based Formulas			
Nestlé	Peptamen® products (Enzymatically hydrolyzed whey protein)	16–25; 99 as peptides	Peptide Size: Percentage by Weight 1: 1 2–4: 18 5–9: 26 10–40: 50 > 40: 5
Novartis	Peptinex® DT (Casein hydrolysate)	20	• Very small peptides and free amino acids • Peptide profile not available
Ross	Perative® (Partially hydrolyzed sodium caseinate)	20.5	Peptide Size: Percentage by Weight 1: 8.7 2–4: n/a 5–9: n/a 10–40: n/a > 40: 75
Immune Enhancing Formulas. All contain arginine (Arg) as a free amino acid			
Nestlé	Crucial® (Enzymatically hydrolyzed casein)	25; 99 as peptides Arg: 15.2 g/L	Peptide Size: Percentage by Weight 1: 15 2–4: 8 5–9: 15 10–40: 34 > 40: 28
Novartis	IMPACT® Sodium and Calcium Caseinate	22 Arg: 12.5 g/L	• Whole protein plus Arg • Peptide profile not available
	IMPACT® (Glutamine wheat protein, hydrolysate, and sodium caseinate)	24 Arg: 16.3 g/L	• Whole protein, peptides plus Arg • Peptide profile not available
Ross	PIVOT™ 1.5 (Partially hydrolyzed sodium caseinate, whey protein hydrolysate)	25 Arg: 13 g/L	Peptide Size: Percentage by Weight 1: 13 2–4: 6.2 5–9: 8 10–40: 5.5 > 40: 74

enhanced diet (IED), it seems most logical to choose a product that contains the majority of its protein as enzymatically produced peptides. (For additional information on implementing an IED, please review the article, "Maximizing the Nursing Nutrition Link: Pressure Ulcers and Nutritional Intervention," published in the January/February 2005 issue of *ECPN*, available online at http://www.extendedcarenews.com.)

Free amino acid-based formulas contain proteins that have been completely hydrolyzed to their basic components, amino acids. These formulas are often referred to as "elemental" and were introduced to help reduce "the work load" of digestion. However, this concept has not proven true. Free amino acid-based diets, as with parenteral nutrition and starvation, have been associated with gut atrophy. In a study[8] by Shou et al., the researchers found that bacterial translocation was 5 times more likely to occur in animals fed free amino acid-based diets compared to those fed peptide-based diets.

Peptide-based formulas contain proteins that have been hydrolyzed to produce peptides of varying lengths and are also referred to as "elemental" diets as well as "partially" or "semi-" elemental. As compared with FAA or whole-protein formulas, peptide-based feedings have been shown to: improve nitrogen retention/balance; improve visceral protein synthesis; improve absorption /reduce diarrhea; maintain/restore gut integrity; reduce bacterial translocation; and improve outcomes.[9] The GI tract has specific and discrete uptake systems and it appears that small peptides consisting of 4–12 amino acids are absorbed more easily and uniformly than corresponding mixtures of FAAs.[16,19]

Peptide-based formulas can vary in the amount of protein provided as peptides and the size of the peptides. Some formulas contain peptides that are very large and similar to whole proteins. Conversely, some contain peptides that are very small and similar to free amino acids. Each formula has a defined peptide profile, which the clinician can use when comparing products. At this point, it should be apparent that not all peptide-based formulas are created equal. Part of justifying the cost of a specialized elemental enteral formula is selecting a product using evidence-based analysis that will be well tolerated by the intended patient population. Otherwise, it will literally be like flushing money down the toilet.

CONCLUSION

Based on the current scientific literature, when selecting a specialized peptide-based formula, particularly for an immune enhancing formula, it makes the most sense for the clinician to choose 1 that is primarily peptide-based with a large percentage as small peptides. Upon request, the formula manufacturer should provide the product's peptide profile. The clinician is responsible for gathering all the product information, reviewing the current literature, and translating it into a formulary that includes a range of products that meet the needs of the institution's population.

Are peptide-based formulas the nutraceuticals of enteral nutrition? You be the judge. ■

Evelyn M. Phillips, MS, RD, LDN, Clinical Nutrition Manager and Researcher at Magee Rehabilitation Hospital in Philadelphia, Pa, has been a clinical dietitian for 18 years. Nicole M. Short, MA, RD, LDN, has been a clinical dietitian at Magee for 4 years. Cheri Turner, RPH, MBA, has been the Director of Pharmacy at Magee for 4 years. Julianne Rece, RN, MSN, CRRN, CWOCN, Wound, Ostomy, Continence Clinical Nurse Specialist, has worked at Magee for 18 years.

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