Anatomy and Physiology of the Small Bowel

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KEYWORDS

• Embryology • Enteric nervous system • Small intestine • Villi • Anatomy • Digestion • Physiology

KEY POINTS

- Embryologically, weeks 9 and 10 are critical time points with the potential for development of malrotation.
- Abnormalities in neural crest cell migration during the first trimester may lead to various neuropathies, one of the most common being Hirshsprung disease.
- The enteric nervous system plays a critical role in gut motility, secretion, and immune function.

EMBRYOLOGY

Development of Morphologic Structures

A review of the gut embryologic process provides a framework for understanding the function of the small bowel as well as the pathways that may lead to small intestinal disease. For the purpose of this review, the development of the small intestine is briefly examined with a focus on the major events outlined in **Table 1**.

Morphogenesis begins with gastrulation, the process of cell migration through the primitive streak, with eventual formation of the three fundamental germ layers of the embryo: ectoderm, mesoderm and endoderm. Although the small intestine is composed of cells that originate in all 3 layers, it is from the endoderm that the gastrointestinal (GI) tract initially develops and ultimately gives rise to the epithelium of the GI tract.[1]

The intestinal lumen first takes the form of an elementary tube during the fourth week of embryogenesis when the cranial, lateral and caudal edges of the trilaminar embryonic disk fold under the dorsal axial structures and are brought together along the now ventral surface of the embryo. The process of tube formation is mediated by several genes, including GATA4, FOXA2, and SOX9.[2] The assignment of biologic fate

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Table 1
Key events in the embryogenesis of the small intestine

Weeks	Major Developmental Milestones
3	Gastrulation: Early tubular gut formation; early formation of major digestive glands
4	Gut tube closes
5	Intestinal loop beginning to form
7	Herniation of intestinal loop
8	Intestine rotates in a counterclockwise direction and recanalizes; early innervation of parasympathetic neural precursors
9	Herniated gut returns into body cavity; epithelial cells differentiate
11	Small intestine begins to develop villi; goblet cells differentiate
12	Intestinal enzymes present
20	Peyer patches seen in small intestine

to small intestine cells, a process called specification, is triggered by CDXC.[3] The acquisition of specialized features of the small intestine is dependent on interactions between the endoderm and mesoderm via the Hox signaling pathway. The resulting simple tubular structure consists of two blind ends on the cranial and caudal sides representing the foregut and hindgut, respectively. Between these two blind ends resides the future midgut. At this stage, the midgut remains largely open to the yolk sac, which has grown at a slower rate than the embryo. As development continues, the edges of the embryonic disc fuse together with the lateral margins of the midgut, forming a lumen, while the prior open connection to the yolk sac is reduced to a narrow tube called the vitelline duct.[4]

In the fifth week, the midgut has elongated to such a degree that it is forced to fold, thus forming the primary intestinal loop; by the sixth week, this loop herniates through the umbilicus (**Fig. 1**). Herniation of the bowel wall is necessary because the length of the gut increases faster than the length of the embryo and due to crowding by the proportionally larger liver and kidneys at this stage of development. The developing intestinal tract returns to the abdominal cavity between weeks 9 to 10 when the abdominal cavity is large enough to accommodate the intestinal tract.[5] During the process of herniation, the intestinal loop rotates counterclockwise 90°, resulting in an ileum that lies in the right abdomen. As the intestinal loop returns into the abdominal cavity, it rotates an additional 180° counterclockwise, resulting in the final configuration of the gut in the abdominal cavity. This process is complete by week 11.

Formation of Villi

The villi of the small intestine form from simple epithelium during week 11. Villi and crypts develop in a coordinated manner, because villi formation is accompanied by invagination into the mesoderm, which eventually forms the intestinal crypts. This process is in part mediated by Shh and Ihh.[6] Beginning during early development, and progressing through adulthood, the epithelial cells of the small intestine need to be constantly replaced due to frequent turnover. Stem cells located at the base of intestinal crypts are integral to this process. Stem cells generate progenitors for the epithelial cells lining the small intestine, a process mediated by several important signaling pathways including Wnt, Notch, and hedgehog.[7–9] As these cells mature, they migrate up the villus, where they eventually interface with the intestinal lumen.