Contents

1

Embryology of the Anorectum

Mercedes Amieva-Balmori*,†, José María Remes-Troche*

*DIGESTIVE PHYSIOLOGY AND GASTROINTESTINAL MOTILITY LABORATORY, INSTITUTE OF MEDICAL AND BIOLOGICAL RESEARCH, UNIVERSITY OF VERACRUZANA, VERACRUZ, MEXICO
†MEXICAN INSTITUTE OF SOCIAL SECURITY, REGIONAL GENERAL HOSPITAL, ORIZABA, MEXICO

1.1 Introduction

Despite a long history of embryologic research, the mechanisms involved in the development of the hindgut, which gives rise to the anorectum, are not completely understood.[1] That limitation of knowledge is related to numerous factors that include: a scarcity of material for appropriate study; technical problems, such as the difficulty in interpreting serial sections; and a lack of experience in performing three-dimensional reconstructions.[2]

In general, four steps are considered in the development of the primitive gut and its derivatives (Fig. 1.1):

1. *Pharyngeal gut* or *pharynx*, which extends from the buccopharyngeal membrane to the tracheobronchial diverticulum;
2. *Foregut*, situated caudal to the pharyngeal tube and arriving caudally at the origin of the liver bud;
3. *Midgut*, begins caudal to the liver bud and extends to the site, in the adult, of the right two-thirds and the left third of the transverse colon; and
4. *Hindgut*, which extends from the left third of the transverse colon to the cloacal membrane.

The formation of the digestive tract begins at week 3 of gestation. It is created from the cranio-caudal and lateral folding of the embryo, resulting in the incorporation of one portion of the endoderm-lined yolk sac into the embryo to form the primitive gut. The other two portions of the endoderm-lined cavity, the yolk sac and the allantois, remain outside of the embryo. The primitive gut forms a blind-ending tube in the cephalic and caudal parts of the embryo, corresponding to the foregut and hindgut, respectively. The middle portion, or midgut, transitorily maintains its communication with the yolk sac through the omphalomesenteric duct, or vitelline pedicle.

The endoderm forms the epithelial lining of the gastrointestinal tract and gives rise to the parenchyma of glands, such as the liver and pancreas. Muscle and peritoneal components of the gut wall, as well as its connective tissue, derive from the splanchnic leaf of the

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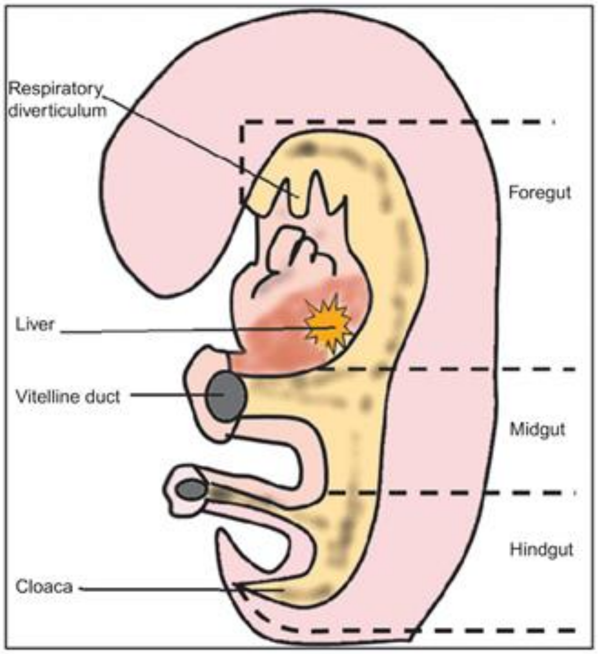

FIG. 1.1 Development of digestive system.

mesoderm. The differentiation of various regions of the gut and its derivatives depends on a reciprocal interaction between the endoderm of the gut tube and the surrounding splanchnic mesoderm. The mesoderm determines the type of structure that can be formed (i.e., the colon).

1.2 Embryology of the Hindgut

The hindgut gives rise to the distal third of the transverse colon, the descending colon, the sigmoid colon, the rectum, and the upper portion of the anal canal. The hindgut endoderm also lines the bladder and the urethra.

The primitive "cloaca" is traditionally considered to be divided by the urorectal septum (which appears at week 4) into an anterior urogenital system (ventral) and a posterior anorectal system (dorsal). The division of the cloaca is completed at week 6, when the urogenital system is fused with the cloacal membrane.

The term "cloaca" has different uses, one of which describes a transitional organ system in human embryos, another refers to a congenital abnormality, and a third describes a normal organ in birds. The terminal portion of the hindgut is continuous with the posterior region of the cloaca, which is the primitive anorectal canal, and the allantois is continuous with the anterior portion of the cloaca, which is the primitive urogenital sinus. The cloaca is an endoderm-lined cavity, whose ventral end is also lined with surface ectoderm. The boundary between the endoderm and ectoderm forms the cloacal membrane. A layer of mesoderm, the urorectal septum, separates the region between the allantois and the hindgut. That septum derives from the fusion of the mesoderm covering the yolk sac with the mesoderm that surrounds the allantois. As the embryo grows and the caudal folding continues, the urorectal septum moves closer to the cloacal membrane, but the two structures never make contact with one another.

At the end of week 7, the cloacal membrane ruptures, creating the opening for the hindgut and a ventral orifice for the urogenital sinus. The tip of the urorectal septum forms the perineal body between the two openings. At that time, ectoderm proliferation closes the region most caudal to the anal canal. During week 9, that region is recanalized, signifying that the caudal portion of the anal canal is of ectodermal origin and is irrigated by the inferior rectal arteries, which are branches of the internal pudendal arteries.

The cranial portion of the anal canal arises from the endoderm and is vascularized by the superior rectal artery, which is the continuation of the inferior mesenteric artery that supplies the hindgut (Fig. 1.2).[3]

1.3 Theories on the Development of the Hindgut

Since the 19th century work of Tourneux and Retterer, it has been accepted that normal development of the primitive hindgut depends on the subdivision of the cloaca by the so-called urorectal septum.[4,5] According to that theory, abnormal septation development would always result in abnormal cloacal development. However, there is no agreement on the nature and formation of that septum and recent studies have presented another form of development. Tourneux thought that the septum moved downwards in a cranial-to-caudal manner "like a French curtain" and Retterer speculated that the lateral folds or ridges appeared in the lumen of the cloaca. Those ridges would become fused at the midline to form the septum, beginning cranially and ending caudally at the level of the cloacal membrane. These theories were supported by numerous researchers. Stephens described a combination of the two theories, which he thought could better explain the different types of anorectal malformations. He stated that the cranial part of the septum would grow downward, as explained by Tourneux, whereas in the caudal portion of the septum, the lateral ridges would fuse to form the septum.[6]

Nevertheless, in 1986, van der Putte rejected the idea that the urorectal septum played the main role in the process of cloacal differentiation.[7] Studying the morphology of rectal malformations in newborns, Bill and Johnson[8] and Gans and Friedman[9] concluded that, in the majority of cases, the fistula could be an ectopic anal opening. They posited that the rectum, situated at a high level, in fact *migrates* toward the anal opening during normal development, and if that process were to be altered the resulting ectopic anal canal would open creating the fistula. However, there is no embryologic evidence of that migration.

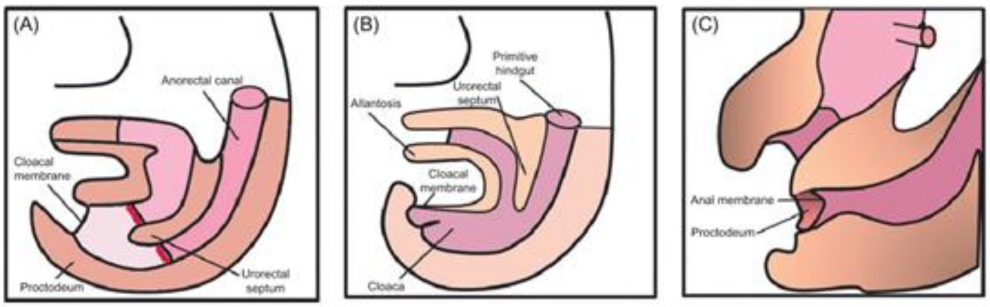

FIG. 1.2 Embryology from 4 to 7 weeks. (A, B) The fusion of the hindgut with the allantois and mesonephric ducts is partitioned by the urorectal septum, creating the urogenital sinus anteriorly and the anorectum posteriorly. The once common chamber terminates blindly at the cloacal membrane, which similarly is divided into the anterior urogenital membrane and posterior anal membrane. (C) The ectodermal layer of the anal membrane gives rise to the surrounding protuberances, the anal folds and creates a central depression, the proctodeum, which develops into the distal anal canal.

At week 7 of gestation the urogenital system and the anorectum are supposed to separate, but in recent studies[10] the mechanism of separation by the urorectal septum has been a subject of debate. Changes in the previously described position of the dorsal cloaca, the process of cloacal membrane rotation, and the transformation of the cloacal configuration have been reported.[11]

In their studies, Kluth et al.[12] evaluated rat embryos through electron microscopy, which allowed them to study the embryologic structures in three dimensions during the development of the hindgut. They concentrated on the following points: (1) the development of the cloacal shape, (2) signs of lateral cloacal wall component fusion, (3) signs of cloacal membrane disintegration, and (4) signs of anal opening migration. They found noticeable ventral growth of the cloaca and a shift of the cloacal membrane from a vertical to a horizontal position that had a fixed point in the fold of the distal portion. The changes in cloacal shape were produced by the outgrowth of the genital tubercles. They found no signs of fusion of the lateral components of the cloacal wall, with respect to the urorectal fold and the cloacal membrane in the normal development of the cloaca. They also stated that the urethral area was larger than the anorectal area. The authors concluded that the microscopic study of rat embryos demonstrated that the subdivision of the cloaca was not the result of lateral cloacal ridges or the fusion of wall components of the lateral cloaca and that their importance had been overestimated in the past. According to the results of the study, hindgut development depends on the normal formation of the cloacal membrane, thus refuting the migration theory. They found that the future anal opening was observed in the dorsal part of the cloacal membrane, near the distal tail groove, in all the embryos.

Embryonic cell differentiation, proliferation, and apoptosis have also been reported, specifically in murine models, to play an essential role in the configuration of the embryonic anorectum.[13,14] Zhang et al.[15] studied 108 human embryos from week 3 to 8 and described the morphologic development of the anorectum in three phases:

1. The cloacal period from week 3 to 5;
2. The development of the urogenital and the anorectum systems from week 5 to 7; and
3. The formation of the anus and perineum from week 8.

During week 8, the urogenital system progressively grows ventrally and its epithelium fuses with the ventral part of the endodermal layer of the cloacal membrane, with persistent epithelium between the mesenchyme of the two structures. The mesenchyme of the urogenital tubercle is inserted into the two layers of the cloacal membrane to form the urethra. The urogenital system confluence with the endoderm and ectoderm of the cloacal membrane forms the perineal body.

Regarding the space-time distribution of apoptosis and the proliferation of the embryonic anorectum, Zhang et al. described the presence of apoptotic cells in the epithelium of the anorectum, urogenital system, and urorectal septum at week 6 that specifically began to appear inside the anal opening. Those cells were observed in the mesenchyme of the terminal rectum and dorsal rectum at week 7 and were not detected in those epithelia at week 8, whereas the fusion of the urogenital system and cloacal membrane remained permanent and strong. The proliferative cells were scarce in the epithelia of the zone at week 6 but were more numerous in the mesenchyme of the urogenital system at week 7 and in the epithelium of the urethra and the anorectum at week 8; especially in the zone of the fused tissue between the urogenital system and the ventral part of the cloacal membrane. The authors described how the urogenital system was not fused with the dorsal cloacal membrane. They therefore concluded that the normal development of the anorectum depends on the dorsal cloaca and the dorsal part of the cloacal membrane, and that the distribution of apoptosis and proliferation in the anorectum and the ventral cloacal mesenchyme plays an essential role in the formation of the anorectum.

In another recent study Hashimoto[16] depicted new forms of development through the analysis of human embryos. He evaluated the embryos from the perspective of the distal portion (tail) and the splanchnic mesenchyme from Carnegie stages 11 to 23, corresponding to day 23 to 60 or, in other words, from week 3 to 9 (the Carnegie stages are used for the study of embryonic development from fertilization to 60 days/8 weeks, because after that date the embryo is called a fetus). Hashimoto carried out the histologic study of 17 embryos, finding that the cloaca that extended caudally to the hindgut enlarged dramatically, particularly in its dorsal portion and its membrane, that is to say the cloacal membrane. The splanchnic mesenchyme that surrounds the hindgut extended ventrally toward the urorectal septum, suggesting its participation in the formation of the septum. No fusion of the urorectal septum with the cloacal membrane was found. The splanchnic mesenchyme proliferated and developed into smooth muscle layers (circular and longitudinal) in a cranial-to-caudal direction along the hindgut. The distal portion (tail) appears to cause both adequate dorsal cloaca dilation and cloacal membrane lengthening. Its dorsal portion in particular is necessary for normal anorectal development. The splanchnic mesenchyme developed and descended toward the pectinate line and formed the internal sphincter muscle at the terminal intestine.

The union between the endodermal and ectodermal portions of the anal canal is represented by the pectinate line that is found immediately under the anal columns. The cylindric epithelium is transformed into stratified epithelium at the level of that line, as previously reported.

In general parts of the traditional theories continue to be adopted, but the advances in the study of embryology have unfolded novel aspects of anorectal embryogenesis. More studies will certainly be conducted, supporting new research and providing a greater understanding of embryology in humans.

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