



# Peptide-Based Therapeutic Nutrition for People with Gastrointestinal Dysfunction



**TOLERANCE  
IS VITAL**



# Objectives

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- ✓ Discuss the consequences of malnutrition and how nutrition intervention can improve patient outcomes
  - ✓ Understand the causes and symptoms of GI intolerance
  - ✓ Describe the current expert guidelines for using peptide-based formulations
  - ✓ Discuss components of enteral nutrition formulas that promote GI tolerance and improve patient outcomes
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# Definition of Malnutrition

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**Malnutrition risk results from inadequate intake of nutrients, as with:**

- ❖ Inadequate intake for day-to-day needs
- ❖ Not enough intake to compensate for malabsorption
- ❖ Intake shortfall relative to excessive nutrient losses
- ❖ Intake insufficient for elevated needs due to illness or injury

**Malnutrition exists when body reserves of macro- and micronutrients become depleted**

**Malnutrition has measurable adverse effects on the body's form and function, and on clinical outcomes.**

# Causes of Malnutrition

## Altered nutrient processing

- Increased or altered metabolic demands, as with infection, surgery, or burns

## Inadequate intake

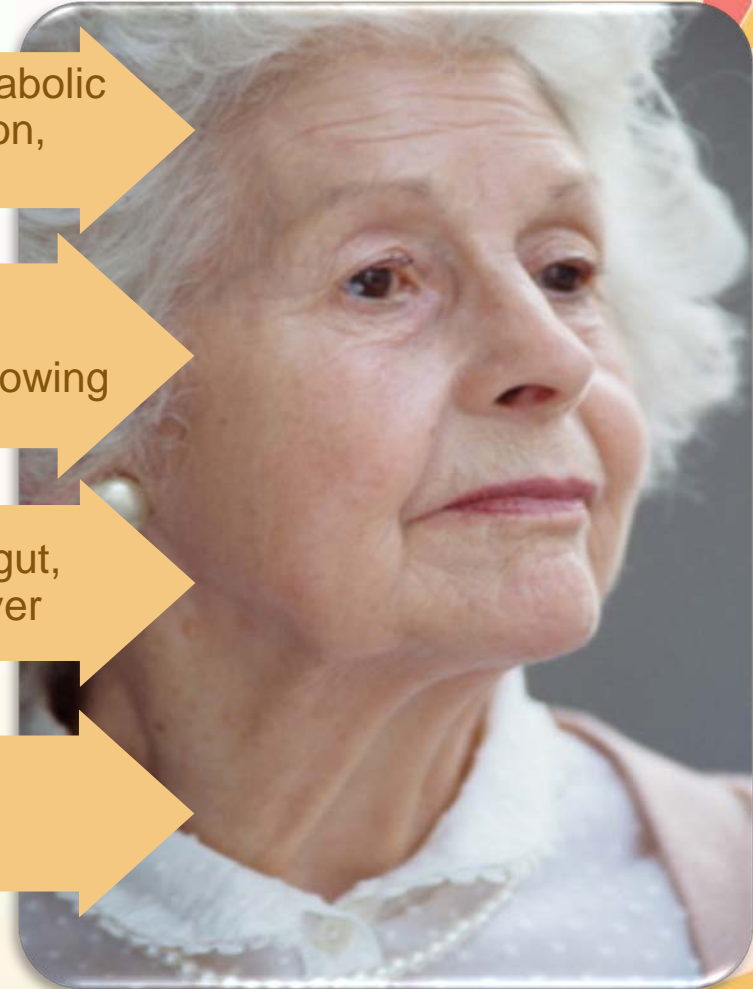
- Poor diet
- Poor appetite
- Problems chewing, swallowing
- Depression

## Malabsorption

- Pathologic conditions in gut, intestine, pancreas, or liver

## Excess loss

- Vomiting
- Diarrhea
- Fistulae



# Malnutrition: Scope of The Problem

## Prevalent across all healthcare settings

Healthcare Setting	Prevalence
Hospital	30-50% <sup>1-4</sup>
Long-term care	21%-51% <sup>5</sup>
Outpatient & Homecare	13-30% <sup>5</sup>

### Risk of malnutrition is increased in<sup>6</sup>:

- ❖ Older adults
- ❖ Critically ill patients
- ❖ Patients with comorbid chronic diseases, e.g., cancer, COPD, chronic kidney disease



1. Coats KG, et al. *J Am Diet Assoc.*1993;93:27-33. 2. Giner M, et al. *Nutrition.*1996;12:23-29. 3. Thomas DR, et al. *Am J Clin Nutr.* 2002; 75:308-313. 4. Somanchi M, et al. *JPEN. J Parenter Enteral Nutr.* 2011;35:209-216. 5. Guigoz Y. *J Nutr Health Aging.* 2006;10:466-487. 6. Jensen GL, et al. *JPEN J Parenter Enteral Nutr.* 2010;34:156-159.



# Malnutrition Negatively Impacts Patient Outcomes



Adapted from Norman K et al. *Clin Nutr.* 2008; 27: 5-15.  
Allaudeen N, et al. *J Hosp Med.* 2011;6(2):54-60.

# Nutrition Therapy is Critical to Improving Outcomes

**Consider enrichment of diet, e.g. with maltodextrin, protein**

**Add oral nutrition supplements**

**Use supportive enteral tube feeding as standard or specialty formula**

**Use parenteral tube feeding; consider combination enteral + parenteral**

# Study Showed ONS Provided During Hospitalization Was Associated With Decreased Costs<sup>1</sup>

**21%**  
decrease  
in length of stay  
(LOS)

**21.6%**  
decrease  
in episode cost

**ONS provided during hospitalization was associated with a reduced probability of 30-day re-admissions for patients with at least one known follow-up<sup>1</sup>**

**6.7%\***  
decrease  
in hospital  
readmissions

\*Re-admission defined as return to study hospital for any diagnosis. Data measured delayed readmission and do not include patients not readmitted due to recovery or death.

1. Philipson T, et al. *Am J Manag Care*. 2013;19(2):121-128.



# Oral Nutritional Supplements Can Improve Patient Outcomes and Decrease Re-admissions

**A study in 445 acutely ill hospitalized patients demonstrated that oral nutritional supplementation for 6 weeks:**

- ❖ Improves nutritional status
- ❖ Reduces the number of non-elective re-admissions at 6 months post discharge (29% in the supplement group compared to 40% in the control group)<sup>1</sup>

**In a 3-month randomized, controlled, post-hospital nutritional supplement study in 80 malnourished patients with nonneoplastic GI disease:**

- ❖ 10 patients in the supplement group were re-admitted during the study period compared to 20 in the control group ( $P = 0.041$ )<sup>2</sup>

1. Gariballa S, et al. *Am J Med.* Aug 2006;119(8):693-699. 2. Norman K, et al. *Clin Nutr.* Feb 2008;27(1):48-56.



# Importance of Feeding The Gut

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## Enteral feeding is associated with<sup>1</sup>:

- ❖ Less gut permeability
- ❖ Lower release and activation of inflammatory cytokines

## Can help maintain GI function

## Can help reduce infection and other complications by maintaining:

- ❖ Intestinal integrity
- ❖ Gut barrier function
- ❖ Systemic Immune response: Support gut immune cells to maintain immune surveillance for recognition and elimination of pathogenic bacteria and viruses<sup>1</sup>
  - ❖ The gut is the site where external pathogens can gain access to the body
  - ❖ Lymphoid cells are responsible for recognizing foreign pathogens
  - ❖ Gut-associated lymphoid tissue (GALT) requires nutrition to maintain integrity

1. Erickson KL, Hubbard NE. *Nutr Rev*, 2009; 67 Suppl 2:S172-82.

# Specialty Oral and Enteral Nutrition Formulas

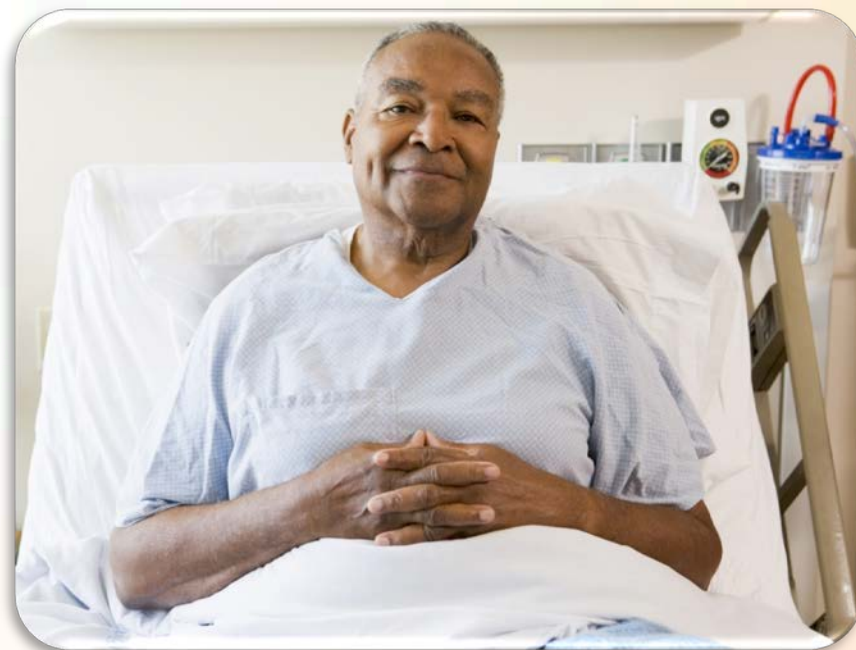
Specialty formulation	Special nutritional needs
Calorically-dense for malnourished or volume-sensitive patients	High energy and/or high protein
Diabetes	Ingredients that help minimize post-meal glucose rise
Chronic kidney disease pre-dialysis	Low protein, low phosphorus
Chronic kidney disease with dialysis	High protein, low phosphorus
Pulmonary disease	Low carbohydrate
Cancer	High protein, anti-inflammatory, and antioxidant ingredients
Malabsorption due to GI disease, feeding intolerance	Peptide-based, medium-chain triglycerides

# Indications for Peptide-based Feeding in Patients With Feeding Intolerance

**Parenteral-to-enteral transition**

**Trophic Feeding**

**Dual-feeding with parenteral and enteral nutrition**





# What Happens When Normal Nutrient Digestion and Absorption Becomes Impaired?

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**Malabsorption:** impaired absorption of macro- and/or micronutrients from the gastrointestinal (GI) tract due to pathological interference with the normal physiological sequence of digestion, absorption, and transport of nutrients

**Maldigestion:** incomplete digestion of food due to impaired secretion or absence of digestive enzymes

**Feeding intolerance:** symptoms of maldigestion and/or malabsorption, intolerance to standard enteral nutrition



# What is Gastrointestinal Dysfunction?

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Any disturbance of GI motility, digestion, or absorption that can affect the delivery of nutrients to the intestinal cells and, in turn, to all body tissues.



# GI intolerance: Symptoms and Consequences<sup>1-8</sup>

Diarrhea

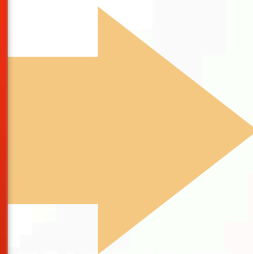
Nausea/Vomiting

Abdominal Pain or Cramping

Bloating/Distension

Delayed Gastric Emptying

Elevated Gastric Residuals



Delay in achieving caloric  
and nutrient goals

Risk of malnutrition

Longer ICU stay

Increased mortality risk

1. McClave SA, et al. *JPEN J Parenter Enteral Nutr.* 2009;33:277-316. 2. Monteio JC, et al. *Intensive Care Med.* 2010;36:1386-1393. 3. Reintam A, et al. *Acta Anaesthesiol Scand.* 2009;53:318-324. 4. Williams MS, et al. *Nutr Clin Pract.* 1998;13:225-227. 5. Chan LN. *Nutr Clin Pract.* 2010;25:10-12. 6. Btaiche IF, et al. *Nutr Clin Pract.* 2010;25:32-49. 7. Fraser RJ, et al. *Nutr Clin Pract.* 2010;25:26-31. 8. Mentec H, et al. *Crit Care Med.* 2001;29:1955-1961.

# Acute and Chronic GI Conditions

Acute GI Dysfunction	Diseases
<ul style="list-style-type: none"><li>• Maldigestion, malabsorption</li><li>• Other situations, based on clinical judgment</li><li>• Critical illness</li><li>• Trauma</li><li>• Burns</li><li>• Sepsis</li><li>• Post-transplant surgery</li><li>• Post-gastric surgery</li></ul>	<ul style="list-style-type: none"><li>• Maldigestion, malabsorption</li><li>• Other situations, based on clinical judgment</li><li>• Pancreatitis (acute or chronic)</li><li>• Pancreatic insufficiency</li><li>• Cystic fibrosis</li><li>• Crohn's disease</li><li>• Ulcerative colitis</li><li>• Short bowel syndrome</li><li>• HIV/AIDS-associated enteropathy</li><li>• Celiac disease</li><li>• Gastritis, duodenitis, enterocolitis</li><li>• Dumping syndrome</li><li>• GI fistulas</li></ul>

# Other Causes of GI and Feeding Intolerance

Medication	Nutrition
<ul style="list-style-type: none"><li>• Laxatives</li><li>• Antibiotics</li><li>• Non-steroidal anti-inflammatory drugs</li><li>• Proton pump inhibitors</li><li>• Antiarrhythmics</li><li>• Antihypertensives</li><li>• Drugs containing magnesium and sorbitol fillers</li></ul>	<ul style="list-style-type: none"><li>• Type of feed</li><li>• Feeding rate</li><li>• Feeding volume</li><li>• Feeding route</li></ul>

Stroud M, et al. *Gut*. 2003 Dec;52 Suppl 7:vii1-vii12.

Young NL, et al. *Arch Phys Med Rehabil*. 2011 Jan;92(1):46-50.

Collins C et al. Managing malabsorption and poor feed tolerance in adults: a practical guide. September 2012.

Accessed 6 September 2012.

Available at <http://www.abbottnutrition.co.uk/support-and-tools/articles/managing-malabsorption-and-poor-feed-tolerance-adults-practical-guide>

# High Prevalence of Feeding Intolerance Calls for Specialized Formula

64% of critically ill patients may experience GI intolerance<sup>1-5</sup>

Up to 60% of enterally fed patients experience diarrhea

(Bowling TE. *Frontline Gastroenterol.* 2010;1:140–143.)

On average 20% of patients are switched to peptide-based feeds due to intolerance of standard feeds\* (Abbott Nutrition, Data on File, 2010)

1. Reintam A, et al. *Acta Anaesthesiol Scand.* 2009;53:318-24. 2. McClave SA, et al. *JPEN J Parenter Enteral Nutr.* May-Jun 2009;33(3):277-316. 3. Mentec H, et al. *Crit Care Med.* Oct 2001;29(10):1955-1961. 4. Montejo JC, et al. *Care Med.* Aug 2010;36(8):1386-1393. 5. Mythen MG. *Cleve Clin J Med.* Nov 2009;76 Suppl 4:S66-71. \*Market research with 15 dietitians from across the UK

# Nutrition Management Goals

**Reduce symptoms of feeding intolerance**

- ❖ Switch to a peptide-based feed

**Support absorption and improve tolerance**

**Improve nutritional intake**

**Improve nutritional status**



# Critical Care Nutrition Guidelines on Peptide-based Formulas

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## Peptide-based feedings: indicated for certain feeding-intolerant patients

- ❖ Patients experiencing diarrhea
- ❖ Patients with pancreatitis
- ❖ Patients who are intolerant to polymeric formula, e.g., patients with Crohn's disease

1. Meier R, et al. *Clin Nutr.* 2006;25:275-284. 2. Mirtallo JM, Forbes A, McClave SA, et al. *JPEN J Parenter Enteral Nutr.* 2012;36(3):284-291. 3. McClave SA, et al. *JPEN J Parenter Enteral Nutr.* 2009;33(3):277-316. 4. [http://www.criticalcarenutrition.com/index.php?option=com\\_content&view=category&layout=blog&id=21&Itemid=10](http://www.criticalcarenutrition.com/index.php?option=com_content&view=category&layout=blog&id=21&Itemid=10)



# Enteral Nutrition Guidelines for Acute Pancreatitis

**ESPEN: Acute pancreatitis:** Peptide-based formulae can be used safely (Grade A) <sup>1</sup>

**International Consensus Guidelines for Nutrition Therapy in Pancreatitis:** For EN, consider a small peptide-based medium-chain triglyceride (MCT) oil formula to improve tolerance (Grade B: Gold)<sup>2</sup>

**SCCM/A.S.P.E.N. K4.** Tolerance to EN in patients with severe acute pancreatitis may be enhanced by... changing the content of the EN delivered from intact protein to small peptides, and long-chain fatty acids to medium-chain triglycerides or a nearly fat-free elemental formulation (Grade: E)<sup>3</sup>

ESPEN=The European Society for Clinical Nutrition and Metabolism

SCCM/A.S.P.E.N.=Society of Critical Care Medicine /American Society for Parenteral and Enteral Nutrition

1. Meier R, et al. *Clin Nutr.* 2006;25:275-284.

2. Mirtallo JM, Forbes A, McClave SA, et al. *JPEN J Parenter Enteral Nutr.* 2012;36(3):284-291.

3. McClave SA, et al. *JPEN J Parenter Enteral Nutr.* 2009;33(3):277-316.

# Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)<sup>1</sup>

- E4.** If there is evidence of diarrhea, soluble fiber-containing or **small peptide** formulations may be utilized (Grade: E)



1. McClave SA, et al. *JPEN J Parenter Enteral Nutr.* 2009;33(3):277-316.



# Canadian Clinical Practice Guidelines

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## 4.3 Strategies for optimizing and minimizing risks of EN: Whole Protein vs. Peptides

- Patients with GI complications, (short bowel syndrome, pancreatitis, etc.) may benefit from peptide-based formulas
- Peptide-based formulas may be considered for their other components i.e., fat content, MCT, glutamine composition, etc.



# The Vital Difference

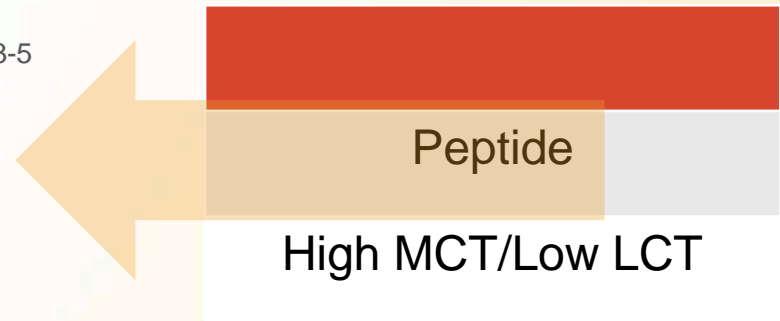
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<b>Nutrient</b>	<b>Standard Formula</b>	<b>Peptide based Formula</b>
Protein	Intact	Peptide
Fat Blend	Low MCT/High LCT	High MCT/Low LCT

# The Vital Difference – Peptide-based Protein

Compared with free amino acids or intact protein, peptide-based proteins have been shown to promote:

- ❖ Enhanced absorption<sup>1-4</sup>
- ❖ Nitrogen absorption, retention, and utilization<sup>3-5</sup>
- ❖ Better maintenance of GI tract integrity<sup>5</sup>
- ❖ Better tolerance<sup>6,7</sup>

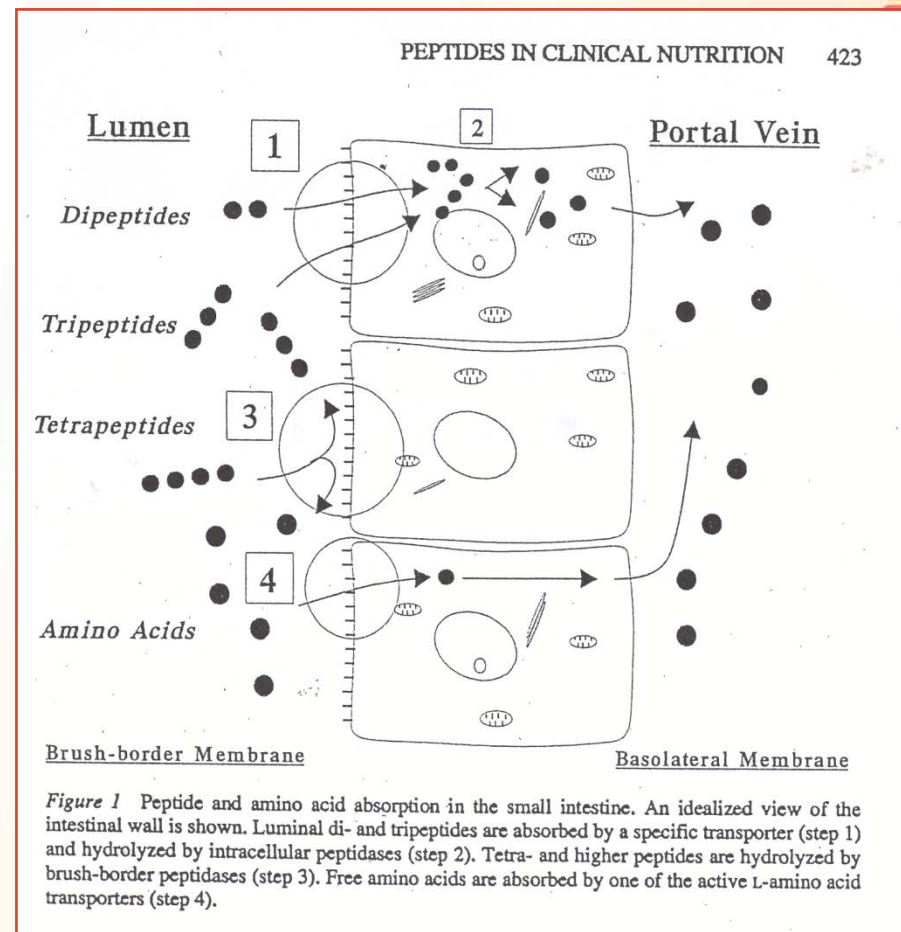


1. Silk DB, et al. *JPEN J Parenter Enteral Nutr.* 1980 Nov-Dec;4(6):548-53.
2. Fairclough PD, et al. *Gut.* 1980;21:829-834.
3. Grimble GK, et al. *Clin Sci.* 1986 Jul;71(1):65-9.
4. Ziegler F, et al. *Gut.* 1990;31:1277-1283.
5. Zaloga GP. Intact proteins, peptides, and amino acid formulas. In: Zaloga GP, ed. *Nutrition In Critical Care.* St Louis: Mosby;1994:59-80.
6. Brinson RR, et al. *Crit Care Med.* 1987;5:506-609.
7. Brinson RR, et al. *Crit Care Med.* 1988;16:130-136.

# Dual Protein Transport System

## Digested protein absorbed via dual-protein carrier system in small intestine

- ❖ Two separate, independent, noncompeting transport systems
- ❖ Dipeptides and tripeptides
- ❖ Free amino acids
- ❖ **Peptides absorbed more rapidly and uniformly than free amino acids<sup>1</sup>**



1. Silk DB, Fairclough PD, Clark ML, et al. Use of a peptide rather than free amino acid nitrogen source in chemically defined "elemental" diets. *JPEN J Parenter Enteral Nutr.* 1980;4(6):548-553.

Source: Grimble GK. The significance of peptides in clinical nutrition. *Annu Rev Nutr.* 1994;14:419-447.

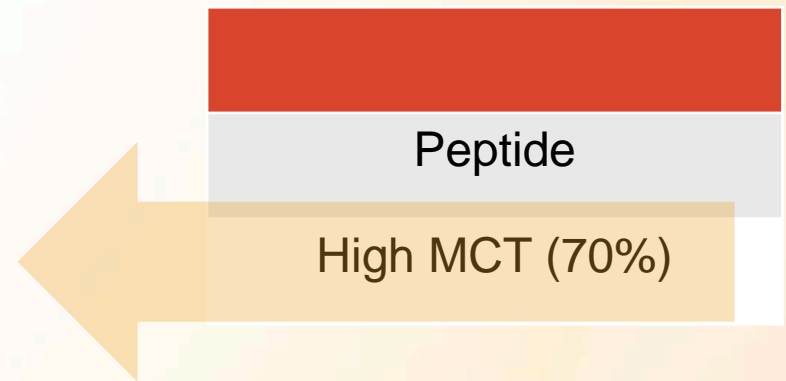
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# The Vital Difference – Fat

## Compared with LCTs, MCTs are:

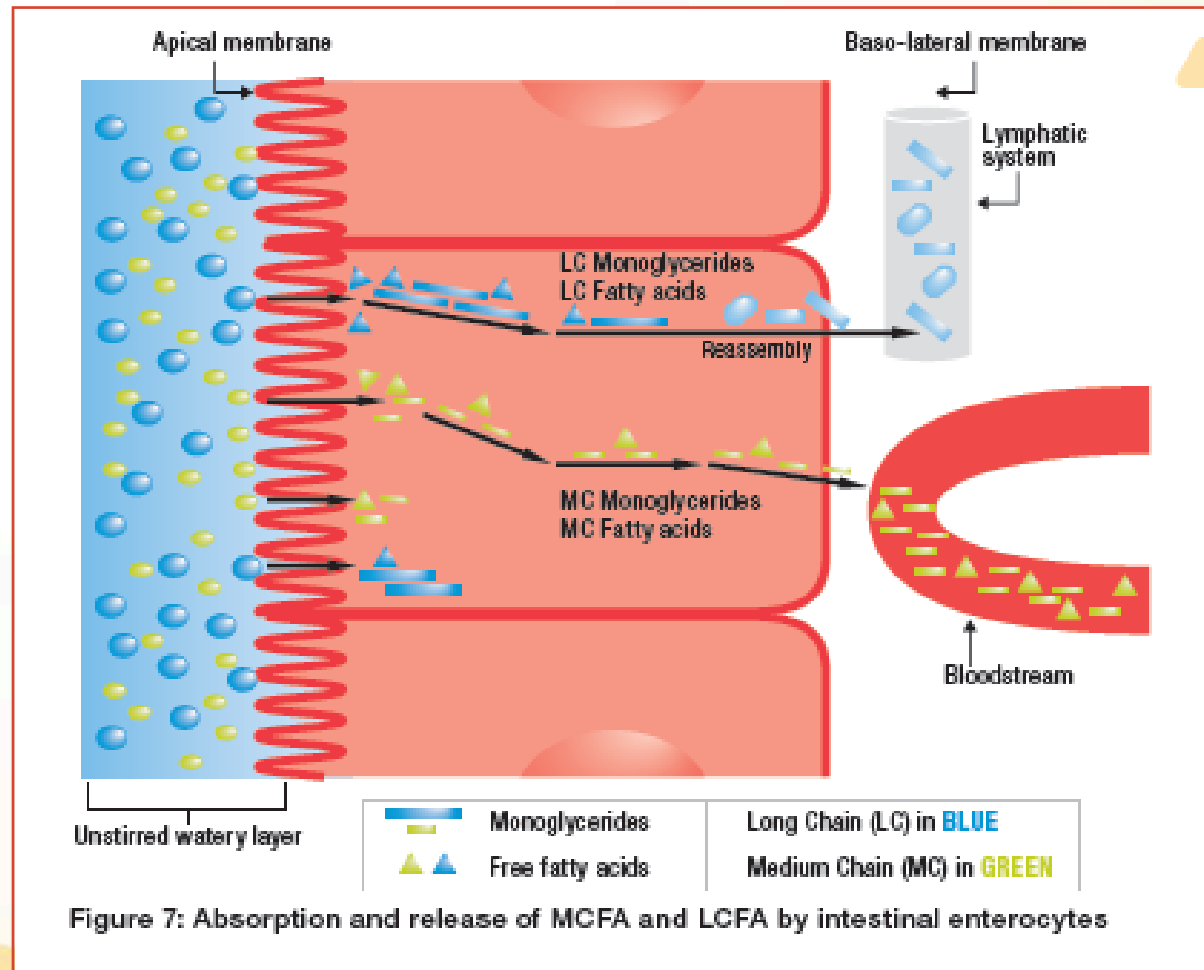
- ❖ Small enough to be water-soluble, with little or no bile salt or pancreatic lipase
- ❖ Quickly absorbed by intestines, metabolized by liver<sup>1,2</sup>
- ❖ Contribute readily available energy<sup>1,2</sup>



1. Bach AC, et al. *Am J Clin Nutr.* 1982;36:950-962.

2. Bach AC, et al. *Clin Nutr.* 1989;8:223-235.

# Fat Digestion and Absorption



Borum PR. The Science and Practice of Nutrition Support. A Case-Based Core Curriculum. Silver Spring, MD, A.S.P.E.N. 2001 pp 17-30.

# Clinical Support

**Peptide-based formulas improve feeding intolerance in patients with:**

- ❖ Severe hypoalbuminemia
- ❖ Acute pancreatitis
- ❖ Crohn's disease
- ❖ Human immunodeficiency virus (HIV disease)





# Hypoalbuminemia

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**Hypoalbuminemia is low serum albumin levels**

**Causes may include:**

- ❖ Poor nutritional state
- ❖ Increased excretion due to:
  - ❖ Kidney dysfunction
  - ❖ Liver disease
  - ❖ Heart conditions
  - ❖ Inflammatory bowel disease
  - ❖ Cancer
  - ❖ Associated GI Symptoms can include diarrhea

# Peptide-based Formulas Improve GI Tolerance in Patients with Severe Hypoalbuminemia

## Objective

Evaluate incidence of diarrhea in medical or surgical ICU patients with hypoalbuminemia randomized to peptide-based or standard enteral nutrition formula

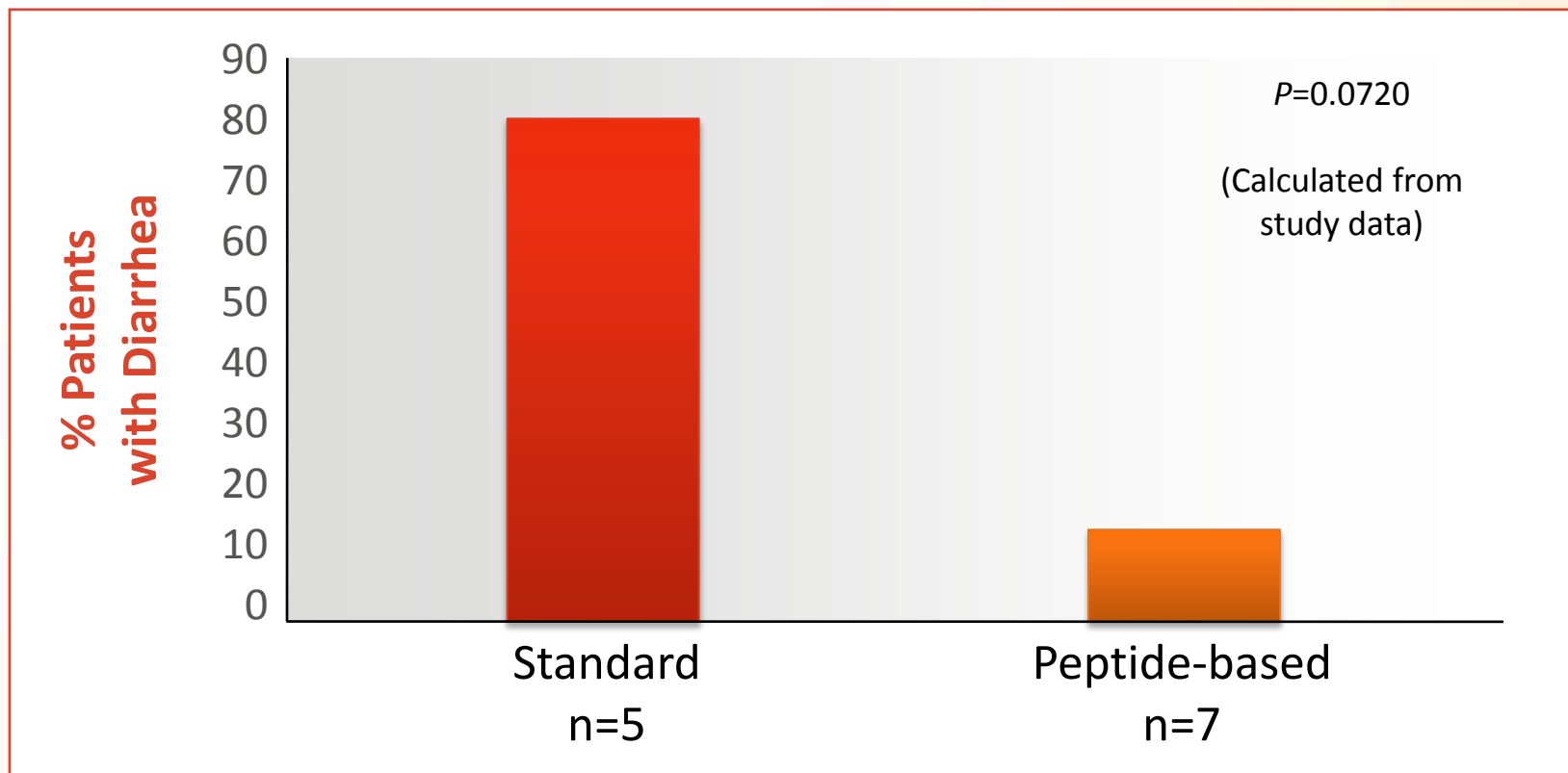
## Subjects

12 patients with hypoalbuminemia ( $< 2.5$  g/dL)

## Design

- ❖ Randomized, prospective study
- ❖ 7 patients received a peptide-based formula
- ❖ 5 patients received a standard isotonic formula (control)
- ❖ Patients were followed for at least 2 weeks or until serum albumin reached 3 g/dL

# Peptide-based Formulas Improve GI Tolerance in Patients with Severe Hypoalbuminemia



**Although not a marker of nutritional status during metabolic stress, a low albumin may be an indication of potential GI intolerance issues**

Brinson RR, Kolts BE. *Crit Care Med.* 1988;16:130-136.





# Acute Pancreatitis

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**Acute pancreatitis refers to acute inflammation of the pancreas causing sudden and severe abdominal pain**

**The most common symptoms and signs include:**

- ❖ Severe upper abdominal pain radiating to the back
- ❖ Nausea
- ❖ Vomiting
- ❖ Diarrhea
- ❖ Loss of appetite

# Peptide-based Formulas Improve Clinical Outcomes in Patients with Acute Pancreatitis (As Compared to Polymeric Formulas)

A peptide-based formula improved clinical outcomes in patients with acute pancreatitis compared to polymeric formula<sup>1</sup>

## Clinical Course After 7 Days Of Enteral Nutrition

Study	peptide based	polymeric	P value
Weight loss (D7-D0) (kg)	-1.3 ± 1.1	-2.4 ± 0.0	0.01
Total hospital stay (days)	23 ± 2	27 ± 1	0.006
Infection (n, %)	1/15 (6)	3/15 (20)	NS

Difference in values between day 7 (D7) and day 0 (D0)  
1. Tiengou LE, et al. *JPEN J Parenter Enteral Nutr.* 2006;30:1-5.



# Crohn's Disease

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**Crohn's disease is a type of inflammatory bowel disease that results in chronic, episodic, inflammation that can affect any part of the gastrointestinal tract from mouth to anus.**

Symptoms may include:

- ❖ Abdominal pain
- ❖ Diarrhea
- ❖ Weight loss
- ❖ Anorexia
- ❖ Nausea

# Peptide-based Formulas Improve Clinical Outcomes in Patients with Crohn's Disease

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## Objective

To evaluate the affect on nutritional status, disease activity, and intestinal permeability of a peptide-based diet compared to steroid treatment in patients with Crohn's disease

## Subjects

20 patients with Crohn's disease

- ❖ 10 received oral peptide-based diet
- ❖ 10 received corticosteroids and normal diet

## Design

- ❖ Prospective, randomized study
- ❖ Patients received treatments for 2 weeks
- ❖ Physical nutritional status and indices of disease activity and intestinal permeability assessed after 2 weeks of treatment

# Results and Conclusion

**After 2 weeks of treatment, the peptide-based diet group experienced significant improvements in:**

- ❖ Crohn's disease activity index ( $5.6 \pm 0.8$  vs.  $2 \pm 1.4$ ,  $P < 0.01$ )
- ❖ Erythrocyte sedimentation rate ( $21.4 \pm 6$  vs.  $16.7 \pm 6.7$ ,  $P < 0.05$ )
- ❖ Permeability index ( $4.9 \pm 5.3$  vs.  $2.1 \pm 2$ ,  $P < 0.01$ )
- ❖ Body mass index ( $18.5 \pm 3$  vs.  $19.2 \pm 3.1$ ,  $P < 0.02$ )
- ❖ Prealbumin ( $22.2 \pm 8$  vs.  $23.5 \pm 7.8$ ,  $P < 0.01$ )
- ❖ Retinol binding protein ( $3.7 \pm 0.7$  vs.  $4 \pm 0.8$ ,  $P < 0.02$ )

**In the corticosteroid group there were significant improvements in:**

- ❖ Crohn's disease activity index ( $4.5 \pm 0.7$  vs.  $3.5 \pm 1.2$ ,  $P < 0.04$ )
- ❖ Fat free mass ( $45.9 \pm 10.5$  vs.  $47.2 \pm 10.7$ ,  $P < 0.05$ )

## Conclusion:

“These data suggest that in the short term, an oral peptide-based diet is at least as effective as steroids in inducing remission of mild-moderately active Crohn's disease but may be more effective in improving the nutritional status via a more rapid restoration of normal intestinal permeability.”




# Human Immunodeficiency Virus (HIV)


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HIV causes a condition in humans (Acquired Immunodeficiency Syndrome [AIDS]) in which progressive failure of the immune system allows life-threatening infections and cancers to thrive. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate or breast milk.

**The most common disease-associated GI symptoms and signs include:**

- ❖ Nausea
  - ❖ Vomiting
  - ❖ Diarrhea
  - ❖ Loss of appetite
  - ❖ Malabsorption
  - ❖ Loss of body weight (lean body mass)
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# An Elemental Diet Containing Medium-chain Triglycerides and Enzymatically Hydrolyzed Protein Can Improve Feeding Tolerance in People Infected with HIV

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## Objective

To quantify both gastrointestinal tolerance and fat absorption (fat tolerance) when patients consumed a complete, oral, elemental diet

## Subjects

23 patients with HIV, 11 subjects completed the study

## Design

Conducted in each subject over 9 days and consisted of 3 continuous phases, each 3 days long



# Design Continued

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## Phase 1 (Study days 1-3)

- ❖ Subjects ingested a diet of their regular food
- ❖ Symptoms of GI intolerance primarily diarrheal in nature documented (frequency, form, and volume)
- ❖ Fat content of stool collected on day 3

## Phase 2 (Study days 4-6)

- ❖ Subjects titrated from food to full intake of the elemental diet (100% of diet)

## Phase 3 (Study days 7-9)

- ❖ Total intake, stool characteristics and fat content in stools collected on study day 9



# Results

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## When fed an elemental diet as compared to a diet of regular food:

- ❖ **6 of the 11** subjects gained weight
- ❖ **91% (10/11)** reported a decrease in stool frequency
- ❖ **64% (7/11)** reported a decrease in stool volume
- ❖ **82%** subjects reported improvement in stool consistency
- ❖ Fecal fat excretion and concentration were significantly lower during phase 3



# Conclusion

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This study indicates that people infected with HIV who experience weight loss and diarrhea can tolerate a nutritionally complete elemental diet and suggests that inadequate intake and fecal nutrient loss can be managed by a carefully selected feeding regimen.

# Case Scenario — Crohn's disease

30-year-old female with Crohn's disease experiencing a 10% weight loss in the past 6 months and an increase in diarrhea over the last month from 1 time per day to now 10 loose stools per day. Patient is now medically managed with steroids and other anti-inflammatory drugs. Diarrhea has improved, but patient is still experiencing some loose stools.



**What would be your nutritional plan for this patient?**

# Case Scenario — Crohn's disease

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## Desired clinical outcomes:

- ❖ Reduce diarrhea
- ❖ Improve nutritional intake to prevent further weight loss
- ❖ Support absorption and improve tolerance

## Nutrition Therapy:

- ❖ Peptide based calorie dense formula via sip feed as a supplement to the oral diet



# Summary

**Malabsorption and feeding intolerance can negatively impact patient outcomes**

**Acute and chronic GI diseases as well as medications and type of feeding can cause feeding intolerance**

**Guidelines support the use of formulas containing small peptides and medium-chain triglycerides to improve feeding tolerance and patient outcomes**

**The peptide based acrie dense formulas support feeding tolerance in people with gastrointestinal dysfunction**

Thank You!

