Evidence-Based Nutritional Solutions for GI-Compromised Children

& the Health Economic Impact Surrounding Them.

When nutrition is overlooked, many hidden costs go unchecked. For example, among critically ill patients, up to 64% experience digestive intolerance.[1] This can delay patients from achieving feeding goals, which can lead to increased length of stay (LOS).[2] And moderate/severe diarrhea costs $2,559 per patient, on average.[3]

1. The Risks of Enteral Feeding Intolerance in Hospitalized Children:

Formula intolerance is a barrier to the delivery of energy and nutrients to critically ill children, and intolerance can prolong the hospitalization of enterally fed children, as more time is taken to achieve full feedings.[2] Improving feeding tolerance makes a difference: a higher percentage of intake of prescribed enteral nutrition is associated with reduced mortality and fewer infectious complications in critically ill children.[4]

A 2012 cohort study by Mehta et al. reviewed nutritional practices and their relationship to outcomes in critically ill children. The authors found that a number of barriers impede achieving full feeds in the PICU, including fluid restriction, feeding intolerance and interruption of feeds due to procedures.[4] The study demonstrated that failure to deliver prescribed energy goals was associated with a higher likelihood of mortality in this population, and the use of a protocol for initiating and advancing nutrition delivery was associated with decreased infectious complications. In this study, mean percentage of daily nutritional intake via enteral nutrition compared to prescribed goals was 38% for energy and 43% for protein.

THE FINDINGS OF MEHTA, ET AL ON NUTRITION IN THE PEDIATRIC ICU[4] ARE NOTABLE FOR:

- A high prevalence of malnutrition on admission;
- A striking inability to deliver the prescribed energy and protein; and
- A higher likelihood of mortality in malnourished children.

"Optimizing protein intake to prevent lean body mass depletion is one of the most important goals of nutrition therapy in the PICU."

Other Findings Related to Inadequacy of Feeding:

Inadequate nutrition intake is pervasive in the early days of hospitalization, and it impairs outcomes and increases healthcare costs.

Malnutrition in pediatric hospitals is widespread, with estimates ranging from 25% to 70% in critically ill children.[5]

A review by Kyle et al. found nutrition delivery in the PICU to be insufficient.[6] During the first 8 days of the PICU stay:

- Actual energy intake was only 75.7% of basal metabolic estimates.
- Only 40% of protein requirements were met.

Suboptimal nutritional intake has been shown to result in cumulative deficits in energy and protein, with anthropometric deterioration in single center reports.[7-9]

Contributors to malnutrition in critically ill children include:[4]

- Delayed initiation, under delivery, under prescription and lack of nutritional knowledge;
- Gastrointestinal intolerance;
- Frequent procedures that can lead to interruption of feedings; and
- Hemodynamic instability, a high criticality score and inflammatory states.

Impaired nutritional status is associated with:[10]

- Higher infection rates,
- Poor wound healing,
- Longer lengths of stay,
- A higher frequency of readmission, and
- Increased costs.

Protein needs are higher in critically ill children:

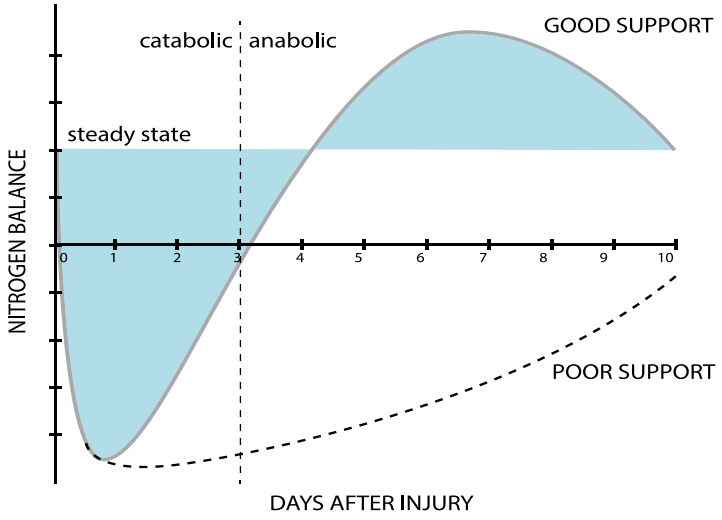


Figure 1: Metabolic response after trauma. Injury quickly leads to negative nitrogen balance. It is believed that the catabolic response cannot be averted, but that adequate nutrition permits faster recovery. Adapted from: Cook RC, Blinman TA. Nutritional support of the pediatric trauma patient. *Seminars in Pediatric Surgery* 2010;19:242-251.

The level of protein delivery required to enhance protein accretion is higher in critically ill children than in healthy children. The American Society for Parenteral and Enteral Nutrition's recommended protein requirements for injured children are 2 to 3 g/kg/day for children aged <2 years, 1.5 to 2 g/kg/day for those aged 2 to 13 years, and 1.5 g/kg/day for those aged 13 to 18 years. These recommendations are not based on results of clinical trials, however.

HEALTH ECONOMIC IMPACT

THE HIDDEN COSTS OF FEEDING INTOLERANCE

When nutrition gets overlooked, unnecessary costs go unchecked:

- ☐ *Up to 64% of critically ill patients experience GI intolerance, which can lead to discomfort, vomiting, or diarrhea.[1]*
- ☐ *Moderate/severe diarrhea costs $2,559 per patient, on average.[3]*
- ☐ *GI dysfunction may lead to inadequate absorption of nutrients, resulting in increased ICU LOS and mortality.[11]*

HEALTH ECONOMIC IMPACT

The right start for children:

- *Early feeding with a well-tolerated formula can help achieve feeding goals faster, which can reduce LOS.[12]*
- *In general, patients who spend fewer days in the ICU use fewer resources.[22]*

2. Improving Feeding Tolerance in a Critical Care Population:

The Role of a 100% Whey, Peptide-Based Diet in Promoting Achievement of Feeds in Pediatric Burn Patients

Burn injury poses significant nutritional challenges due to massive nitrogen losses, metabolic aberrations and the potential for multiple accompanying medical conditions. Children with burns have a considerable propensity for feeding intolerance.

In one institution, a retrospective chart review of enterally fed children with burn injuries exceeding 20% total body surface area revealed more rapid achievement of full feeds with enteral feedings of a whey-based peptide formula compared to casein-based intact protein formula.[12] Diarrhea was also reduced in the children receiving the whey-based peptide formula. The specific benefits in days to full feeds and reduced diarrhea days are presented in Table 1.

TABLE 1: More rapid achievement of goal feedings with a whey-based peptide formula in the pediatric burn ICU

A retrospective chart review of 17 pediatric burn patients who required enteral tube feeding. The mean total burn surface area was 45% (±17%).

RESULTS		
	Whey-based peptide formula	Casein-based intact protein formula
Days to Achieve Goal Feeding Rate	**8.3 ± 5.2**	**15.4 ± 12**
Incidence of Diarrhea (days)	**0.67 ± 1.2**	**2.6 ± 2.6**
Percent of Patients Requiring Formula Hold for High Gastric Residuals	**56%**	**88 %**

"Whey-based tube feeding offers many advantages for the pediatric burn population. Research in our own institution has shown that whey-based formulas improve gastric emptying and minimize reliance on PN in patients receiving nasogastric feedings."[13]

Although less clearly documented in pediatrics, several factors related to critical illness have been reported to be associated with gastric dysmotility and feeding intolerance in adult patients, including hyperglycemia, mechanical ventilation, sedatives, cytokine release and splanchnic hypoperfusion due to shock and sepsis. Delayed gastric emptying affects approximately 50% of mechanically ventilated patients and 80% of patients with increased cranial pressure following head injury.[14]

The right formula can make a difference in feeding tolerance associated with delayed gastric emptying. Several studies have found faster gastric emptying with the use of formulas containing hydrolyzed whey compared with formulas containing mostly casein.[12,15-18] In the acidic environment of the stomach, casein curdles, whereas whey remains liquid.

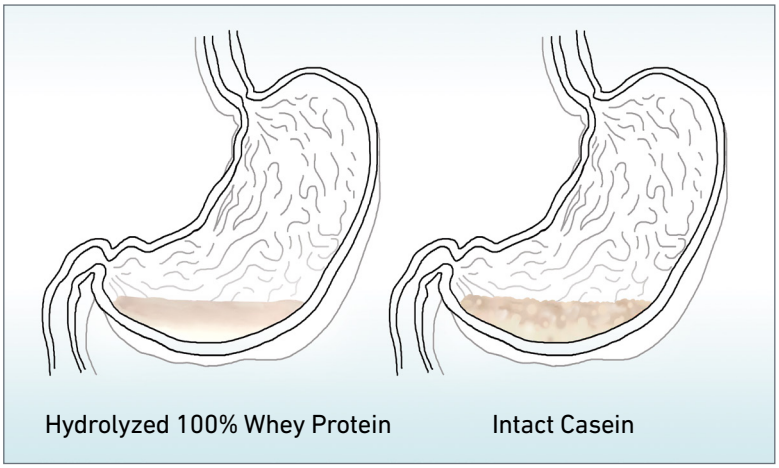


Figure 4: Hydrolyzed 100% whey protein compared to intact casein.

In the stomach, casein behaves like solids, which have a slower gastric-emptying time than liquids. In the small intestine, casein breaks down into beta-casomorphins, a form of opioid not produced after feeding hydrolyzed whey formulas. It has been postulated that these opioid peptides decrease gastrointestinal motility through direct interaction with gut opiate receptors.[19-20] Because children are already at risk for disordered gut motility after trauma (e.g., ileus, gastroparesis after TBI, etc.), using a whey-based enteral formula may improve tolerance.[21]

3. Evidence-Based Approaches to Preventing and Overcoming Feeding Intolerance:

Achieving and maintaining full enteral feedings is dependent upon many factors, including consistent feeding tolerance. Many patients are fed gastrically, even in cases where post-pyloric feeds may be indicated. Gastric emptying can be enhanced via appropriate positioning, prokinetic medications and appropriate formula selection. In some cases, isotonic, 100% whey, peptide-based diets may be advisable. Whey protein is unable to form a curd at gastric pH, which appears to contribute to its improved gastric emptying compared to casein.[18]

PROMOTE FEEDING TOLERANCE FROM THE START

1. Address the causes of the feeding intolerance with medical staff.
2. Consider the effects of analgesics and sedatives.
3. Consider using low long-chain fat, elemental or semi-elemental formulas.[23]

Figure 3: Improving nutrition therapy by achieving energy and protein goals may impact important clinical outcomes in critically ill children.[4]

USE OF FEEDING PROTOCOLS

A 2014 study by Hamilton et al. demonstrated that the implementation of an enteral nutrition algorithm significantly improved enteral nutrition delivery and decreased reliance on parenteral nutrition in critically ill children. In addition, the energy intake goal was reached earlier in a higher proportion of patients.[24]

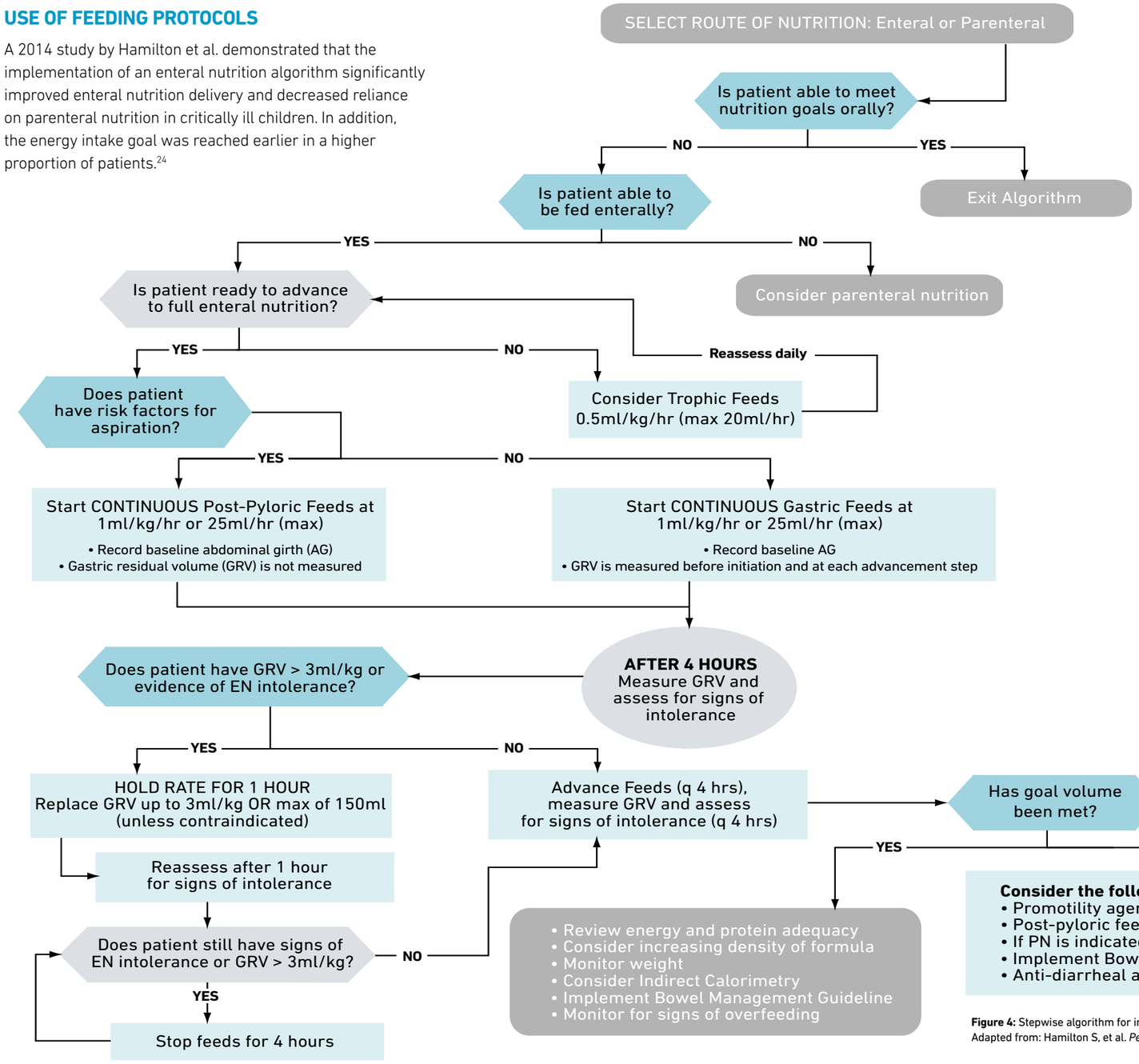


Figure 4: Stepwise algorithm for initiating and advancing enteral nutrition (EN) in the PICU. Adapted from: Hamilton S, et al. *Pediatr Crit Care Med* Sept 2014;15(7):583-589.

HEALTH ECONOMIC IMPACT

Formula intolerance can keep children in the ICU longer:

- *Early use of well-tolerated formulas may help children return home sooner and reduce the overall cost of care.*[22]
- *Fewer episodes of intolerance also allow nurses to attend to more critical tasks, thereby increasing staff efficiency.*[2,22]

4. Nutrition Challenges and Solutions in Chronically Ill Children

Feeding Intolerance is Common in Children with Serious Neurologic Impairment Who Require Enteral Feeding.

Children with severe cerebral palsy (CP) commonly have GI dysfunction. Gastroesophageal reflux, a frequent complication in patients with cerebral palsy, may result in undernutrition and aspiration pneumonia.[26] Delayed gastric emptying is an important factor in GE reflux in children older than three years, especially those with cerebral palsy.[26,27] The rate of gastric emptying associated with a formula is affected by the type of protein the formula contains: gastric emptying occurs more slowly in patients fed a casein-predominant formula than in those fed whey-based formulas.[16-18]

THE ROLE OF WHEY PROTEIN IN GASTRIC EMPTYING

A 2012 pilot study demonstrated that children who have severe cerebral palsy (CP), with a gastrostomy and fundoplication had significantly faster gastric emptying (GE) with whey-based enteral formulas (either 50% whey or 100% whey) compared to a casein predominant formula.[28] The results indicate that enteral formula selection may be particularly important for children with severe CP and delayed GE.

Median time to empty half of the gastric contents (GE t1/2) as a combined group was 40% faster with a whey-based formula (33.9 [25.3-166.2] min) compared to the casein-based formula (56.6 [46-191] min) (P = .033). Both of the whey-based formulas produced a similar acceleration in GE compared to the casein-based formula (see Figures 5 and 6).

In a prospective study looking at infants with reflux, Tolia et al. found a significantly longer gastric emptying time with casein-dominant formulas compared to whey-dominant formulas.[15] This has also been demonstrated in older children (ages 3-18 years) with spastic quadriplegia and severe developmental delays. When fed a whey-predominant, whey hydrolysate or whey hydrolysate with a high MCT content, a lower mean gastric residual content was demonstrated at 60 and 120 minutes post feeding.[18]

HEALTH ECONOMIC IMPACT

Demand for home care is strong:

- *Demand for in-home pediatric care is increasing.*[31]
- *Annual growth in home medical equipment is 8.2%.*[32-35]
- *It is a cost-effective alternative to inpatient care.*[32,36,37]
- *It is the preferred location for recovery.*[33]

Effects of a Whey-Based Formula on Gastric Emptying Time

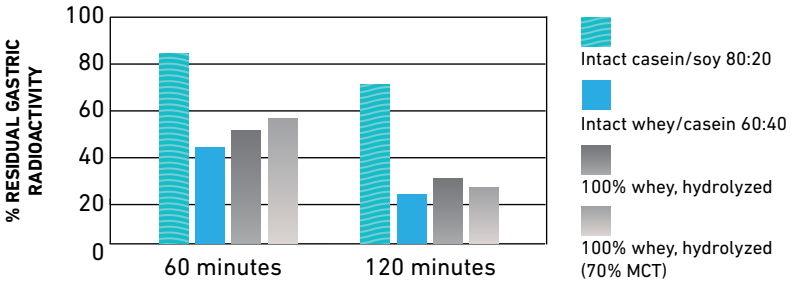


Figure 7: Effects of a whey-based formula on gastric emptying time over 60 minutes and 120 minutes.

Other studies have demonstrated a significant reduction in gagging, retching and emesis in children with neurological impairment with formulas containing at least 50% of the protein source as whey protein,[29,30] with one study demonstrating improved acceptance and tolerance of solid food that in some cases led to better weight gain.[30]

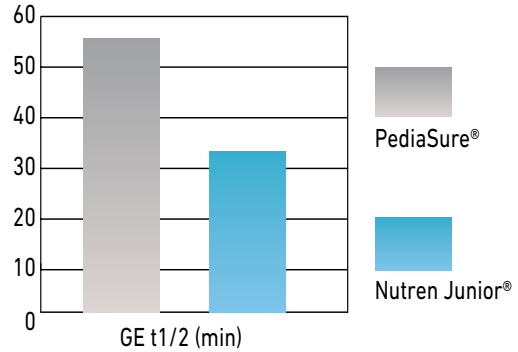


Figure 5: Median scores for gastric half emptying time (GE t1/2) in minutes for casein formula (PediaSure®) and 50% WWP (Nutren Junior®).

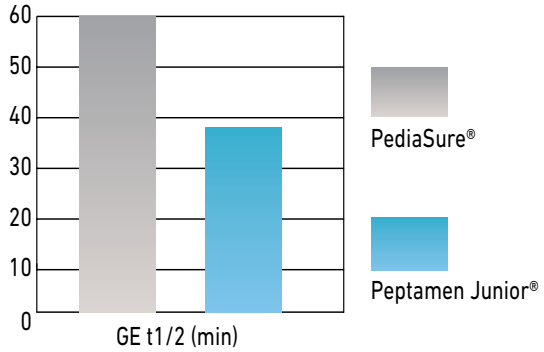


Figure 6: Median scores for gastric half emptying time (GE t1/2) in minutes for casein formula (PediaSure®) and 100% WPHP formula (Peptamen Junior®).

5. The Peptamen® Family of Formulas to Improve Feeding Tolerance and Achieve Goal Feeds Sooner

Delayed gastric emptying and dysmotility can be a barrier to feeding success in many chronic and acute diagnoses and conditions:

- **Critical illness**
- **Mechanically ventilated patients**
- **Traumatic brain injury**
- **Burn injury**
- **Trauma**
- **Neurological impairment/cerebral palsy**

THE PEPTAMEN® FAMILY OF FORMULAS PROVIDES:

1. 100% whey protein to facilitate gastric emptying.[18]
2. High-quality whey protein, as documented by five analytical markers:

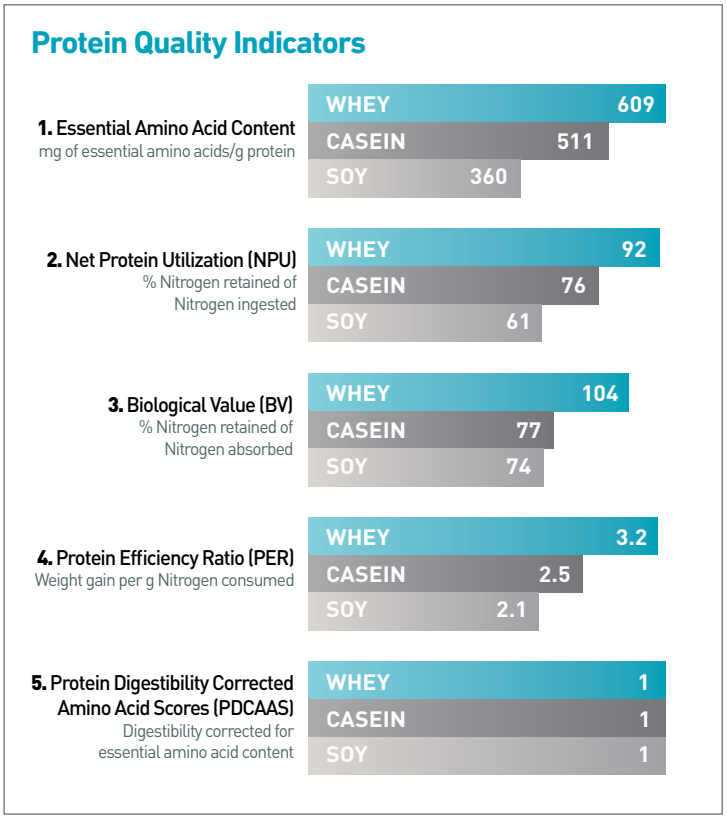


Figure 8: Nutritional quality of cow's milk and soy proteins used in infant formulas.

Reference Manual for US Whey and Lactose products. US Dairy Export Council June 2008. P. 14. http://usdec.files.cms-plus.com/PDFs/2008ReferenceManuals/Whey_Lactose_Reference_Manual_Complete2_Optimized.pdf. Accessed June 2012.

FAO/WHO ad hoc Committee of Experts on Energy and Protein: Requirements and Recommended Intakes. http://www.fao.org/docrep/010/ai407e/AI407E28.htm. Accessed June 2012.

3. A protein source that is enzymatically hydrolyzed:

- Hydrolysis of protein results in fewer protein bonds for the compromised GI tract to break down.
- Intact casein has a median molecular weight (MMW) of more than 10 times that of partially hydrolyzed whey.

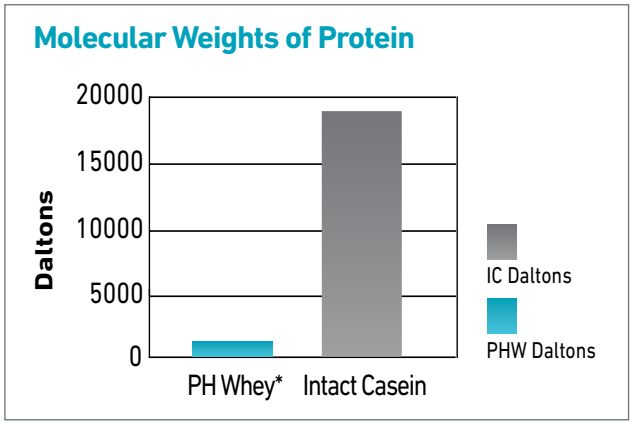


Figure 9: Approximate median molecular weight of partially hydrolyzed whey vs intact casein.[25]
*Average size of the peptides in Peptamen Junior® as determined by analysis of multiple lots.

Feeding challenges in critically and chronically ill children can include delayed gastric emptying, vomiting, diarrhea, retching and gagging. All of these challenges may lead to delay in reaching feeding goals and result in children not getting the nutrition they need. The Peptamen® family of formulas has been shown to address such feeding challenges.

THE PEPTAMEN® SOLUTION:

FEEDING CHALLENGES	PEPTAMEN® FAMILY OF FORMULAS AS A SOLUTION
Delayed Gastric Emptying	Whey protein demonstrates faster gastric emptying than casein[16-18,28]
Feeding Intolerance	Shown to be associated with improvement in diarrhea in pediatric burn patients[12] and vomiting in children with CP with documented delayed gastric emptying[18] Using a whey-based enteral formula may improve tolerance in pediatric trauma patients[21]
Achievement of Goal Feedings	More rapid achievement of goal feedings with a whey-based peptide formula in pediatric burn ICU[12]

The PEPTAMEN JUNIOR® family offers a variety of solutions for patients with GI dysfunction.

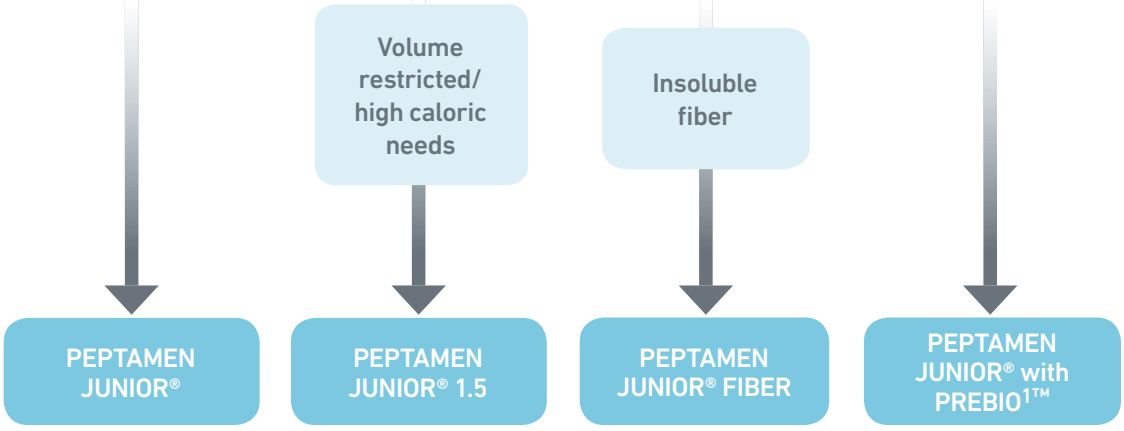
Complete peptide-based nutrition with MCT for:

Impaired GI function, which may result from:

- Short bowel syndrome
- Cerebral palsy
- Cystic fibrosis
- Crohn's disease

Malabsorption
Chronic diarrhea
Delayed gastric emptying
Growth failure
Early enteral feeding
Transition from or dual feeding with TPN

PREBIO1™ soluble fiber to help promote the growth of beneficial bacteria to support digestive health



USE UNDER MEDICAL SUPERVISION
www.NestleHealthScience.us • 1-800-422-ASK2 (2752)

NestléHealthScience

PPTJ-13252-0315

References:

1. Montejo JC, et al. Gastric residual volume during enteral nutrition in ICU patients: The REGANE study. *Intensive Care Med* 2010;36(8):1386–1393. **2.** Taha AA, et al. Effect of early nutritional support on intensive care unit length of stay and neurological status at discharge in children with severe traumatic brain injury. *J Neurosci Nurs* 2011;43(6):291–297. **3.** Dranitsaris G, et al. Estimating the cost of illness in colorectal cancer patients who were hospitalized for severe chemotherapy-induced diarrhea. *Support Care Cancer* 2005;13:318-324. **4.** Mehta NM, et al. Nutritional practices and their relationship to clinical outcomes in critically ill children — An international multicenter cohort study. *Crit Care Med* 2012;40(7):2204–2211. **5.** Prieto MB, et al. Malnutrition in the critically ill child: The importance of enteral nutrition. *Int J Environ Res Public Health* 2011;8:4353–4366. **6.** Kyle UG, et al. Nutrition support in critically ill children: Under delivery of energy and protein compared with current recommendations. *Journal of the Academy of Nutrition and Dietetics* 2012;112(12):1987–1992. **7.** Mehta NM, et al. Cumulative energy imbalance in the pediatric intensive care unit: Role of targeted indirect calorimetry. *JPEN J Parenter Enteral Nutr* 2009;33:336–344. **8.** Hulst JM, et al. The effect of cumulative energy and protein deficiency on anthropometric parameters in a pediatric ICU population. *Clin Nutr* Dec 2004;23(6): 1381–1389. **9.** Mehta NM, et al. Severe weight loss and hypermetabolic paroxysmal dysautonomia following hypoxic ischemic brain injury:the role of indirect calorimetry in the intensive care unit. *JPEN J Parenter Enteral Nutr* 2008;32(3):281–284. **10.** Corkins MR, et al. Malnutrition diagnoses in hospitalized patients: United States, 2010. *JPEN J Parenter Enteral Nutr* 2014;38(2):186–195. **11.** Mentec H, et al. Upper digestive intolerance during enteral nutrition in critically ill patients: Frequency, risk factors and complications. *Crit Care Med* 2001;29(10): 1955–1961. **12.** Dylewski ML, et al. Whey-based formulas improve tube feeding tolerance in pediatric burn patients. *Nutrition Poster 72; ASPEN Clinical Nutrition Week* 2006. **13.** Prelack K, et al. Nutrition support in the pediatric burn patient. *Support Line* Dec 2013;35(6): 3–13. **14.** Ukleja A. Altered GI motility in critically ill patients: Current understanding of pathophysiology, clinical impact and diagnostic approach. *Nutr Clin Pract.* 2010; 25(1):16–25. **15.** Tolia V, et al. Gastric emptying using three different formulas in infants with gastroesophageal reflux. *J Pediatr Gastroenterol Nutr* 1992;15(3):297–301.**16.** Billeaud C, et al. Gastric emptying in infants with or without gastroesophageal reflux according to the type of milk. *Eur J Clin Nutr* 1990;44(8): 577–583. **17.** Fried M & Feinle C. The role of fat and cholecystokinin in functional dyspepsia. *Gut* 2002;51:154–157(suppl 1). **18.** Fried MD, et al. Decrease in gastric emptying time and episodes of regurgitation in children with spastic quadriplegia fed a whey-based formula. *J Pediatr* 1992;120(4):569–572. **19.** Daniel H, et al. Effect of casein and B-casomorphins on gastrointestinal motility in rats. *J Nutr* 1990;120: 252–257. **20.** Sturner RA & Chang KJ. Opiod peptide content of predigested infant formulas. *Pediatr Res* 1991;29:A670. **21.** Cook RC & Blinman TA. Nutritional support of the pediatric trauma patient. *Seminars in Pediatric Surgery* 2010;19:242–251. **22.** Arabi Y, et al. A prospective study of prolonged stay in the intensive care unit: Predictors and impact on resource utilization. *Inj J Qual Health Care* 2002;14:403–410. **23.** Tempest M. Enteral nutrition intolerance in critical illness. *Today's Dietitian* Feb 2011;13(2):30. **24.** Hamilton S, et al. A stepwise enteral nutrition algorithm for critically ill children helps achieve nutrient delivery goals. *Pediatr Crit Care Med* Sept 2014;15(7): 583–589. **25.** Data on file. Nestlé Nutrition. **26.** Sondheimer JM & Morris BA. Gastroesophageal reflux among severely retarded children. *The Journal of Pediatrics* 1979;94(5):710-714. **27.** Di Lorenzo C, et al. Gastric emptying with gastroesophageal reflux. *Arch Dis Child* 1987;62: 449-453. **28.** Savage K, et al. Whey- vs casein-based enteral formula and gastrointestinal function in children with cerebral palsy. *JPEN J Parenter Enteral Nutr* 2012;36:118S.26. **29.** Graham-Parker C, et al. Effect of whey-based diet on incidence of vomiting in G-tube fed children with severe neurodevelopmental delay. *JPEN J Parenter Enteral Nutr* 2001;25:S14(0051). **30.** Barsky DL. Whey-based pediatric enteral formula can improve food acceptance for children with feeding difficulties. *NCP* 2002;17:51(N7). **31.** www.homecaremag.com/news/market-research-forecasts-strong-demand-hme. **32.** Elias ER, et al. Home care of children and youth with complex health care needs and technology dependencies. *Pediatrics* 2012;129:996–1005. **33.** Committee on child health financing. *Pediatrics* 2006;118:834–838. **34.** Perrin JM. Health services research for children with disabilities. *Milbank Q* 2002;80(2):303–324. **35.** Simon TO, et al. Children with complex chronic conditions in inpatient hospital settings in the United States. *Pediatrics* 2010;126(4):647–655. **36.** Close P, et al. A prospective, controlled evaluation of home chemotherapy for children with cancer. *Pediatrics* 1995;95(6):896–900. **37.** Fields A, et al. Home care cost effectiveness for respiratory technology-dependent children. *Am J Dis Child* 1991;145(7):727–728.