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Neonatal intestinal physiology and failure

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ABSTRACT

The neonatal intestine is a complex organ that regulates the absorption of nutrients essential for growth and development. Intestinal failure results from insufficient or functionally inadequate bowel and can lead to failure of neonatal growth and development. Current literature on neonatal intestinal physiology and failure was reviewed and summarized. A homeostatic interplay of electrolytes, enzymes, and hormonal regulators is essential to achieve the physiologic balance needed for adequate intestinal performance. Physiologic consequences of intestinal failure are dependent on the length and anatomic location of the diseased or surgically resected bowel. Intestinal failure leads to disruption of normal intestinal physiology and may have long-term consequences for growth and development if inadequately treated. Parenteral nutrition remains the mainstay of treatment for neonatal intestinal failure.

Introduction

The neonatal intestine is the site of absorption of the nutrients essential for growth and development. A complex interplay of electrolytes, enzymes, and hormonal regulators is required for the physiologic balance needed for adequate intestinal performance. Insufficient or functionally inadequate bowel results from a variety of disease states and leads to metabolic derangements and the inability to maintain growth, a condition that can be incompatible with life for the developing neonate. Herein we describe the physiology of the neonatal intestine with a specific focus on intestinal failure.

Intestinal physiology

The physiology of nutrient absorption in the small intestine relies on specific cellular, hormonal, and enzymatic mechanisms. Specialized intestinal epithelial cells, some localized in the proximal small intestine (duodenum and jejunum) and others in the distal small intestine (ileum), perform unique functions. The intestine digests and absorbs carbohydrates, proteins, lipids, vitamins, and bile salts. Understanding the specialized physiologic functions of the proximal and distal small bowel allows the health care practitioner to understand the physiologic derangements observed with loss of specific segments of the intestine. In addition, the prenatal and neonatal periods are characterized by immaturity of some physiologic mechanisms that can significantly impact nutrition and gastrointestinal disease in preterm infants.

Intestinal development begins in the third week of gestation with the formation of an endodermal tube surrounded by mesenchyme.[1] The formation of finger-like projections of intestinal epithelium, or villi, from the endoderm for increased absorptive surface area is initiated by 9–10 weeks of gestation.[1] By the end of the first trimester, all types of intestinal epithelial cells are present and proliferating, each with specialized functions in intestinal physiology.[2] The enterocyte is the basic unit of absorptive function of the small bowel, with Paneth cells, enteroendocrine cells, M-cells, and goblet cells each performing specific and critical supportive functions (Table 1).[3]

Duodenum and jejunum

The bulk of carbohydrate and protein absorption takes place in the proximal small intestine, specifically the duodenum and jejunum.[4] The entry of protein and fat into the small intestine from the stomach stimulates the release of several intestinal hormones that play specific roles in orchestrating a concerted response to allow the entry of pancreatic enzymes, bile, and acid-neutralizing bicarbonate into the small intestine and to regulate gastric emptying.[5] Cholecystokinin (CCK), in response to the presence of fatty acids and amino acids in the intestinal lumen, stimulates the secretion of pancreatic enzymes and contraction of the gallbladder.[6] Gastrin is stimulated by amino acids and produced by G-cells of the gastric mucosa and upregulates gastric acid secretion and proliferation of gastric epithelium.[6] The acidic pH in the lumen of the duodenum leads to increased production of

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Table 1
Epithelial cells of the small intestinal tract.

Cell type	Function
Enterocyte	Columnar epithelial cells lined with transporters for absorption of a range of electrolytes and nutrients and enzymes involved in the digestion of carbohydrates, proteins, and lipids.
Goblet cell	Mucus-secreting cells that aid in protecting the intestinal mucosa from digestion and serves as a medium for probiotic organisms.
Paneth cell	Cells that aid in epithelial cell defenses to pathogens. Secrete antimicrobial peptides that can kill bacteria.
M-cell	Found in Peyer's patches, aggregations of lymphoid cells in the intestine. Sample luminal contents to assist in developing immunity.
Enteroendocrine cells (D-, K-, I-, L-, M-, and S-cells)	Secrete gastrointestinal hormones and peptides in response to changes in luminal contents.

secretin, which stimulates secretion of water and bicarbonate from the pancreas. Gastric-inhibitory peptide (GIP), stimulated by fat and glucose, inhibits gastric secretion and motility and potentiates the release of insulin from pancreatic beta cells in response to hyperglycemia.[7] The concerted motility of the stomach and small bowel is regulated by motilin, and though the specific stimulation for its production is unclear, it is secreted during the fasting state.[7] A review of the relevant hormones and their site of production and function is provided in Table 2.[6,7]

Carbohydrate digestion begins in the mouth with salivary amylase, which is inactivated by the acidic environment of the stomach. The presence of pancreatic amylase within the duodenum allows carbohydrate digestion to resume. Thereafter, a multitude of saccharidases found on the enterocyte (e.g., maltase, lactase, and galactase) complete the breakdown of polysaccharides to monosaccharides for absorption into the bloodstream via membrane-bound sodium–glucose co-transporters.[4] Neonates notably have a transient physiologic insufficiency of duodenal amylase, which resolves with maturation of the exocrine pancreas by approximately 1 year of age.[8]

Protein absorption begins in the stomach; however, the majority of digestion takes place in the proximal small intestine. The transit of chyme from the stomach to the duodenum stimulates the release of enterokinase. Enterokinase cleaves trypsinogen to active trypsin, resulting in the zymogen-activating cascade of a multitude of proteases.[3] Resulting peptides and amino acids can then be absorbed into the bloodstream.

Lipid metabolism involves emulsification by bile acids and hydrolysis by lipases. Bile acids from the liver and gallbladder solubilize the micelles of lipids produced by the churning of the stomach and action of lingual lipase. Hydrolysis is completed by pancreatic lipases in the duodenum.[9] The fatty acids generated are subsequently brought into the enterocyte through poorly understood mechanisms. Like sugars and amino acids, medium-chain fatty acids [or medium-chain triglycerides (MCTs)] are directly absorbed into the portal circulation and do not require re-esterification. Long-chain fatty acids (LCFAs) are re-esterified, packaged into chylomicrons, and absorbed into lymphatic circulation in the jejunum. Lymph rich in chylomicrons then drains into the lymphatic system, which flows into the bloodstream, where blood-born chylomicrons are disassembled and their constituent lipids are utilized in the rest of the body.[3,10] LCFAs are also critical for the absorption of fat-soluble vitamins A, D, E, and K. The fat-soluble vitamins, phosphorus, folate, and water-soluble vitamins are primarily absorbed in the jejunum.[11–14]

The duodenum is also the primary site of calcium uptake, mediated by calbindin, a vitamin D-dependent calcium-binding protein found in duodenal enterocytes. Vitamin D-independent passive paracellular transport of calcium also occurs in the

Table 2
Overview of hormones secreted by enteroendocrine cells of the small intestine. (Adapted from Rehfeld[6] and Drozdowski and Thomson.[7])

	Site of production	Function
Cholecystokinin	I-cells of duodenum and jejunum (also in neurons of ileum and colon)	Contraction of gallbladder Relaxation of sphincter of Oddi Secretion of pancreatic enzymes Inhibition of gastric emptying
Gastric inhibitory peptide	K-cells of duodenum and jejunum	Increased insulin release Increased lipoprotein lipase activity
Vasoactive intestinal peptide	Neurons of enteric nervous system	Smooth muscle relaxation Secretion of water and electrolytes Inhibition of intestinal absorption Increased pancreatic bicarbonate
Secretin	S-cells of duodenum	Secretion of pancreatic bicarbonate Stimulates bile secretion from liver and gallbladder Inhibits gastric acid secretion
Motilin	M-cells of duodenum and jejunum (not the same M-cell as in Peyer's patch)	Stimulate production of pepsin Stimulates migrating myoelectric complex—promotes gastrointestinal motility
Somatostatin	D-cells of duodenum, stomach, and delta islet cells of pancreas	Decreases gastrin, gastric acid, and pancreatic enzyme secretion Decreased bile flow from liver
Glucagon-like peptide-1	L-cells of ileum	Stimulates insulin secretion Inhibits glucagon secretion Inhibits gastric acid secretion and motility Promotes satiety
Neurotensin	Enteroendocrine cells of ileum	Smooth muscle contraction Stimulates histamine release
Peptide YY	L-cells of ileum and colon	Suppresses pancreatic secretions Promotes satiety