

Embryology, comparative anatomy, and congenital malformations of the gastrointestinal tract

Melinda Danowitz, Nikos Solounias

ABSTRACT

Evolutionary biology gives context to human embryonic digestive organs, and demonstrates how structural adaptations can fit changing environmental requirements. Comparative anatomy is rarely included in the medical school curriculum. However, its concepts facilitate a deeper comprehension of anatomy and development by putting the morphology into an evolutionary perspective. Features of gastrointestinal development reflect the transition from aquatic to terrestrial environments, such as the elongation of the colon in land vertebrates, allowing for better water reabsorption. In addition, fishes exhibit ciliary transport in the esophagus, which facilitates particle transport in water, whereas land mammals develop striated and smooth esophageal musculature and utilize peristaltic muscle contractions, allowing for better voluntary control of swallowing. The development of an extensive vitelline drainage system to the liver, which ultimately creates the adult hepatic portal system allows for the evolution of complex hepatic metabolic functions seen in many vertebrates today.

Human digestive development is an essential topic for medical students and physicians, and many common congenital abnormalities directly relate to gastrointestinal embryology. We believe this comprehensive review of gastrointestinal embryology and comparative anatomy will facilitate a better understanding of gut development, congenital abnormalities, and adaptations to various evolutionary ecological conditions.

Keywords: Anatomy education, Digestive, Embryology, Gastrointestinal tract

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INTRODUCTION

The gastrointestinal tract is one of the earliest organ systems to form in the human embryo; it develops as a diverticulum off the yolk sac. The most primitive fishes exhibit a tubular digestive tract, functioning proximally in transport and distally in nutrient breakdown and absorption. The expansion of this early gut tube into an intricate digestive system involving accessory organs and intestinal rotation reflects the evolution of more complex dietary habits. Several features of gastrointestinal

development also demonstrate the transition from water to land organisms. A recent article reviewed head and neck embryology with links to evolutionary anatomy, to provide context to the morphology of primitive structures, and explain complexities in head development [1]. Similarly, we believe the study of digestive comparative anatomy puts the embryology and modern anatomy into perspective, and facilitates a deeper comprehension of the human gastrointestinal tract.

Feeding to obtain nutrients, such as pre-synthesized amino acids, carbohydrates, and smaller biomolecules is an essential process common to all multicellular organisms. It is crucial to absorb organic molecules and water, and subsequently break down the materials to be used in various cellular processes. There are three types of multicellular organisms: fungi, plants, and animals. Fungi are composed of filaments that invade decomposing materials such as fruits or carcasses. They absorb the nutrients at the site and incorporate them into their own cells [2]. Plants rely on solar energy, which is converted to usable nutrients via chlorophyll molecules. They also obtain minerals and water from their roots that penetrate the surrounding soil [3, 4]. Animals ingest food, which is subsequently processed by a tubular digestive system. The food particles are broken down mechanically and chemically by digestive enzymes and intestinal bacteria. Both absorption and digestion take place in the intestines, and wasted bacteria and unused food material is excreted.

Comparative anatomy and evolutionary biology provide context to the development of early digestive structures, however these courses have been lost in the pre-medical and medical curricula [5]. A key concept in anatomy involves relating form to function; comparative anatomy demonstrates how structural adaptations can meet environmental or changing physiologic needs. A current recommendation by the American Association of Medical Colleges is to incorporate evolutionary biology in medical education [6]. Many articles argue the importance of Darwinian medicine in training future physicians [7–9]. Evolutionary biology teaches medicine at the molecular level, for example demonstrating the virulence of viruses via genetic mutations, and at the epidemiological level, such as relating malarial resistance to the sickle-cell trait carrier by natural selection [10, 11]. Studies in North America and in the UK showed a need for evolutionary biology to be incorporated into standard medical education courses [12, 13].

In this article, we summarize the key embryological events in human gastrointestinal development, while providing connections to comparative digestive anatomy. The evolutionary history of the gut tube puts the modern anatomy and development into context, and enriches the medical student knowledge of digestive adaptations by relating structure to function. We also describe important congenital anomalies of the gastrointestinal tract; an understanding of these anomalies helps reinforce

knowledge of the normal embryology. We believe this comprehensive review of gastrointestinal embryology and comparative anatomy will enable medical students to better understand gut development and adaptations to various evolutionary ecological conditions.

THE GENERAL DEVELOPMENT OF THE GASTROINTESTINAL TRACT

During third to fourth week of development, the embryo folds and the innermost endodermal layer forms the gut tube, which communicates ventrally with the yolk sac (Figure 1). The gut forms as a diverticulum off of the yolk sac. The gut tube is divided regionally into the foregut, which terminates cranially in the oropharyngeal membrane, midgut, and the hindgut, which terminates caudally in the cloacal membrane. The oropharyngeal and cloacal membranes are the only two regions in the body where ectoderm directly contacts endoderm. These membranes eventually rupture, making the gut tube a patent pathway proximally and distally. As folding and gut tube lengthening continue, the ventral connection between the midgut and yolk sac narrows and elongates to form the vitelline duct. The endodermal gut tube is surrounded by lateral plate splanchnic mesoderm, which forms the lamina propria, submucosal, and mucosal layers of the gastrointestinal tract. The splanchnic mesoderm also forms the smooth muscles of the intestines and of the lower esophagus. Neural crest cells migrate to the developing gut tube and form the enteric nervous system. The autonomic (parasympathetic and sympathetic) innervation is also formed, largely by neural crest, and connects the gastrointestinal system

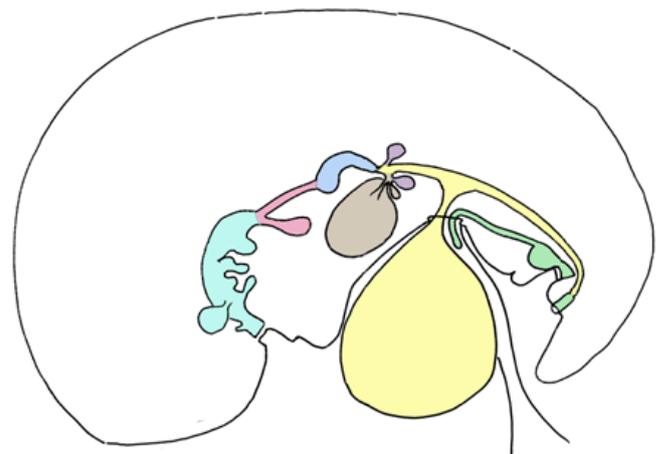


Figure 1: Lateral view of the developing embryo depicting the yolk sac, gastrointestinal tract and diverticula. The pharynx is shown in turquoise, the esophagus and respiratory diverticulum are shown in pink, the stomach is shown in blue, the yolk sac and intestines are shown in yellow, the liver and gallbladder are shown in brown, the pancreatic buds are shown in purple, and the derivatives of the cloaca (urogenital sinus, allantois, and distal anus) are shown in green.

to the brain. Therefore, the gut tube is controlled by two nervous systems [14].

The gut tube is surrounded by the splanchnopleure, which ultimately forms the visceral peritoneum. A broad layer of mesenchyme initially attaches the abdominal gut tube to the body wall. This attachment subsequently thins and forms the dorsal mesentery. The gut tube becomes suspended in the peritoneal cavity, and the viscera therefore are intraperitoneal. These intraperitoneal structures are suspended in mesenteries, but are still mobile. Retroperitoneal structures are organs deep to the abdomen, or posterior to the peritoneal cavity. Primarily retroperitoneal structures originate behind the peritoneal cavity, and are never suspended; these include the kidneys, adrenals, ureters, and bladder. Some regions of the gut tube that develop initially within the peritoneal cavity are rotated and fuse to the posterior body wall; these are termed “secondarily retroperitoneal” and include the duodenum, pancreas, ascending colon, and descending colon [15].

Evolutionary link

In primitive fishes and amphibians, the developing gut tube was comprised of a single pouch of endoderm with cells rich in yolk material. The richness in yolk preceded the origin of a true yolk sac. In more advanced groups, endoderm grows to surround the yolk, enclosing it in a yolk sac. The yolk is progressively digested during development, and the connection between the yolk sac and growing endoderm thins, eventually forming a stalk, or the vitelline duct [16].

The regional delineations of the foregut, midgut, and hindgut are not common to all species. In the more primitive form, such as in sharks and certain fishes, there is minimal anatomical distinction between the small and large intestines, and often there is no discrete outpouching to form the stomach. The pylorus, however, which delineates the transition from stomach to intestines, is common to most vertebrates. Primitively, the gut tube regions proximal to the pyloric constriction functioned in food transport from the mouth, and regions distal to the pylorus were responsible for digestion and absorption. The foregut evolves to play a larger role in nutrient breakdown and food storage, and the stomach becomes pivotal for chemical and mechanical digestion [17].

GREATER SAC, LESSER SAC, AND MESENTERIES

Initially, the pancreas, spleen, stomach, and liver are aligned dorsoventrally in the median plane, and are connected by ligamentous or mesenteric attachments. The pancreas and spleen are joined within the dorsal mesogastrum, the spleen and stomach are connected by the gastrosplenic ligament, the stomach and liver are joined by the hepatogastric ligament, and the liver connects

to the ventral wall with the falciform ligament (Figure 2). This line of organs divides the abdominal cavity into two initially equal areas. However, as abdominal organs enlarge and rotate, the dorsal mesogastrum is repositioned and creates a small space behind the stomach

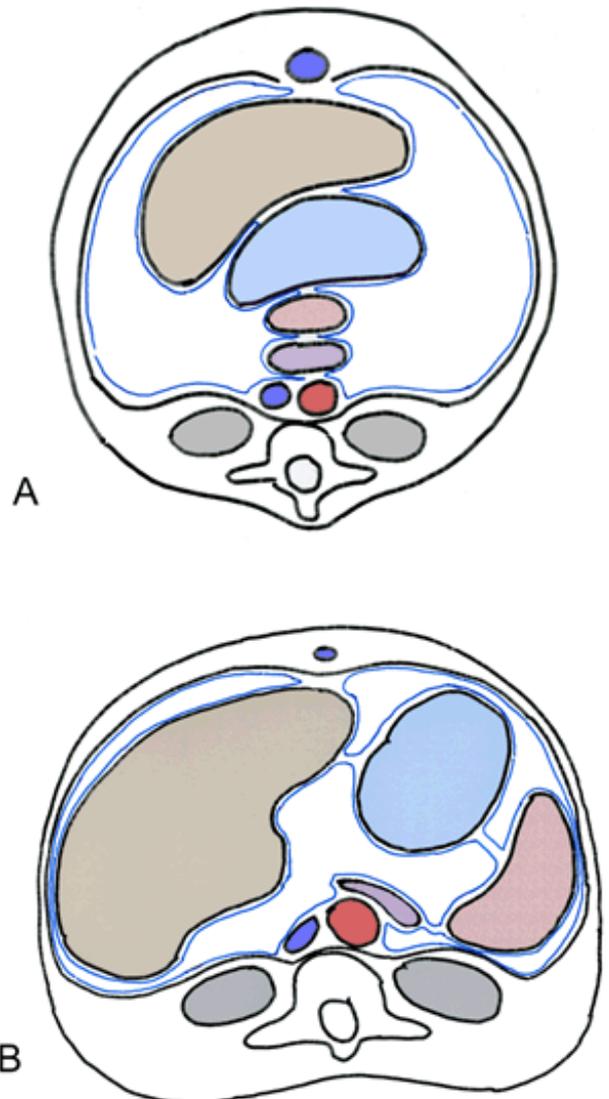


Figure 2: Transverse view of the abdomen, where the organs are connected dorso-ventrally with ligamentous and mesenteric attachments. (A) Abdominal organs initially aligned in the median plane around 36 days. The lesser sac on the right and the greater sac on the left are initially equal areas, (B) Rotation of the abdominal organs around sixth week, bringing the pancreas in the retroperitoneal space, along with the kidneys, aorta, and inferior vena cava. The liver, stomach, and spleen remain suspended in mesenteries within the intraperitoneal space. The structures depicted from ventral to dorsal include: umbilical vein within the falciform ligament (blue), liver (brown), stomach (light blue), spleen (peach), pancreas (purple), abdominal aorta (red), inferior vena cava (blue), kidneys (gray), and thoracic vertebra. The blue line represents the visceral (intimately touching the organs) and parietal peritoneum.

termed the lesser peritoneal sac. The remainder of the peritoneal cavity, comprising the majority of the abdomen becomes the greater peritoneal sac; the two spaces are connected via the epiploic foramen. The epiploic foramen represents the central point of embryonic rotation [18].

The stomach attaches to the posterior body wall via the dorsal mesogastrium. The double-layered dorsal mesogastrium extends caudally during rotation of the stomach, and fuses with the double-layered mesentery of the transverse colon to create the greater omentum. The greater omentum is thus composed of four layers of visceral peritoneum. The lesser omentum extends from the stomach and duodenum to the liver and includes the hepatogastric ligament, which joins the liver with the stomach, and the hepatoduodenal ligament, which connects the liver to the duodenum. The hepatoduodenal ligament contains the portal triad (bile duct, portal vein, and hepatic artery) [19].

Evolutionary link

The rotation of the stomach and concurrent pulling of the dorsal mesogastrium to form the greater omentum likely began with the evolution of jawed vertebrates. In reptiles and birds, the lungs are separated from the peritoneal (abdominal) cavity by an oblique septum, thus allowing for a more extensive respiratory system to develop. In mammals, this is accomplished by the development of the diaphragm from the embryonic transverse septum, which not only separates the thoracic and abdominal cavities, but also functions in drawing air into the lungs during respiration. The liver of vertebrates grows into the transverse septum, and as the liver wall expands, it spreads the septum to form its serosal covering, as well as the coronary ligament cranially, and the falciform ligament ventrally [20].

ESOPHAGUS

The esophagus is the cranial-most structure formed from the foregut. The respiratory diverticulum forms on the ventral surface of the developing esophagus; this will further differentiate to form the trachea, bronchi, and lungs. The respiratory diverticulum is separated from the cranial foregut by the tracheoesophageal septum. The esophagus is initially a short structure that progressively grows to span the length of the thoracic cavity. The inner wall of the esophagus is comprised of endoderm. The musculature of the upper esophagus is striated muscle, derived from branchial arch mesoderm, and the musculature of the lower esophagus is smooth muscle, derived from splanchnic mesoderm [21].

Evolutionary link

In primitive fishes, the esophagus, and majority of foregut in general, is reduced to a simple tube connecting the mouth and pharynx to the intestines. The inner surface is ciliated, facilitating transport in water (Figure 3). In

many more advanced fishes, the stomach develops, and a sphincter is often present to control passageway from the esophagus into the stomach. The evolution of a discrete esophagus coincides with the development of land vertebrates. This occurs with the reduction of gills and therefore the pharynx, allowing the esophagus to elongate and eventually span the length of the neck and thoracic cavity. In land mammals, the ciliated epithelium is often lost, and striated and smooth musculature surrounding the esophageal wall appears. Therefore, ciliary transport, which is better adapted for particle transport in water, is replaced by peristaltic muscular contractions, allowing for voluntary control of swallowing on land. The development of esophageal musculature also allows for reverse transport from the stomach to the mouth, which serves as a protective mechanism to expel potentially toxic substances. This also facilitates regurgitation of partially digested food material, a behavior exhibited by ruminants for specialized digestion and birds for feeding their young. Birds have an additional esophageal adaptation where a distensible sac is present, termed the crop, which is a temporary site for food storage before regurgitation (Figure 3) [17].

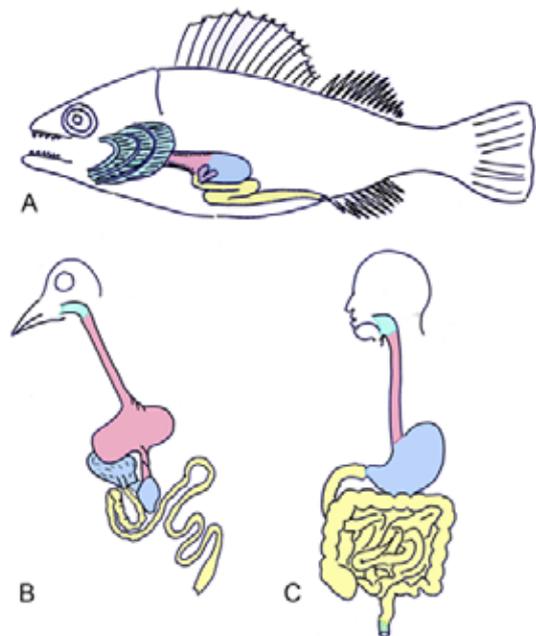


Figure 3: The gastrointestinal tract of a fish, bird, and human. (A) Gut tube in a fish. The pharynx comprises a large portion of the cranial body cavity, and thus restricts the length of the esophagus. The inner lumen of the esophagus is ciliated, facilitating particle transport in water, (B) Gut tube in a bird. The esophagus has a large out pouching distally termed the crop, which allows for the storage and regurgitation of partially digested food material to feed their young. The stomach has a separate section termed the gizzard, where swallowed pebbles are stored and facilitate mechanical digestion, to compensate for the lack of teeth in the beak, and (C) Gut tube in a human. From proximal to distal, the structures shown include the pharynx (turquoise), esophagus (pink), stomach (blue), intestines (yellow), and anus (green).

STOMACH AND DUODENUM

The stomach forms as a dilatation of the foregut. The developing stomach initially connects to the ventral body wall via the septum transversum. This eventually thins and forms the ventral mesentery. Around fifth week, the stomach wall grows asymmetrically; the dorsal wall grows faster and creates the greater curvature, and the ventral wall forms the lesser curvature. During weeks seven and eight, the stomach rotates 90 degrees around a longitudinal axis, bringing the greater curvature to the left and the lesser curvature to the right (Figure 4). This rotation creates the C-shaped loop characteristic of the duodenum, and moves it towards the dorsal body wall, with which it fuses to form the lesser sac. The duodenum delineates the caudal portion of the foregut and cranial portion of the midgut, and is thus supplied by both the celiac and superior mesenteric arteries [22].

Evolutionary link

In early fishes, there is no muscular dilatation of the foregut that characterizes a distinct stomach. In these species, food particles are passed directly into the

intestines, without delay in transport or true digestion. The evolution of the stomach allows for storage of food before passage into the intestines, thus permitting more complex feeding habits, such as the ingestion of large quantities of material that would otherwise overwhelm the intestines. Storage of food in the stomach and selective transport through the pylorus at neurally regulated time intervals prevents overwhelming the intestines during large meals, and maximizes digestion and absorption of nutrients. Many bird species further exploit this function and store meals and subsequently regurgitate the partially digested material to feed their young. The stomach also develops mechanical and chemical digestive capabilities, likely with the evolution of jawed fishes that ingest larger meals at irregular intervals. Many variations of stomach shape exist in living vertebrates: the gizzard of birds allows for mechanical digestion using swallowed pebbles, largely reducing the need for teeth (Figure 3). The four-chambered stomach of mammalian ruminants (Figure 4) allows for regurgitation of cud and more extensive breakdown of plant nutrients; the first three chambers secrete liquid and house microorganisms that help breakdown cellulose, and the fourth chamber contains the regions of a “typical” mammalian stomach (cardiac, fundic, and pyloric). Although the stomach shape is highly variable, the majority of living species exhibit an asymmetry of the left and right stomach wall (greater and lesser curvatures) and a general curvature to the left, reflecting the overgrowth of the dorsal wall and rotation of the entire organ seen in human development [17].

LIVER AND GALLBLADDER

The liver forms as a diverticulum from the foregut. Liver hepatoblasts differentiate into the hepatocytes, bile canaliculi, and hepatic ducts. The connection between the liver and duodenum narrows during development, forming the bile duct. The liver gains its hematopoietic function via migrating stem cells from the yolk sac, which is the initial site of hematopoiesis in the embryo. The liver loses its hematopoietic function shortly after the birth of the fetus, at which time the bone marrow becomes the primary site of red and white blood cell production. The liver is supplied by the vitelline vein, which brings nutrient rich blood from the yolk sac. The vitelline vein forms the adult portal vein, which drains the digestive tract. The majority of the liver is endodermal in origin, with mesodermal stromal support from the septum transversum and splanchnic mesoderm. The liver parenchyma is penetrated by branches of the vitelline and umbilical veins, forming the hepatic sinusoids. The gallbladder and cystic duct develop from the cystic diverticulum, which forms from the bile duct. The cystic duct and bile duct merge to form the common bile duct, which opens into the major duodenal papilla [21].

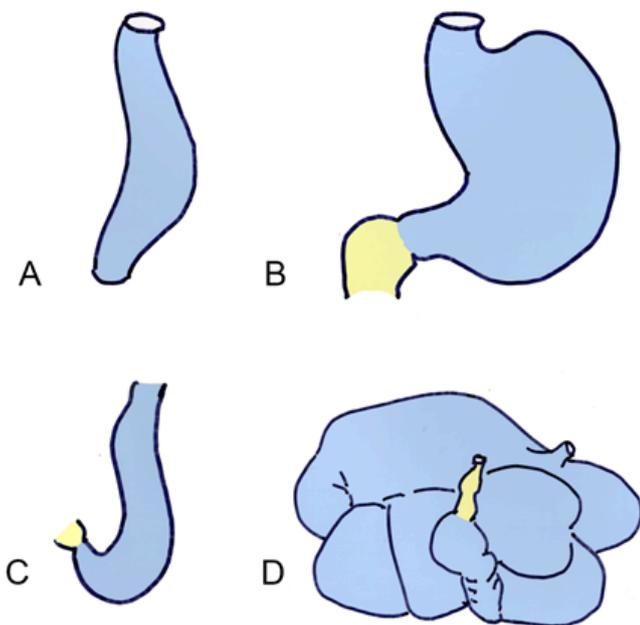


Figure 4: The stomach of a developing human, adult human, shark, and ruminant. (A) Human stomach around 28 days. The dorsal wall of the stomach will grow faster, creating the greater curvature, and the ventral wall will form the lesser curvature. The stomach then rotates 90 degrees around a longitudinal axis, (B) Adult human stomach, where the greater curvature is rotated to the left and the lesser curvature is positioned on the right, (C) Stomach of an adult shark. Note the similarity in shape and orientation with the 28-day human stomach, and (D) Four chambered stomach of a ruminant; the various chambers house bacteria and allow for more extensive digestion of plant cellulose and regurgitation of cud for further mechanical digestion in the mouth.

Evolutionary link

The liver is a structure common to all vertebrates, and it always occupies a considerable space in the ventral abdominal cavity. The mammalian liver closely resembles a glandular gut diverticulum seen in early taxa such as *Amphioxus*, suggesting its most primitive function was in digestive enzyme production. This is reflected in its drainage into the duodenum, allowing for direct transport of digestive material such as bile into the intestinal lumen. The liver also gains an extensive metabolic role, and it produces, alters, and stores fats, proteins, sugars, vitamins, and many other materials. This systemically crucial role of the liver is supported by its extensive venous supply, where all gastrointestinal organs first drain into the hepatic portal system before ultimately reaching the heart (see “vasculature” below). The presence of the gallbladder and drainage of the cystic duct is variable. Interestingly, among the relatively closely related ungulates, cervids lack a gallbladder, bovids possess a gallbladder, and giraffids possess a gallbladder during fetal life but lack one as adults [16, 23–25].

PANCREAS

Like the liver and gallbladder, the dorsal and ventral buds of the pancreas form as diverticula from the duodenum. The ventral bud forms the uncinuate process and the caudal part of the head, and migrates posteriorly around the duodenum to fuse with the dorsal bud, which forms the cranial part of the head, as well as body, and tail of the pancreas (Figure 5). This migration occurs concurrently with the posterior rotation of the duodenum. The ductal systems of both buds fuse, and the ducts from the dorsal bud drain into the ventral ducts, creating the main pancreatic duct. This drains into the duodenum at the ampulla of Vater, along with the common bile duct. The pancreatic endoderm differentiates into cells that perform the many functions of the pancreas. The exocrine (acinar) cells function in digestion, the ductal cells function in transport, and the endocrine cells produce hormones such as insulin, glucagon, and somatostatin. The endocrine cells aggregate into islets, which become functional around the fifth month of development [14].

Evolutionary link

Many primitive fish species lack a discrete pancreas, but instead possess a mass of enzyme secreting cells aggregated at the proximal intestines near what will become the major duodenal papilla. Later in evolution, pancreatic tissues develop as an outgrowth of the bile duct, and still retain their position adjacent to the liver. Correspondingly, as the pancreas develops as a separate organ, its duct system is shared with the drainage of bile from the liver, and the two systems drain into a common opening in the duodenum, which marks the original location of pancreatic cells seen in primitive organisms. In fishes, the dorsal and ventral buds form separate

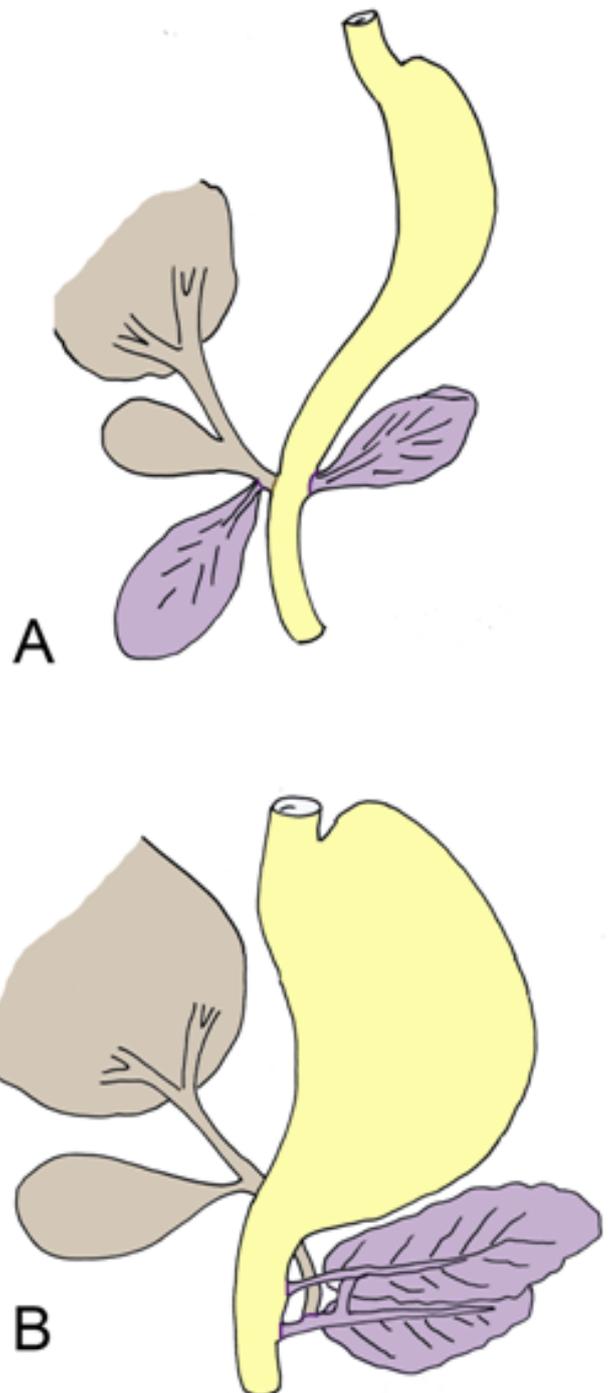


Figure 5: The development of the liver, gallbladder, and pancreas. (A) The hepatic diverticulum arises from the duodenum and forms the liver, bile duct, and cystic diverticulum. The cystic diverticulum further differentiates into the cystic duct and gallbladder. The dorsal and ventral pancreatic buds originate as two separate pancreatic masses with initially independent drainage into the duodenum, and (B) The dorsal and ventral pancreatic buds migrate around the duodenum around week 5, and fuse to form the adult pancreas. The duct systems fuse to form the main pancreatic duct, which opens into the major duodenal papilla, along with the common bile duct that drains the liver and gallbladder. The dorsal pancreatic bud can also drain to the duodenum separately via the accessory pancreatic duct, which empties into the minor duodenal papilla.

structures with independent drainage. This resembles the occasional condition seen in humans, where drainage of the dorsal and ventral buds does not fuse, forming the main and accessory pancreatic ducts respectively [20].

ROTATION OF THE MIDGUT

Around week 5, the midgut undergoes rapid elongation, and forms a hairpin loop around the superior mesenteric artery termed the primary intestinal loop (Figure 6). The cranial limb of the loop creates the jejunum, and parts of the duodenum and ileum, and the caudal limb of the loop develops into the cecum, appendix, ascending colon,

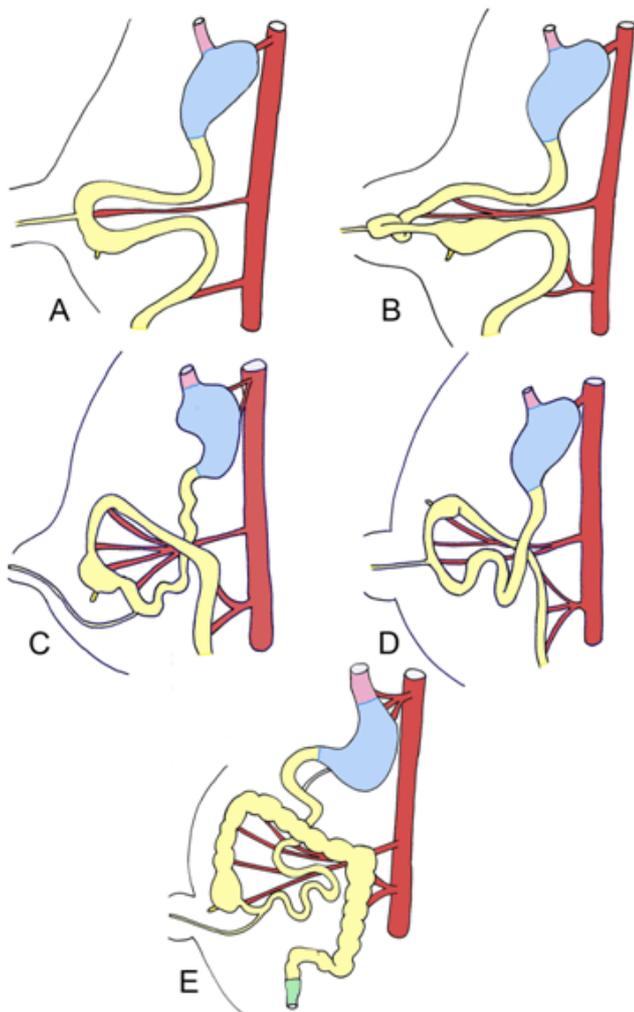


Figure 6: Rotation of the midgut around the superior mesenteric artery. (A) Formation of a hairpin loop around the superior mesenteric artery around fifth week. (B) Herniation of the midgut into the umbilicus around sixth week, and rotation 90 degrees counterclockwise around the superior mesenteric artery, (C) Return of the intestines into the abdomen around 10th week, (D) Further rotation of the intestines within the abdominal cavity around 11th week, so that the cecum is positioned in the right upper quadrant, (E) Fixation of the cecum in the right lower quadrant, thus completing intestinal rotation (270 degrees total).

and parts of the ileum and transverse colon. As the liver rapidly expands in size, the abdominal cavity becomes temporarily too small to accommodate the proliferating intestinal loop, and the intestinal loop thus herniates into the umbilicus. The midgut rotates around the superior mesenteric artery 90 degrees counterclockwise in the umbilicus, and another 180 degrees as the elongated intestines fall back into the abdomen around week 10. The jejunum and ileum also coil and loop separately from the colon. The final midgut rotates an additional 180 degrees counterclockwise, placing the cecum at the right lower quadrant. The midgut, in total, rotates 270 degrees. The ascending and descending colon contact the dorsal body wall upon their return into the abdominal cavity, and eventually fuse, becoming secondarily retroperitoneal [15].

Evolutionary link

Sharks, and some primitive fishes lengthen the intestinal surface area with spiral valves within the intestinal tube. The spiral folds of mucosa extend from one end of the intestine to the other. Vertebrates expand the absorptive capacity of the intestines by extending the mucosal surface into villi and crypts, thus increasing the surface area. In many vertebrates, the intestine itself is elongated and coiled, thus necessitating its herniation into the umbilical cord to accommodate for massive lengthening during development. In mammals and birds, this elongation and rotation can generate intestinal lengths 7–8 times the height of the entire body. The absolute length of the intestines is highly variable, and often relates both to body size and dietary habits. In frog tadpoles, which are largely herbivorous, the intestines are long and extensively coiled, allowing for better plant digestion, whereas the adult frogs after metamorphosis possess shortened intestines, as they are mainly carnivorous and don't require extensive nutrient breakdown. Herbivorous species generally have more elongated intestines, allowing for the ingestion of cellulose plant material, which necessitates more extensive digestion and larger surfaces for absorption [20].

HINDGUT AND CLOACA

The distal-most portion of the embryonic hindgut as well as the developing urinary and reproductive tracts is continuous with the cloaca (Figure 7). The cloaca forms the anorectal canal posteriorly and urogenital sinus (future bladder, urethra, prostate, and vestibule of the vagina) anteriorly. The anus and urogenital sinus become separated by the urorectal septum, which forms the perineal body [21].

The cloacal membrane is endodermal dorsally and ectodermal ventrally, with no mesoderm in between. The membrane ruptures, allowing the anal canal to open to the exterior, thus making the gastrointestinal

tract a patent pathway. In the anus, ectodermal cells of the anal membrane proliferate and temporarily plug the lumen. The membrane obliterates around week 8, and its location is marked by irregular mucosal foldings, forming the pectinate line. Anything proximal to this is formed from the endoderm of the hindgut, and distal to the pectinate line is formed by the ectoderm of the cloaca. The distal third of the anal canal is referred to as the proctodeum. As the distal and proximal anal canal have different embryologic origins, they are supplied by separate vasculature and innervation (Table 1) [14].

Evolutionary link

The colon of most mammals is larger in diameter than the small intestines, and contains characteristic intestinal outpouching and longitudinal muscle fibers. As aquatic organisms evolve to live on land, the colon undergoes substantial lengthening. One of the major functions of

the colon is to reabsorb water, and as vertebrates become adapted for terrestrial life, longer large intestines facilitate better water retention. The general shape involves a right-sided ascending colon and left-sided descending colon. In primates, a transverse colon is present and extends the connection between the ascending and descending colon, thus increasing the surface area of haustrated intestines. Herbivores increase the length of the colon with additional coiling [26].

Several groups of animals, including amphibians, reptiles, and birds, maintain the distal connection between the urinary, genital, and gastrointestinal tracts as a cloaca. The formation of a cloaca at some point during development is common to all vertebrates, however in most mammals, this distal cavity is partitioned into the anorectal canal and urogenital sinus by the urorectal septum. This septum creates separate external openings for the gastrointestinal and genitourinary tracts. In monotremes, such as the platypus, the subdivision of the cloaca is partially completed, and a fold marks the delineation between but does not fully separate the distal intestines from the distal urinary and reproductive tracts [17].

VASCULATURE

The yolk sac is initially a large and major embryonic structure, and it contains its own blood supply arising from the dorsal (abdominal) aorta. The gastrointestinal tract and associated organs derive from the yolk sac, thus the vitelline arteries persist in the adult to supply the digestive organs. The vitelline arteries arise from the aorta caudal to the diaphragm, and form in the adult the celiac artery (foregut), superior mesenteric artery (midgut) and inferior mesenteric artery (hindgut). During early development, these arteries bring deoxygenated blood from the heart towards the yolk sac [22].

The embryo has three venous systems: the vitelline system, the umbilical system, and the cardinal system. The umbilical and vitelline veins bring blood from the placenta and yolk sac, respectively, into the liver and heart. The vitelline and umbilical systems contribute to the ultimate venous drainage of the developed gastrointestinal tract. The vitelline veins traverse the developing liver and create the liver sinusoids. Around the third month, the left vitelline vein regresses, and the right vitelline vein drains the entirety of the gastrointestinal tract and diverticula. The vitelline venous system creates the portion of the inferior vena cava between the liver and heart, portal vein, splenic vein, and the veins draining the gastrointestinal tract, including the superior mesenteric vein and inferior mesenteric vein (Figure 8) [14].

The umbilical veins drain oxygenated blood from the placenta to the embryonic heart. The right umbilical vein ultimately regresses, and the left umbilical vein persists as the ductus venosus. The ductus venosus is an anastomosis between the inferior vena cava and umbilical

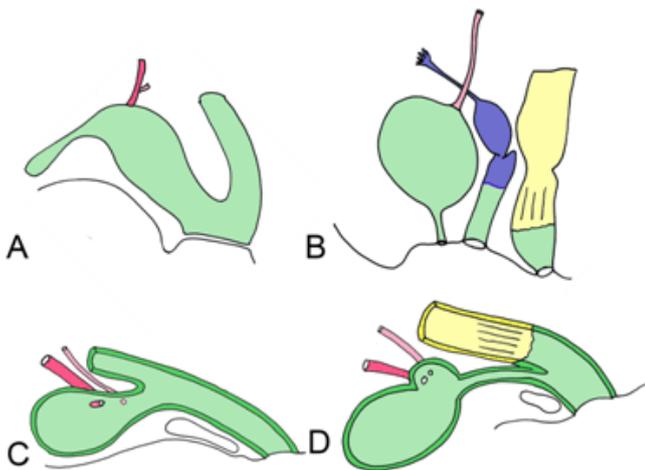


Figure 7: Development of the cloaca. (A) Cloaca of a human embryo around fifth week, when the embryo is anatomically sexually indifferent. The urogenital sinus is positioned anteriorly (left), and the distal anus is positioned posteriorly (right); both systems initially drain into a common opening. Arising from the urogenital sinus is the allantois that enters the umbilical cord anteriorly as the primitive excretory system, and the mesonephric duct with the ureteric bud, (B) Cloacal derivatives in a female embryo. The structures from anterior to posterior include the bladder and ureter, vagina and uterus, and anorectal canal. The upper portion of vagina as well as the uterus and fallopian tubes are formed from the paramesonephric duct, and the upper portion of the anus above the pectinate line is formed from gut endoderm, (C) Cloaca of a male reptile, where the ureter, ductus deferens and distal intestines terminate in a common opening, (D) Cloaca of a male monotreme, where the ureter, ductus deferens, and distal intestines terminate in a common opening, but a deeper fold begins to incompletely separate the genitourinary tract from the gastrointestinal tract. Paramesonephric duct structures are shown in blue, mesonephric duct structures are shown in pink, gut endodermal structures are shown in yellow, and cloacal structures are shown in green.

Table 1: Regional delineations of the human digestive system and their associated autonomic/somatic innervation and vascular supply

Portion of Digestive Tract and Embryologic Origin	Sympathetic Innervation	Parasympathetic Innervation	Somatic Innervation	Arterial/Venous Supply
Foregut: Mouth to second portion of the duodenum Diverticula: liver, gallbladder, pancreas	T5-T9 via the greater splanchnic nerve	CN X (Vagus nerve)		Celiac trunk/splenic vein, portal veins
Midgut: Third portion of the duodenum through the proximal 2/3 of the transverse colon	T10-T11 via the lesser splanchnic nerve	CN X (Vagus nerve)		Superior mesenteric artery/superior mesenteric vein
Hindgut: distal 1/3 of the transverse colon, to anus above pectinate line	L1-L2 via the lumbar splanchnic nerve	S2-S4: Pelvic splanchnic nerves		Inferior mesenteric artery/inferior mesenteric vein
Cloaca: anus below the pectinate line			Pudendal nerve (via inferior rectal nerves)	Middle and inferior rectal artery/middle and inferior rectal vein

Abbreviations: CN: Cranial nerve

vein, allowing oxygenated blood to bypass the liver and drain directly into the right atrium. This channel is closed after birth, as the placenta no longer supplies oxygenated blood, and creates the ligamentum venosum [21].

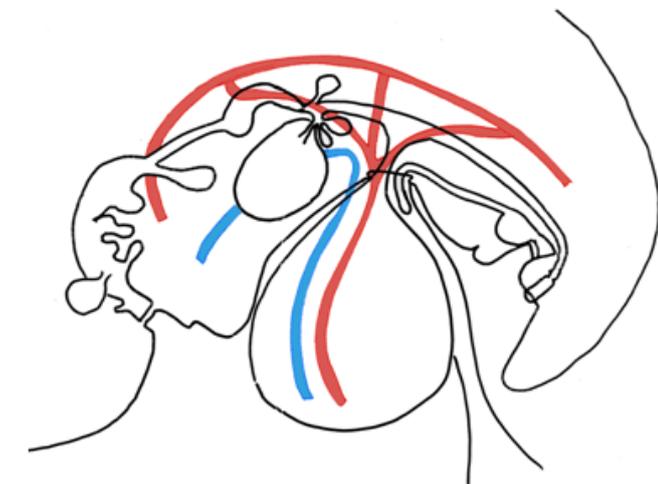


Figure 8: Vitelline vasculature of the human embryo. The vitelline arteries (red) arise from the abdominal aorta and supply blood to the yolk sac and derivatives. In the adult, these form the celiac trunk, superior mesenteric artery, and inferior mesenteric artery. The vitelline vein (blue) drains blood from the yolk sac to the developing heart. The vein first traverses the liver, creating the hepatic sinusoids. All yolk sac derivatives first drain to the liver, thus creating the adult hepatic portal system. The vitelline vein also forms the portion of the inferior vena cava between the liver and heart.

Evolutionary link

In fishes and amphibians, the yolk sac does not have its own vasculature, and is instead supplied by systemic arteries and veins. In mammals, birds, and reptiles, however, the yolk sac evolves its separate drainage, thus forming the vitelline arteries and veins. As the liver develops into a massive abdominal structure, the vitelline veins are divided into smaller hepatic sinusoids as they traverse the liver towards the heart; all gut veins first converge in the liver, thereby forming the hepatic portal system common to all vertebrates. The development of the vitelline drainage system allows for the evolution of extensive hepatic metabolic functions, as all nutrients absorbed in the digestive tract are drained directly to the liver. In many fishes, blood from the liver is drained directly into the sinus venosus of the developing heart; in mammals, reptiles, amphibians, and birds, however, the vitelline system creates the portion of the inferior vena cava between the liver and heart, and thus hepatic blood flow drains first into this large composite vein [27].

CONGENITAL ABNORMALITIES

Tracheoesophageal fistula

Failure of the tracheoesophageal septum to fully separate the proximal foregut from the developing respiratory tree. Several variations exist; the most common anomaly presents as a blind ending esophagus (esophageal atresia), and distal anomalous connection between the esophagus and trachea. During development, the blind ending esophagus prevents the normal swallowing of amniotic fluid, resulting in a dilated proximal esophagus, and polyhydramnios. This greatly increases the risk of

aspiration after birth, and can present with drooling, choking, and cyanosis with feeding. This is component of “VACTERL” association, which is a group of congenital anomalies that commonly coexist, and are often seen with chromosomal disorders. The VACTERL association includes vertebral anomalies, anal atresia, cardiovascular anomalies, tracheoesophageal fistula, esophageal atresia, renal anomalies, and limb defects [28].

Pyloric stenosis

The pylorus of the developing stomach hypertrophies, causing gastric outlet obstruction. This creates an “olive” mass, created from the thickened pyloric circular muscle. After birth, this presents as non-bilious projectile vomiting; bile is absent since the constriction is proximal to the bile duct [29].

Annular pancreas

The pancreas develops as a bilobed ventral bud, rather than the typical dorsal and ventral buds. One lobe migrates posteriorly and the other migrates anteriorly, and the two buds join to form a ring around the duodenum. The buds compress the duodenum causing obstruction. This prevents the fetus from swallowing amniotic fluid during development, causing polyhydramnios, and leads to vomiting and abdominal distension after birth [30].

Intestinal malrotation

Rotation of the midgut is not complete by the 10th-12th week. The cecum is positioned adjacent to the duodenum, and is anomalously attached to the vasculature of the mesentery. This allows for torsion around the attachment, possibly leading to obstruction and necrosis. This presents with bilious vomiting, and on imaging exhibits an “apple peel” appearance of the jejunum [31].

Midgut volvulus

Fixation of the midgut to the body wall via fibrous bands, termed “Ladd’s bands” due to intestinal malrotation. This can compress the vasculature supplying the intestines, leading to necrosis, or cause obstruction leading to bilious vomiting [32].

Meckel’s diverticulum

Failure of the vitelline duct to fully regress, which typically occurs around weeks 5–8. This is a true diverticulum that involves all layers of the intestinal wall. Meckel’s diverticulum can present as ectopic gastric or pancreatic tissue secreting acid or digestive enzymes, causing ulceration. After birth, this leads to painless bleeding (melena), right lower quadrant pain, peritonitis, or obstruction within the first two years of life. A variation of Meckel’s diverticulum is an omphalomesenteric fistula, where the ileum maintains an open connection with the

umbilicus. This would present as meconium leaking through the umbilicus after birth [33].

Umbilical hernia

Protrusion of bowel through the umbilical ring. This often regresses spontaneously by age 5 [34].

Omphalocele

Herniation of bowel through the umbilical ring, covered with a membranous sac. This is often seen with chromosomal abnormalities [35].

Gastroschisis

Herniation of the bowel through the weakness in the anterior abdominal wall, lateral to the umbilicus. The herniated bowel is not contained in a sac [35].

Imperforate anus

Dysfunction of the urorectal septum, which normally separates the cloaca into the urogenital sinus and anorectal canal. The rectum opens into the reproductive or urinary tract (as a fistula between the bladder, urethra, or vagina), or a low lesion where the rectum ends in a blind pouch. After birth, this presents as failure to pass meconium, with a “dimple” where the anus should be [36].

Hirschsprung’s disease

Failure of the neural crest cells to migrate to the distal anus, thus creating an aganglionic segment of colon. This section is unable to relax and pass stool. At birth, this presents as obstruction and failure to pass meconium, and can lead to the condition termed megacolon [37].

CONCLUSION

Studying evolutionary anatomy helps put human embryology into perspective; the concepts help explain why humans develop the way we do, rather than just memorizing how. Comparative anatomy helps link form to function, and leads to an overall deeper understanding of the embryology and anatomy, and an appreciation for the complexity of other animals. Studying congenital anomalies helps reinforce embryological concepts, and learning these anomalies in their developmental context facilitates long-term retention of knowledge. We believe reviews of each system of embryology supplemented with the evolutionary anatomy and associated congenital anomalies will help students better understand human development.

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Conflict of Interest

Authors declare no conflict of interest.

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REFERENCES

1. Danowitz M, Zheng H, Guigova A, Solounias N. A combined approach of teaching head development using embryology and comparative anatomy. *J Anat Embryo* 2016;3:17–27.
2. Talbot NJ. Growing into the air. *Curr Biol* 1997 Feb 1;7(2):R78–81.
3. Schulze ED. Plant life forms and their carbon, water and nutrient relations. In: Lange OL, Nobel PS, Osmond CB, Ziegler H eds. *Physiological plant ecology*. New York: Springer; 1982. p. 615–76.
4. Niklas KJ, Kutschera U. The evolution of the land plant life cycle. *New Phytol* 2010 Jan;185(1):27–41.
5. Miller SA, Perrotti W, Silverthorn DU, Dalley AF, Rarey KE. From college to clinic: reasoning over memorization is key for understanding anatomy. *Anat Rec* 2002 Apr 15;269(2):69–80.
6. Nesse RM, Bergstrom CT, Ellison PT, et al. Evolution in health and medicine Sackler colloquium: Making evolutionary biology a basic science for medicine. *Proc Natl Acad Sci U S A* 2010 Jan 26;107 Suppl 1:1800–7.
7. Nesse RM, Williams GC. Evolutionary biology in the medical curriculum: What every physician should know. *Bioscience* 1997;47(10):664–66.
8. Childs B, Wiener C, Valle D. A science of the individual: implications for a medical school curriculum. *Annu Rev Genomics Hum Genet* 2005;6:313–30.
9. Harris EE, Malyango AA. Evolutionary explanations in medical and health profession courses: are you answering your students’ “why” questions? *BMC Med Educ* 2005 May 10;5(1):16.
10. MacCallum CJ. Does medicine without evolution make sense? *PLoS Biol* 2007 Apr;5(4):e112.
11. Nesse RM, Stearns SC, Omenn GS. Medicine Needs Evolution. *Science* 2006;311(5764):1071.
12. Nesse RM, Schiffman JD. Evolutionary Biology in the Medical School Curriculum. *BioScience* 2003;53(6):585–87.
13. Downie JR. Evolution in Health and Disease: The Role of Evolutionary Biology in the Medical Curriculum. *Bioscience Educ* 2004;4(1):1–18.
14. Schoenwolf GC, Bleyl SB, Brauer PR, Francis-West PH. *Larsen’s human embryology*, 4ed. Philadelphia: Churchill Livingstone; 2009. p. 1–687.
15. Standring S. *Gray’s anatomy: the anatomical basis of clinical practice*, 41ed. Philadelphia: Churchill Livingstone; 2015. p. 1–15843.
16. Feduccia A, McCrady E. *Torrey’s Morphogenesis of the Vertebrates*, 5ed. New York: John Wiley & Sons; 1991. p. 1–528.
17. Romer AS, Parsons TS. *The Vertebrate Body*, 5ed. Philadelphia: W.B. Saunders Company; 1986. p. 1–624.
18. Clemente CD. *Anatomy: A Regional Atlas of the Human Body*, 6ed. Baltimore: Williams & Wilkins; 2010. p. 1–752.
19. Hamilton WJ, Mossman HW. *Human embryology*, 4ed. Baltimore: The Williams and Wilkins Company; 1972. p. 1–646.
20. Wake MH. *Hyman’s Comparative Vertebrate Anatomy*, 3ed. Chicago: The University of Chicago Press; 1979. p. 1–768.
21. Sadler TW. *Langman’s Medical Embryology*, 13ed. Philadelphia: Lippincott Williams & Wilkins; 2014. p. 1–400.
22. Cochard LR. *Netter’s atlas of human embryology*. Philadelphia: Saunders; 2012. p. 1–288.
23. Cave AJE. On the liver and gall-bladder of the Giraffe. *Proc Zool Soc Lond* 1950;120(2):381–93.
24. Braun U, Hausammann K. Ultrasonographic examination of the liver in sheep. *Am J Vet Res* 1992 Feb;53(2):198–202.
25. Geist V. *Deer of the world: their evolution, behavior, and ecology*. Mechanicsburg: Stackpole Books; 1998. p. 1–421.
26. Kardong KV. *Vertebrates: comparative anatomy, function, evolution*, 7ed. Boston: McGraw-Hill; 2014. p. 1–816.
27. Stephan F. Morphologie Générale du Système Circulatoire. In: Grasse PP ed. *Traité de Zoologie Volume 12*. Paris: Masson et Éditeurs Libraires de L’academie de Médecine; 1954. p. 854–973.
28. Kovesi T, Rubin S. Long-term complications of congenital esophageal atresia and/or tracheoesophageal fistula. *Chest* 2004 Sep;126(3):915–25.

29. Hernanz-Schulman M. Infantile hypertrophic pyloric stenosis. *Radiology* 2003 May;227(2):319–31.
30. Ravitch MM, Woods AC. Annular pancreas. *Ann Surg* 1950 Dec;132(6):1116–27.
31. Ford EG, Senac MO Jr, Srikanth MS, Weitzman JJ. Malrotation of the intestine in children. *Ann Surg* 1992 Feb;215(2):172–8.
32. Seashore JH, Touloukian RJ. Midgut volvulus. An ever-present threat. *Arch Pediatr Adolesc Med* 1994 Jan;148(1):43–6.
33. Williams RS. Management of Meckel's diverticulum. *Br J Surg* 1981 Jul;68(7):477–80.
34. Skinner MA, Grosfeld JL. Inguinal and umbilical hernia repair in infants and children. *Surg Clin North Am* 1993 Jun;73(3):439–49.
35. deVries PA. The pathogenesis of gastroschisis and omphalocele. *J Pediatr Surg* 1980 Jun;15(3):245–51.
36. Stafford SJ, Klein MD. Surgical conditions of the anus and rectum. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF eds. *Nelson Textbook of Pediatrics*, 19ed. Philadelphia: Elsevier Saunders; 2011. p. 1355–62.
37. Amiel J, Lyonnet S. Hirschsprung disease, associated syndromes, and genetics: a review. *J Med Genet* 2001 Nov;38(11):729–39.

SUGGESTED READING

- Moore KL. *The developing human*, 9ed. Philadelphia: W.B. Sanders Company; 2014. p. 1-560.
- Stevens CE, Hume ID. *Comparative physiology of the vertebrate digestive system*. Cambridge: Cambridge University Press; 2004. p. 1-420.

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