Aligning Nutritional Support with Gastrointestinal Physiology

A case for peptide-based nutrition

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Undifferentiated gastrointestinal (GI) symptoms are a frequent feature of clinical practice. Estimates suggest that 1 in 10 GP consultations involve a gastrointestinal concern[1] and functional GI disorders account for approximately 12% of primary care workload.[2]

Across long-term conditions, the prevalence of gastrointestinal symptom reporting is considerable:

- Up to 80% of patients receiving cancer treatment[3]
- 94% of women in perimenopause and menopause[4]
- Up to 50% of adults with diabetes[5]
- Up to 80% of people with liver cirrhosis[6]
- Over 75% of patients with pancreatic enzyme insufficiency (PEI).[7]

Within this landscape, referrals for nutrition support are common but, as GI symptoms span multiple underlying conditions, an accurate clinical picture depends on systematic evaluation of bowel patterns and symptom clusters within a structured assessment framework. This standardised approach is particularly important when gastrointestinal symptoms include persistent diarrhoea, steatorrhoea – bulky, pale, foul-smelling, oily stools – and unintentional weight loss, where malabsorption should be considered[8, 9] before progressing down a standard nutritional support pathway.

Recognising malabsorption in complex GI presentations

Malabsorption often presents with overlapping gastrointestinal symptoms, making assessment necessarily layered and interpretive rather than linear. Bowel evaluation should integrate symptom patterns, anthropometry, medication history and psychosocial context to construct a coherent clinical picture.

Anthropometric and functional measures are particularly informative when interpreted collectively. Unintentional weight loss combined with reduced hand grip strength should prompt consideration of malabsorption, whereas weight loss with preserved grip strength makes significant maldigestion less likely. Considering these measures together can provide greater diagnostic clarity than body mass index (BMI) or weight change alone.

Stool assessment is central, though frequently complicated by symptom mislabelling. For instance, 'diarrhoea' may be reported despite bowels opening with normal frequency and Type 7 stool (watery with no solid pieces) occurring simultaneously with Type 1 (hard, separate lumps on the Bristol Stool Chart), consistent with constipation and overflow rather than true diarrhoea. Interpreting stool form, frequency, urgency, nocturnal opening, colour and pain patterns in combination is essential to distinguish functional conditions from possible malabsorption.

Medication effects can further obscure interpretation, and the influence of the gut-brain axis should also be considered. Stress, anxiety and depression can alter motility, visceral sensitivity and symptom perception.

When gastrointestinal symptoms occur simultaneously with functional and anthropometric changes, malabsorption should remain firmly within the differential diagnosis.

PEI: The missed diagnosis

When malabsorption is suspected, PEI should also be considered within the differential diagnosis. In essence, PEI reflects reduced pancreatic exocrine activity in the intestine, impairing normal digestion and resulting in secondary malabsorption.

PEI is well recognised in chronic pancreatitis (30–90%)[10] and pancreatic cancer (66–94%),[11] but it is also observed in diabetes (Type 1: 26–57%; Type 2: 20–36%)[12] and following bariatric surgery (23%).[13] These associations place PEI within routine clinical practice rather than as a rare or specialist diagnosis.

However, because its symptoms overlap with functional bowel disorders, PEI is frequently overlooked. Where diarrhoea, steatorrhoea and anthropometric/functional decline converge, PEI should be actively considered, as recognition has direct implications for enzyme replacement therapy as well as nutritional strategy.

PEI in practice: A reframed diagnosis

A 53-year-old male was referred for nutrition support due to significant weight loss. His history included chronic pancreatitis, longstanding 'IBS', and a recent diagnosis of type 2 diabetes with markedly elevated HbA1c.

His assessment revealed 25% unintentional weight loss and hand grip strength below the 10th centile. Stools were described as orange, pale, floating and malodorous – features consistent with steatorrhoea. Although diarrhoea was not always prominent, regular loperamide use may have masked stool frequency, potentially obscuring the underlying picture.

Taken together – pancreatic disease, new-onset diabetes, steatorrhoea and anthropometric and functional decline – the features were consistent with PEI. The diabetes diagnosis in this context raised suspicion of Type 3c diabetes with associated exocrine dysfunction.

The referral was for nutritional support; the assessment identified malabsorption. Management included pancreatic enzyme replacement therapy (PERT) alongside peptide-based oral nutritional supplementation, aligning nutrition strategy with impaired GI function.

The physiological case for peptide-based oral nutritional supplements (ONS)

Taking all this into consideration, the clinical distinction between inadequate intake and impaired digestion is fundamental when considering nutritional intervention. When maldigestion or malabsorption is present, simply increasing calories or prescribing standard polymeric oral ONS may not achieve the intended effect.

Standard polymeric ONS contain intact macronutrients[14] and assume adequate digestive function[15] – an assumption that holds true in many clinical contexts. But for those with compromised GI function, digestion and/or absorption of these macronutrients may be difficult.[16]

Intact protein must be digested by proteases into amino acids, dipeptides and tripeptides before absorption (see **Figure 1**).[17]

Long-chain triglycerides (LCTs), which form the predominant lipid component of polymeric formulas, require pancreatic lipase and bile salts for emulsification and absorption (see **Figure 2**).[17]

Symptoms such as bloating, worsening diarrhoea or persistent weight loss despite supplementation should prompt consideration of whether maldigestion is limiting therapeutic success.

Importantly, this consideration should not only arise after intolerance has occurred. Where assessment findings indicate likely malabsorption, it is clinically appropriate to consider whether a polymeric formulation is suitable as first-line therapy. Nutritional strategy should be aligned with GI function from the outset.

Peptide-based ONS: A targeted physiological approach

Peptide-based ONS are formulated to reduce reliance on intact GI processes. They contain enzymatically hydrolysed protein in the form of smaller peptides – predominantly dipeptides and tripeptides – which do not require extensive proteolytic breakdown prior to absorption.[17] This may be beneficial where protease activity is reduced, particularly in the context of pancreatic exocrine insufficiency.

In addition, these formulations contain a higher proportion of medium-chain triglycerides (MCTs). Unlike long-chain triglycerides (LCTs), MCTs do not require pancreatic lipase-dependent hydrolysis or bile salt-mediated micelle formation to the same extent. They are absorbed more directly across the intestinal mucosa, thereby reducing dependence on pancreatic-biliary function.[17]

In patients with exocrine insufficiency, impaired bile flow, altered post-surgical anatomy or chronic diarrhoeal states, digestion of intact macronutrients may be inefficient. In these circumstances, reducing reliance on luminal digestion may improve tolerance and support nutritional rehabilitation.

Figure 1

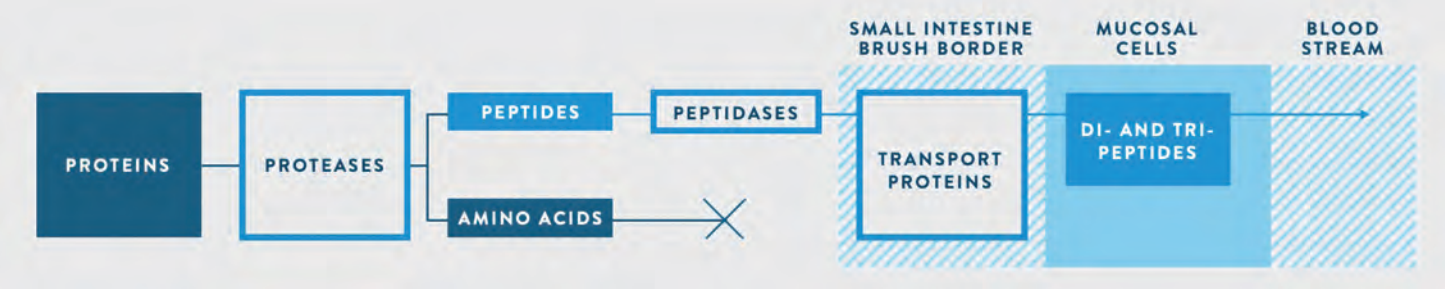
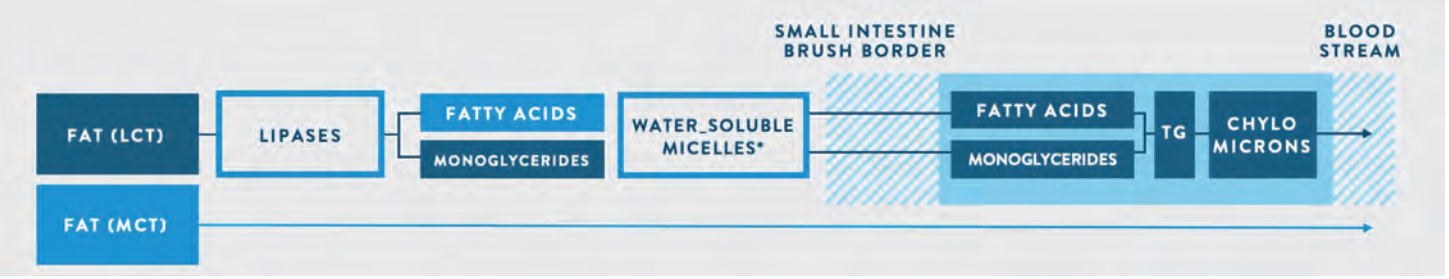


Figure 2



Clinical scenarios in which peptide-based ONS merit consideration could include:

- Confirmed or suspected PEI
- Post-pancreatitis diabetes (particularly where Type 3c is suspected)
- Post-hepatobiliary or bariatric surgery
- Persistent diarrhoea accompanied by anthropometric and functional decline
- Ongoing gastrointestinal intolerance to polymeric supplementation.

In such contexts, introducing a peptide-based formulation may be clinically appropriate either as first-line therapy when malabsorption is strongly suspected, or when tolerance to intact macronutrients is limited.

The decision to use peptide-based ONS should therefore be assessment-led, guided by stool characteristics, anthropometry, underlying pathology and overall clinical trajectory. Used in the right patients, peptide-based ONS offer a targeted strategy to support nutritional rehabilitation where maldigestion is contributing to clinical decline.

Case study: Severe GI intolerance and functional decline

A 63-year-old male with a history of liver transplant following autoimmune hepatitis presented with severe gastrointestinal symptoms and a 10-year history of diarrhoea. He reported marked reduction in functional ability and had significant frailty, with grip strength measuring 11.5 kg (reference range 33.4-44 kg). A trial of standard polymeric ONS was poorly tolerated.

At the time of assessment, the differential diagnosis remained broad, without a confirmed underlying cause. However, the combination of chronic diarrhoea, intolerance to intact macronutrients and objective evidence of malnutrition suggested impaired GI function.

Rather than waiting for definitive diagnostic clarification, a pragmatic decision was made to align nutritional support with the physiology observed. A trial of peptide-based oral nutritional supplementation was introduced. Tolerance improved, nutritional intake increased, and the patient reported a marked functional benefit, describing the intervention as having *"changed my life."*

This case illustrates an important clinical principle: while definitive diagnosis remains essential, nutritional intervention need not be delayed when GI impairment is evident. Even in the absence of complete diagnostic certainty, matching formulation to GI capability can be both rational and impactful.

A physiological approach to nutritional strategy

In clinical nutrition, focus often begins with intake – calories consumed, protein targets achieved, supplements prescribed. In complex gastrointestinal presentations, equal attention must be given to digestion and absorption.

Polymeric ONS remain appropriate and effective for many patients. However, when persistent diarrhoea, steatorrhoea and anthropometric and functional decline suggest impaired digestion – or when tolerance to intact macronutrients is limited – formulation choice becomes clinically significant.

Peptide-based ONS offer a physiologically aligned option in such circumstances. By reducing reliance on pancreatic enzyme activity and bile-mediated fat digestion, they may better match nutritional intervention to compromised GI function.

Several clinical principles underpin this approach:

- Reassessing inherited diagnostic labels, particularly where symptoms persist or evolve.
- Interpreting stool patterns in context – considering form, frequency, urgency, colour and nocturnal symptoms together.
- Evaluating anthropometry and function collectively; weight change and grip strength offer complementary insight.
- Reviewing medications that may mask or modify gastrointestinal presentation.
- Maintaining early awareness of malabsorption when symptom clusters converge.
- Aligning supplementation choice with GI function.

The key question is therefore not simply:

"Does this patient require nutritional support using ONS?"

But:

"If ONS is required, which formulation best aligns with this patient's GI function?"

For selected patients with malabsorption, that distinction can meaningfully influence tolerance, nutritional adequacy and functional recovery.

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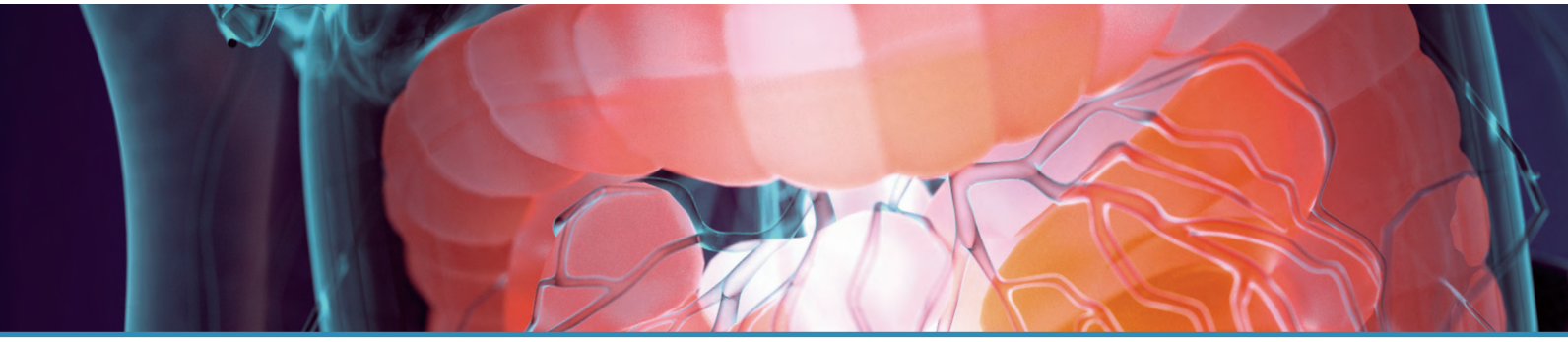

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