

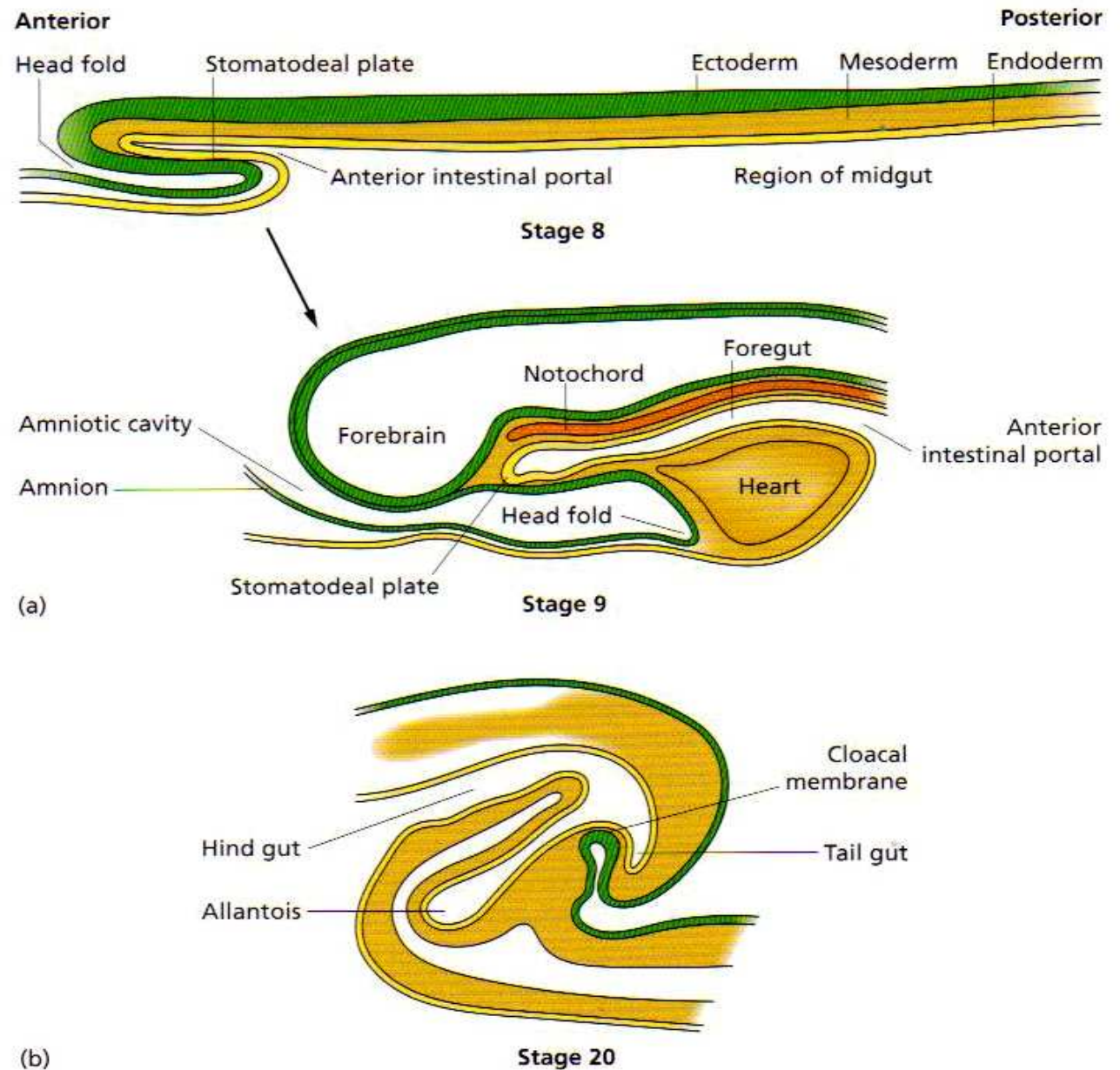
6.2. DEVELOPMENT OF ENDODERMAL ORGANS

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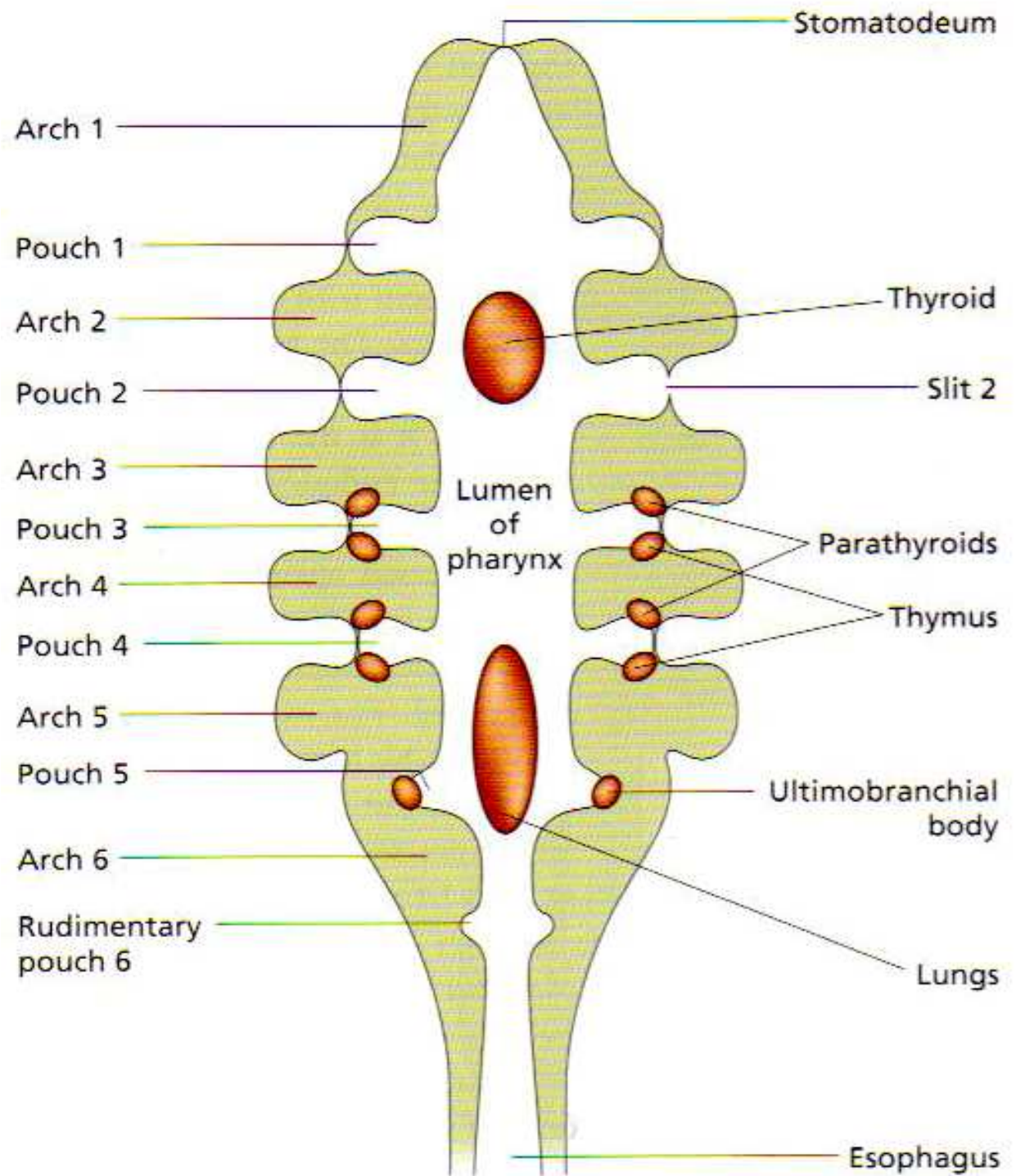
Endoderm forms the **epithelial lining** of the gut together with its outgrowths – liver, pancreas and respiratory system. The outer coats of these organs - smooth muscle, connective tissue and blood vessels are formed from **splanchnic mesoderm**. Splanchnic mesoderm + endoderm = **splanchnopleure**.

GUT DEVELOPMENT

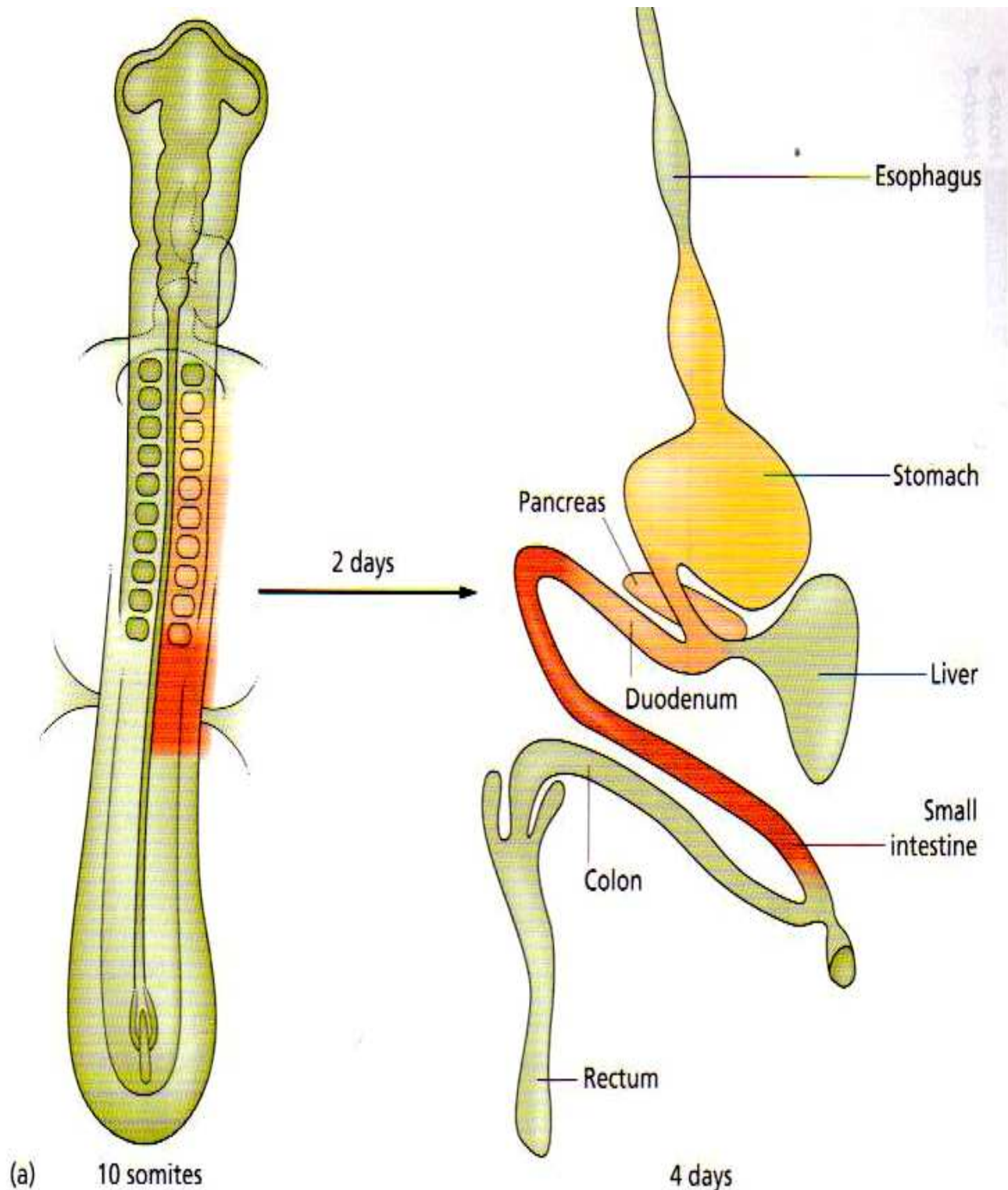
In chick, the endoderm is formed as lower layer of definitive endoderm that emerges from the primitive streak. The gut lumen originates from the space beneath the blastoderm. The gut tube itself is formed by the folding of the body away from the blastoderm.



ORGANIZATION OF THE GUT TUBE: In the region of the pharynx are formed the **pharyngeal pouches**, there are 4 major pouches and two or more rudimentary. Buds from the 1st pouch form the cavities of the **middle ear** and the **Eustachian tubes**. The ventral midline region forms the **thyroid gland**. The 2nd pair forms the **tonsils**, 3rd pair the **thymus**, 4th pair the **parathyroid**. In the ventral midline opposite to the pouches the trachea forms and produces the paired buds that later generate **bronchi** and **lung tissue**. The floor of pharynx becomes the **tongue**.



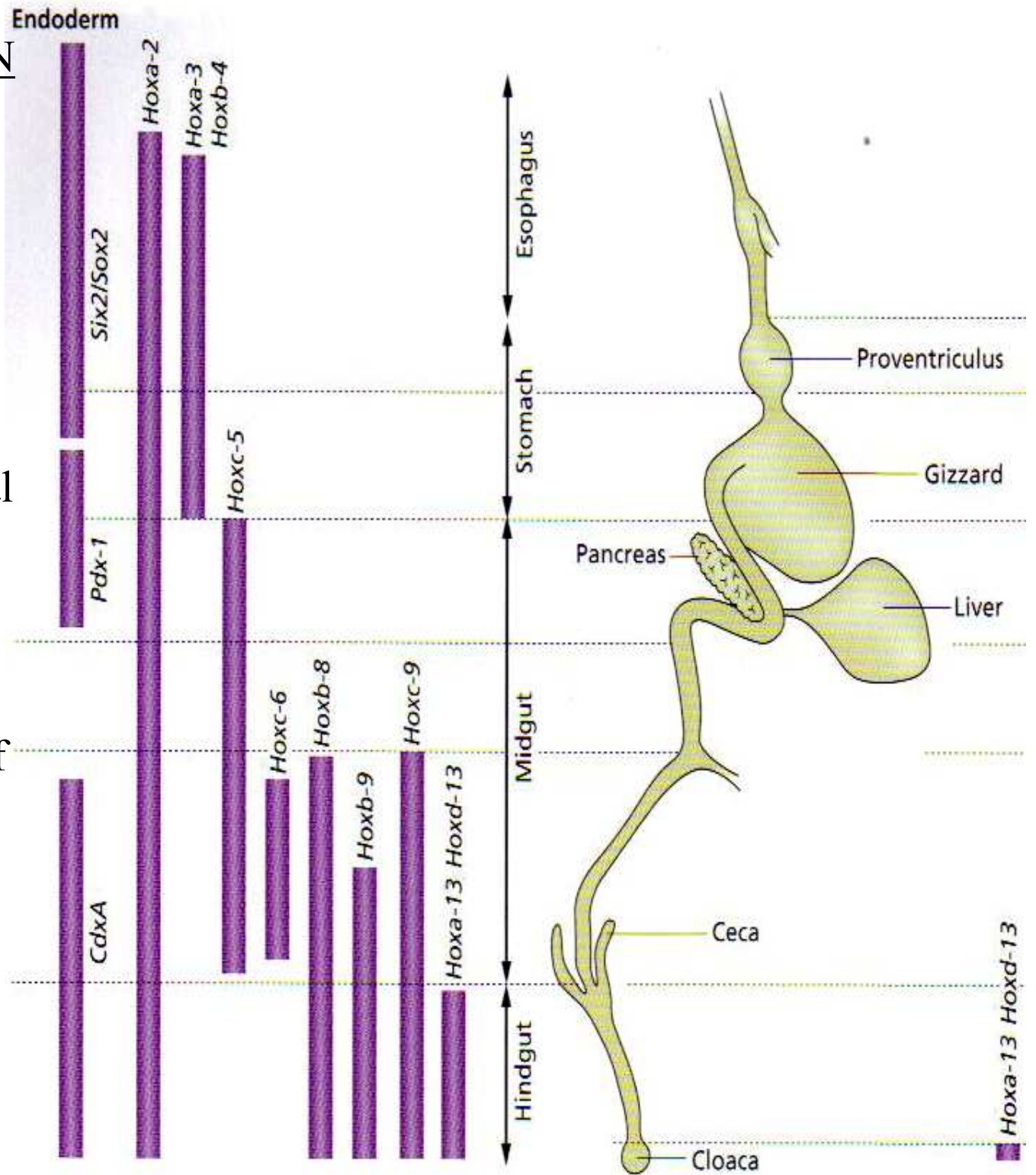
Esophagus and **stomach** follow the pharyngeal region. At the exit of the stomach is the **pyloric sphincter** leading to **small intestine**. The **liver** is ventral outgrowth of the endodermal epithelium that expands to the adjacent ventral mesentery. The **pancreas** arises from a large dorsal bud and a small ventral bud, that later fuse to form a single organ. The junction between small and large intestine is often marked by presence of outgrowth called **caeca**. At the posterior end the large intestine becomes **rectum** in and mammals joins the exterior through the **anal sphincter**.



DETERMINATION OF THE ENDODERM: The initial formation of the endoderm has been mainly characterized in *Xenopus* and zebrafish. In *Xenopus* the endoderm forms from the tissue corresponding to the eight most vegetal blastomeres at the 32-cell stage. The endoderm is formed by the action of transcription factors **VegT**, **Sox17**, **Mix1**, **Mixer** and **GATA1-4**. Some of these factors require intercellular signaling out of which the critical is **nodal** signaling. Animals with **nodal loss-of-function** can not form the **definitive endoderm**. The transcription factors mentioned above specify endoderm as a germ layer rather than any specific type of epithelium or organ.

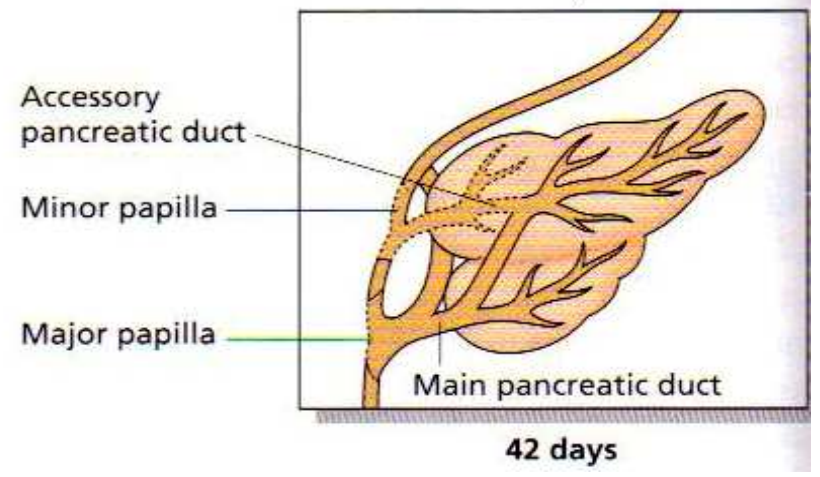
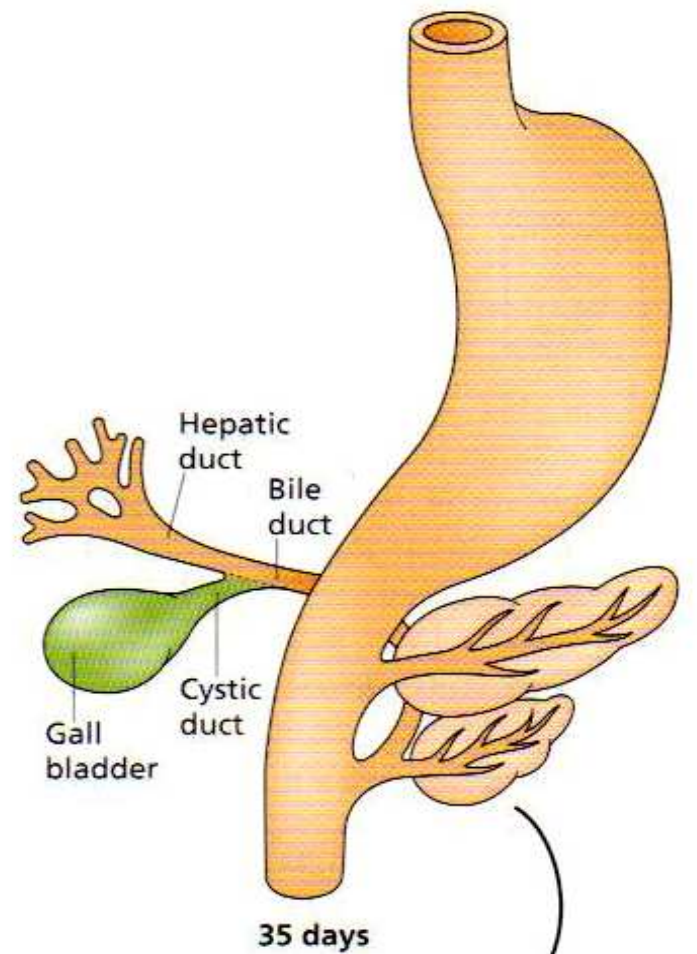
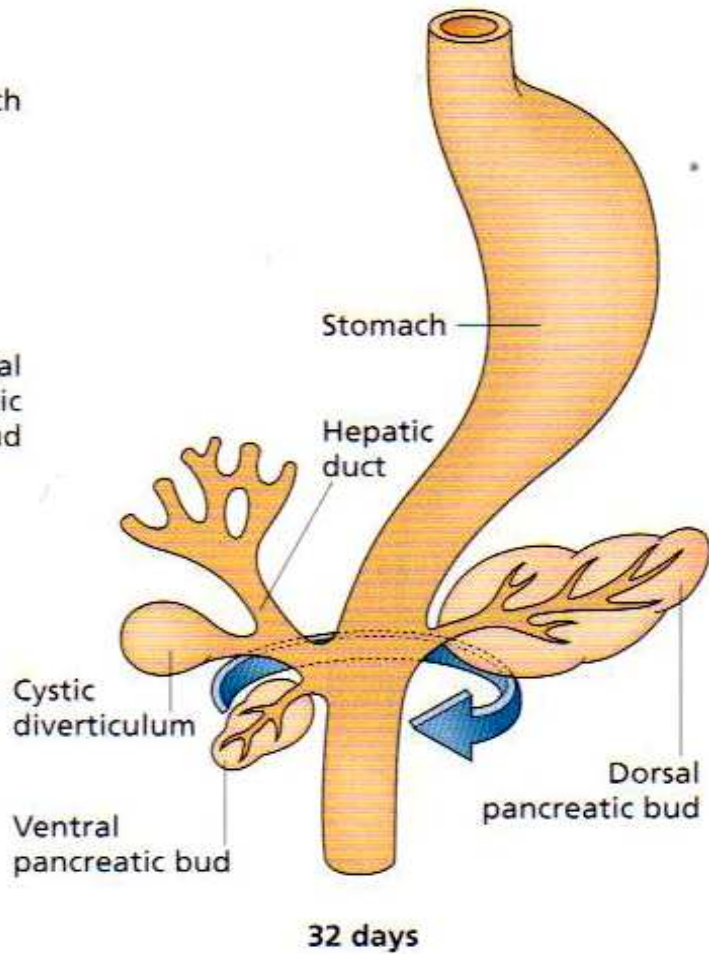
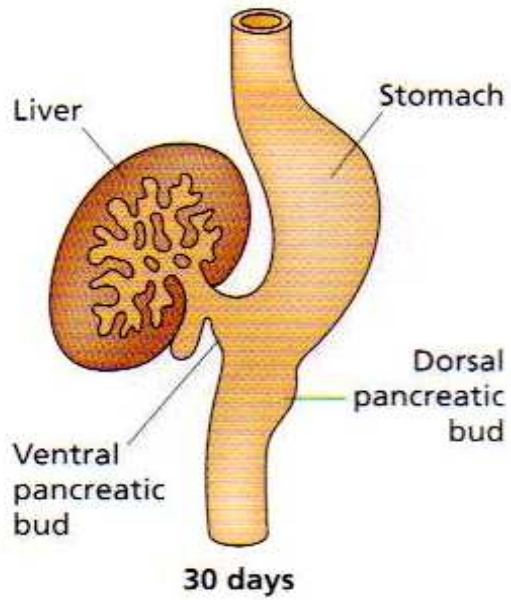
REGIONAL SPECIFICATION

OF ENDODERM: Many transcription factors are expressed locally in endoderm and are important for regional specification. These include **pax9** that is critical for development of thymus and parathyroid, **Nkx2.1** is essential for thyroid and lungs, **Pdx1** that is a critical regulator of pancreas development, and **FoxA2** which loss-of function leads to lack of development of fore- and midgut.



PANCREATIC DEVELOPMENT

INDUCTION OF PANCREATIC BUDS: Both dorsal and ventral buds give rise to the same range of pancreatic cell they arise in different ways. The dorsal bud appears the region where notochord contacts the gut roof. It is the region of suppression of the otherwise ubiquitous expression of **Shh** and **Indian hedgehog (Ihh)**. The effect of notochord can be mimicked by administration of **Activin** or **FGF**. The ventral pancreas is formed from the adjacent region of the foregut floor to the liver only in the **absence** of FGF, that functions in maintaining the Shh. It thus appears that dorsal bud is induced by FGF whereas the ventral bud develops because of an absence of FGF, although the common factor is suppression of Shh expression in the endoderm. Once both buds are formed, their continued outgrowth and differentiation depends on close proximity of the pancreatic mesenchyme, that executes a **permissive effect** on bud outgrowth. A signal that carries this function appears to be **FGF10**.



PANCREATIC TRANSCRIPTION FACTORS: **Pdx1** is essential for pancreas formation and is expressed in a region of the duodenum including the prospective territories of the pancreatic buds. Later in the development, the Pdx expression is downregulated but persists in β -cells where it serves as transcription factor for insulin. **Hb9** precedes Pdx1 expression and the K.O. animals do not develop dorsal pancreas. **PTF1** is essential for expression of various exocrine genes, its K.O. do not develop ventral bud. **Pax4**, **Pax6** and **neurogenin 3 (Ngn3)** are essential for endocrine cell development.

