

Development of the Liver and Pancreas

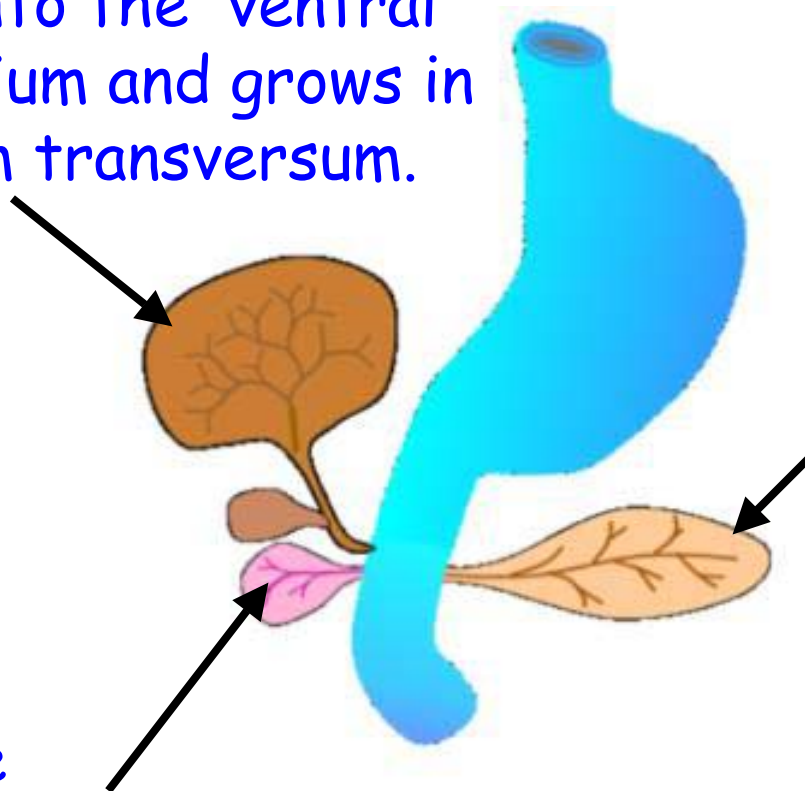
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Three glandular buds arise from the distal end of the foregut during the fourth week

Day 22 - The hepatic bud projects into the ventral mesogastrium and grows in the septum transversum.



Day 26 - The dorsal pancreatic bud grows into the dorsal mesogastrium

Day 28 - The ventral pancreatic bud grows into the ventral mesogastrium

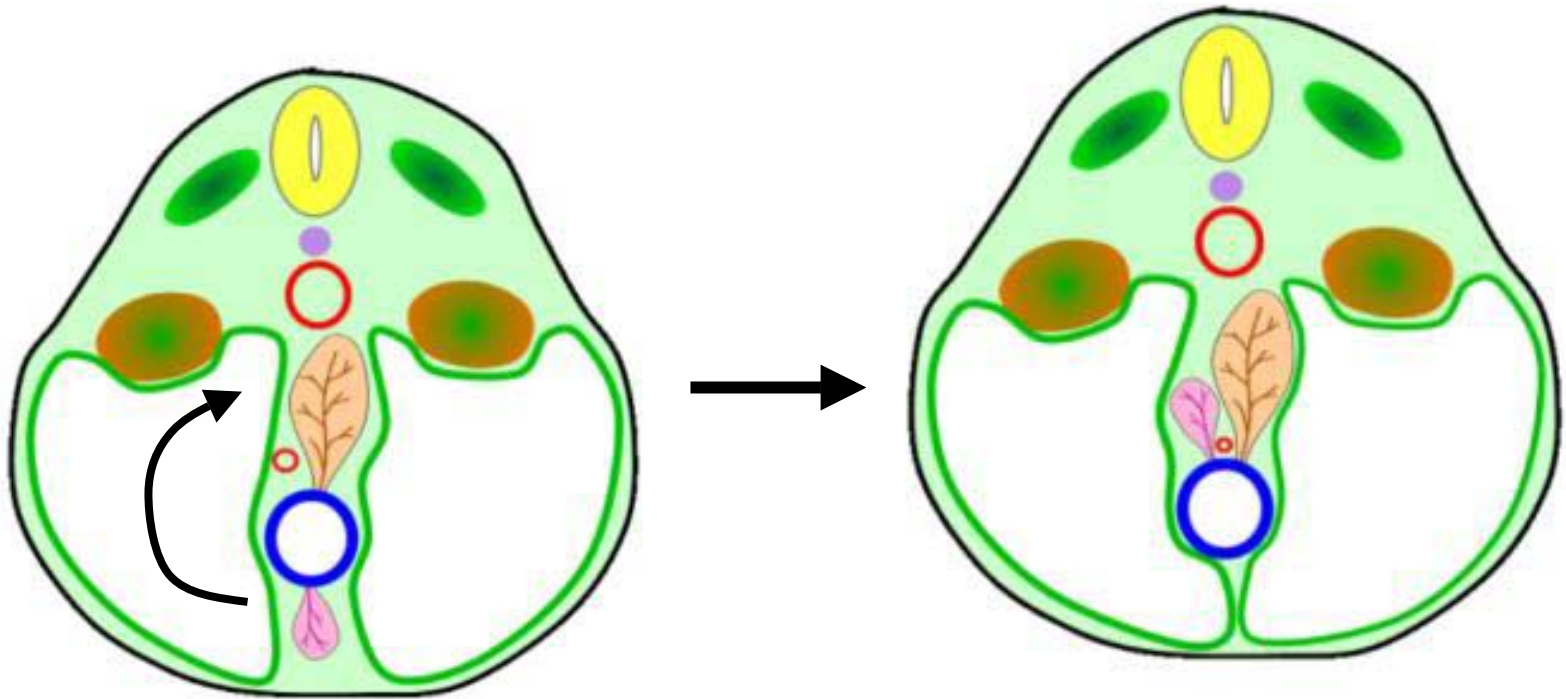
Two pancreatic buds develop from the distal end of the foregut endoderm during the fourth week

Day 26 -
The dorsal pancreatic bud
grows into the dorsal
mesentery

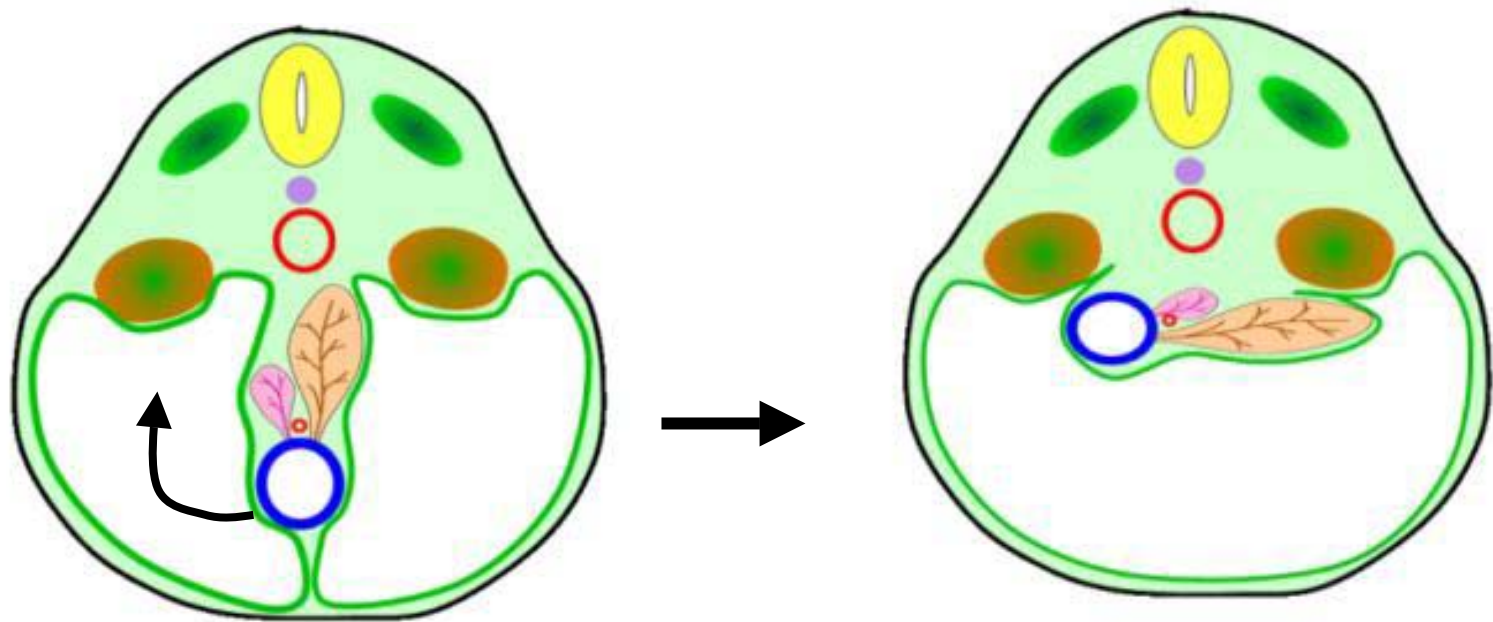


Day 28 -
The ventral pancreatic bud
grows into the ventral mesentery
just distal to the bile duct

The Position of the Pancreatic Buds Is Altered by Two Rotations



1. The ventral pancreas migrates to the dorsal aspect of the foregut.
The superior mesenteric artery is trapped between the two pancreatic rudiments



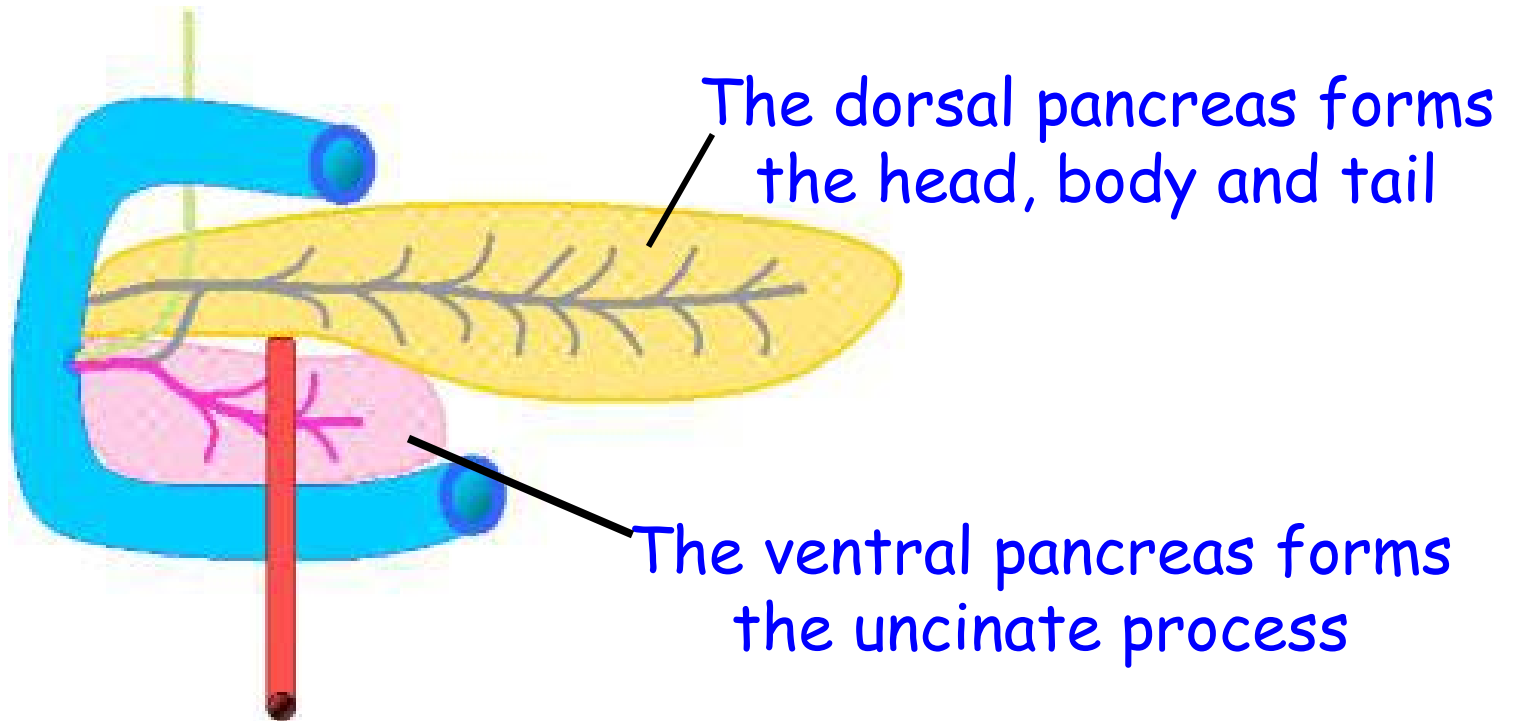
2. The foregut and dorsal mesentery fold to the right

As a result:

- The dorsal mesentery is obliterated
- The pancreas becomes retroperitoneal

The dual origin of the pancreas explains the anatomical relations of the pancreas

The two pancreatic buds fuse in the 6th week to form the definitive pancreas



The superior mesenteric artery emerges dorsal to the body and ventral to the uncinete process

The two pancreatic ducts are re-arranged to form a common opening into the duodenum.

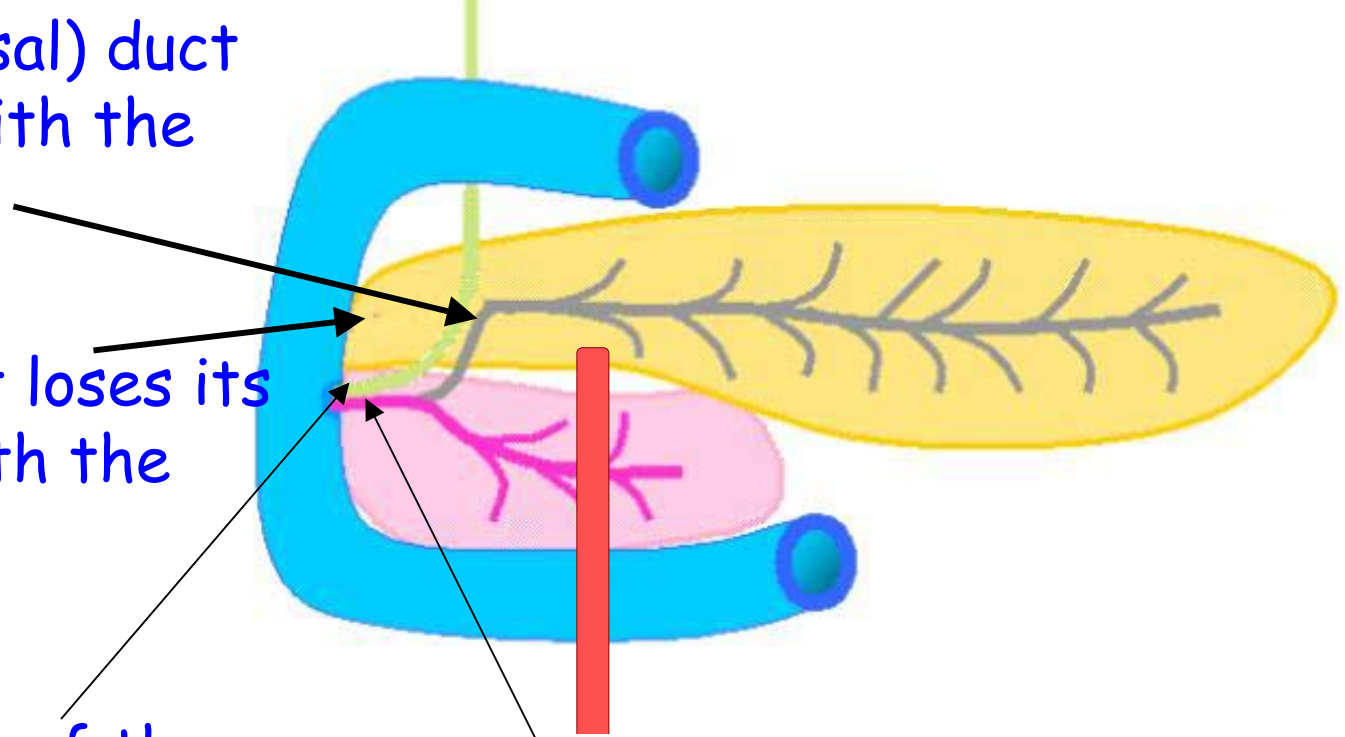
The main (dorsal) duct anastomosis with the ventral duct.

The main duct loses its connection with the duodenum.

The opening of the ventral duct becomes the main opening.

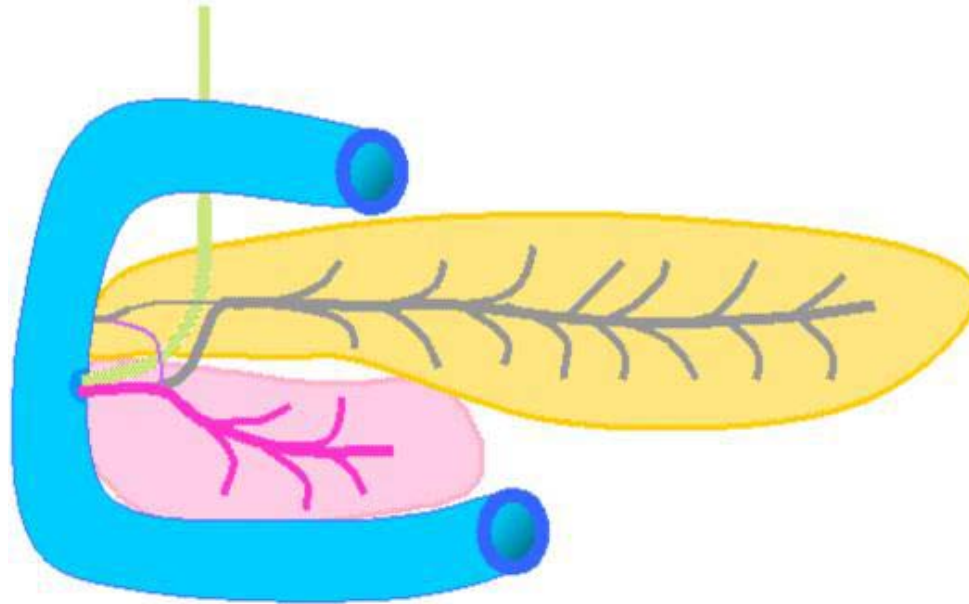
The pancreatic duct and bile duct open into a common ampulla of Vater.

Sphincter of Oddi develops from mesenchyme at 12 weeks



An Accessory Pancreatic Duct (of Santorini) Is Often Present in Normal Individuals.

It is due to anomalous anastomoses between the ventral pancreatic duct and the opening of the dorsal duct.



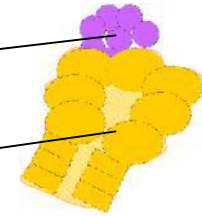
- When present, the accessory pancreatic duct:
- receives the ducts from the uncinete process,
 - opens into the duodenum proximal to the major papilla
 - often communicates with the main duct.

The acini and islets of Langerhans both differentiate from the foregut endoderm.

They arise from distinct cell clusters.

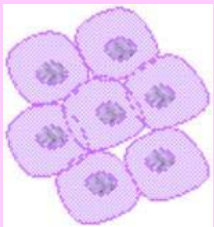
Islet cells

Acinar cells



The **pancreatic acini** begin to form zymogen granules from the 8th week. They secrete digestive enzymes at 30 weeks (7 months).

The **islets of Langerhans** differentiate into distinct cell types during the 8th - 9th weeks in the following order:



α -cells: glucagon

β -cells: insulin

δ -cells: somatostatin

PP-cells: pancreatic polypeptide

Specific granules are evident by the 9th week.
Islets secrete insulin at 21 weeks (5 months).

Development and Differentiation of the Pancreas

The dorsal pancreas is induced by the notochord.
The ventral pancreas is induced by hepatic mesoderm

Differentiation of the acini depends on the presence of mesoderm, but this need not be pancreatic mesoderm.

Differentiation of the islets of Langerhans does not require the presence of mesoderm or of pancreatic acini.

It was originally thought that the Islets were derived from the neural crest. Evidence from quail-chick chimera cell tracers and transgenic animals indicates that islet cells are derived from foregut endoderm.

Anomalies of the Pancreas

1. Annular pancreas:

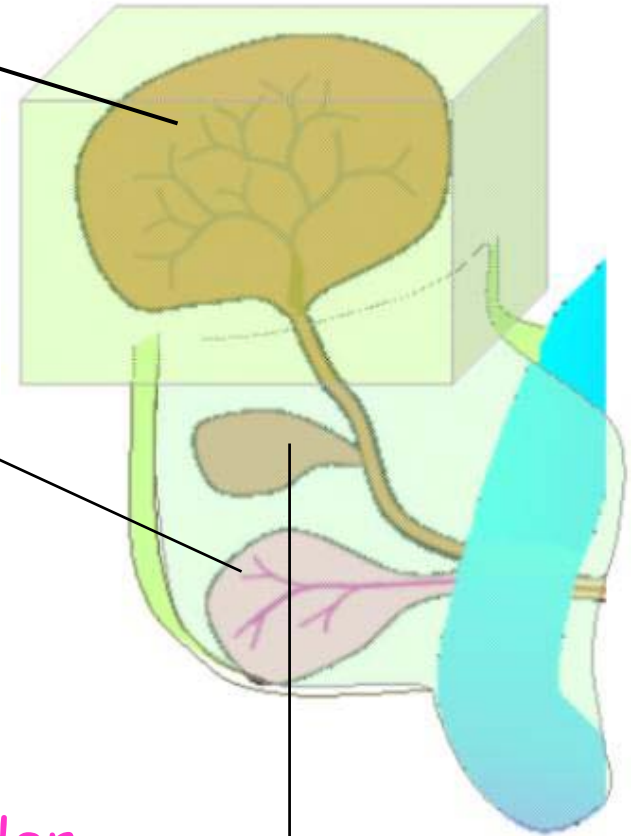
- thought to arise from the ventral pancreas migrating on both sides of the duodenum
- It may cause duodenal obstruction
- It is often associated with duodenal atresia

2. Ectopic pancreatic tissue:

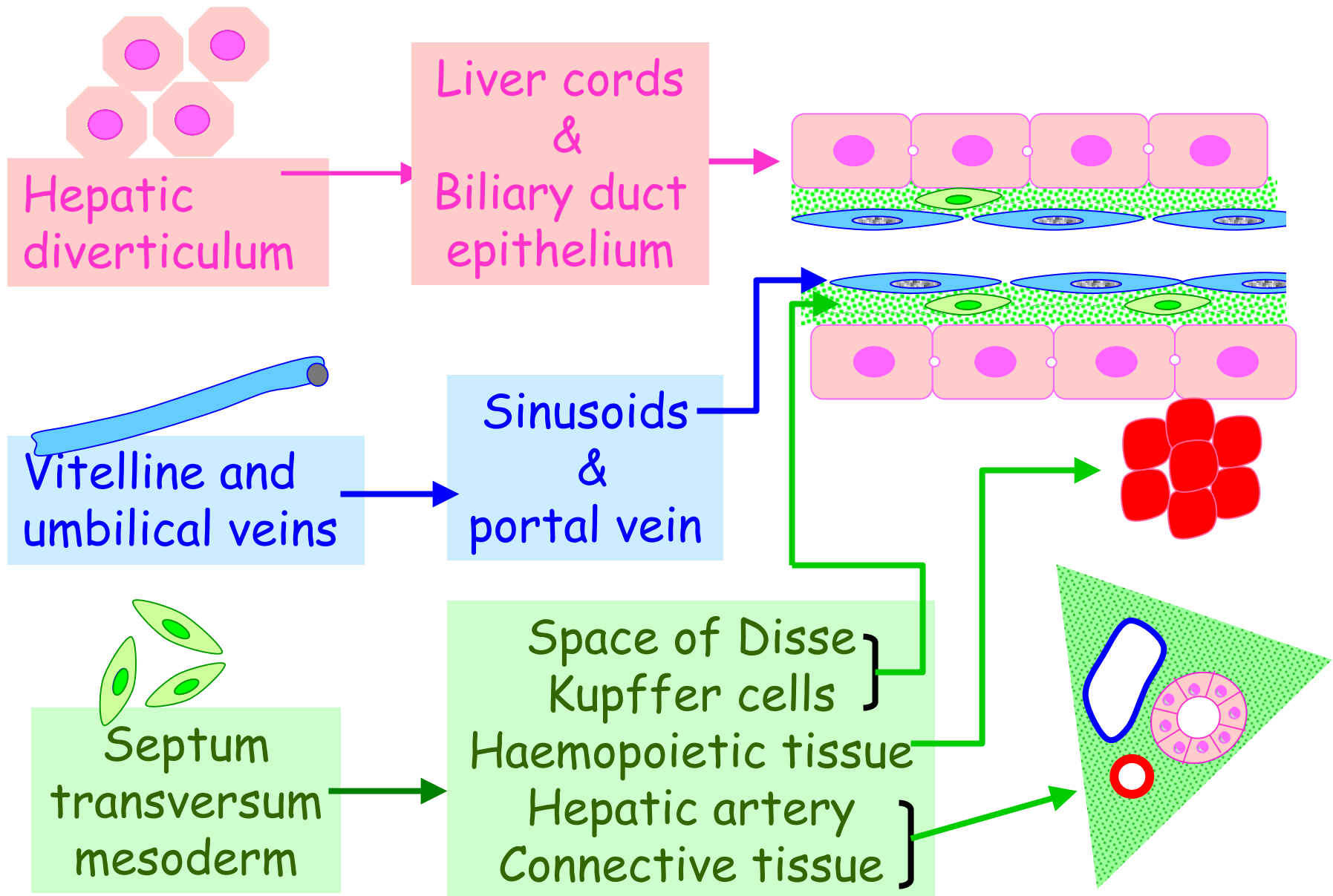
- may occur in the duodenum, stomach or Meckel's diverticulum or rarely in the appendix, biliary tract, ileum or lungs
- causes vague abdominal pain due to the ectopic secretion of proteolytic enzymes
- may simulate peptic ulcer or appendicitis
- difficult to diagnose clinically

The liver and biliary system develop from the hepatic diverticulum

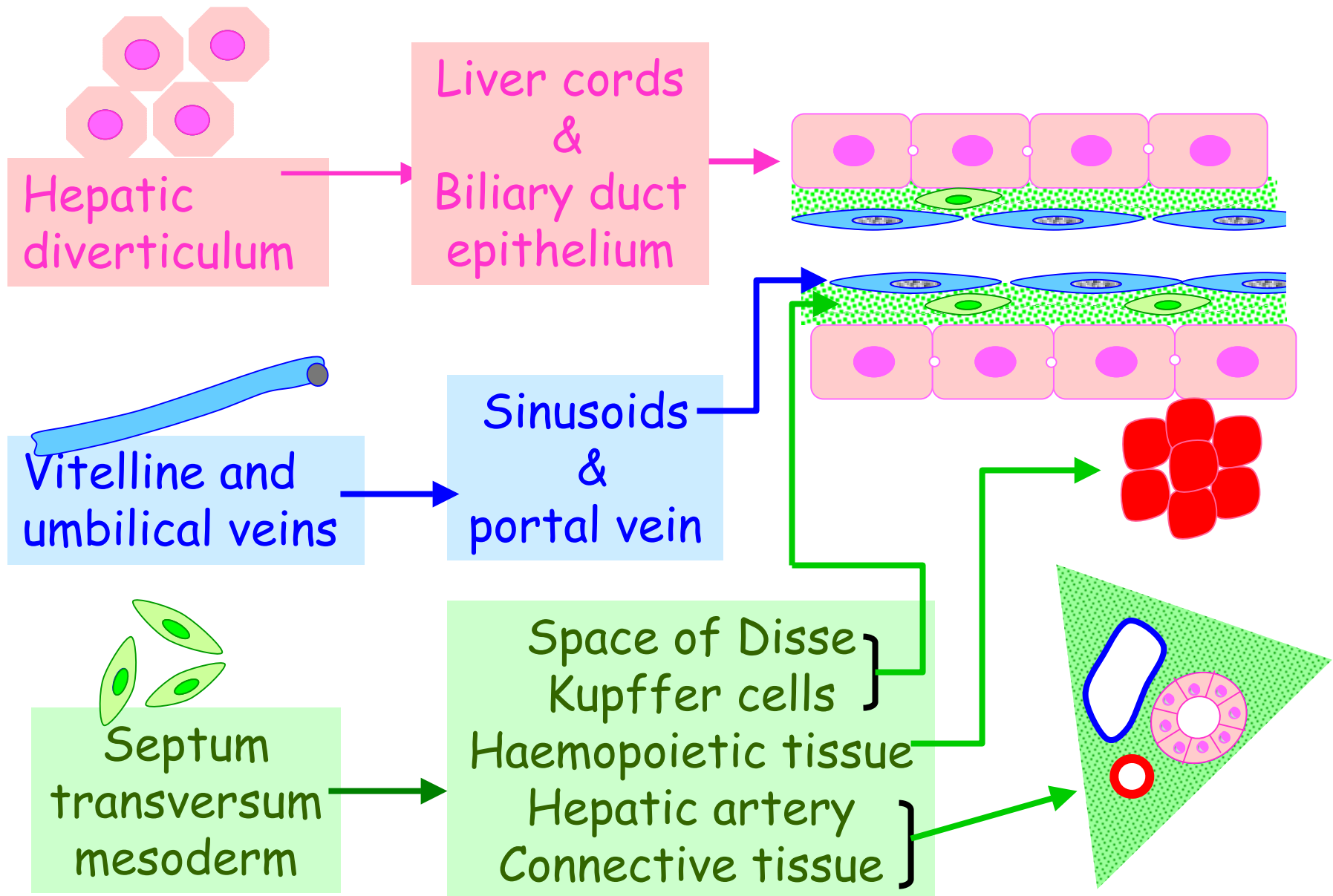
- The distal end proliferates rapidly in the **septum transversum** to form the **hepatocytes** and **intra-hepatic biliary system**
- The proximal part in the **ventral mesogastrium** proliferate slowly, becomes relatively narrow and forms the **extrahepatic biliary system**.
 - A secondary outgrowth from it forms the **gall bladder** and **cystic duct** during the 4th week (day 24)



Rudiments of the Liver and Biliary system



Rudiments of the Liver and Biliary system



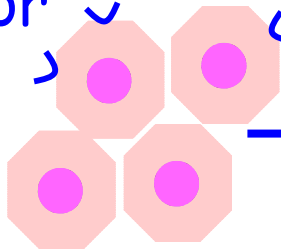
The septum transversum mesoderm has an inductive influence on hepatic bud endoderm.

Septum transversum mesoderm

Hepatic growth factor

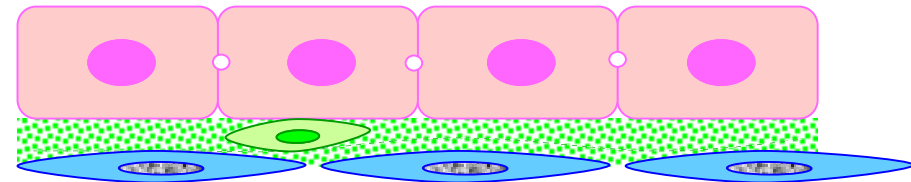
It releases hepatic growth factor that interacts with receptors on the liver cells.

C-met receptor



Hepatic diverticulum

Liver cords

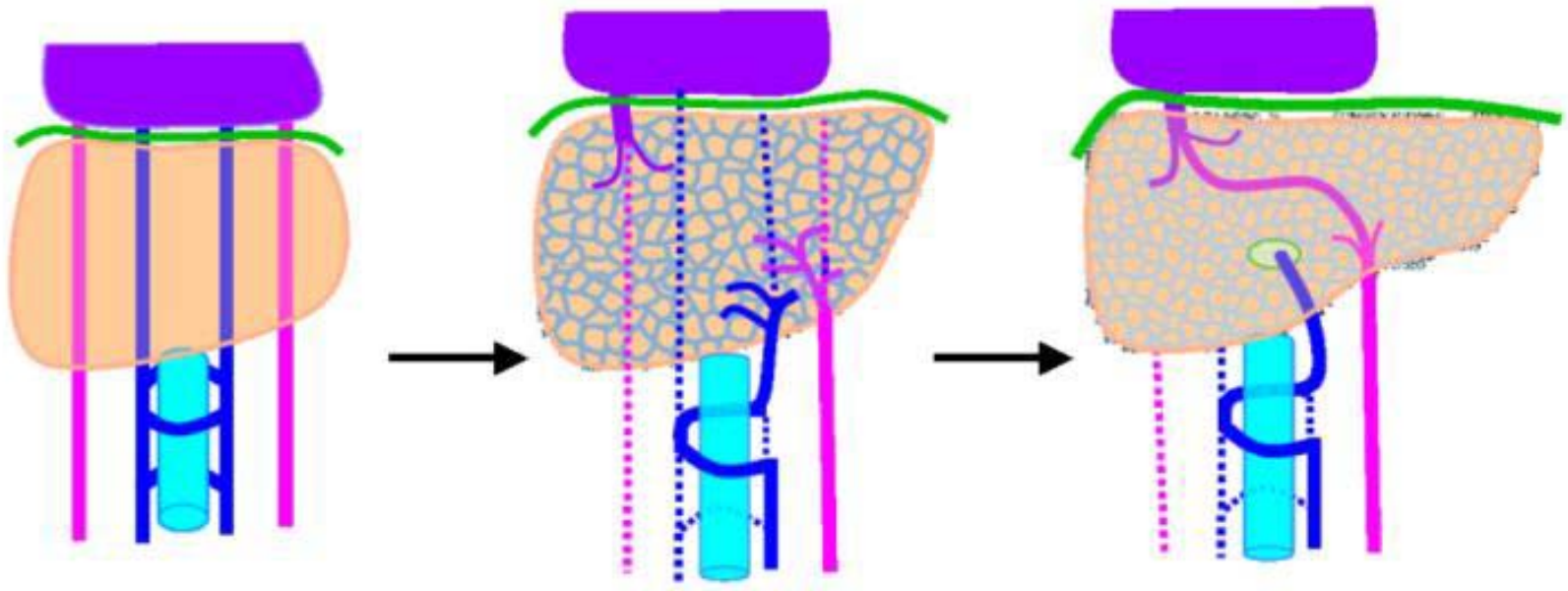


Development of Liver Function

- Synthesis of serum **albumin** - 5th week
- Secretion of **bile** - 12th week
 - From the 4th month till birth the intestinal contents are dark green and termed **meconium**.
- **Glycogen storage** - late foetal life

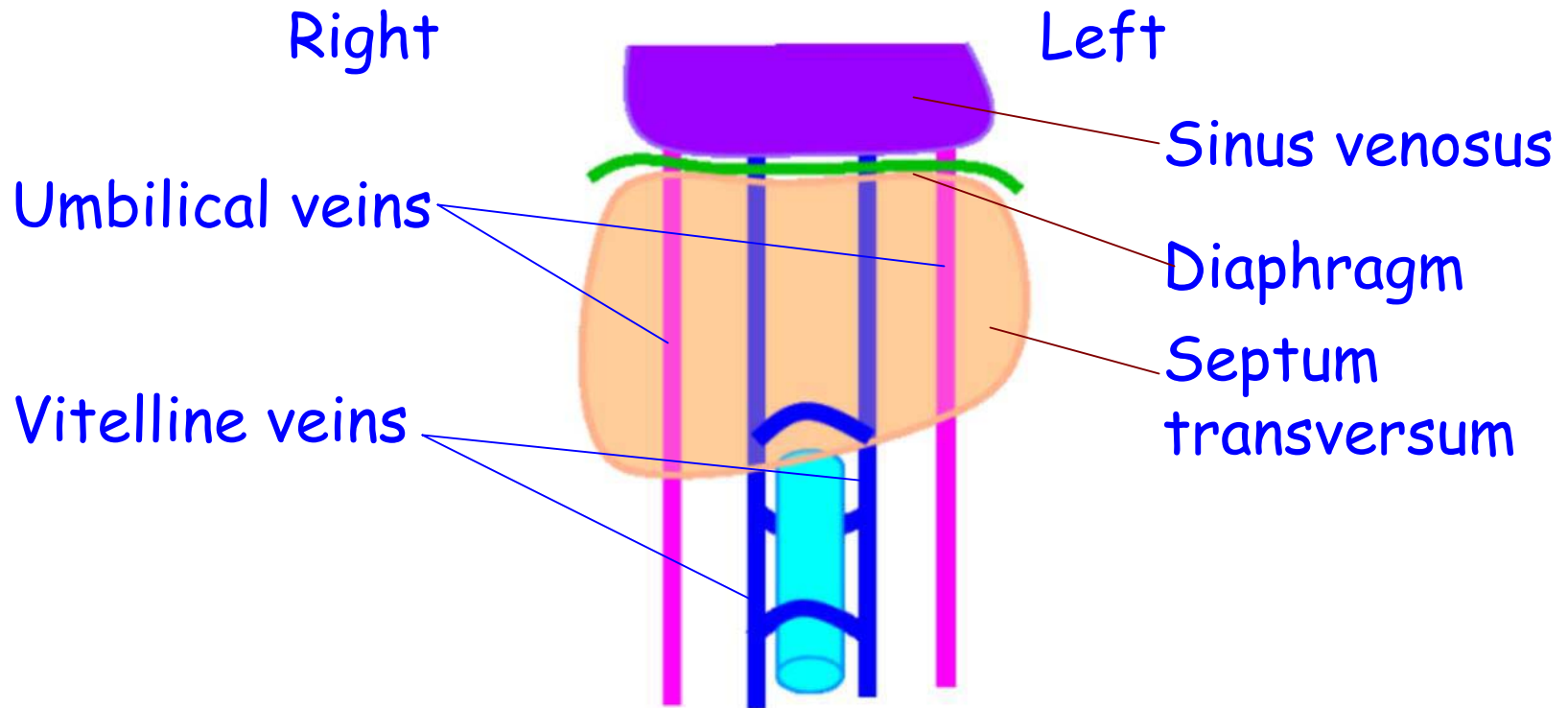
- **Haemopoiesis** is a major function of the liver from the 4th week to birth
 - Haemopoietic cells:
 - are derived from septum transversum mesoderm
 - are situated in clusters in spaces between hepatic cells.

Changes in the veins coursing through the septum transversum account for some anatomical features of the liver



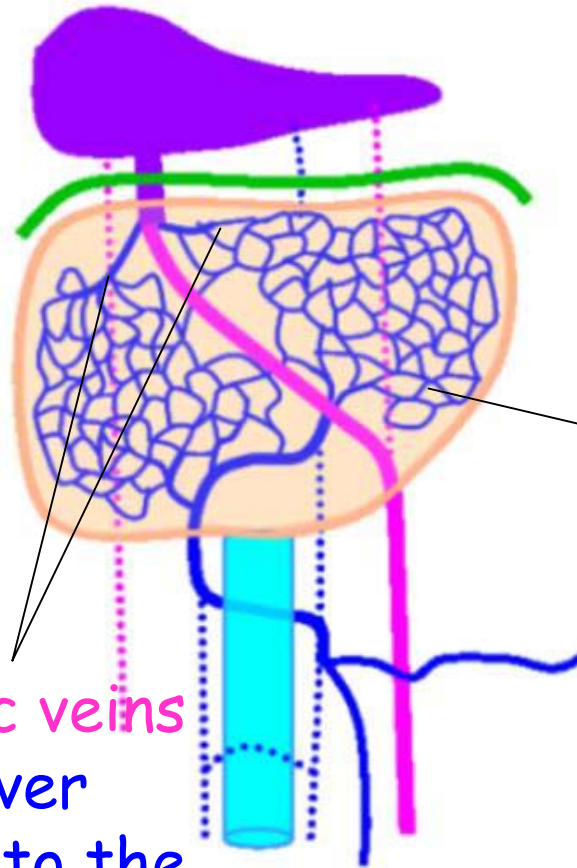
Initially veins are symmetrical

Paired umbilical and vitelline veins course through the septum transversum and drain into the sinus venosus



A series of **anastomoses** connect the right and left vitelline veins. Two anastomoses lie ventral and one dorsal to the terminal part of the foregut. The most cranial anastomosis lies within the septum transversum.

Proliferation of cells of the hepatic diverticulum disrupts the symmetrical pattern of the veins coursing through the septum transversum



The vitelline veins break up into a plexus that surrounds the rapidly growing cords of hepatic cells and forms the liver sinusoids

The hepatic veins drain the liver sinusoids into the right vitelline veins.

As the left horn of the sinus venosus regresses, all the veins are shunted to the right vitelline vein.

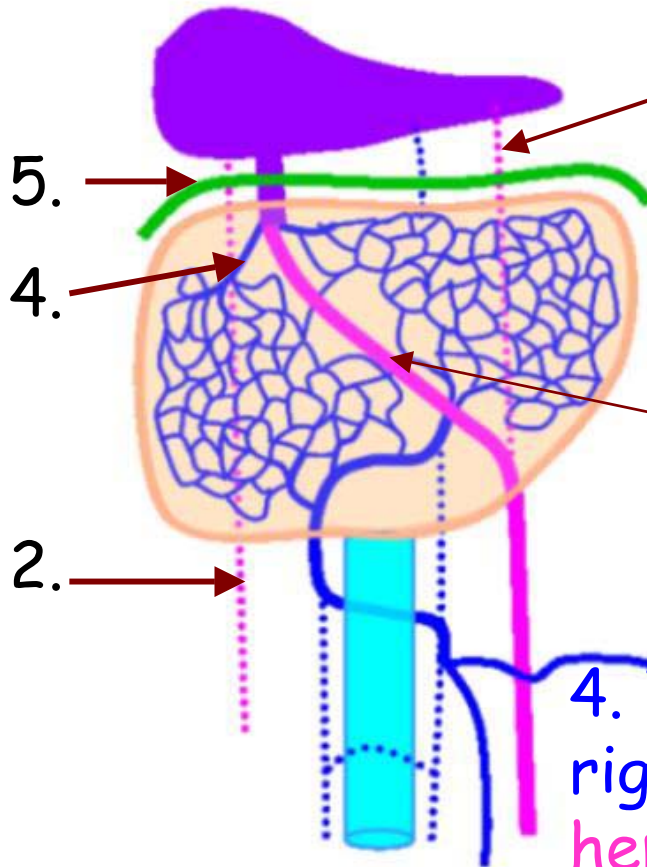
1. The left vitelline and umbilical veins lose their connections with the left horn of the sinus venosus

2. The right umbilical vein disappears completely

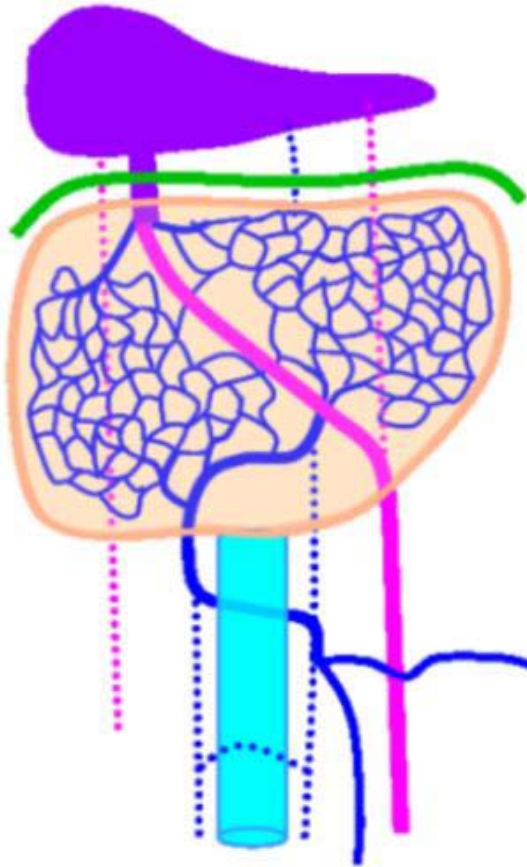
3. The **ductus venosus** shunts blood from the left umbilical to the cranial end of the right vitelline vein.

4. The liver sinusoids drain into the right vitelline veins through the **hepatic veins**

5. The cranial part of the right vitelline vein enlarges and forms part of the of the IVC



The Umbilical Veins



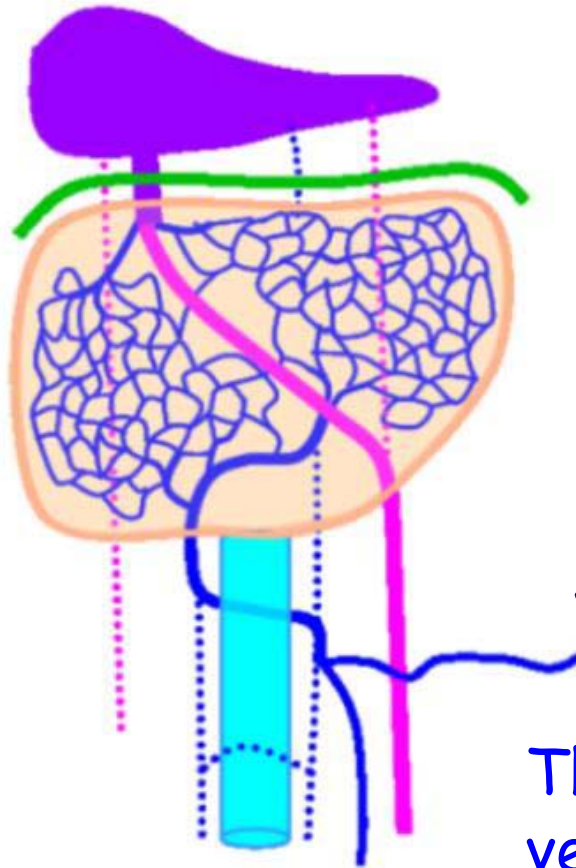
1. The right umbilical vein disappears completely

2. The left umbilical veins lose its connection with the left horn of the sinus venosus

3. The **ductus venosus** shunts blood from the left umbilical to the cranial end of the right vitelline vein.

Remember! The umbilical cord has only one vein (the left umbilical vein)

Re-arrangement of the paired vitelline veins gives rise to the portal vein

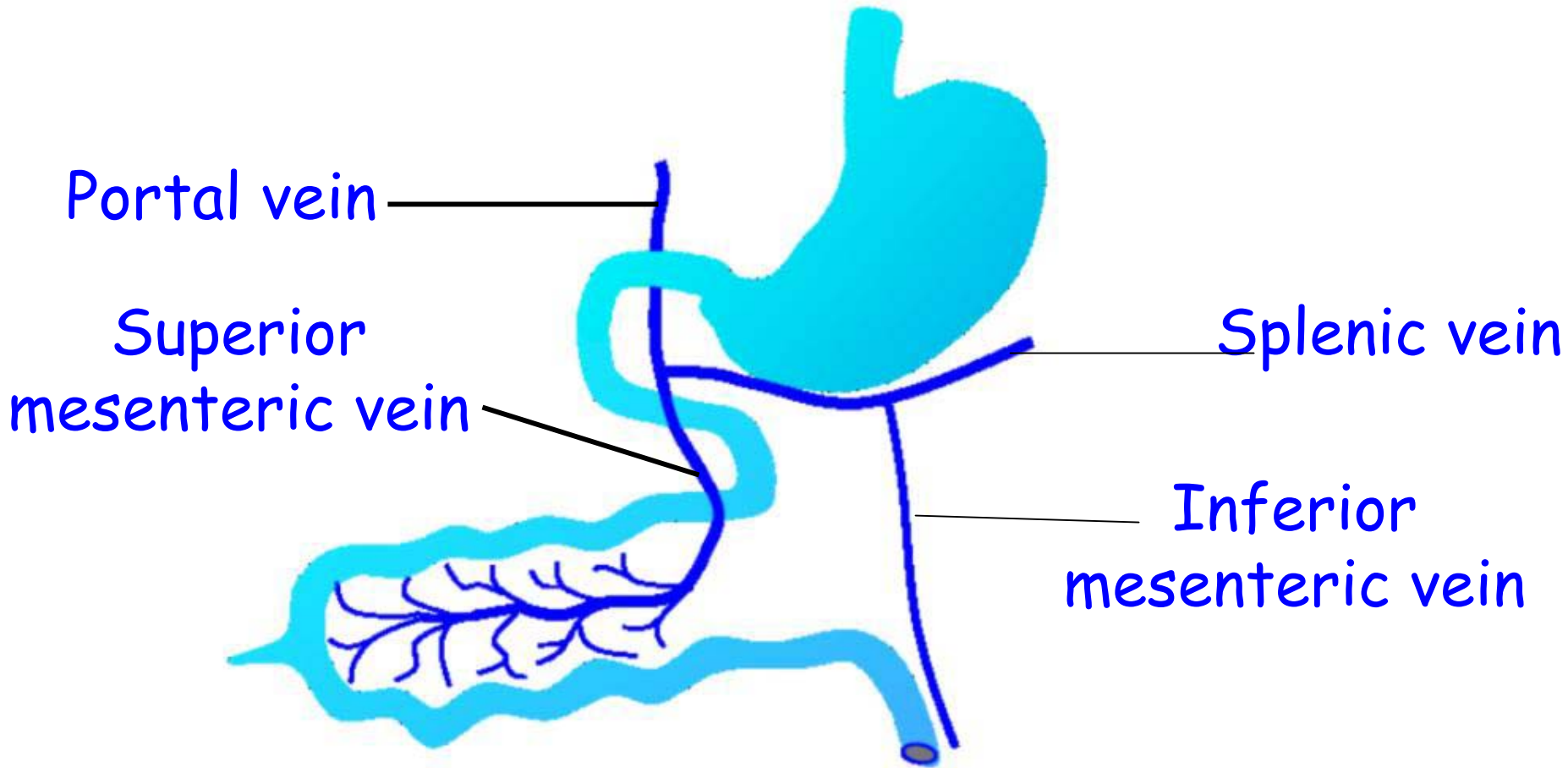


In the septum transversum - Parts of the right and left vitelline veins and the ventral anastomosis give rise to the right and left branches of the portal vein

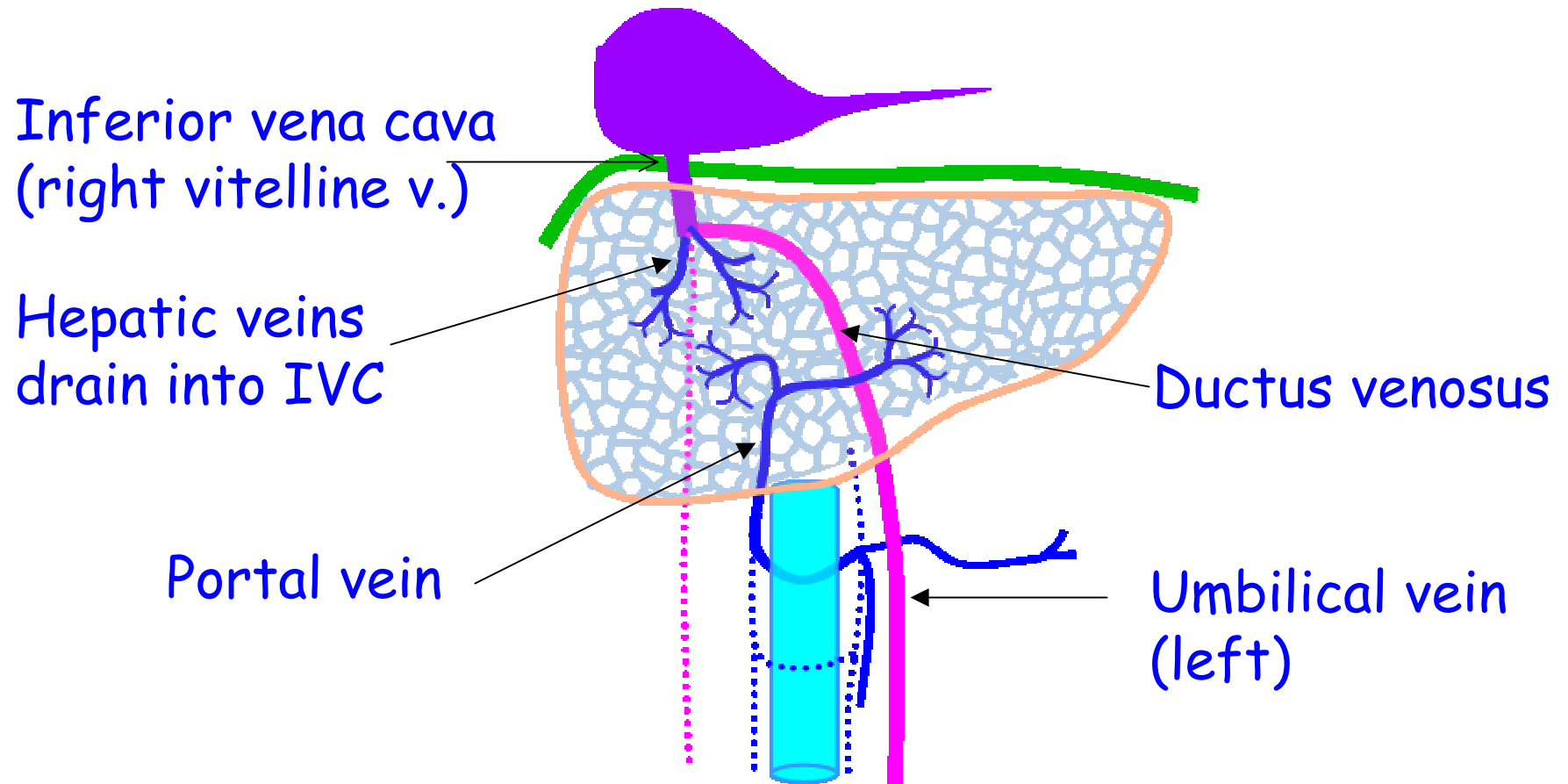
Outside the septum transversum - The portal vein develops from parts of the right and left vitelline veins and the dorsal anastomosis.

The splenic and superior mesenteric veins develop join the left vitelline vein; later, the inferior mesenteric vein joins the splenic vein.

The portal vein develops partly from the dorsal anastomosis. This explains why it passes dorsal to the first part of the duodenum.

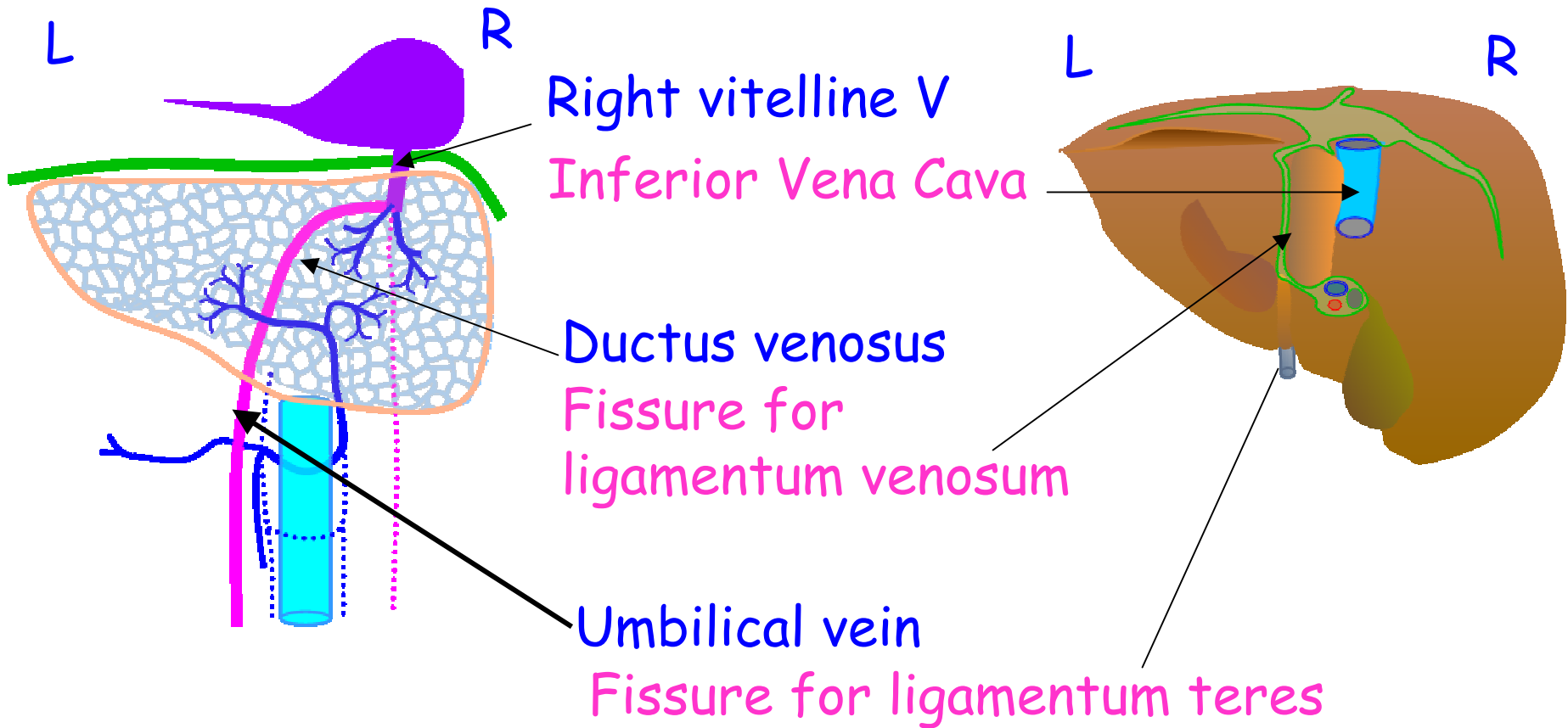


The development of the veins explain some of the anatomical features of the liver.



Embryological veins and their derivatives in the mature liver.

A mirror image of the previous diagram illustrates the liver as seen from the posterior aspect, in order to facilitate comparison with the derivatives in the mature liver.



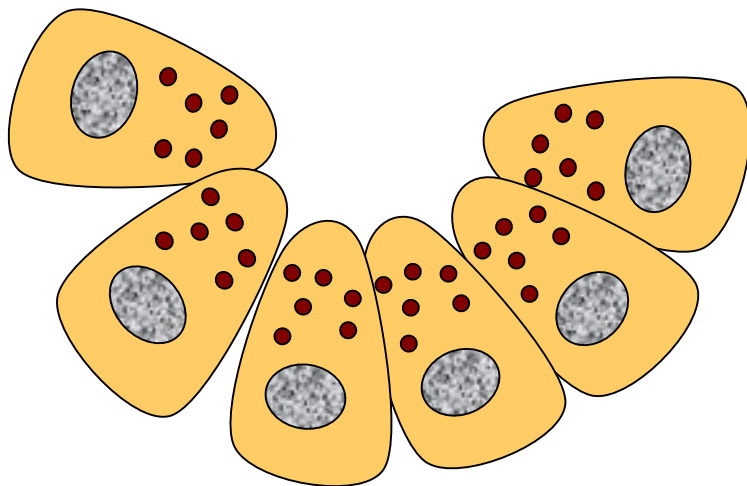
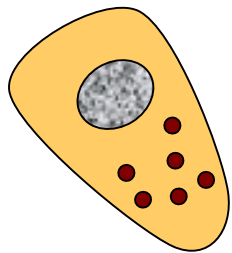
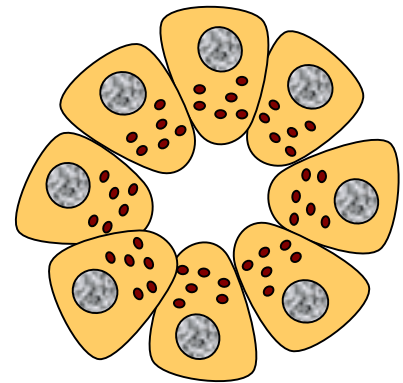
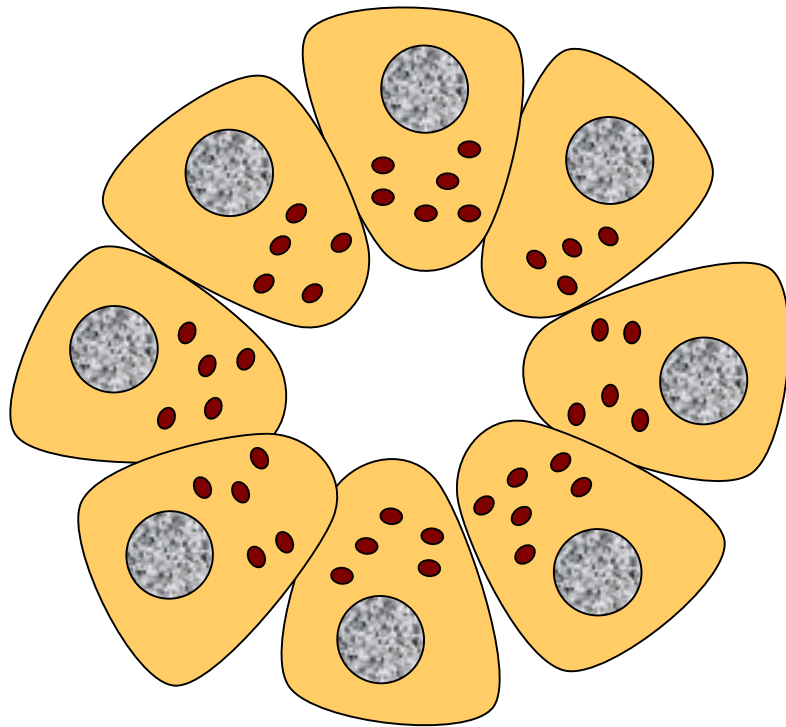
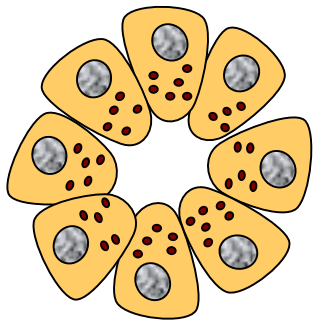
Anomalies of the Liver and Biliary System

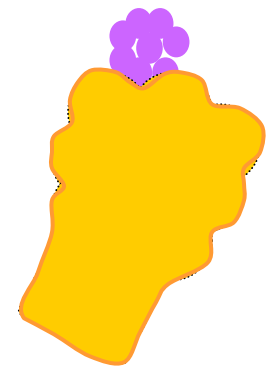
1. Duplication of the gall bladder, sharing the same common bile duct

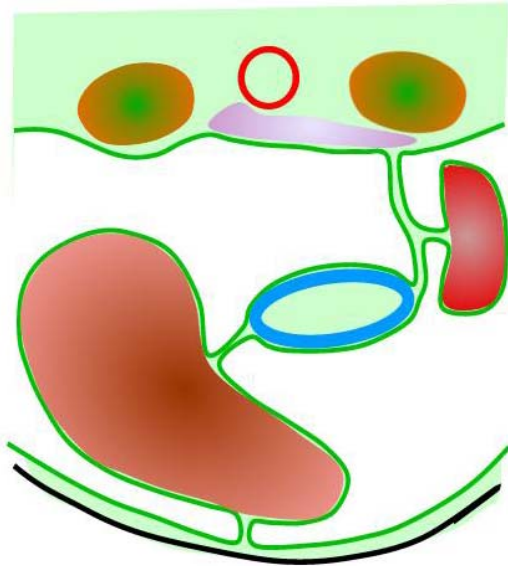
2. Extrahepatic biliary atresia

- variable absence of part or all of the biliary tree
- causes severe jaundice shortly after birth
- requires surgery to relieve the obstruction (e.g. cholecysto-gastrostomy)
- prognosis depends on site and extent of the atresia; more severe if proximal part is involved

3. Biliary hypoplasia due to intrahepatic biliary atresia







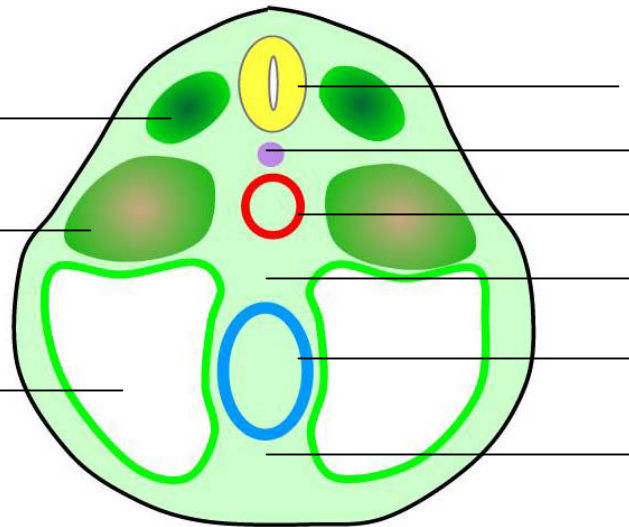
The stomach develops in the septum transversum and has dorsal and ventral mesenteries

Lateral structures

Paraxial mesoderm

Intermediate cell mass

Pleuro-peritoneal canal



Midline structures

Neural tube

Notochord

Dorsal aorta

Dorsal mesentery

Developing Stomach

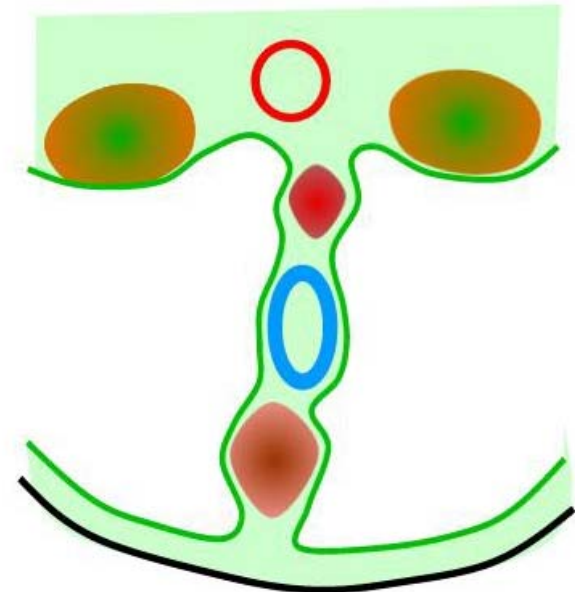
Ventral mesentery

28 day embryo:

TS at the level of septum transversum

The spleen develops in the dorsal mesentery.

The liver develops in the ventral mesentery.



The liver and biliary system develop from the hepatic diverticulum

- The distal end of the hepatic diverticulum proliferates rapidly in the septum transversum to form the hepatocytes and intra-hepatic biliary system
- The proximal part in the ventral mesogastrium does not proliferate rapidly, becomes relatively narrow and forms the extrahepatic biliary system. A secondary outgrowth from it forms the gall bladder and cystic duct during the 4th week (day 24)
- The vitelline and umbilical veins, disrupted by growth of hepatic cells in the septum transversum, form the liver sinusoids
- The septum transversum mesoderm surrounding the hepatic cords forms the Kupffer cells and haemopoietic cells