بِسْمِ اللهِ الرَّحْمَـٰنِ الرَّحِيم

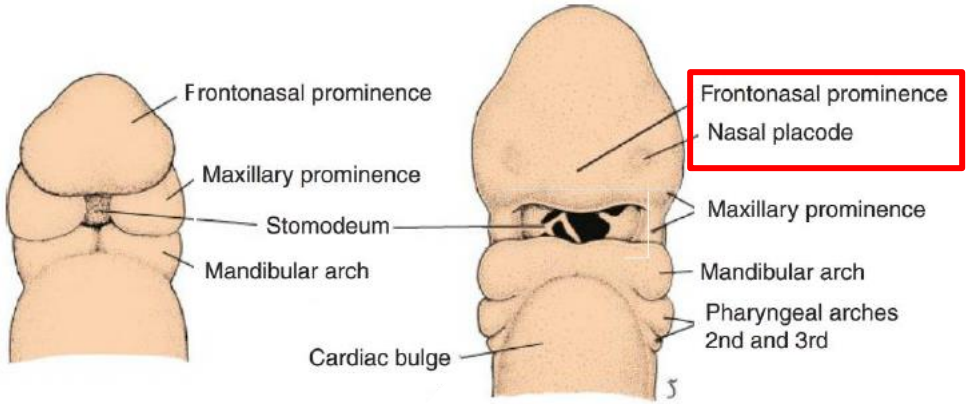
DONE BY AHMAD AYMAN | DOCTOR
2019 | JU

Respiratory System Embryology

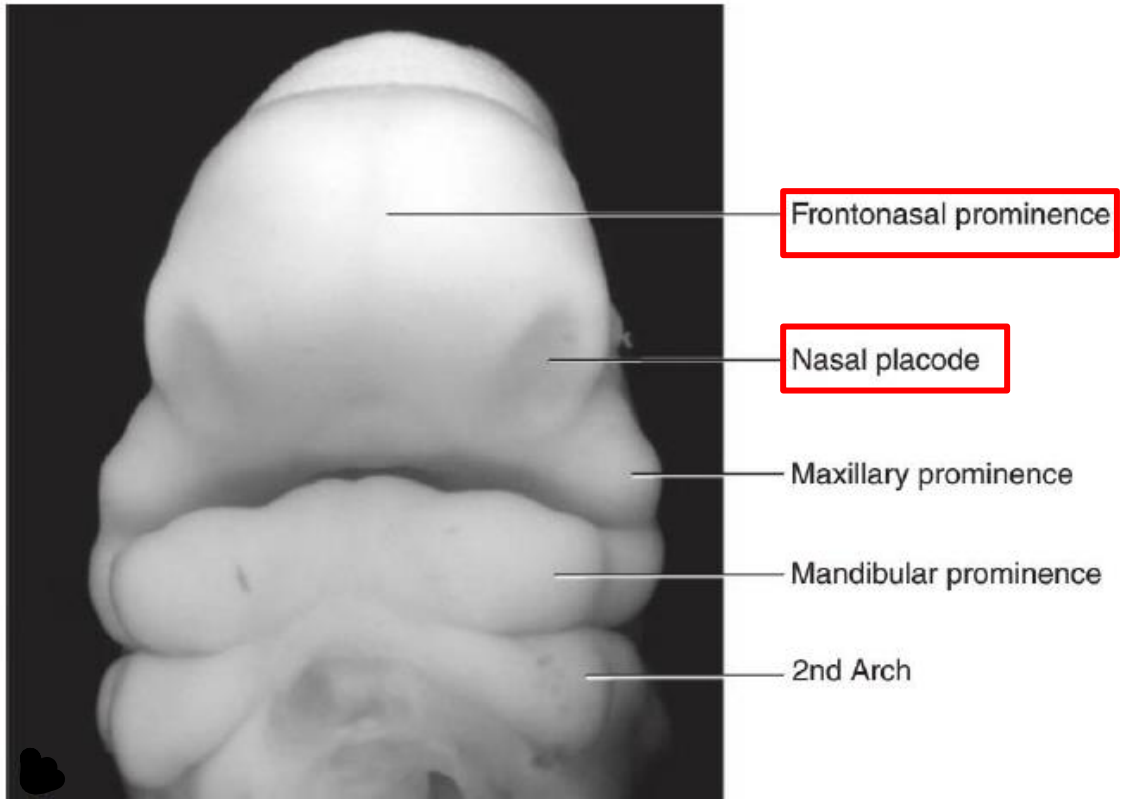
Done By: Ahmad Ayman

DEVELOPMENT OF THE NOSE

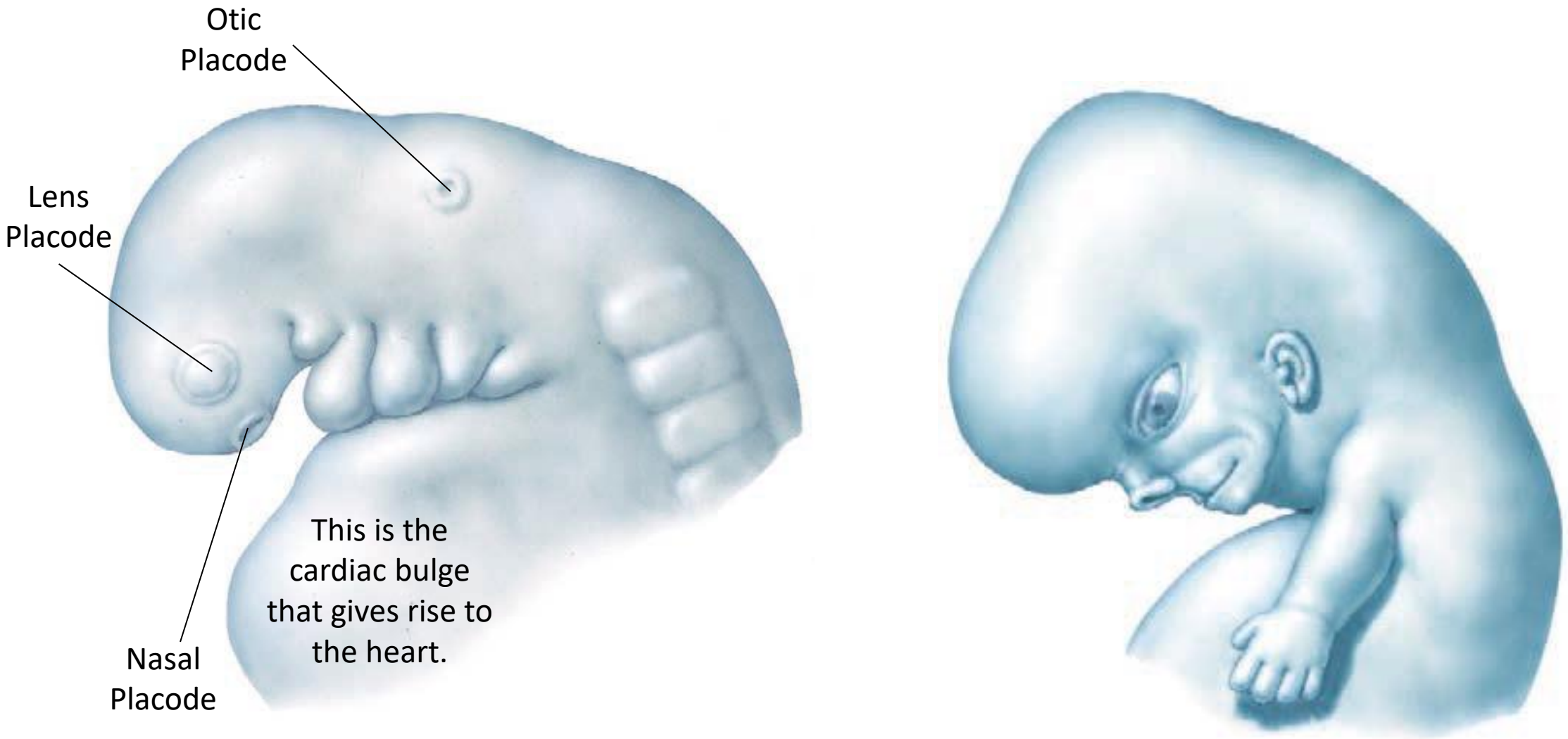
At the end of the fourth week, facial prominences consisting primarily of neural crest-derived mesenchyme and formed mainly by the first pair of pharyngeal arches appear.
The frontonasal prominence, formed by proliferation of mesenchyme ventral to the brain vesicles, constitutes the upper border of the stomodeum.
On both sides of the frontonasal prominence, local thickenings of the surface ectoderm, the nasal (olfactory) placodes, originate under inductive influence of the ventral portion of the forebrain, these placodes give rise to the nostrils.



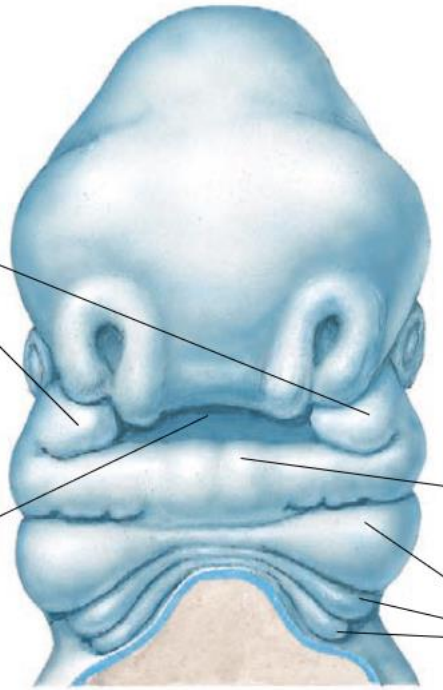
To understand the embryology of a certain organ, we must be familiar with its anatomy, we know that the nose has nostrils anteriorly, it has a septum, and lateral walls, and the choanae posteriorly, the lateral wall of the nose has conchae and meatuses.



Note: just like we have nasal placodes that gives rise to the nose 👃 , we have otic placodes that give rise to the ears 👂 and lens placodes that give rise to the eyeballs 🎯 .



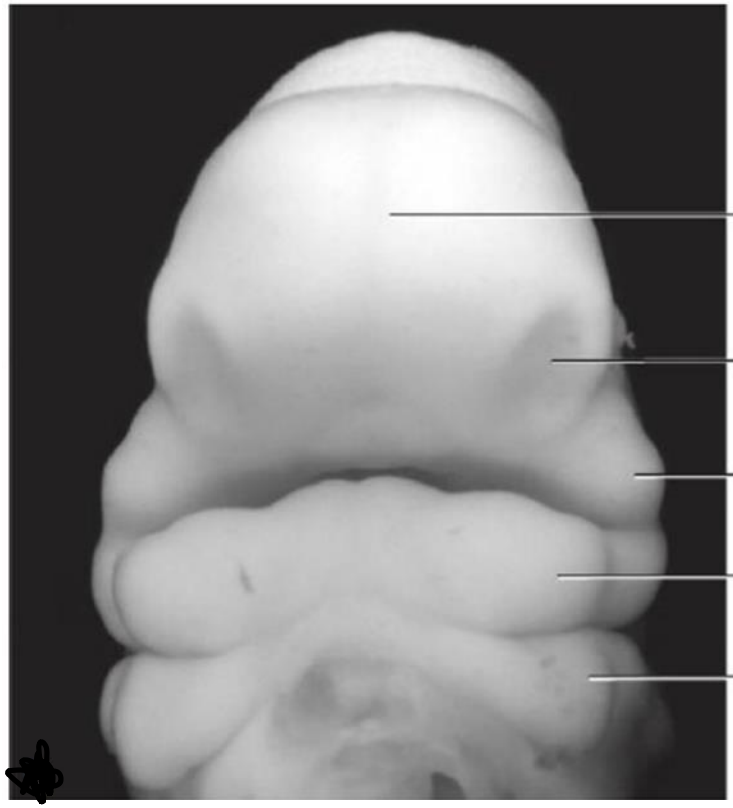
on the sides of the stomodeum, we have the Maxillary Prominences

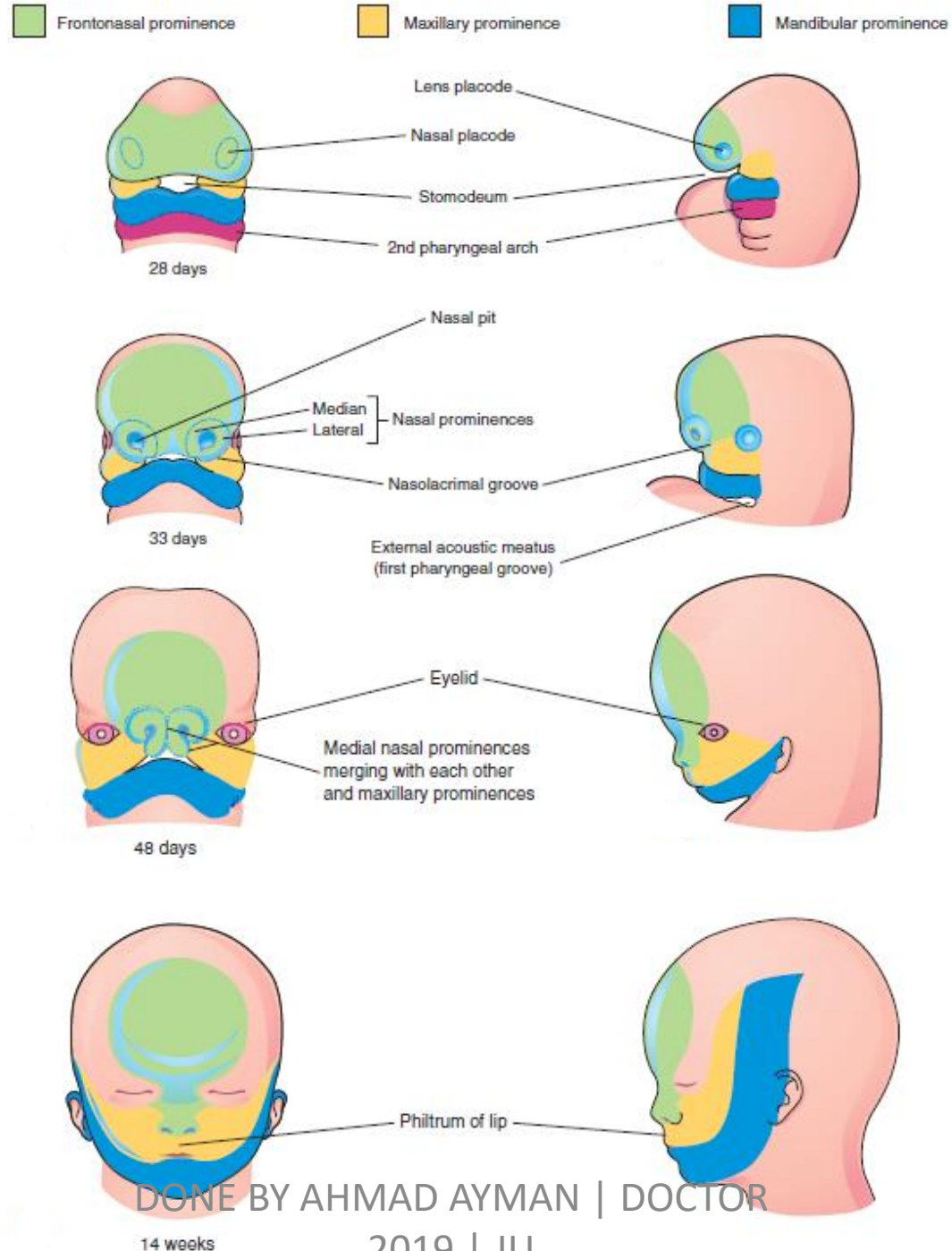


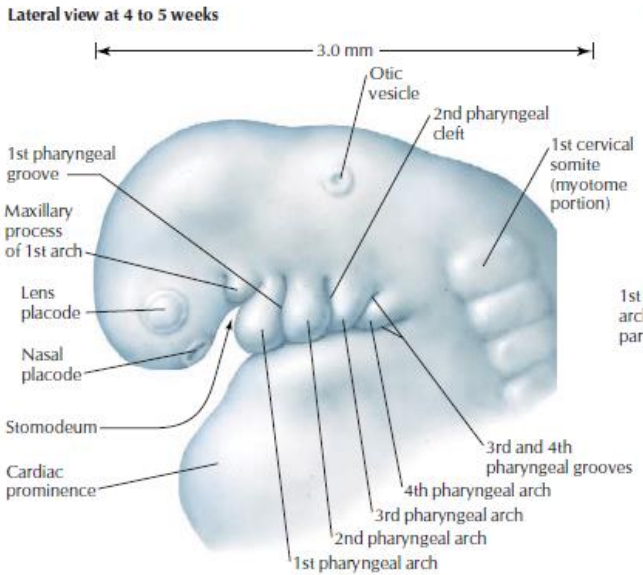
The stomodeum, gives rise to the oral cavity.

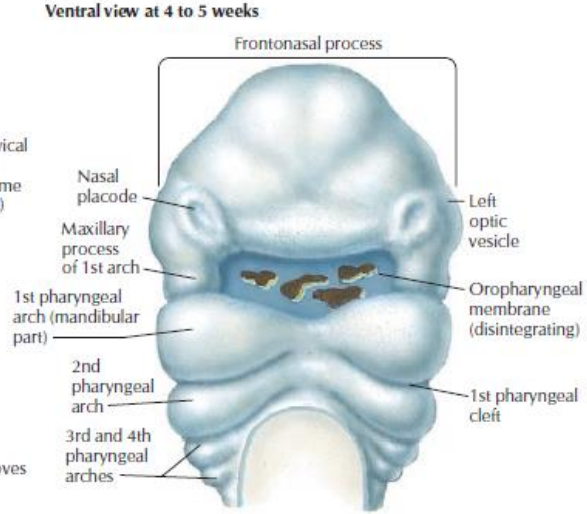
Rest of Pharyngeal Arches

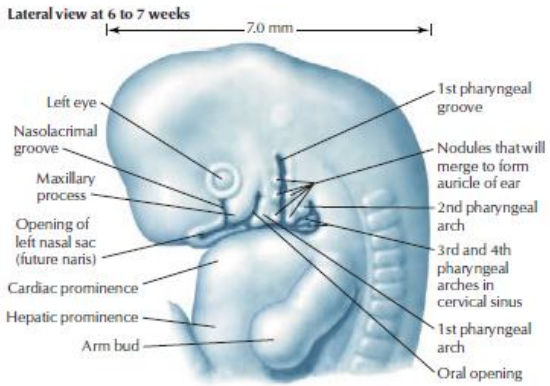
Under the stomodeum, we have the mandibular prominence, both maxillary and mandibular prominences are derived from the 1st pharyngeal arch

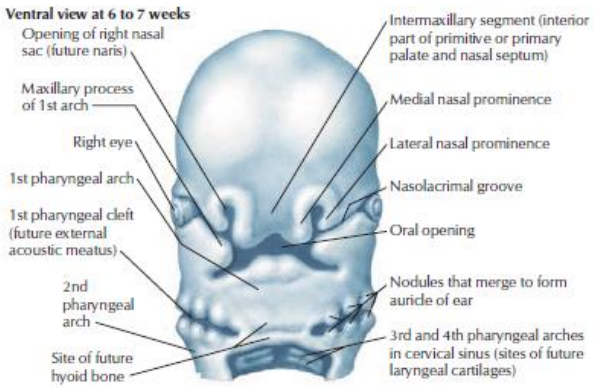


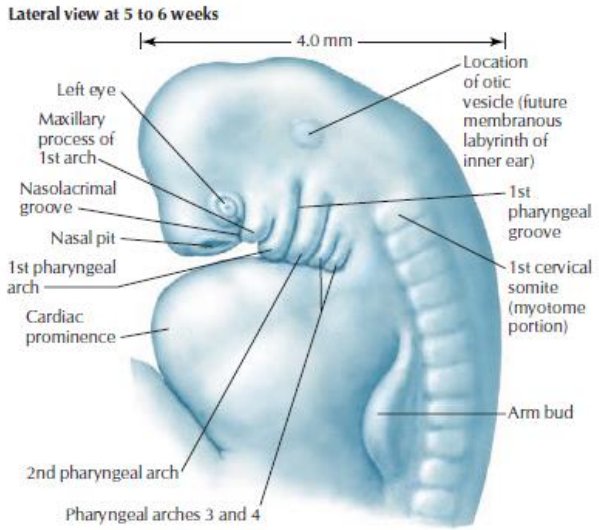


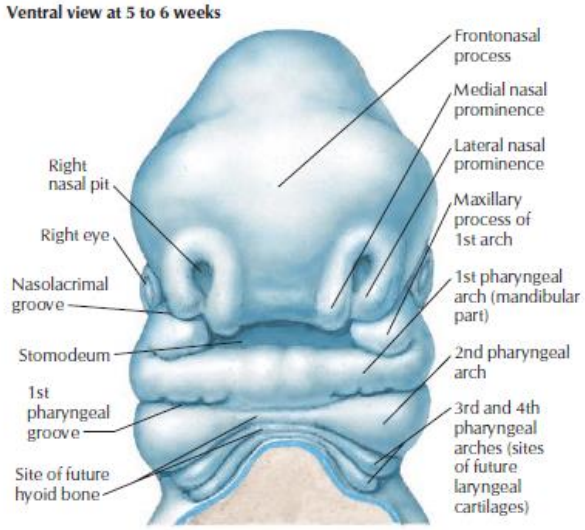


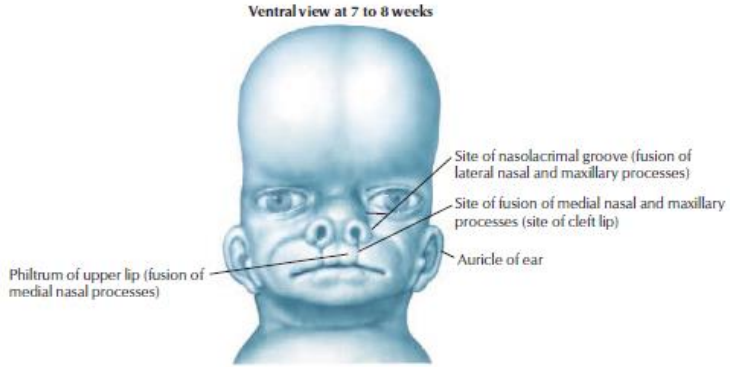


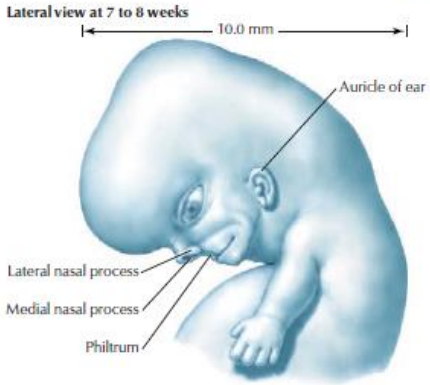


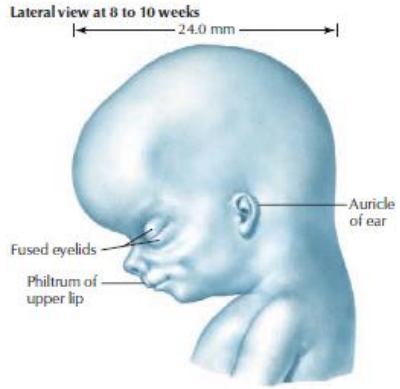




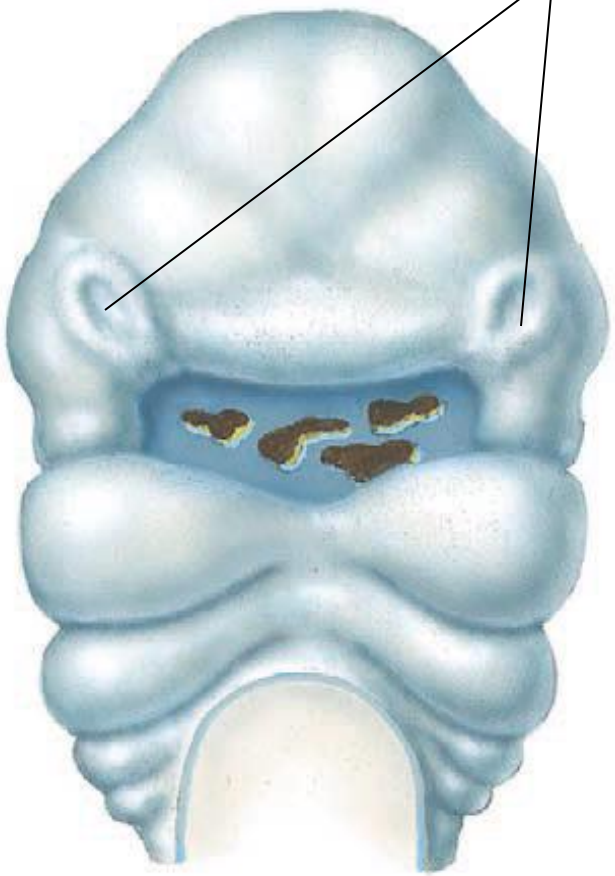


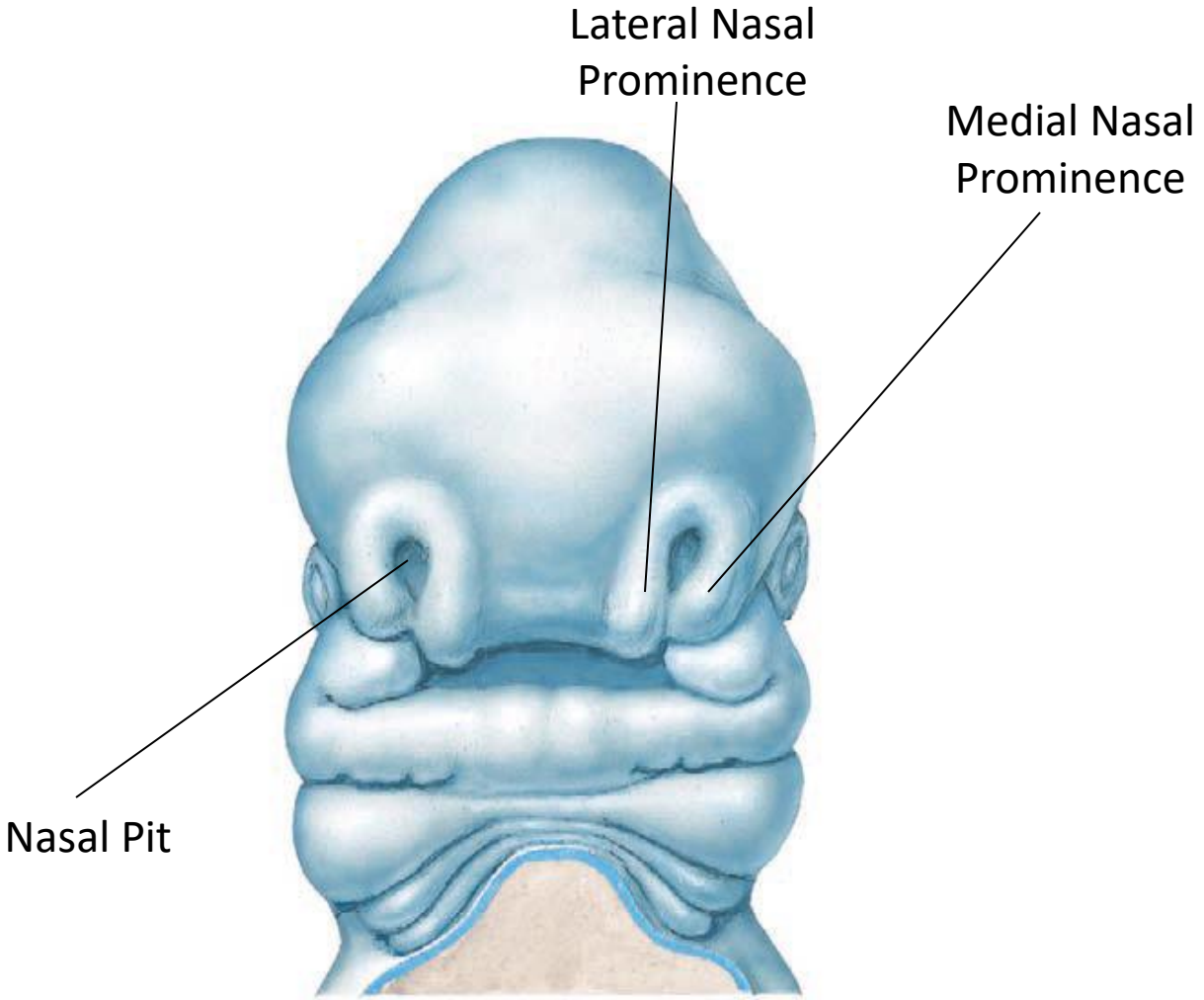




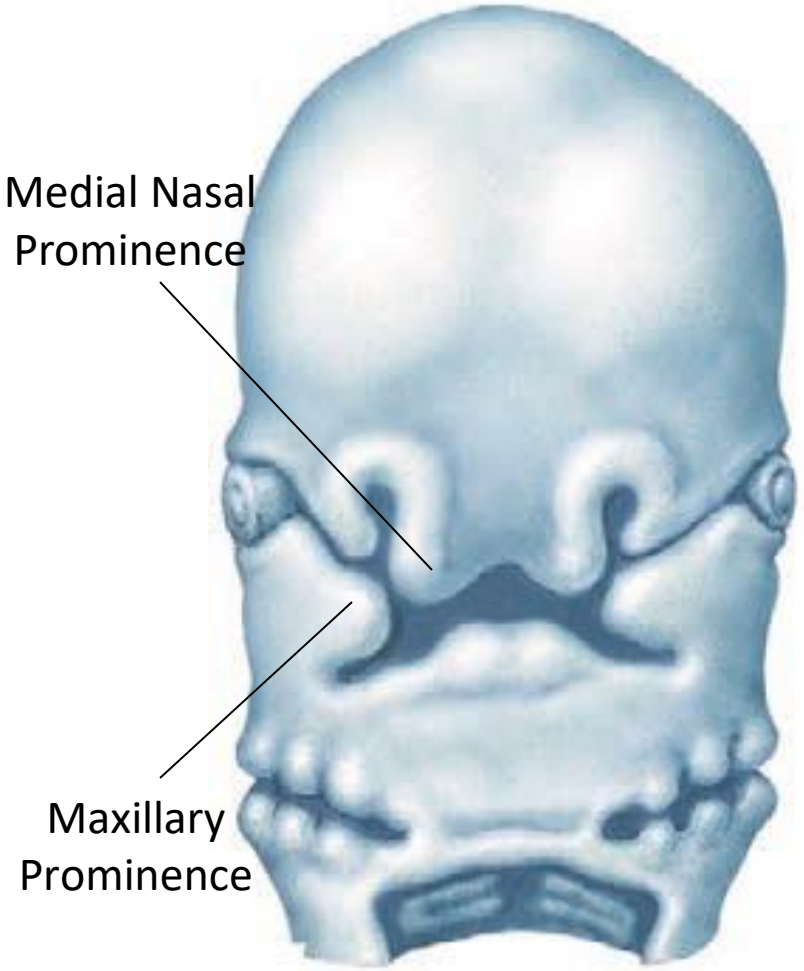


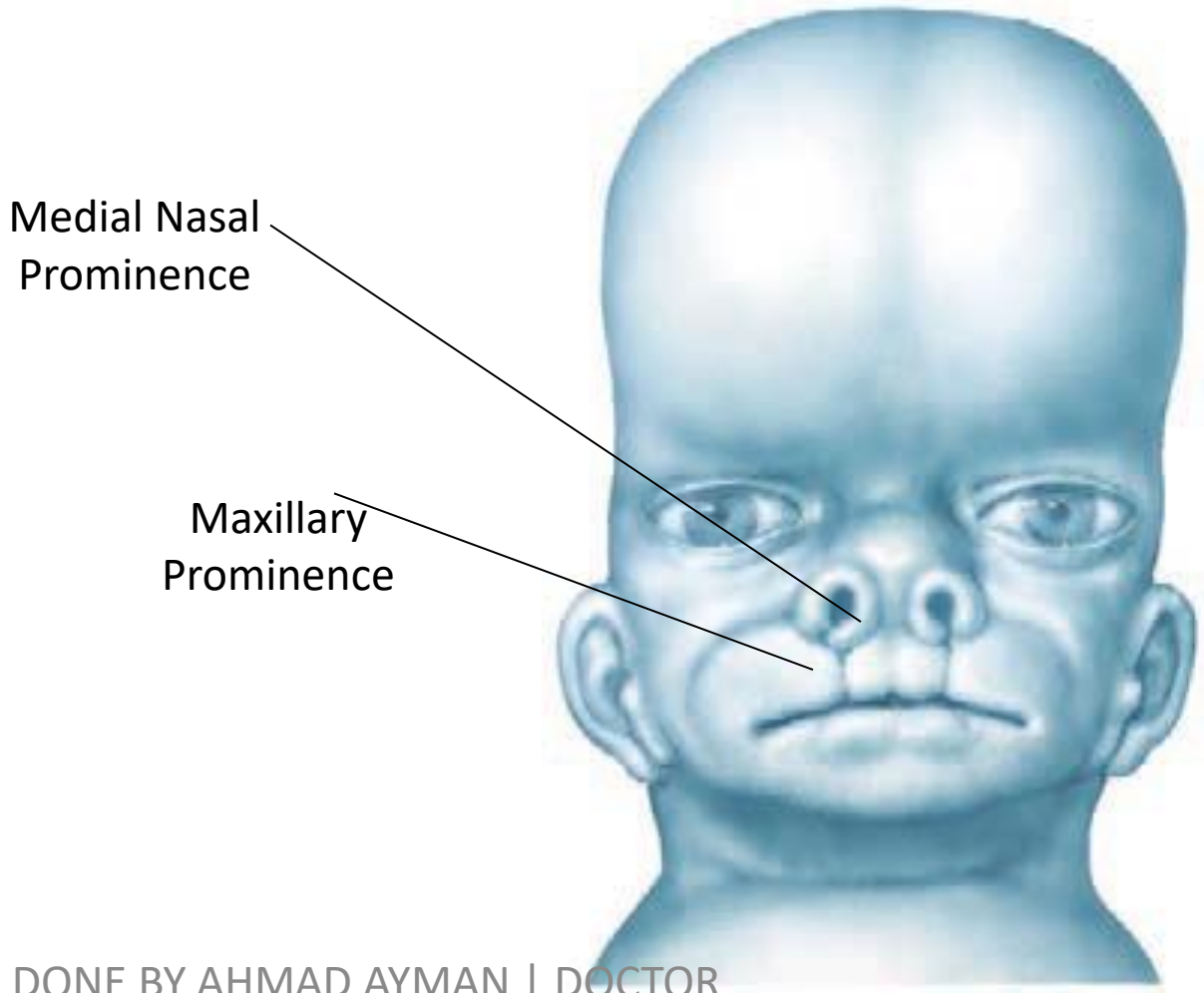
During the fifth week, the nasal placodes invaginate to form nasal pits (nostril).
In so doing, they create a ridge of tissue that surrounds each pit and forms the nasal prominences.
The prominences on the outer edge of the pits are the lateral nasal prominences; those on the inner edge are the medial nasal prominences.



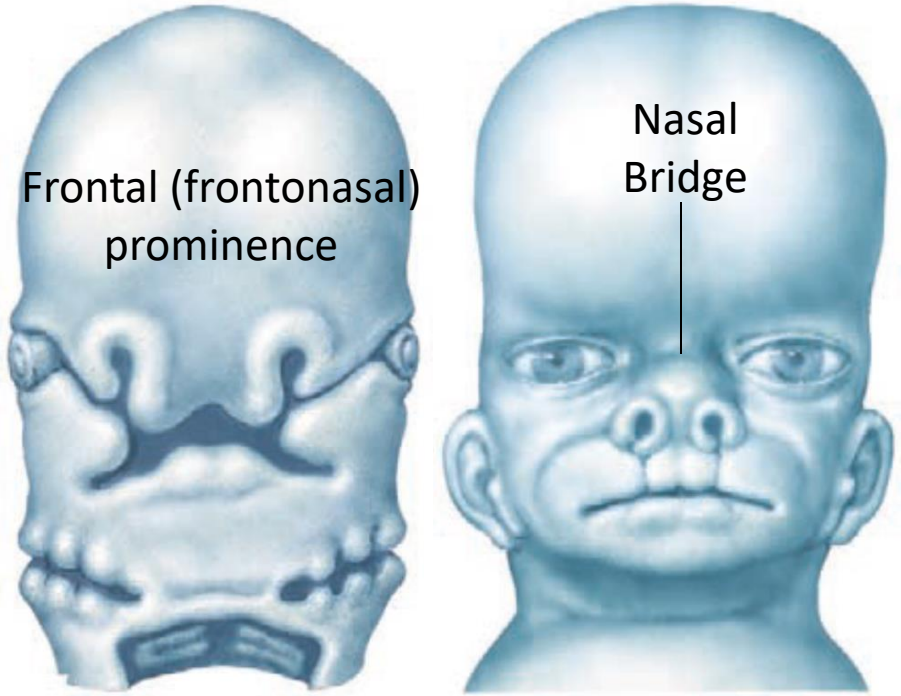


During the following two weeks (in the 6th week), the maxillary prominences continue to increase in size, simultaneously, they grow medially, compressing the medial nasal prominences toward the midline, subsequently the cleft between the medial nasal prominence and the maxillary prominence is lost, and the two fuse.

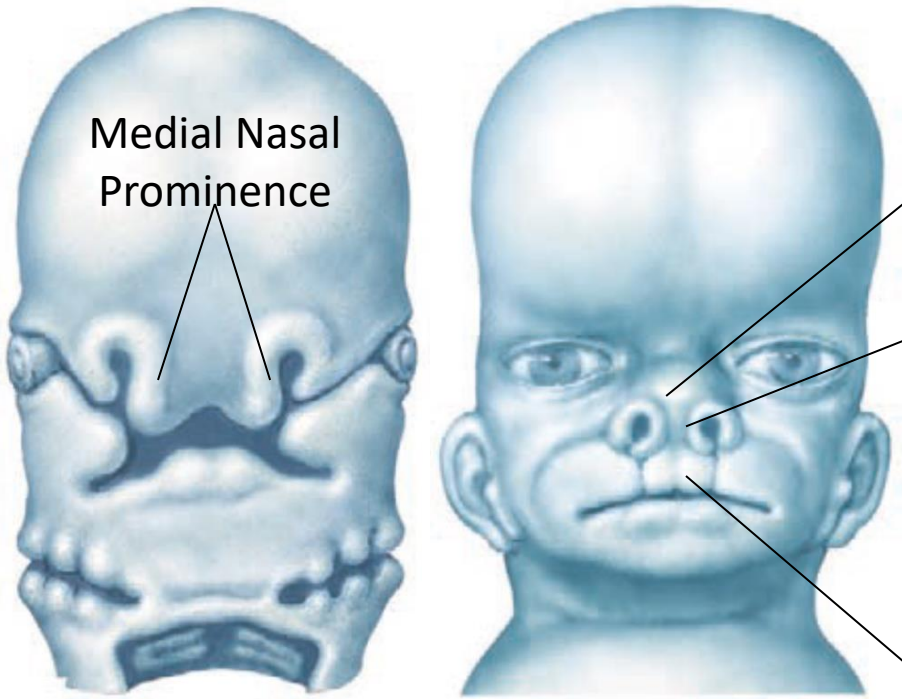




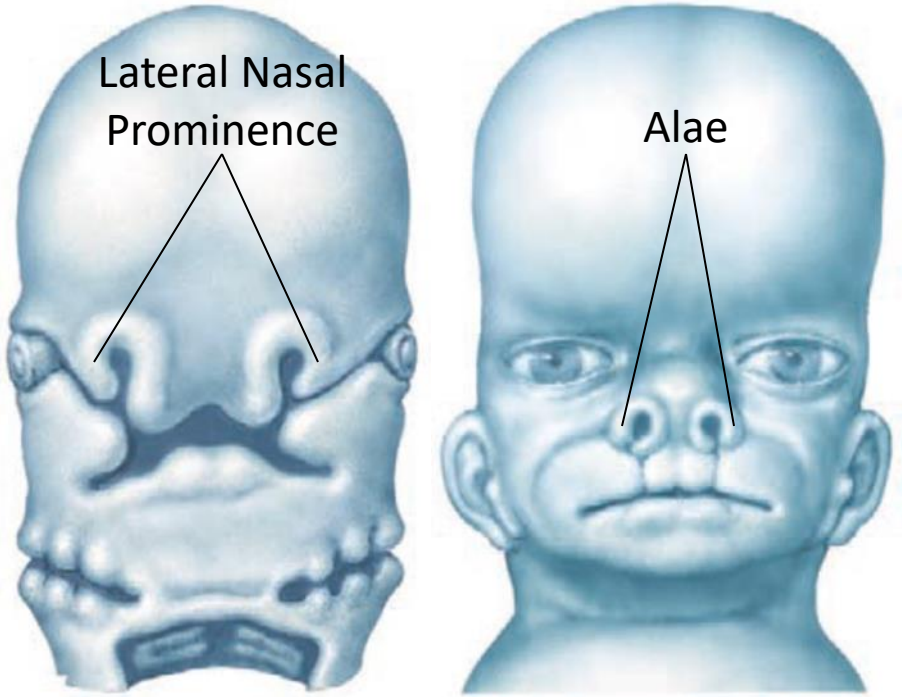
The nose is formed from five facial prominences:



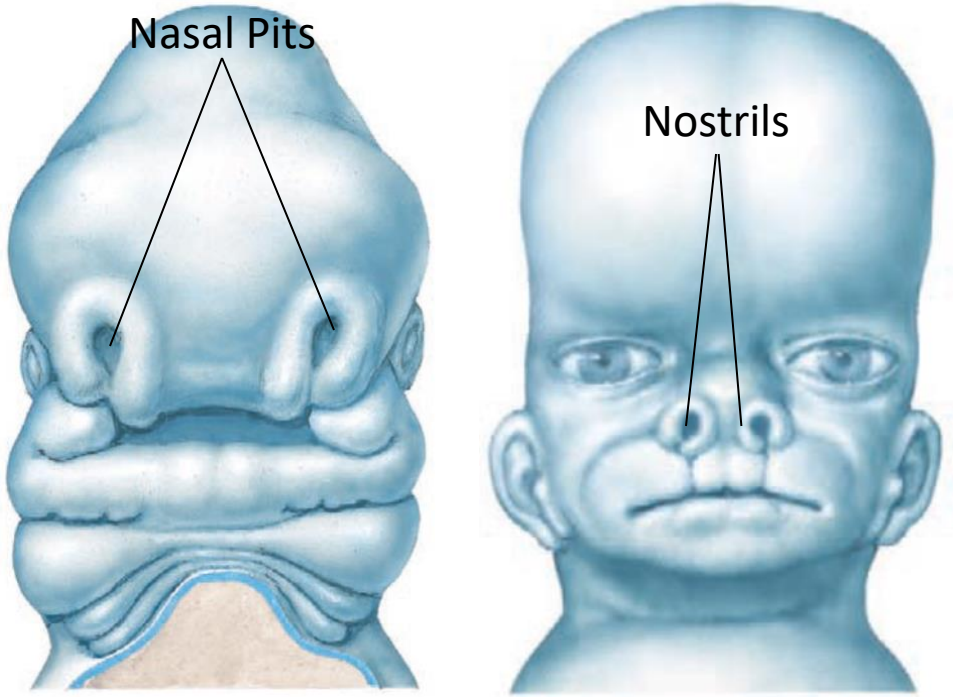
The frontal prominence gives rise to the bridge of the nose and the nasal septum.



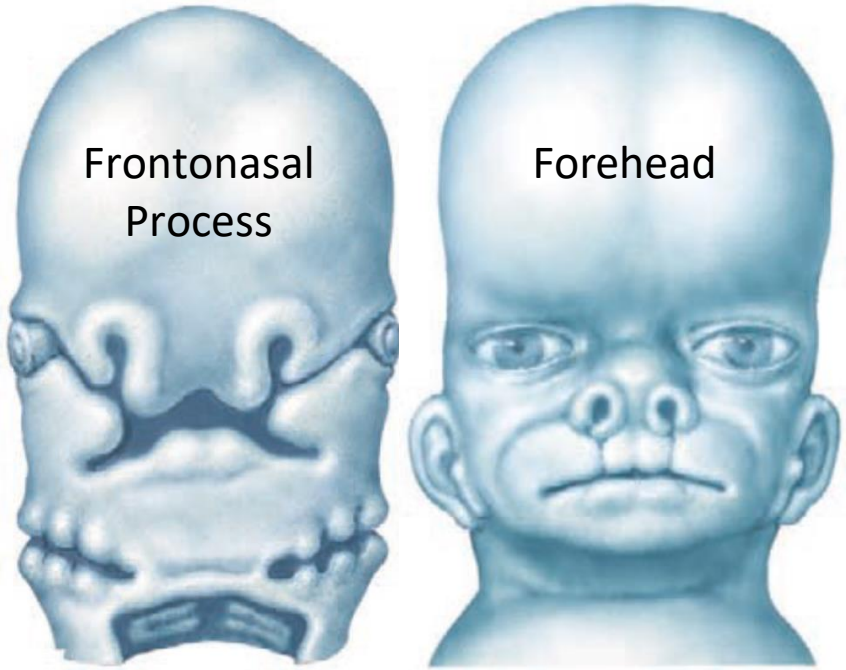
The merged medial nasal prominences provide the crest and tip of nose, and the labial philtrum.



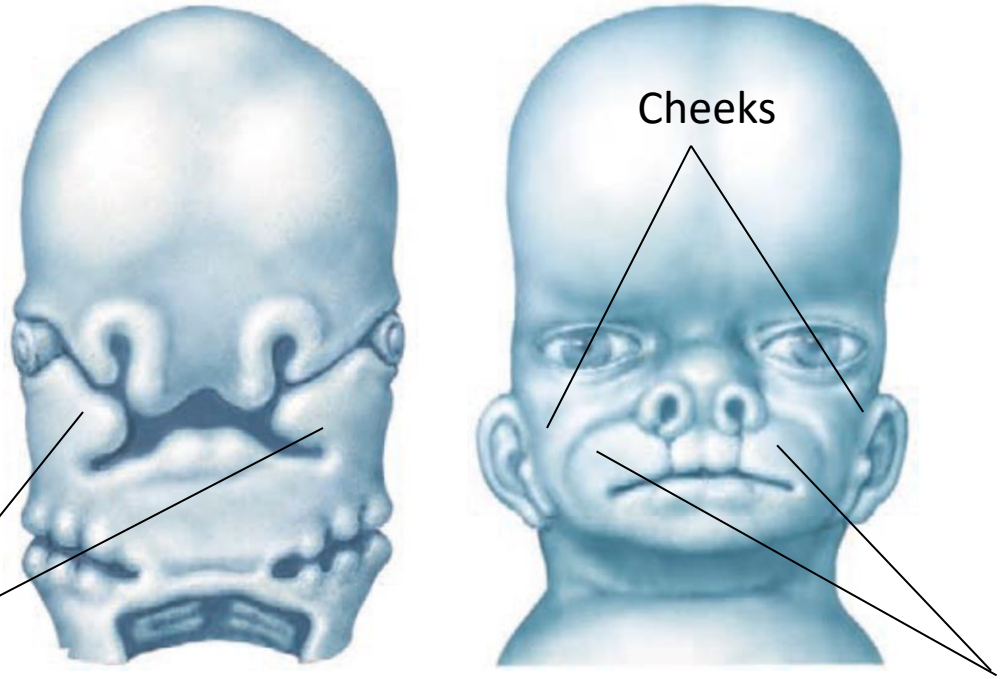
The lateral nasal prominences form the sides (alae).



Olfactory (nasal) pit, which is derived from the nasal placode forms the nostril and then becomes deeper (invaginates) to form a blind sac that forms The nasal vestibule.
(This blind sac unites with the respiratory tube which forms the rest of the nasal cavity)



In addition to the frontonasal nasal bridge, nasal septum and the medial and lateral nasal prominence, the frontonasal process gives rise to the forehead.

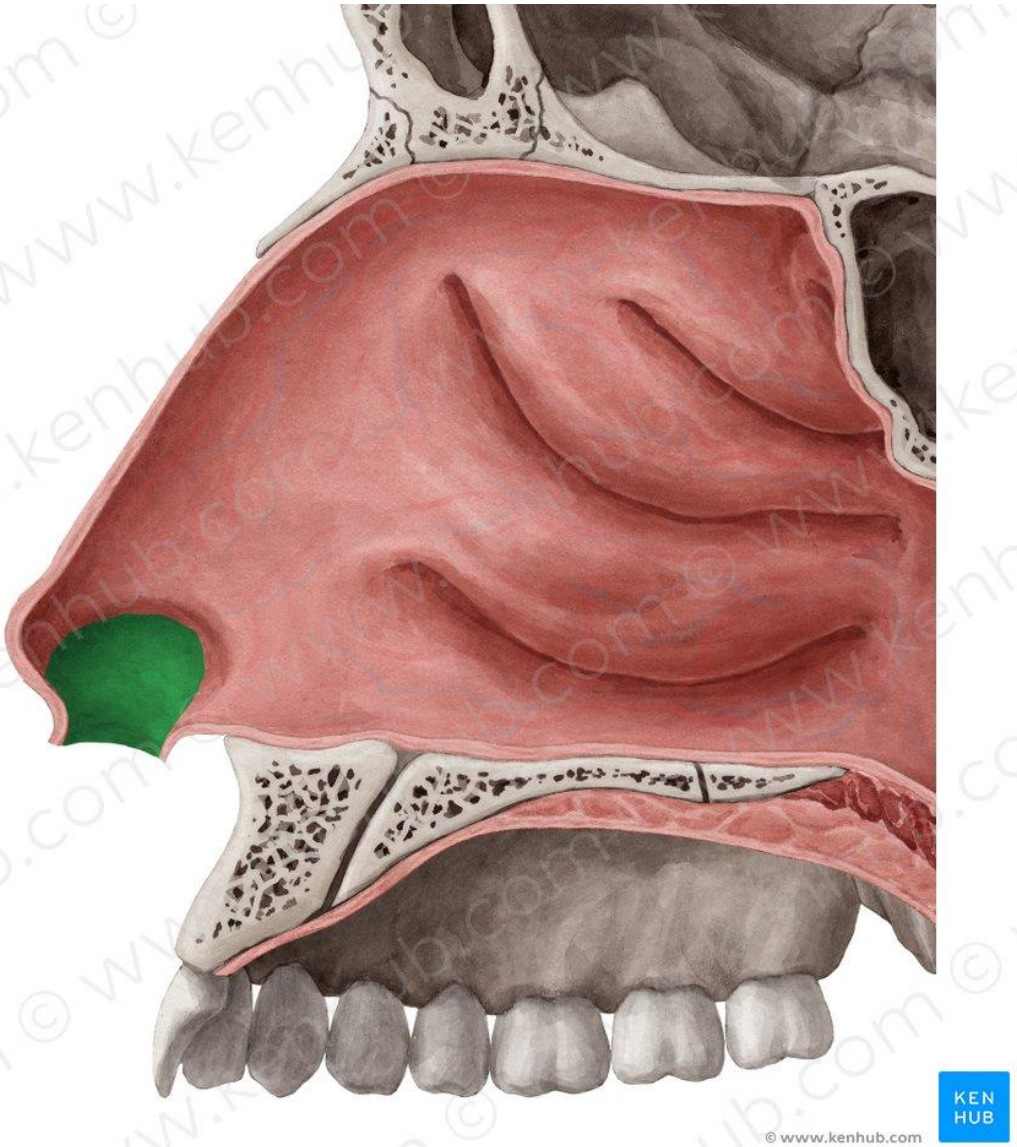


The maxillary Process

The maxillary process gives rise to the Cheeks and the lateral portion of the upper lip.

Portions of the upper lip derived from the maxillary process

Just to remember: this is the nasal vestibule.



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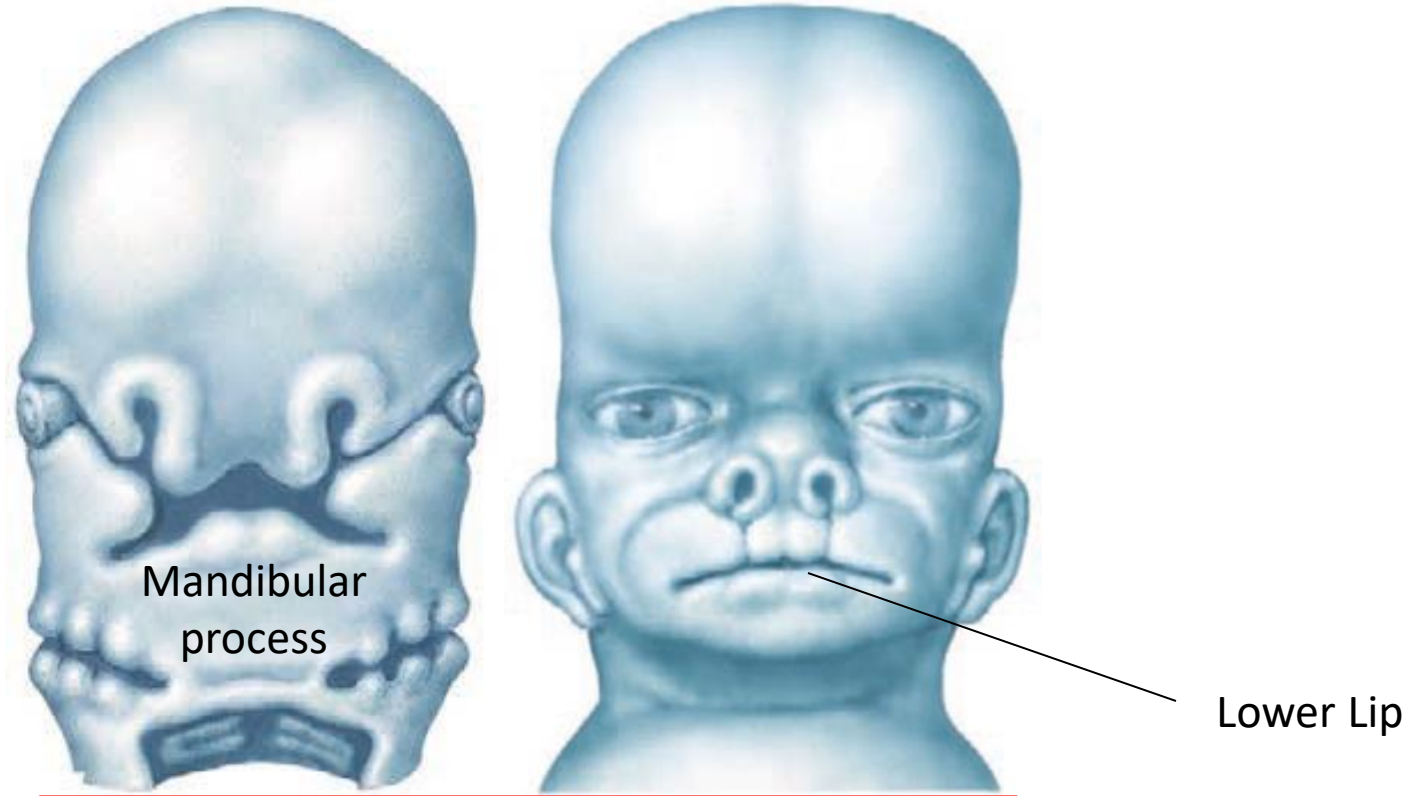
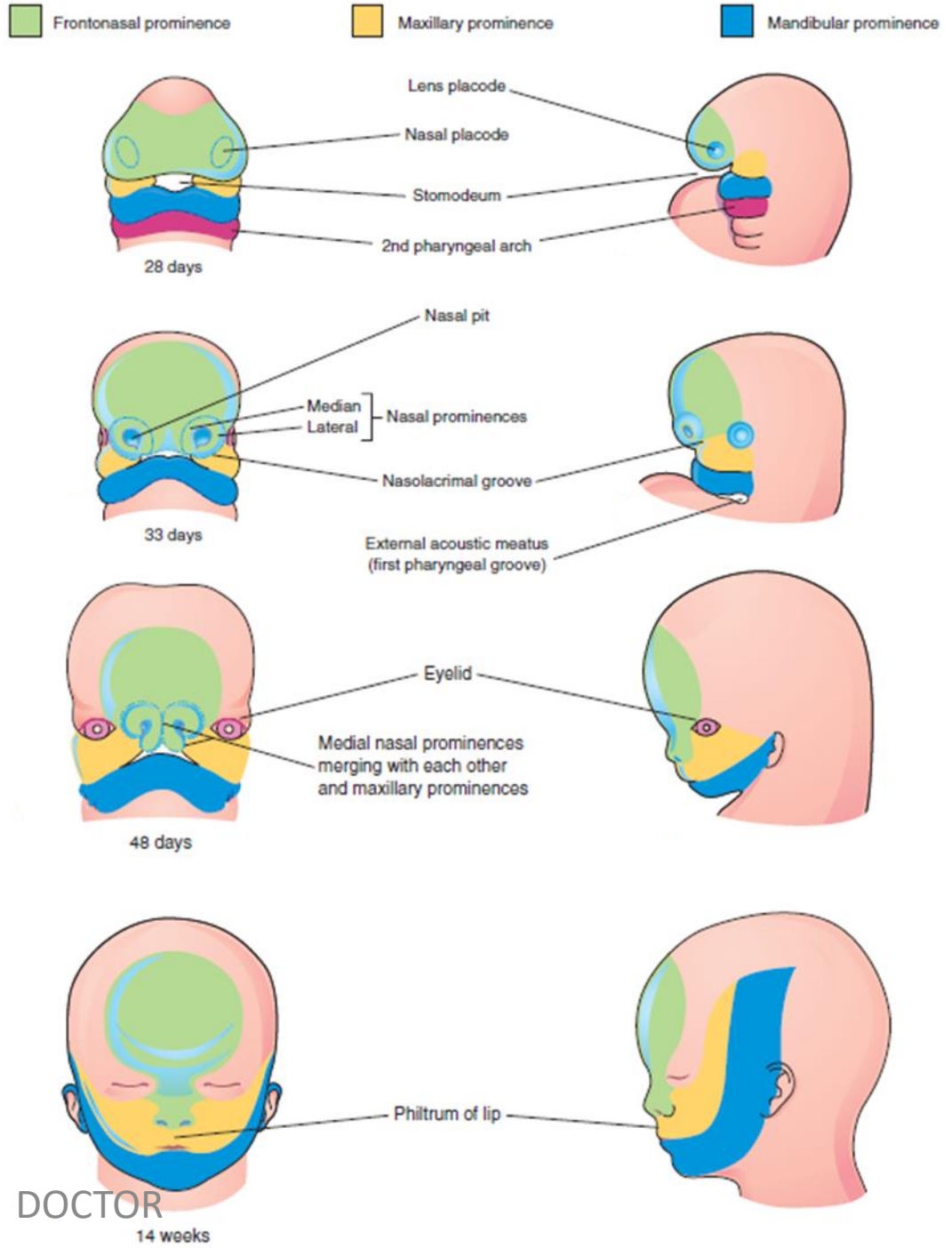


The mandibular process gives rise to the lower lip, it does not contribute to the nose by any means.

Prominence	Structures Formed
Frontonasal[a]	Forehead, bridge of nose, medial and lateral nasal prominences
Maxillary	Cheeks, lateral portion of upper lip
Medial nasal	Philtrum of upper lip, crest and tip of nose
Lateral nasal	Alae of nose
Mandibular	Lower lip

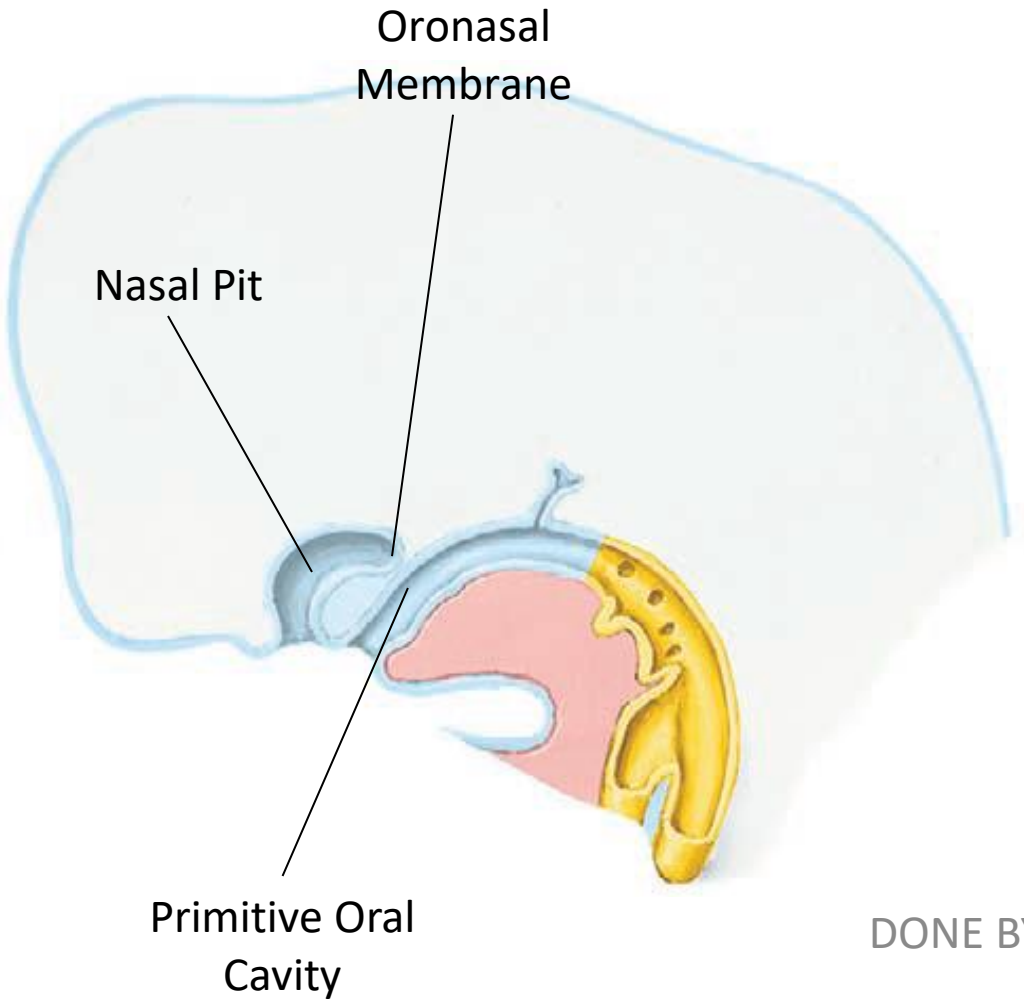
[a] The frontonasal prominence is a single unpaired structure; the other prominences are paired.

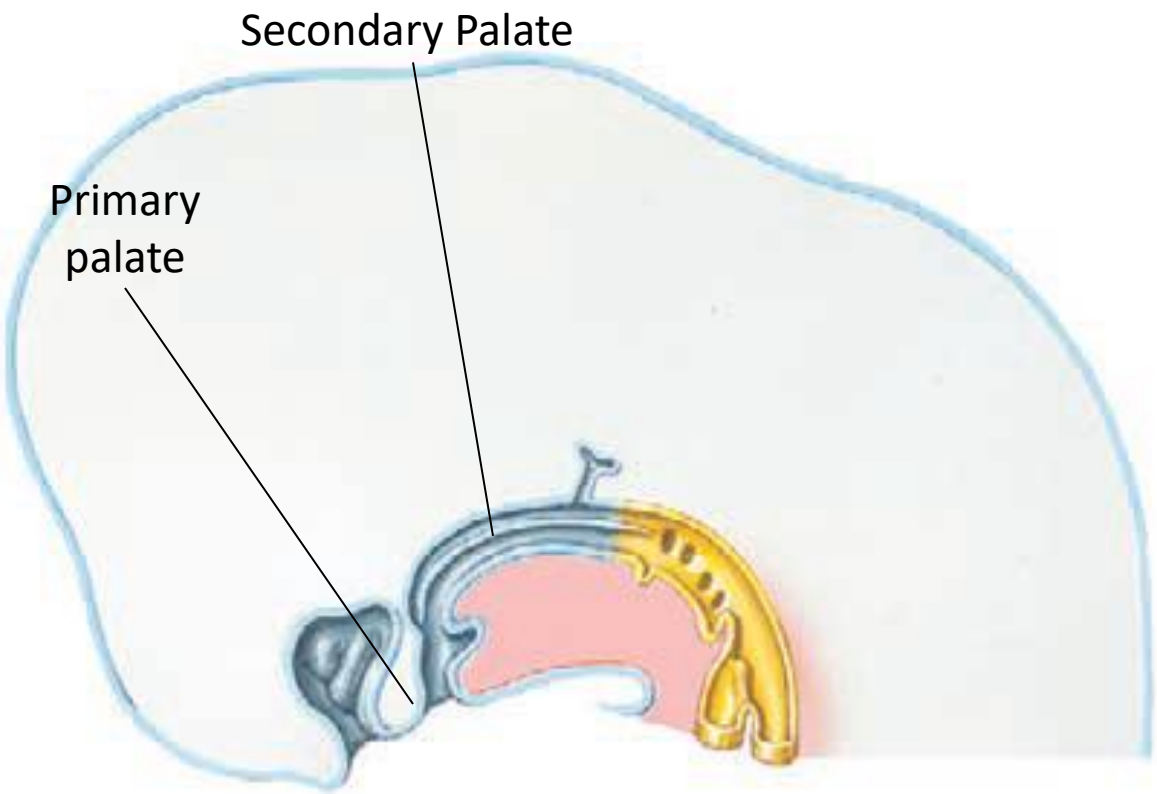


During the sixth week, the nasal pits deepen considerably, partly because of growth of the surrounding nasal prominences and partly because of their penetration into the underlying mesenchyme

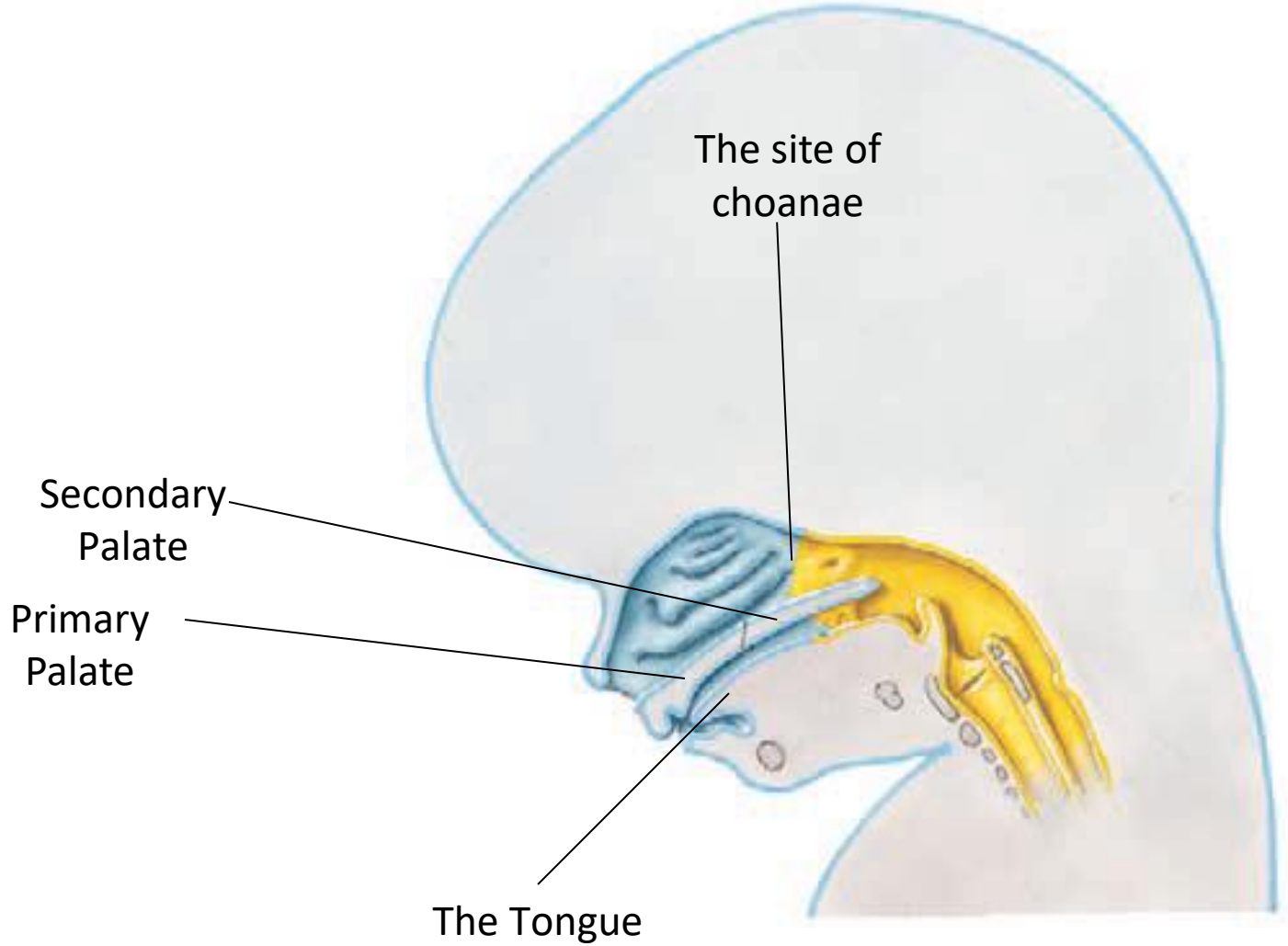
At first the oronasal membrane (floor of the nose) separates the pits from the primitive oral cavity by way of the newly formed foramina, the primitive choanae, this membrane ruptures then, allowing communication between oral and nasal cavities, then the palate develops and re-separates them.

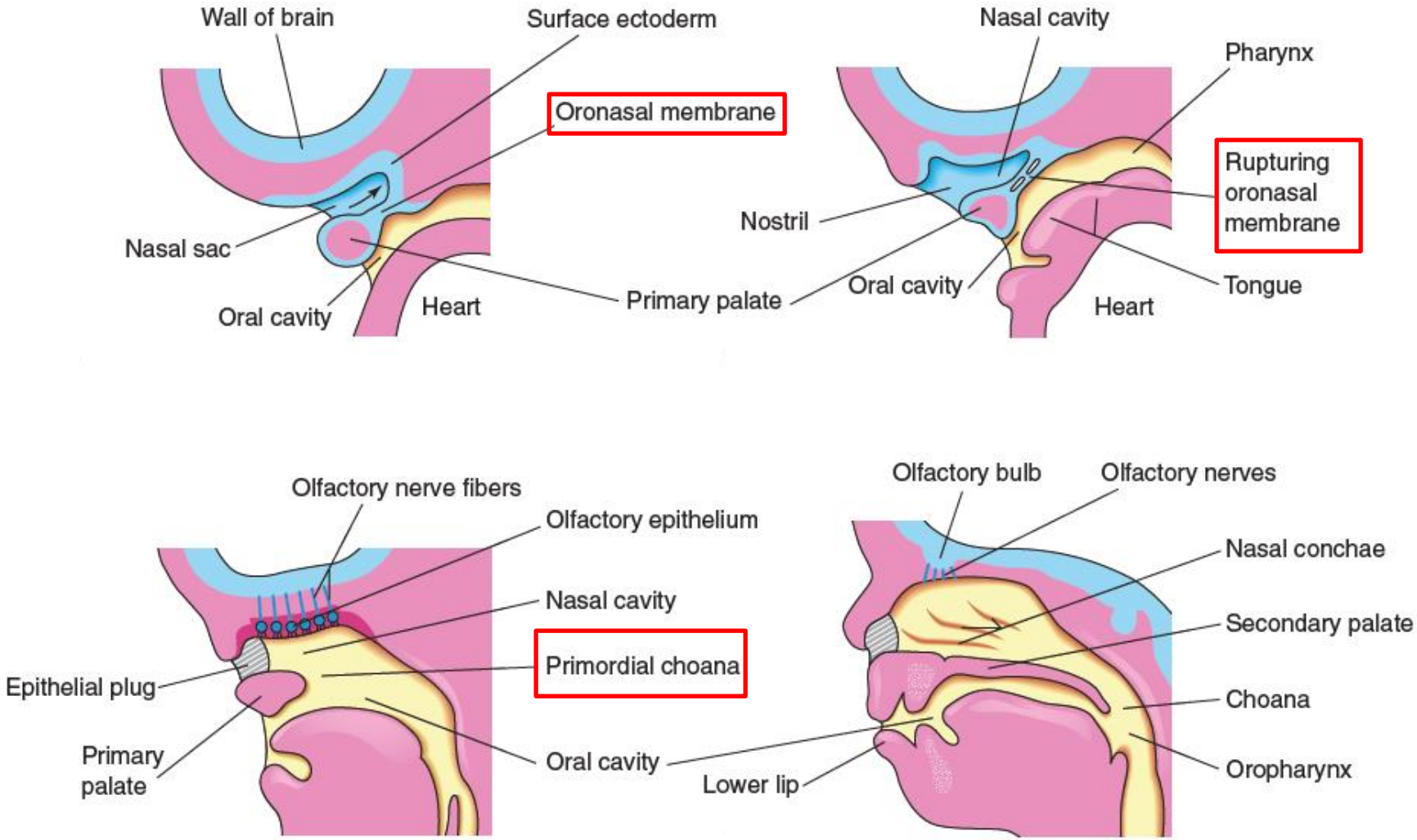
These choanae lie on each side of the midline and immediately behind the primary palate.





Later, with formation of the secondary palate and further development of the primitive nasal chambers, the definitive choanae will lie at the junction of the nasal cavity and the nasopharynx.

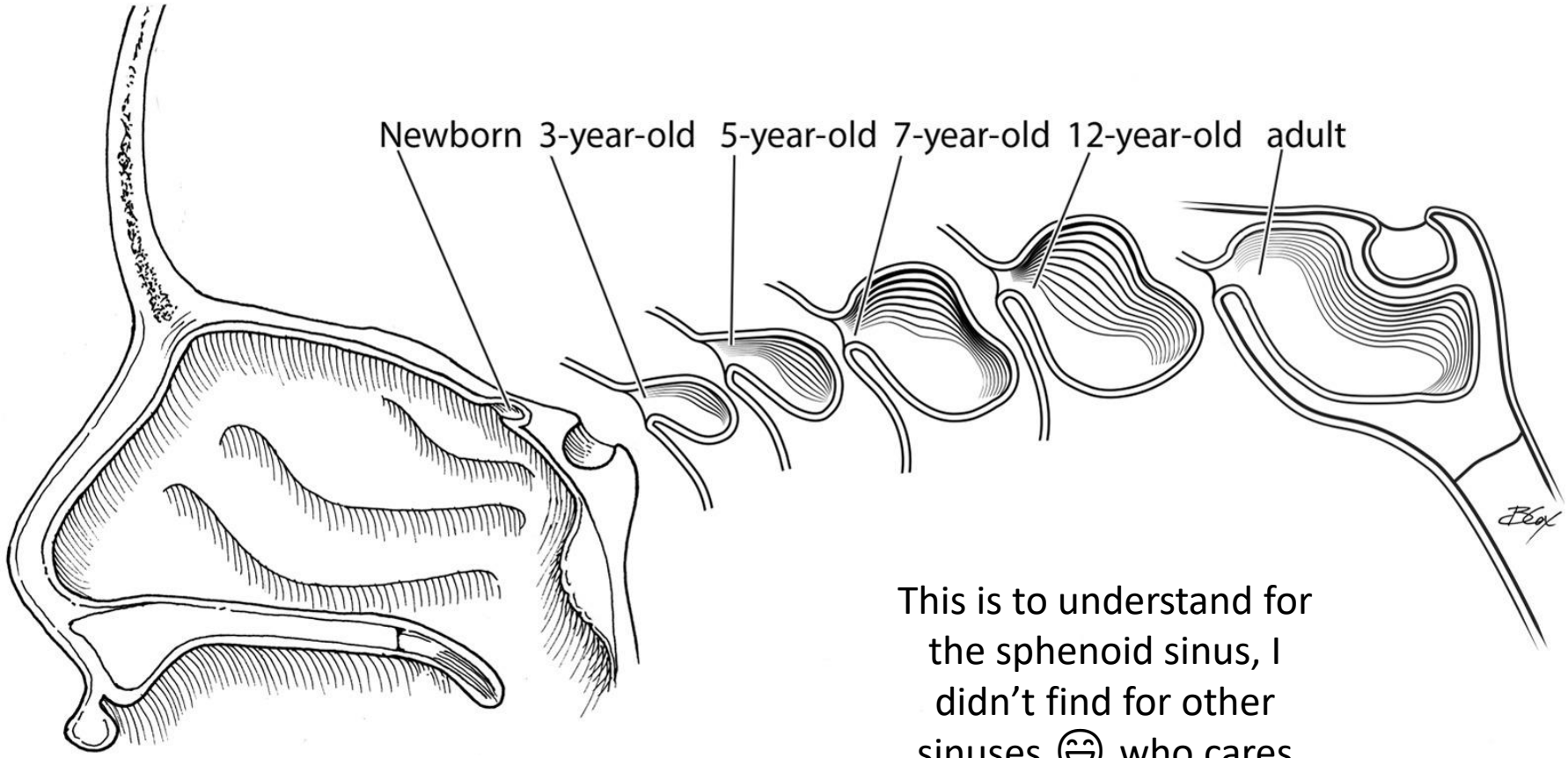



Wall of brain
Surface ectoderm
Oronasal membrane
Nasal sac
Oral cavity
Heart
Primary palate
Nasal cavity
Pharynx
Rupturing oronasal membrane
Nostril
Oral cavity
Tongue
Heart
Olfactory nerve fibers
Olfactory epithelium
Nasal cavity
Primordial choana
Epithelial plug
Primary palate
Oral cavity
Olfactory bulb
Olfactory nerves
Nasal conchae
Secondary palate
Choana
Oropharynx
Lower lip

DEVELOPMENT OF PARANASAL AIR SINUSES

Paranasal air sinuses develop as diverticula of the lateral nasal wall and extend into the maxilla, ethmoid, frontal, and sphenoid bones.

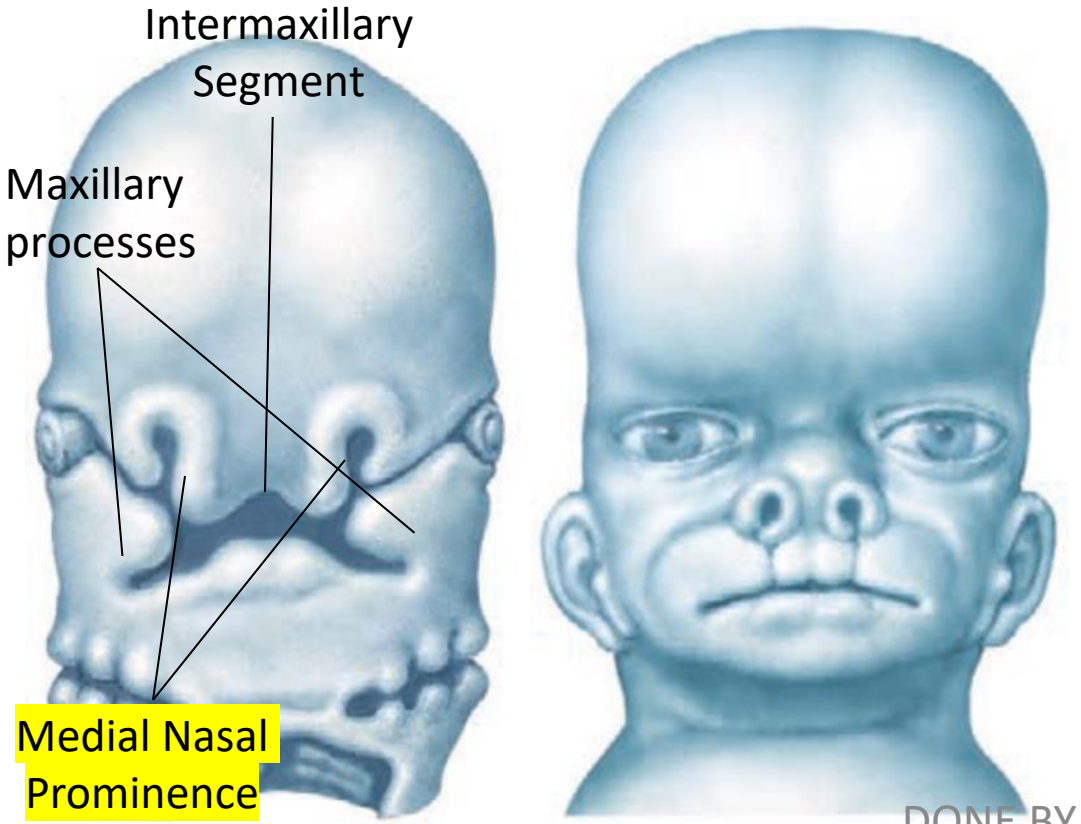
They reach their maximum size during puberty and contribute to the definitive shape of the face.

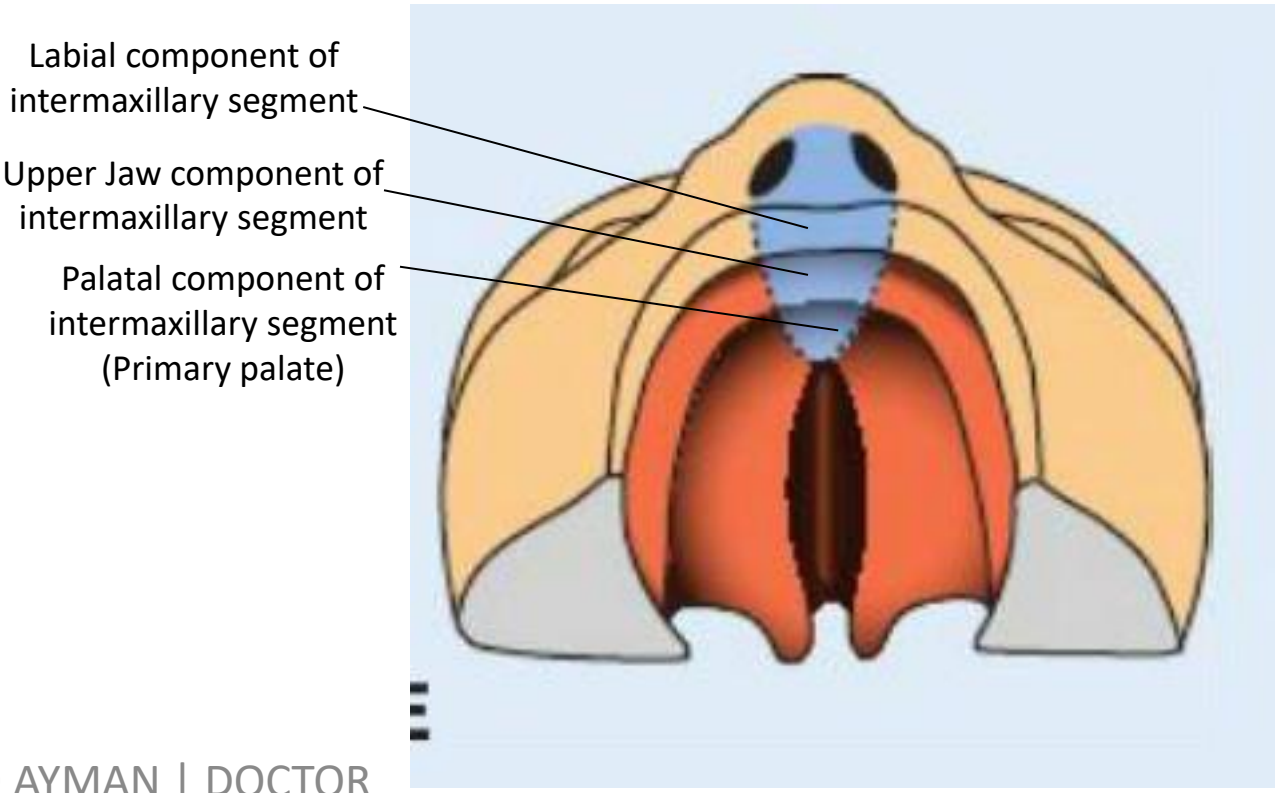


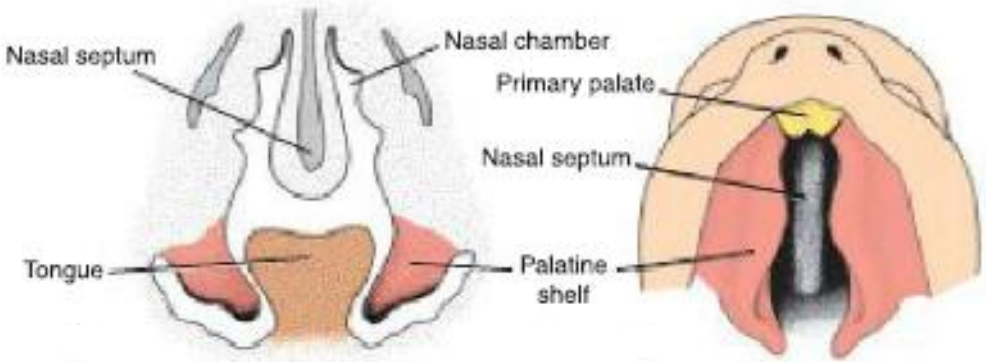
This is to understand for the sphenoid sinus, I didn't find for other sinuses 😄 who cares how paranasal sinuses develop anyways ? 😐

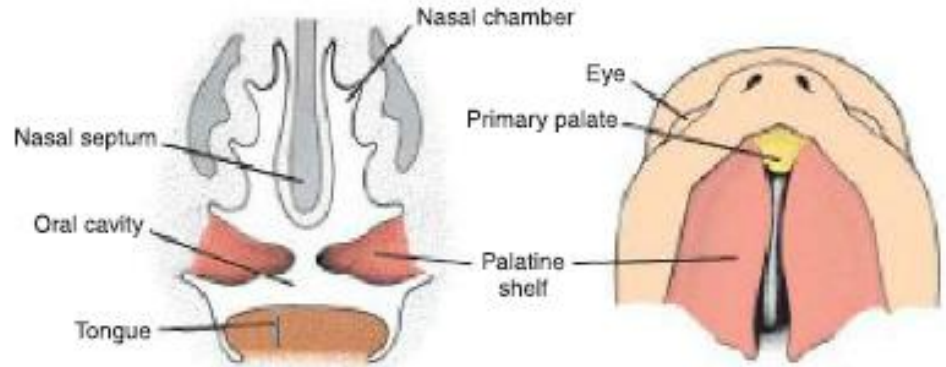
DEVELOPMENT OF THE PALATE

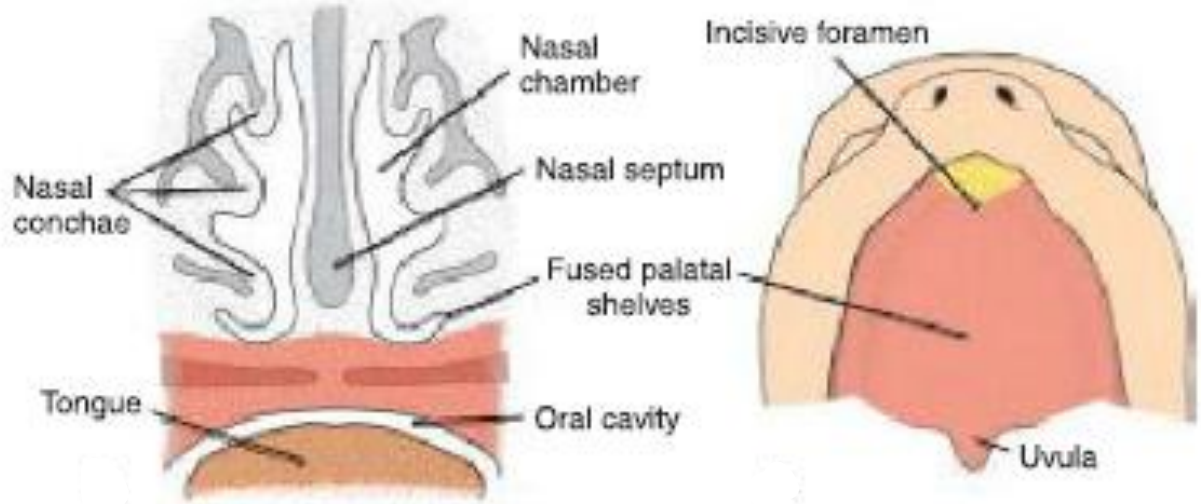
- As a result of medial growth of the maxillary prominences, the two medial nasal prominences merge not only at the surface but also at a deeper level, the structure formed by the two merged nasal prominences is the intermaxillary segment.
- The intermaxillary segment it is composed of a labial component, which forms the philtrum of the upper lip, an upper jaw component, which carries the four incisor teeth, and a palatal component, which forms the triangular primary palate.
- The intermaxillary segment is continuous with the rostral (inferior) portion of the nasal septum, which is formed by the frontonasal prominence.



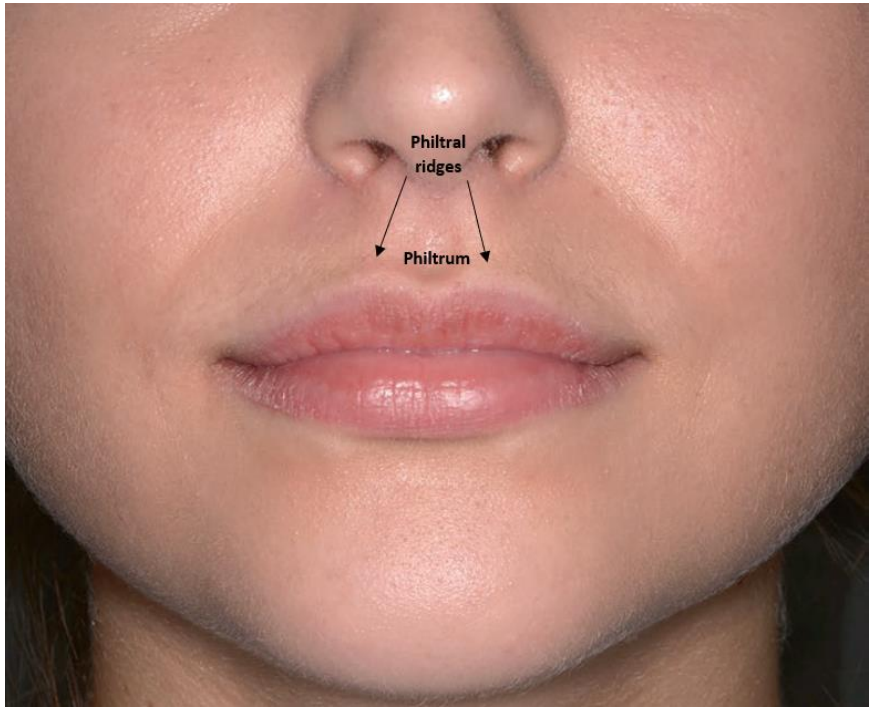


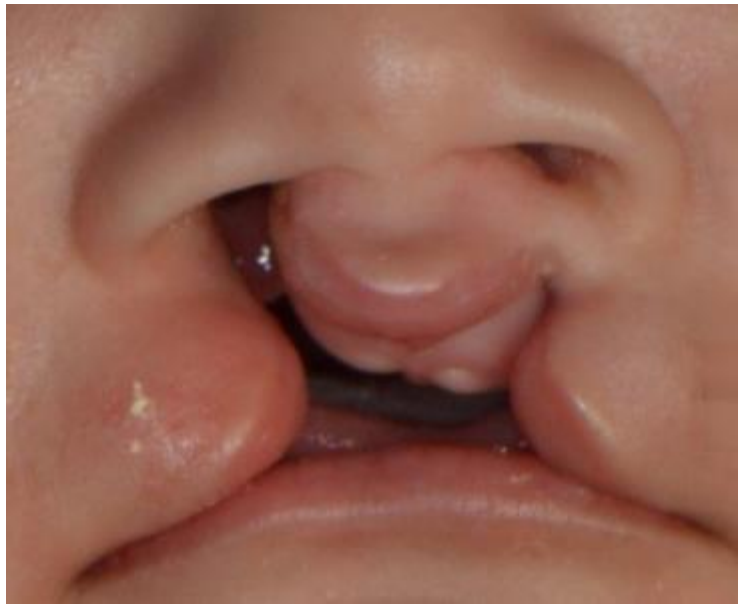

Nasal septum
Nasal chamber
Primary palate
Nasal septum
Tongue
Palatine shelf


Nasal chamber
Eye
Primary palate
Nasal septum
Oral cavity
Palatine shelf
Tongue

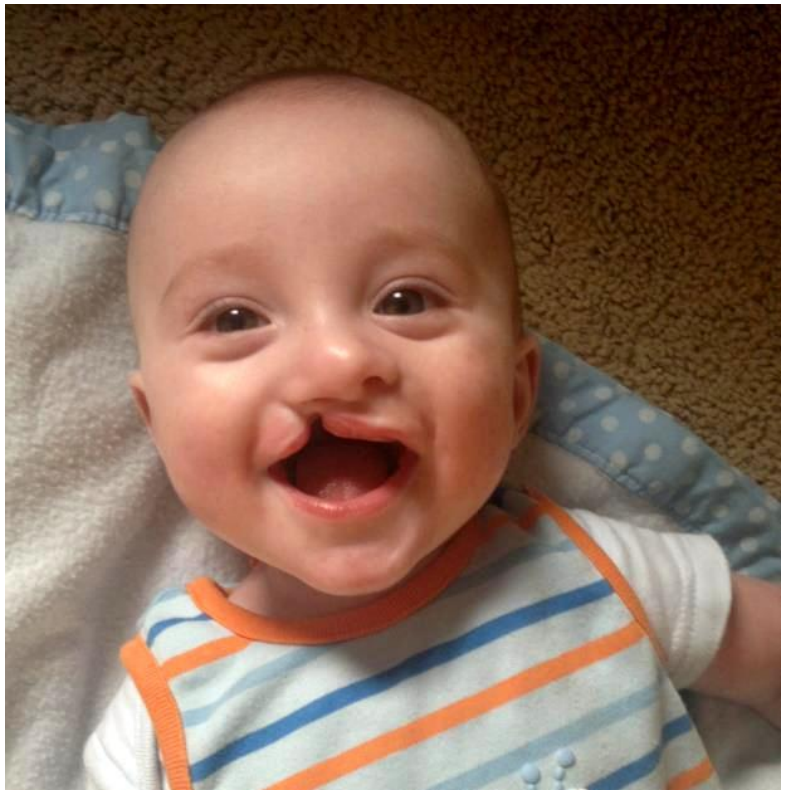

Nasal chamber
Incisive foramen
Nasal septum
Nasal conchae
Fused palatal shelves
Tongue
Oral cavity
Uvula

Note: the labial component of the intermaxillary segment of the frontonasal process fuses with the maxillary prominence on each side to form the upper lip, this fusion is marked by the ridges of philtrum, failure of this fusion would result in a cleft lip, which might be unilateral or bilateral.



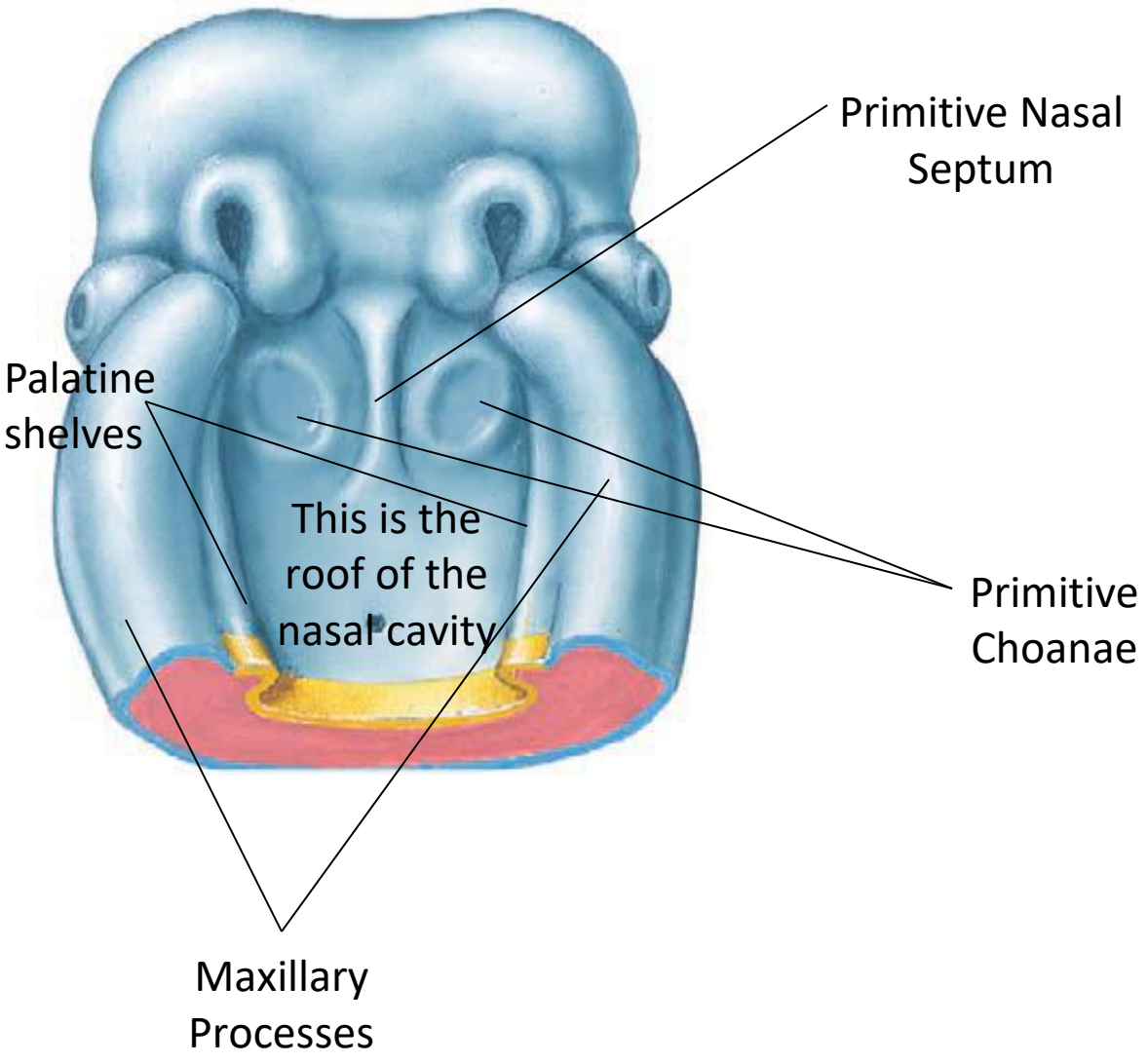


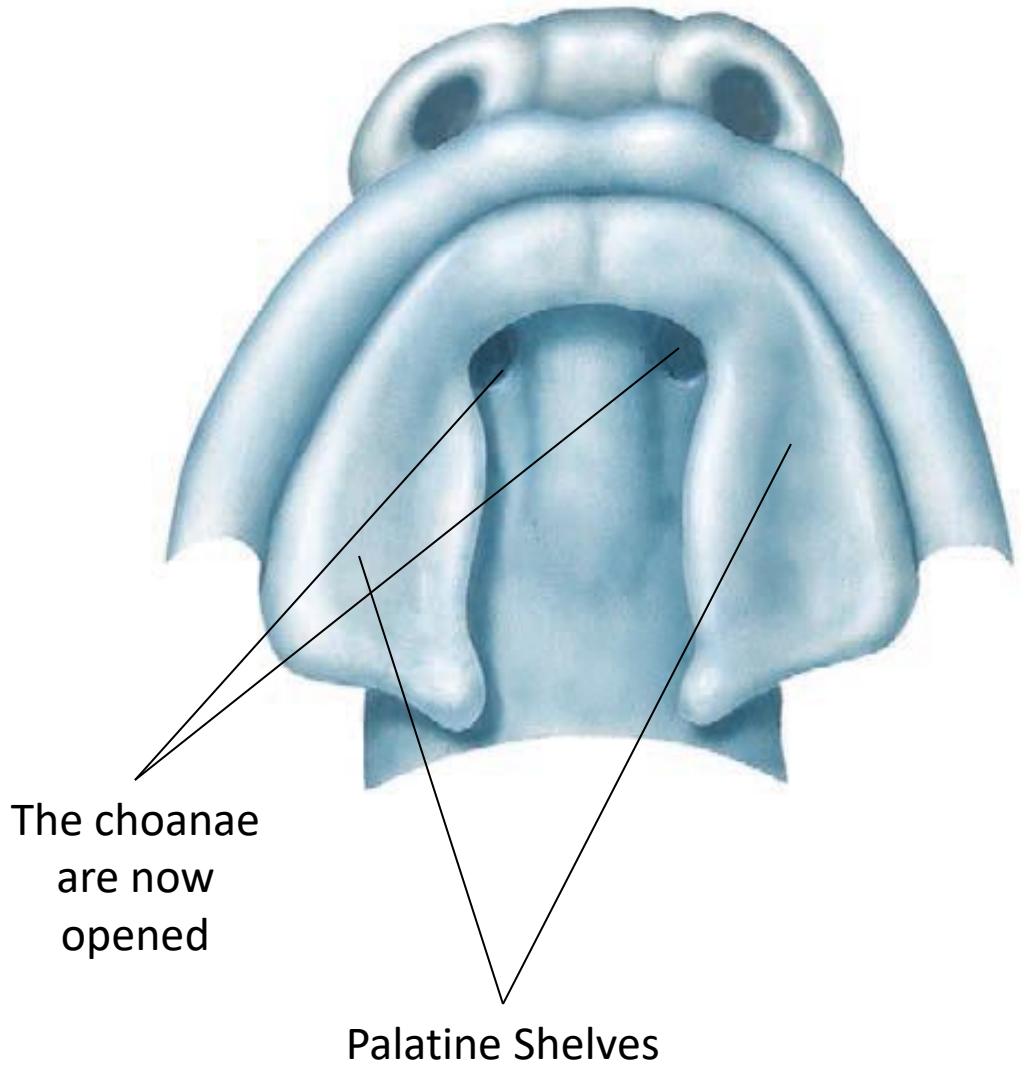
Bilateral Cleft Lip



Unilateral Cleft Lip

The main part of the definitive palate is formed by two shelf-like outgrowths from the maxillary prominences. These outgrowths, the palatine shelves , appear in the sixth week of development and are directed obliquely downward on each side of the tongue.

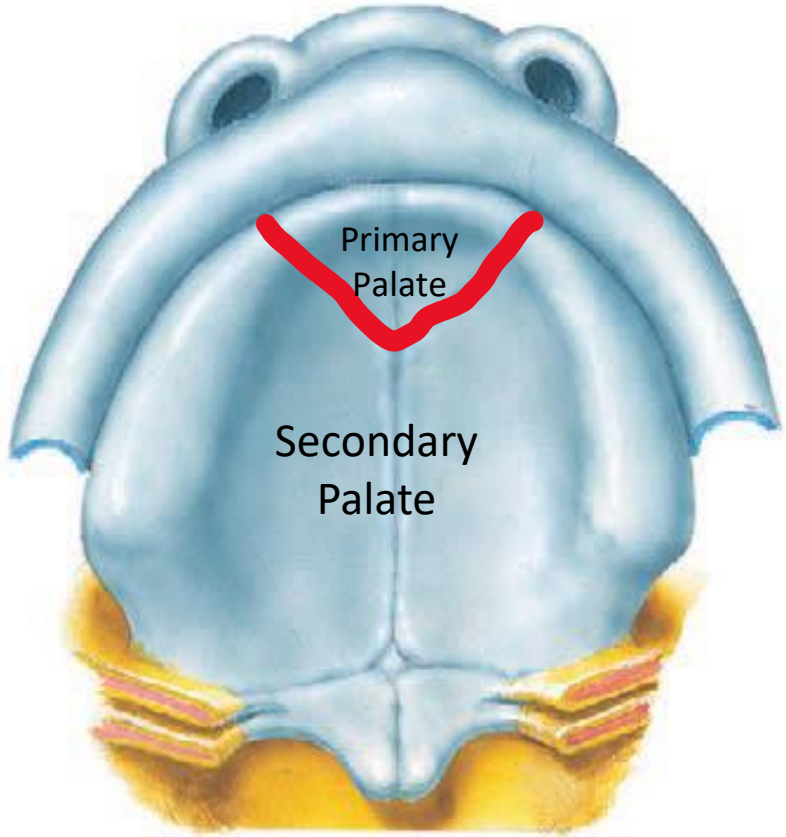


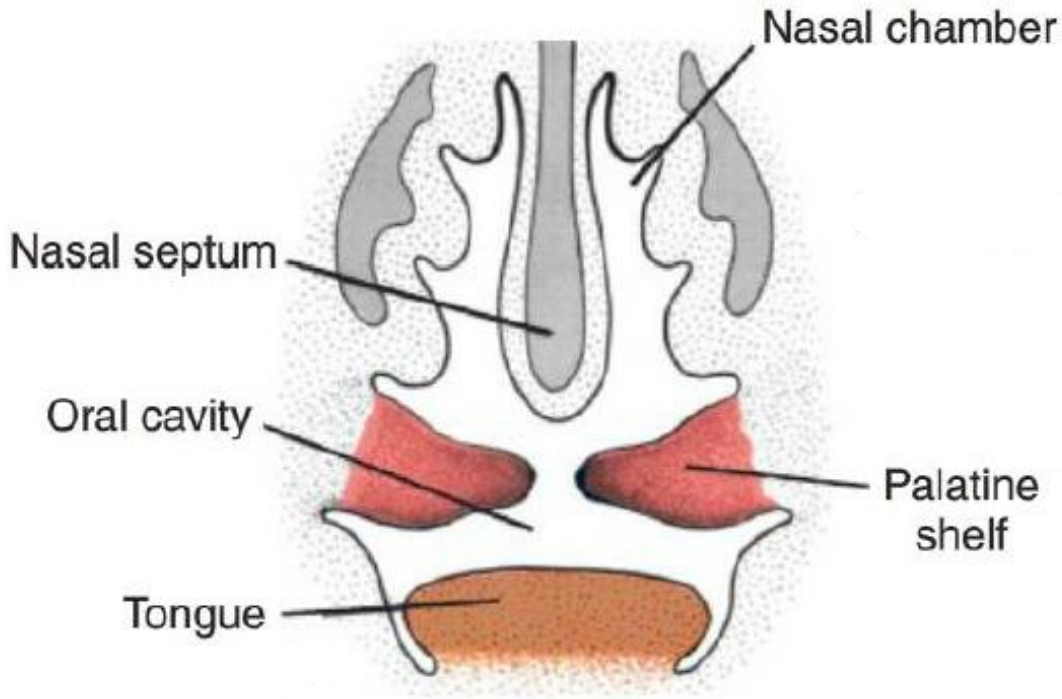


In the seventh week, however, the palatine shelves ascend to attain a horizontal position above the tongue and fuse, forming the secondary palate.

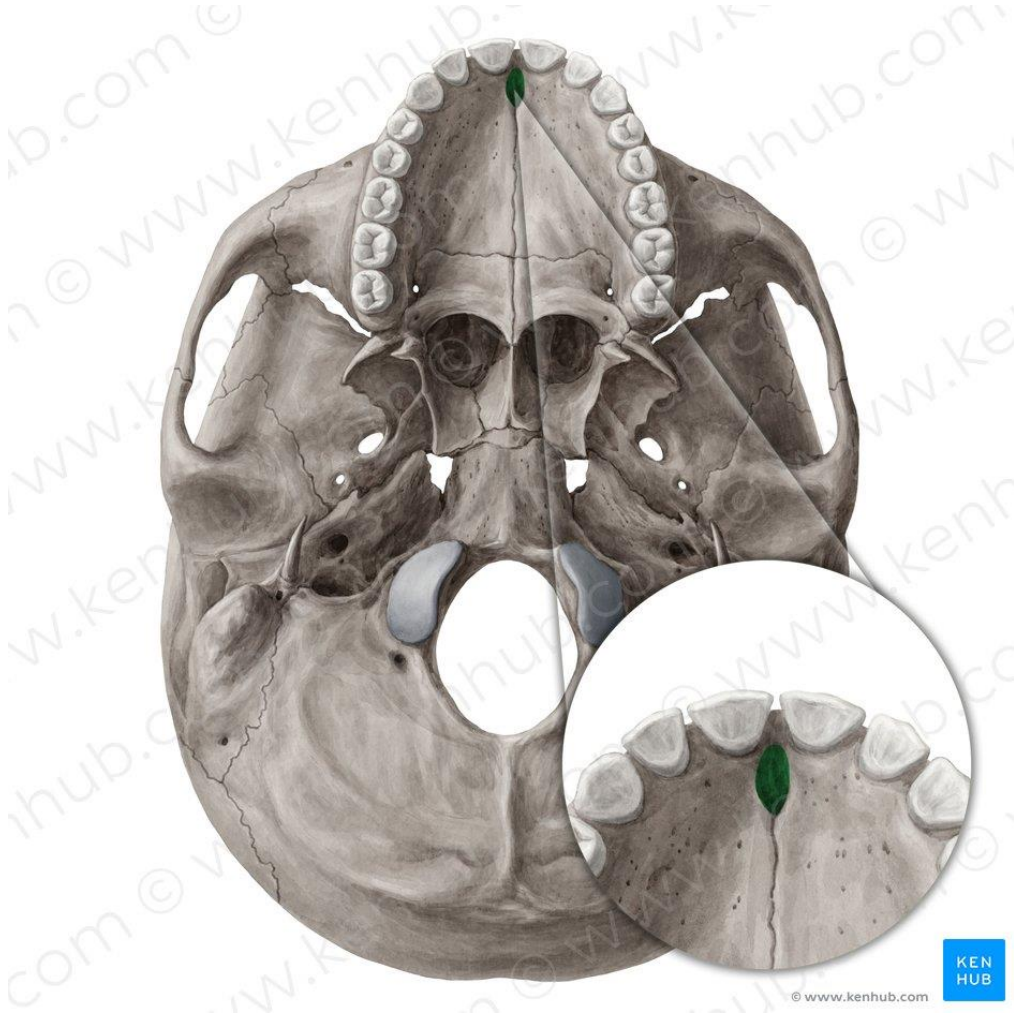
Anteriorly, the shelves fuse with the triangular primary palate, and the incisive foramen is the midline landmark between the primary and secondary palates.

At the same time as the palatine shelves fuse, the nasal septum grows downward and joins with the cephalic aspect of the newly formed palate.





Just to remember: this is the incisive foramen.



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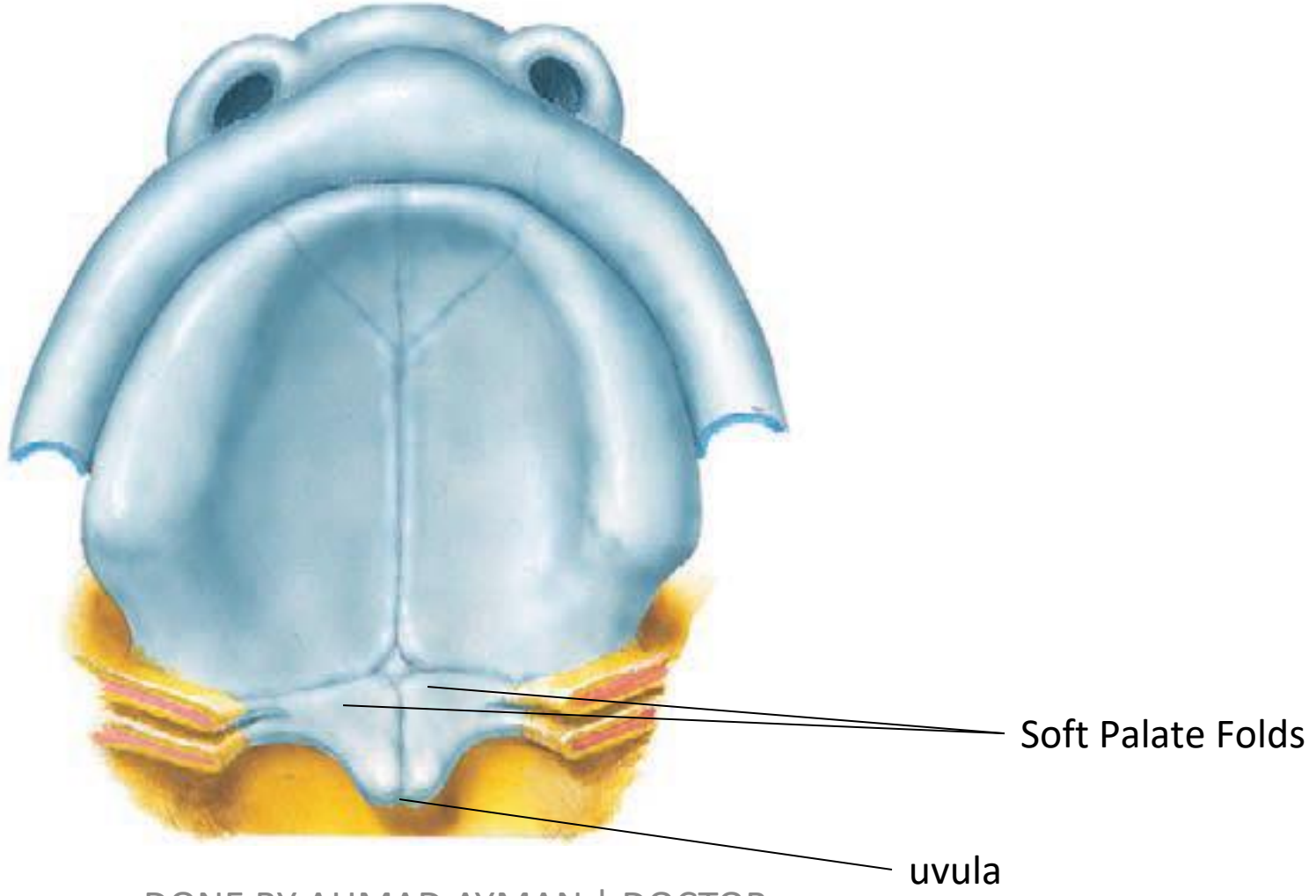
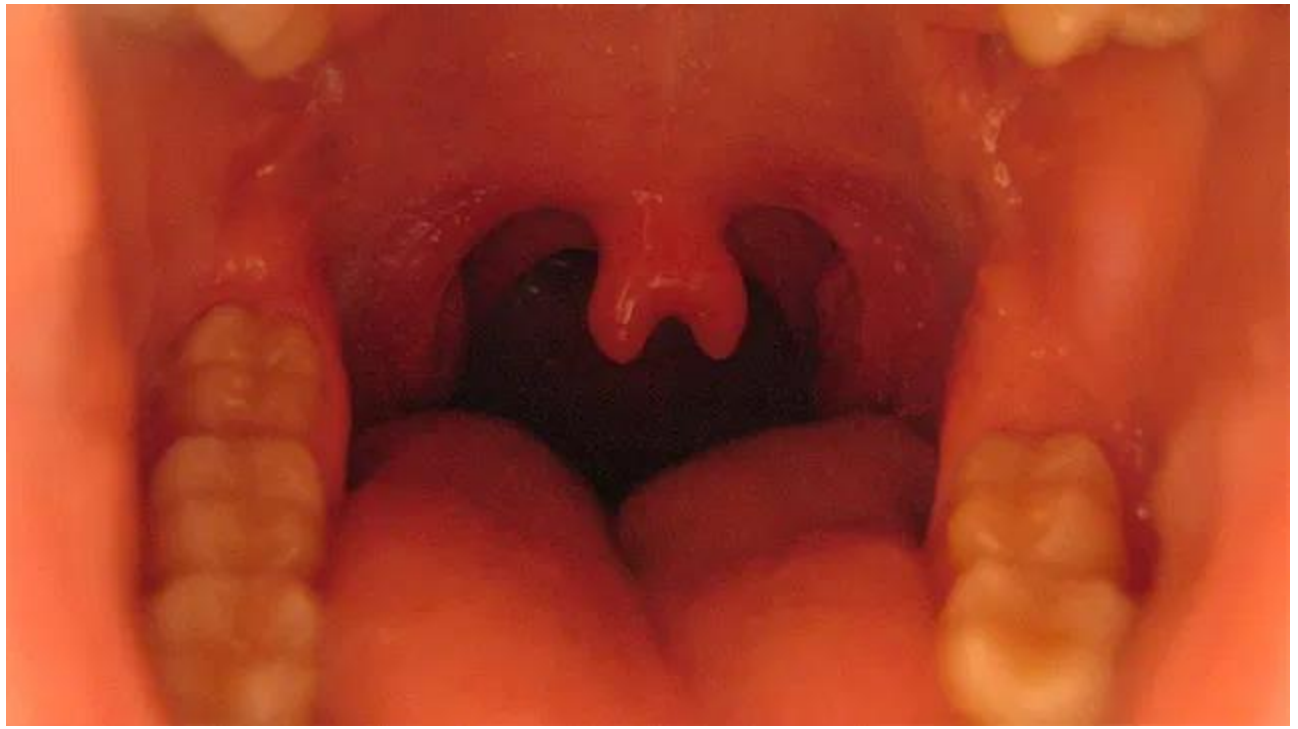
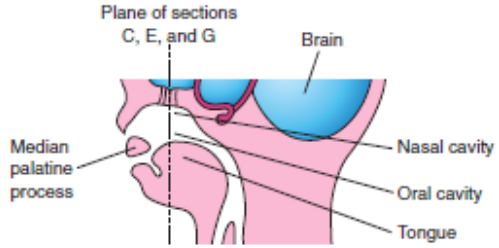
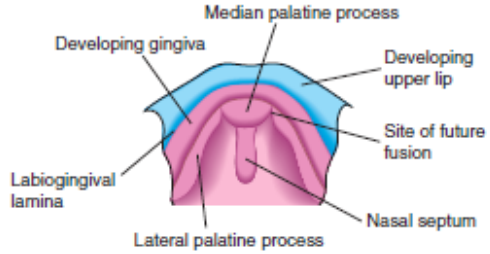
Two folds grow posteriorly from the edge of the palatine process to form the soft palate and the uvula, the union of these two folds of the soft palate occurs during the eighth week, while the two parts of the uvula fuse in the midline during the eleventh week.

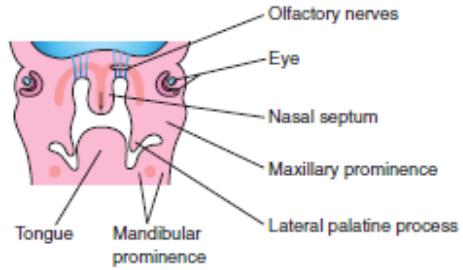


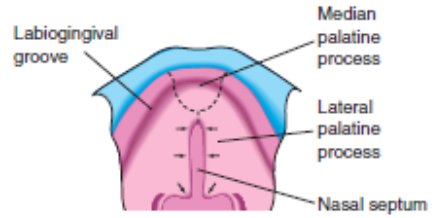
Failure of the uvulae to fuse results in a cleft uvula.

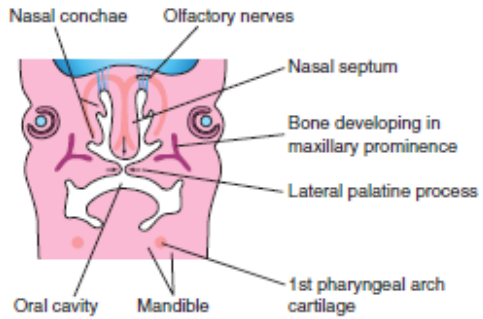


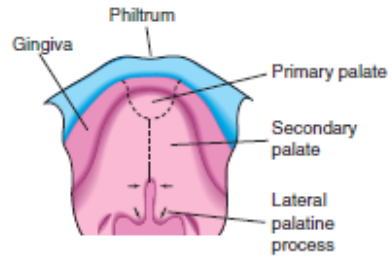


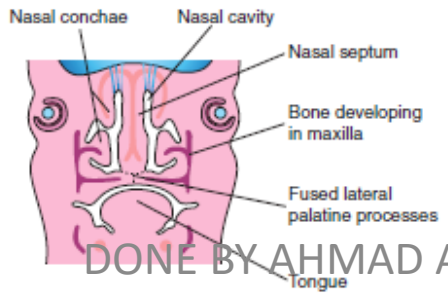


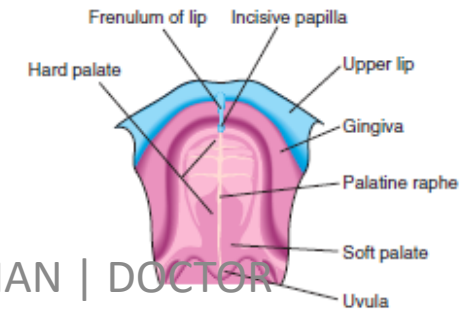




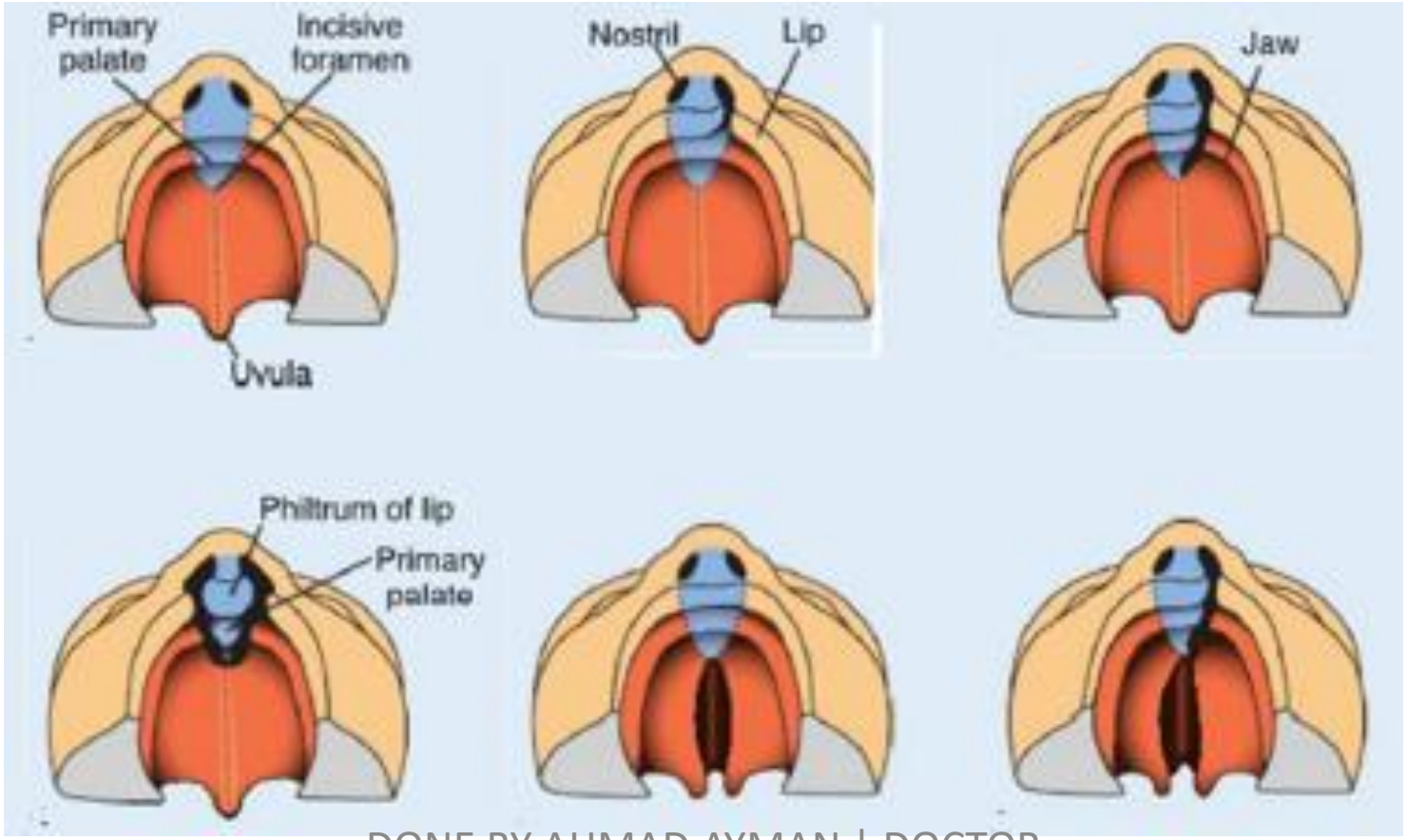








Just like cleft lips, failure of the primary palate (which is derived from the intermaxillary segment of the frontonasal prominence, which is in turn derived from the medial nasal processes) to fuse with the secondary palate (which is derived from the palatine shelves of the maxillary prominences), would result in a cleft palate, which might be unilateral or bilateral, moreover, a cleft palate might or might not be accompanied with a cleft lip (if failure of primary and secondary palates to fuse is accompanied by failure of labial component of the intermaxillary segment to fuse with maxillary prominences), a cleft palate might also result if the two palatine shelves fail to fuse. A cleft might also be complete or incomplete.

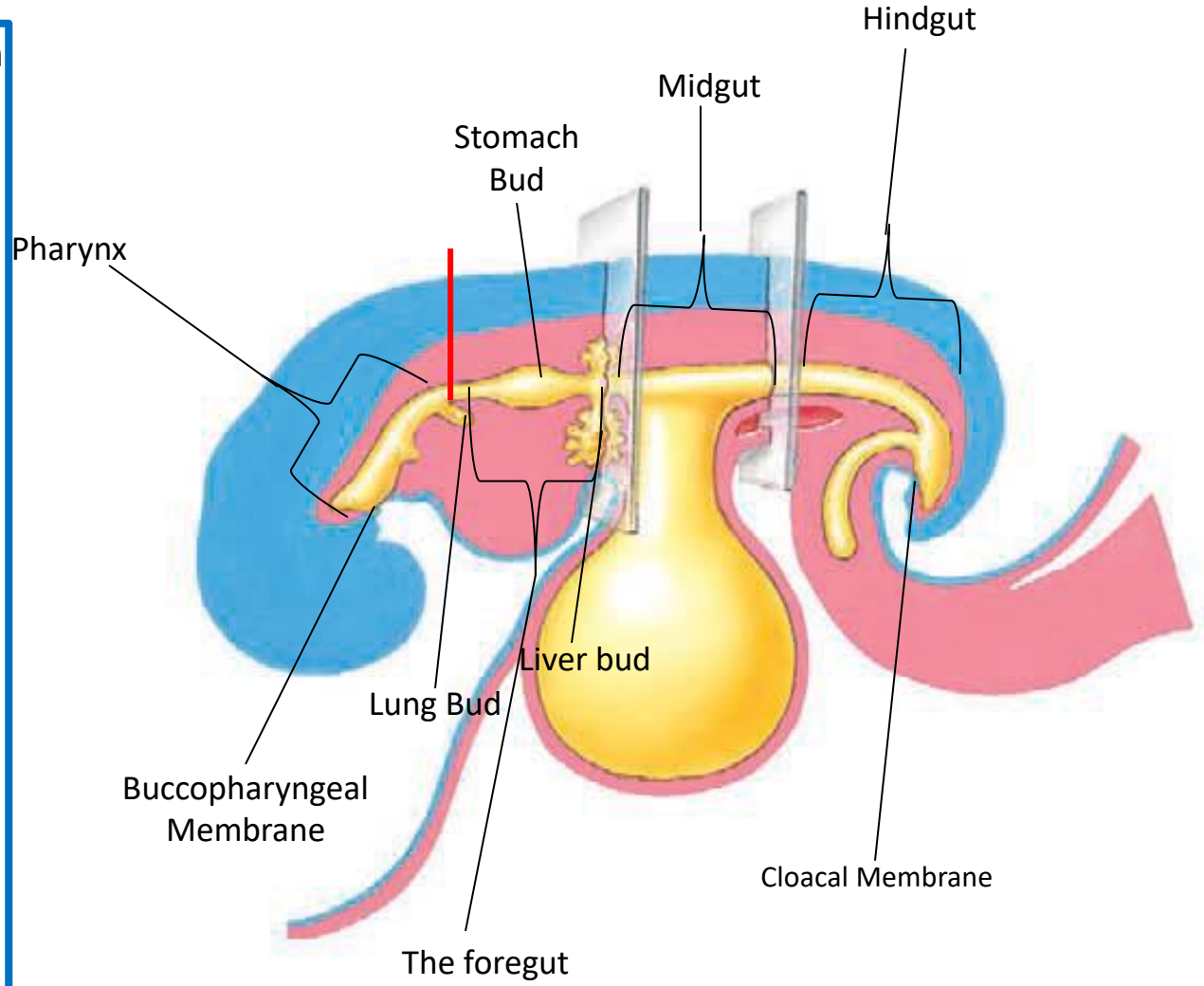


Note that the cleft might extend into the nose.

DEVELOPMENT OF THE PRIMITIVE GUT

Development of the primitive gut and its derivatives is in four sections:

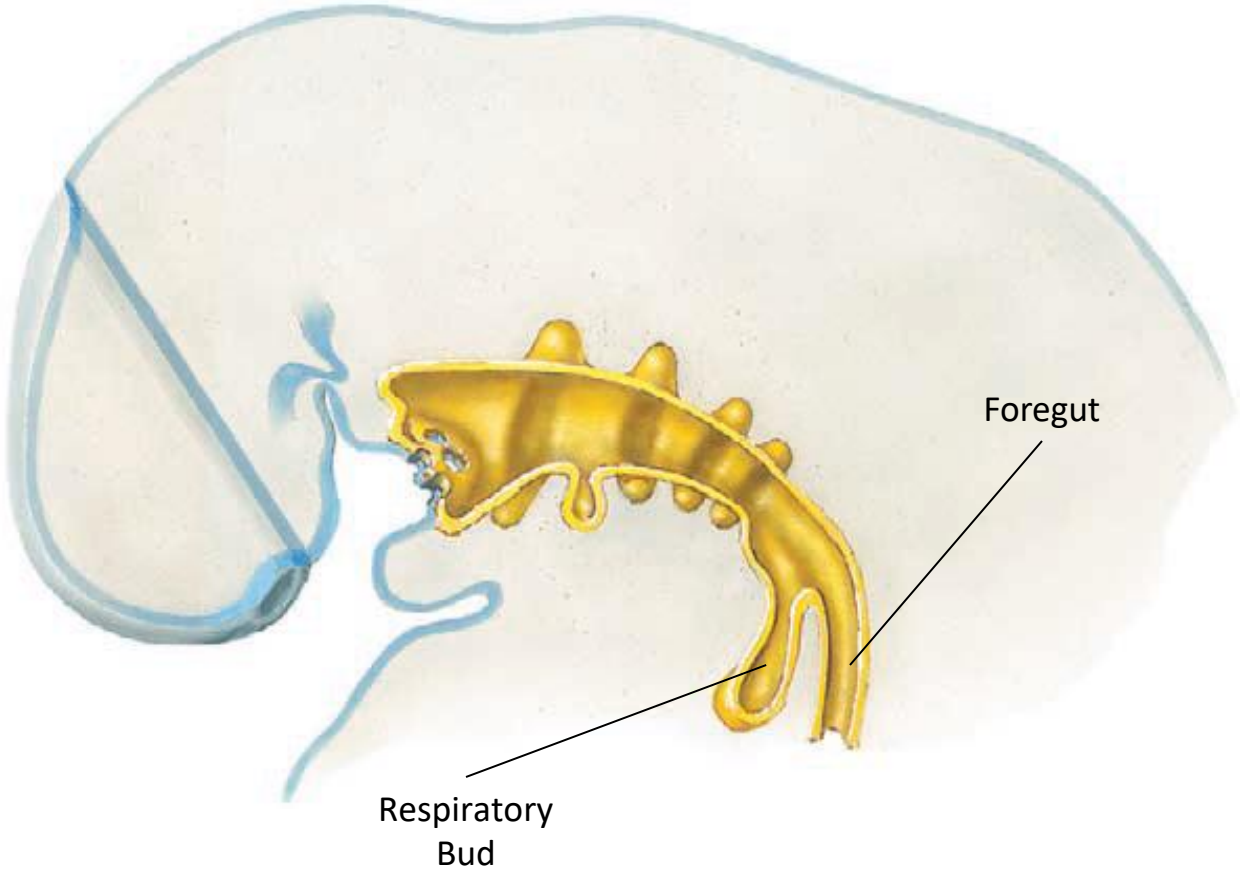
- The pharyngeal gut, or pharynx, extends from the buccopharyngeal membrane (which ruptures to give rise to the oral fissure) to the tracheobronchial diverticulum (which gives rise to the trachea and lungs).
- The foregut lies caudal to the pharyngeal tube and extends caudally as far as the liver outgrowth, it gives rise to the esophagus, stomach, 1st two parts of duodenum, liver, biliary tree, and the pancreas, derivatives of the foregut are supplied by branches of the coeliac trunk.
- The midgut begins caudal to the liver bud and extends to the junction of the right two-thirds and left third of the transverse colon in the adult, it gives rise to the last two parts of the duodenum, jejunum, ileum, and the large intestine till the proximal 2/3s of the transverse colon, derivatives of the midgut are supplied by branches of the superior mesenteric artery.
- The hindgut extends from the left third of the transverse colon to the cloacal membrane (which ruptures to give rise to the anus), it gives rise to the distal third of the transverse colon and the rest of the large intestine till the lower half of the anal canal, derivatives of the hindgut is supplied by branches of the inferior mesenteric artery.

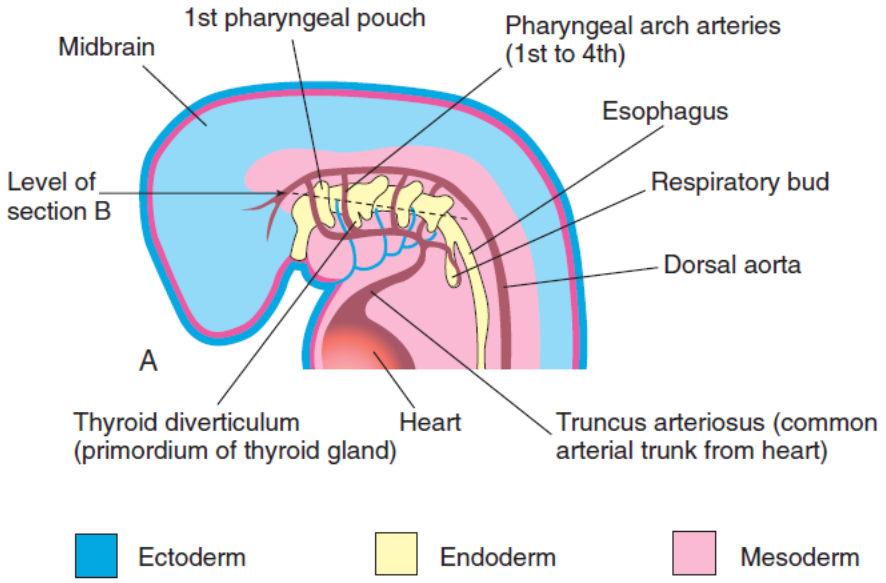


Note: after the third week of development and embryonic folding, the embryo is much like a tube that has three layers in its wall, those are the ectoderm which gives rise to the skin, the mesoderm which gives rise to bones, muscles and other connective tissue, and the endoderm which gives rise to our viscera

THE RESPIRATORY DIVERTICULUM

When the embryo is approximately four weeks old, the respiratory diverticulum which is also called the lung bud, appears as an outgrowth from the ventral wall of the foregut.
The location of the bud along the gut tube is determined by signals from the surrounding mesenchyme, including fibroblast growth factors (FGFs) that instruct the endoderm.

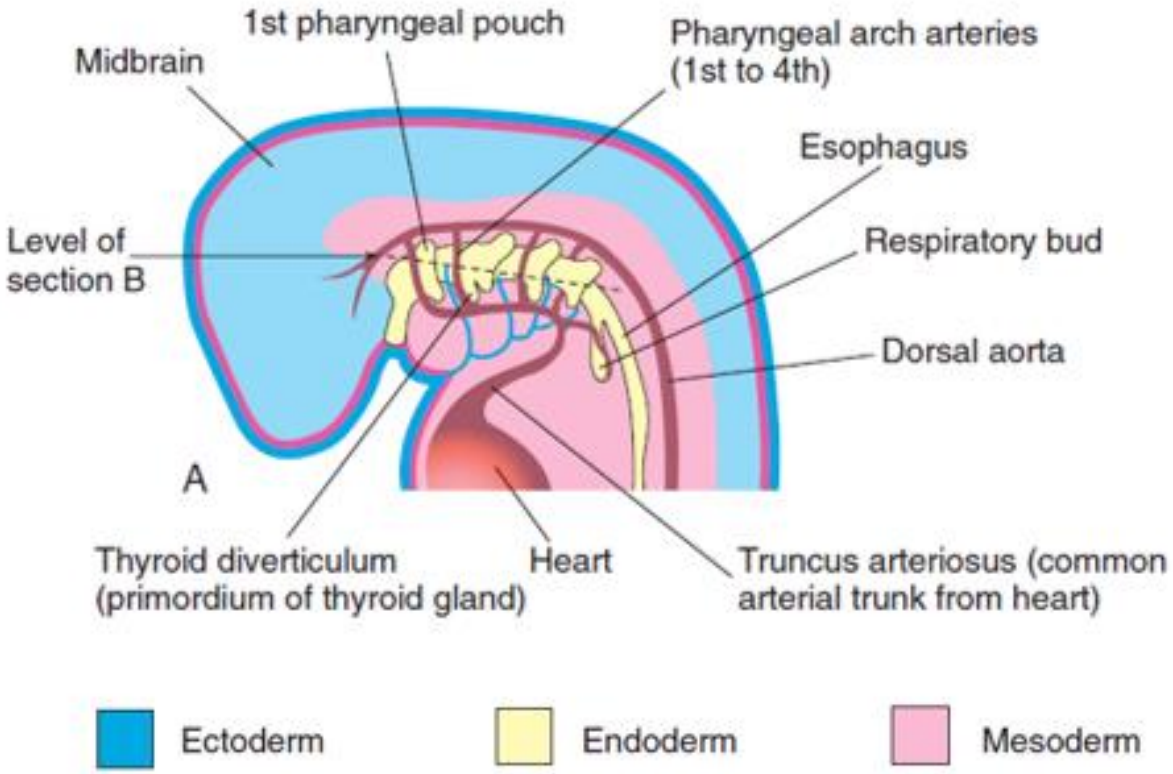




The epithelium of the internal lining of the larynx, trachea, and bronchi, as well as that of the lungs, is entirely of endodermal origin.

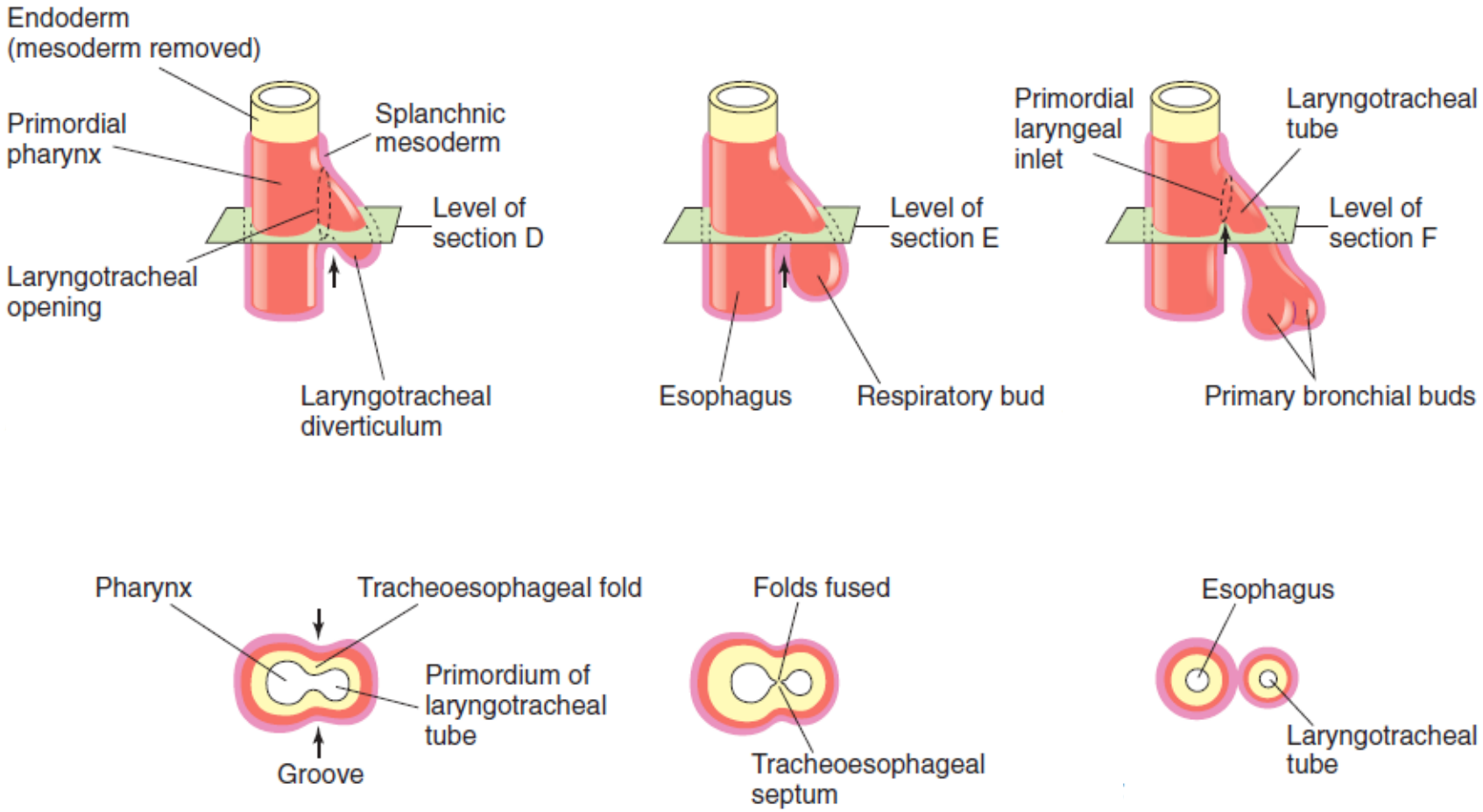
The cartilaginous, muscular, and connective tissue components of the trachea and lungs are derived from splanchnic mesoderm surrounding the foregut.

Initially, the lung bud is in open communication with the foregut.

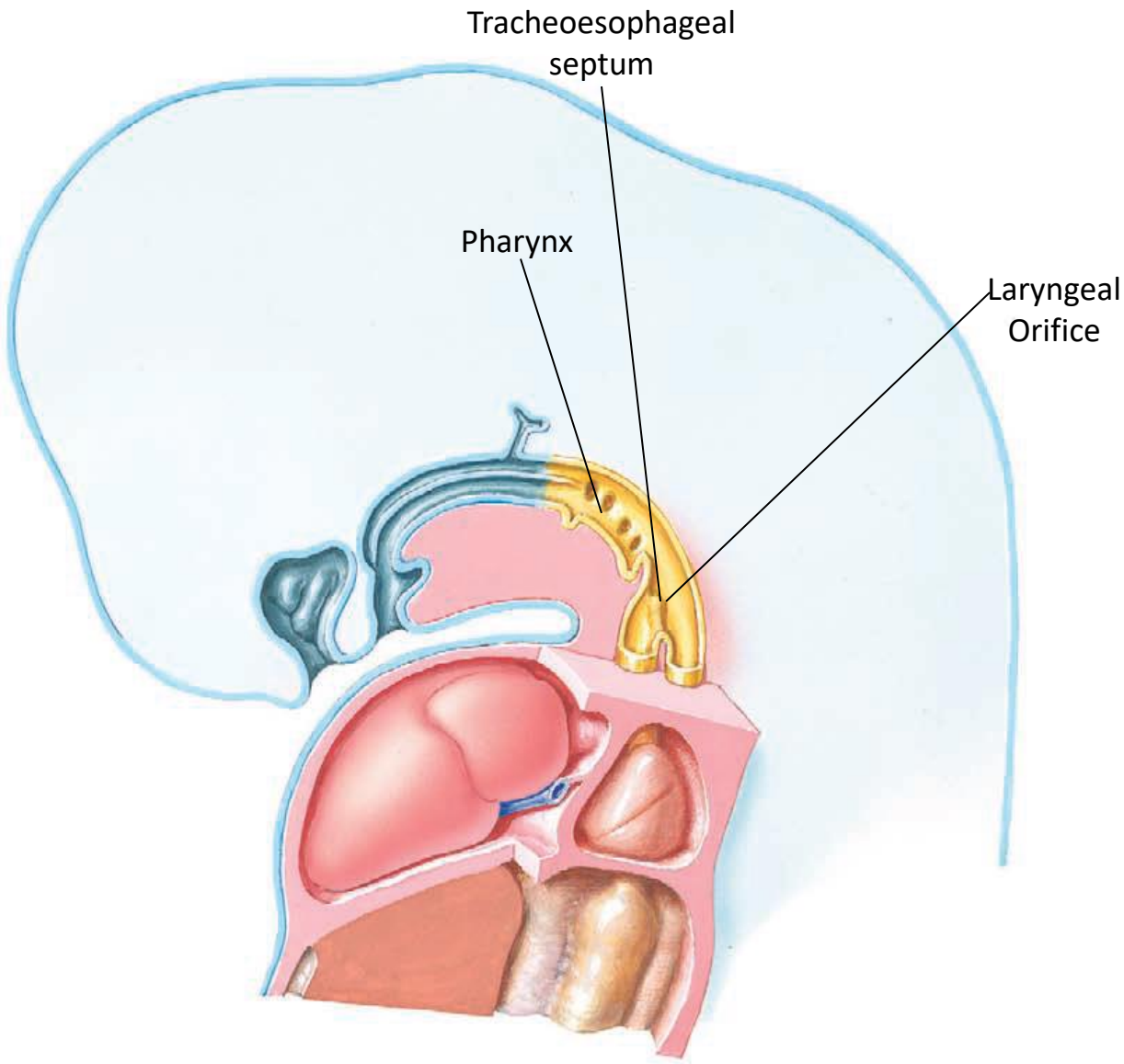


When the respiratory diverticulum expands caudally, two longitudinal ridges, the tracheoesophageal ridges, separate the respiratory diverticulum from the foregut.

Subsequently, when these ridges fuse to form the tracheoesophageal septum, the foregut is divided into a dorsal portion that forms the esophagus, and a ventral portion that forms the trachea and lung buds.

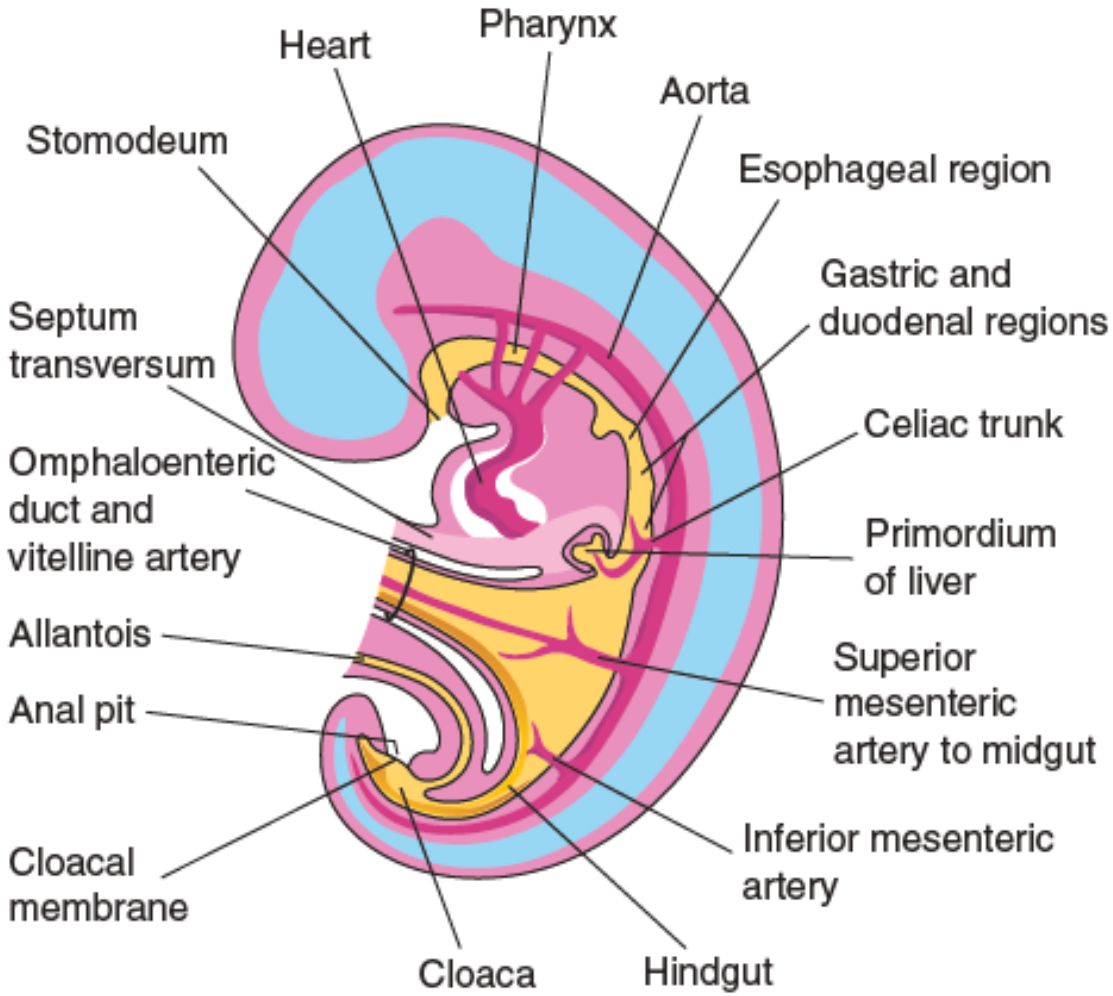


The respiratory primordium maintains its communication with the pharynx through the laryngeal orifice.



The laryngeal orifice must be there to ensue adequate passage of air into the respiratory tract after birth.

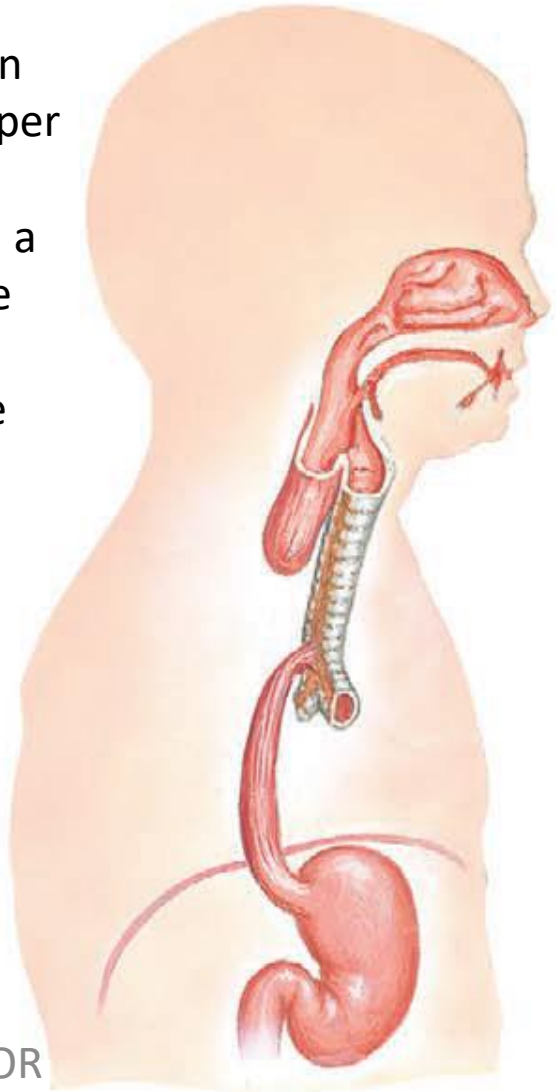
- At first the esophagus is short, but with descent of the heart and lungs it lengthens rapidly.
- The muscular coat, which is formed by surrounding splanchnic mesenchyme, is striated in its upper two-thirds and innervated by the vagus nerve, however, the muscular coat of the esophagus is smooth in the lower third and is innervated by the splanchnic plexus.

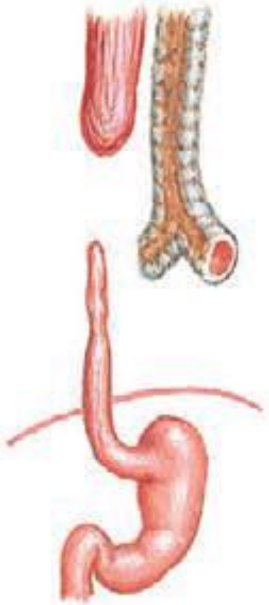


ANOMALIES OF THE TRACHEA AND THE ESOPHAGUS: TRACHEOESOPHAGEAL FISTULAS (TEFs)

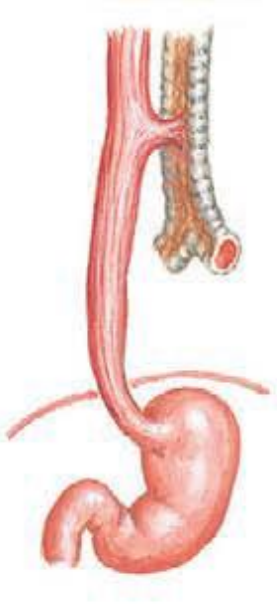
Abnormalities in partitioning of the esophagus and trachea by the tracheoesaphageal septum result in esophageal atresia with or without tracheoesaphageal fistulas.
These defects occur in approximately in 1/3000 births, and 90% result in the upper portion of the esophagus ending in a blind pouch and the lower segment forming a fistula with the trachea.
Predominantly affect male infants.

The most common form of TEF, the upper portion of the esophagus ends in a blind end and the lower portion is connected to the trachea.



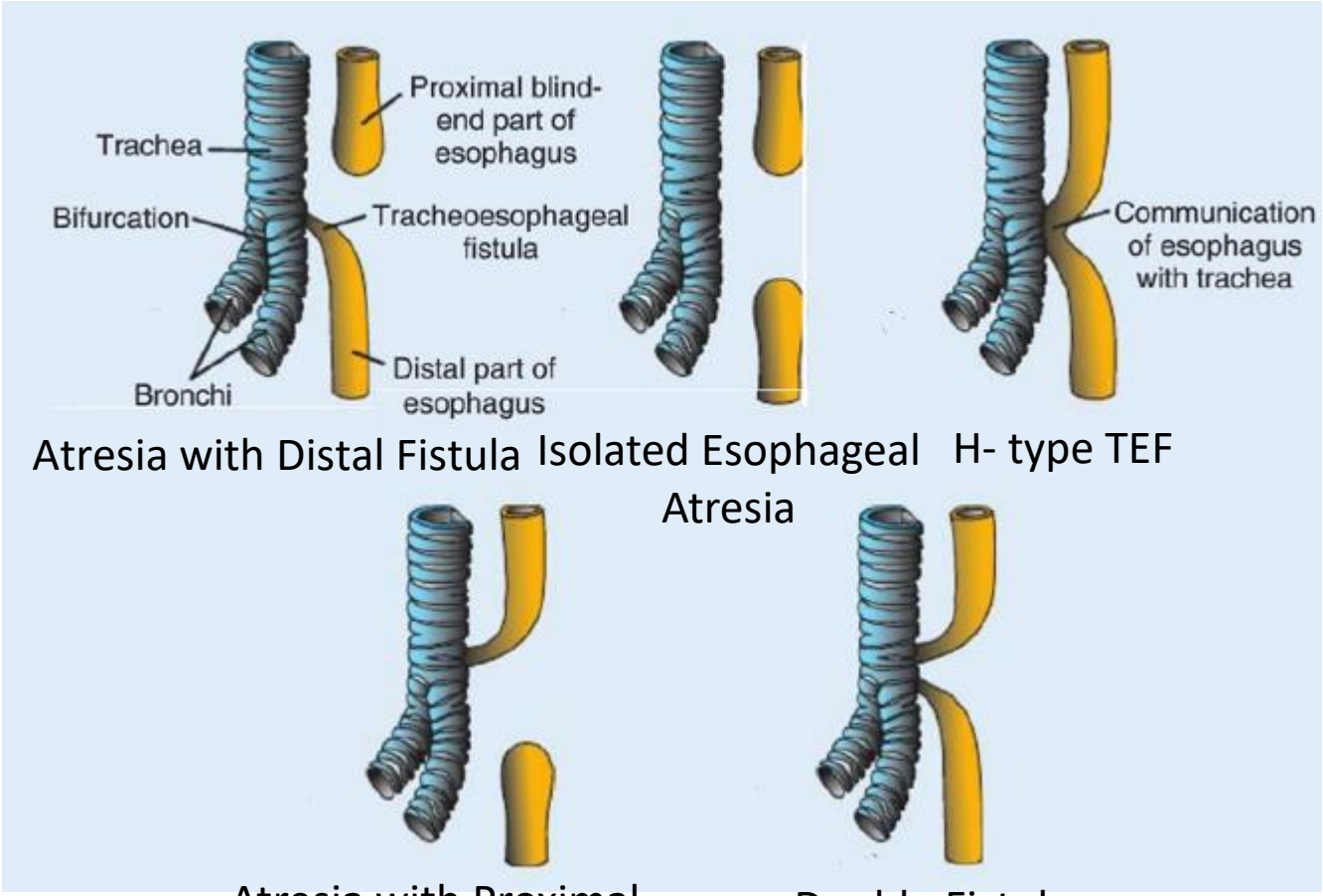


Isolated Esophageal Atresia



H-type Tracheoesophageal Fistula

Isolated esophageal atresia and H-type TEF without esophageal atresia each account for 4% of these defects.



Atresia with Distal Fistula

Isolated Esophageal Atresia

H- type TEF

Atresia with Proximal Fistula

Double Fistula.

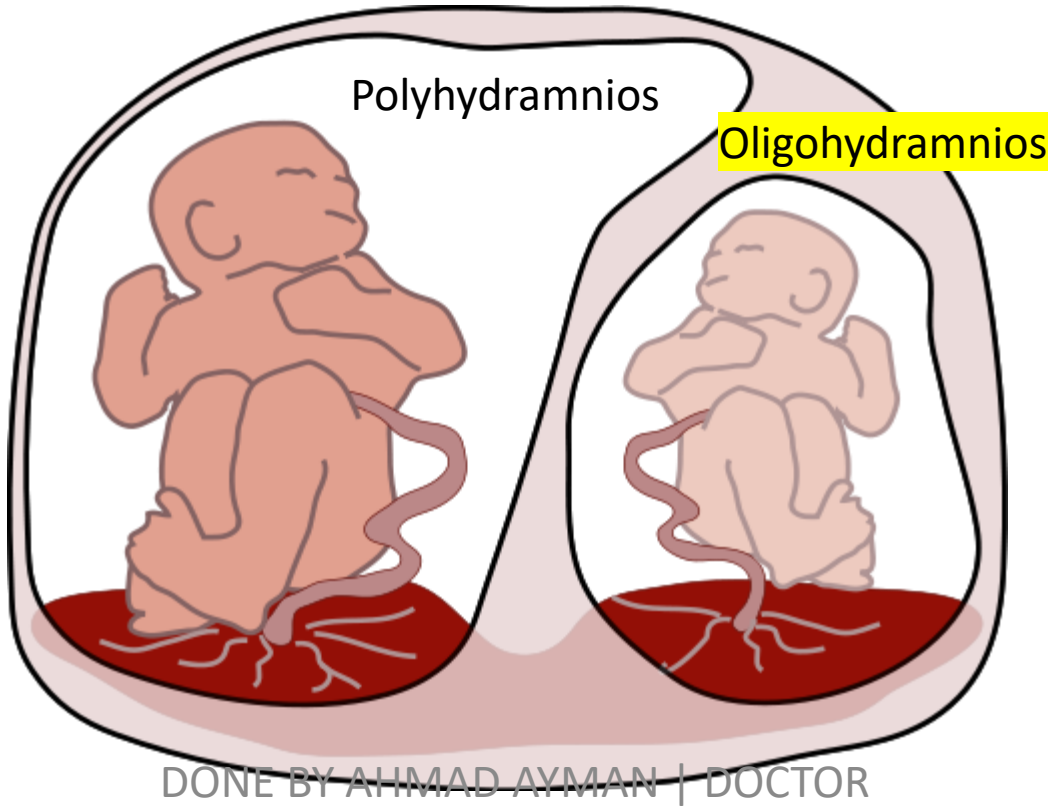
Other variations account only for 1% of these defects.

SIGNS AND SYMPTOMS OF TRACHEOESOPHAGEAL FISTULA

Tracheoesophageal fistula is the most common anomaly in the lower respiratory tract, infants with common type TEF and esophageal atesia cough and choke because of excessive amounts of saliva in the mouth (which cannot pass into the stomach and intestine), so when the infant tries to swallow milk, it rapidly fills the esophageal pouch and is regurgitated.

A complication of some TEFs is polyhydramnios (polyhydramnios means increased amount of amniotic fluid around the fetus, because normally, the embryo swallows the amniotic fluid and urinates in it, if it cannot be swallowed, it will increase), since in some types of TEF amniotic fluid does not pass to the stomach and intestines.

Also, gastric contents and/or amniotic fluid may enter the trachea through a fistula, causing pneumonitis and pneumonia.



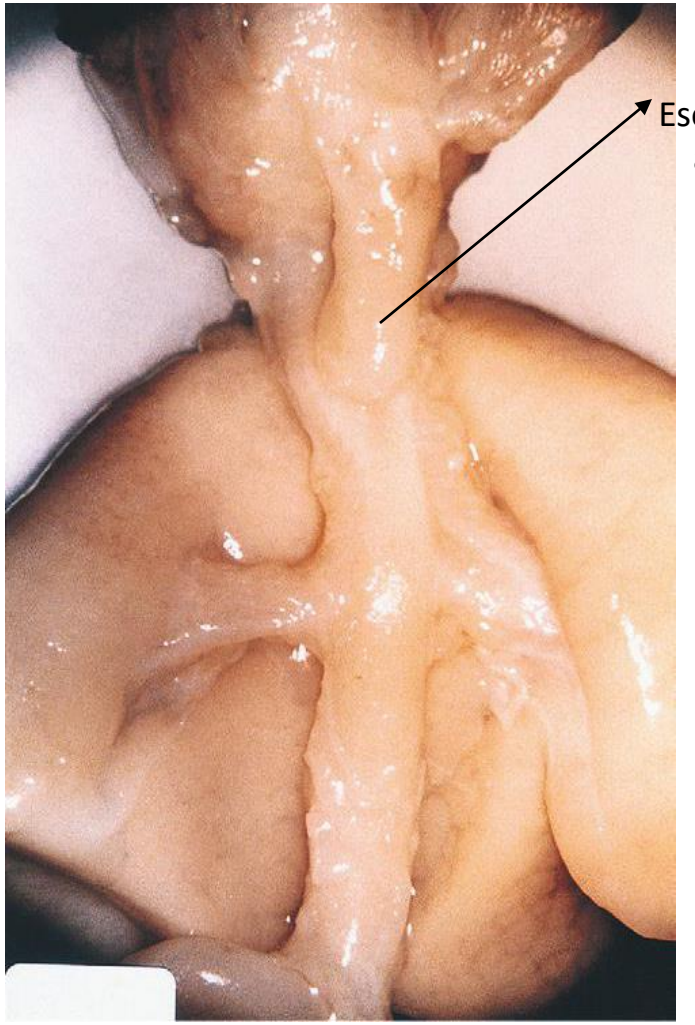
Note: the opposite of polyhdraminos is oligohydramnios where we have a very small amount of amniotic fluid, we'll talk about that later on.

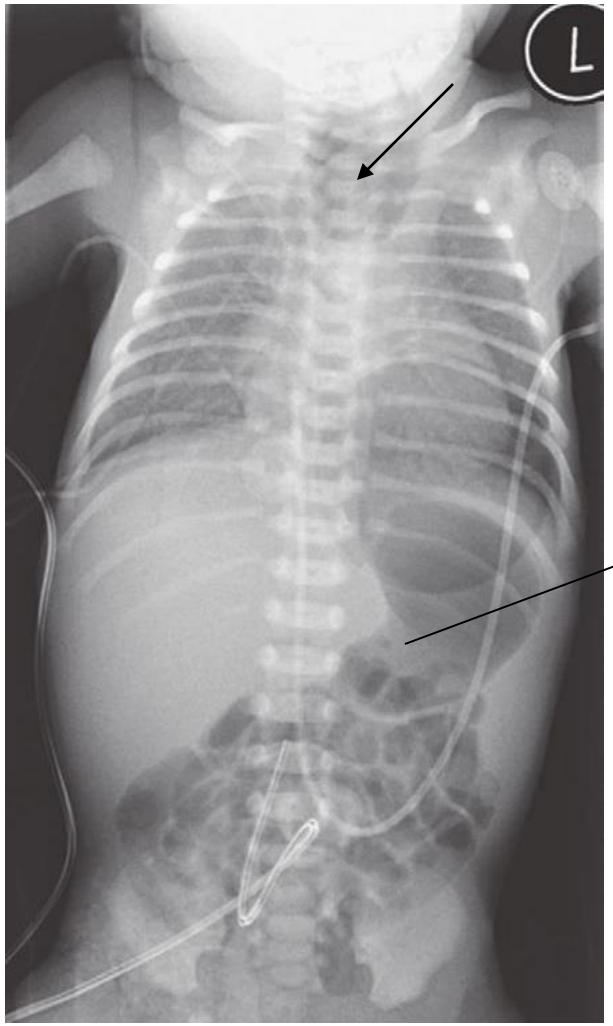
Thracheoesophageal abnormalities are associated with other birth defects, including cardiac abnormalities, which occur in 33% of these cases.

In this regard TEFs are a component of the **VACTERL** association (**V**ertebral anomalies, **A**nal atresia, **C**ardiac defects (like atrial or ventricular septal defects, tetralogy of Fallot, these are found most commonly), **T**racheoesophageal fistula, **E**sophageal atresia, **R**enal anomalies, and **L**imb defects)

VACTERL association is a collection of defects of unknown causation, but occurring more frequently than predicted by chance alone.

Because a TEF might result in air entering the stomach, you might see that the baby's abdomen is getting bigger upon breathing or crying.



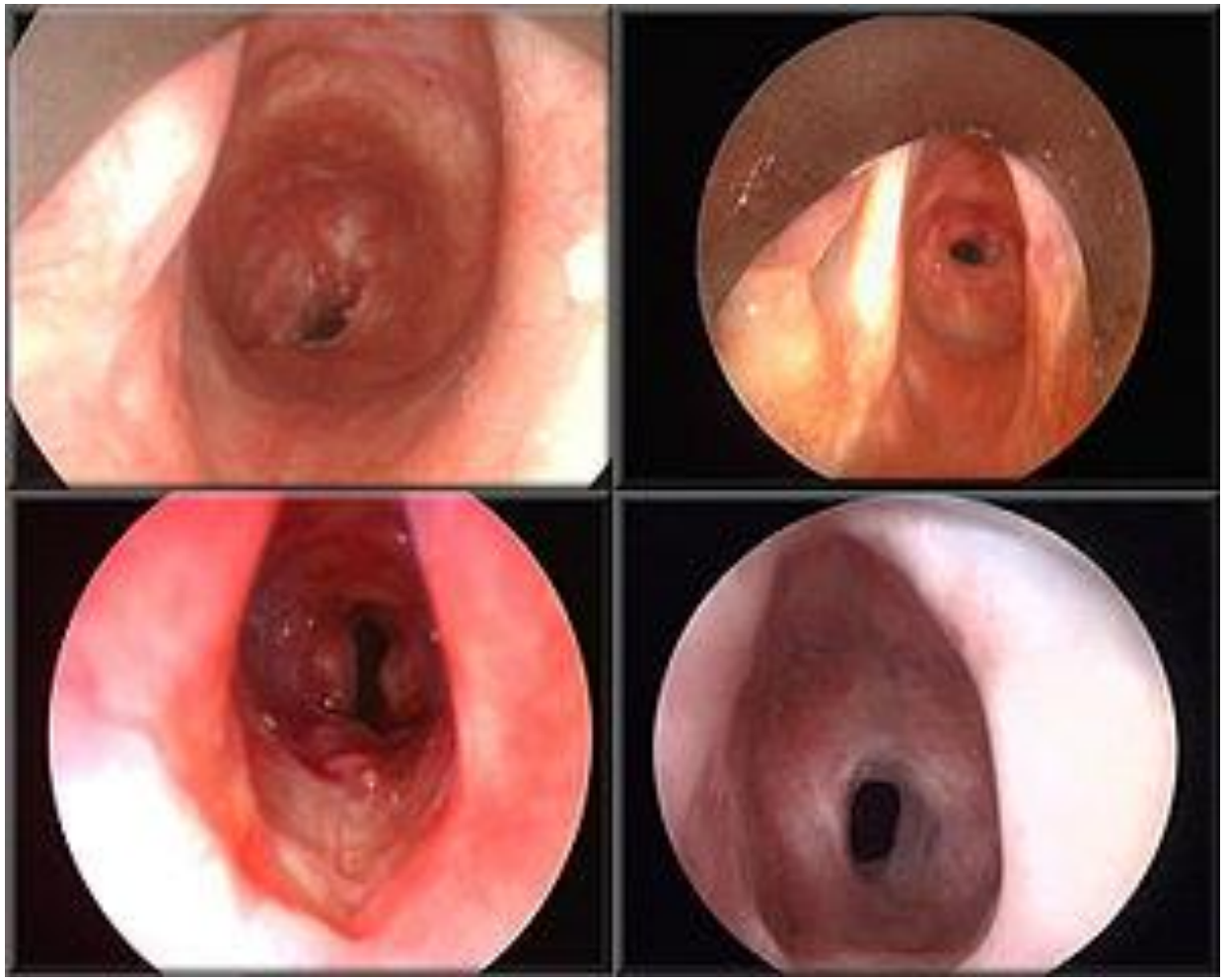


Notice that the stomach and the GI tract of this baby contain a lot of air.

TRACHEAL ATRESIA AND STENOSIS

Tracheal atresia and stenosis are uncommon anomalies and usually associated with one of the verities of TEF

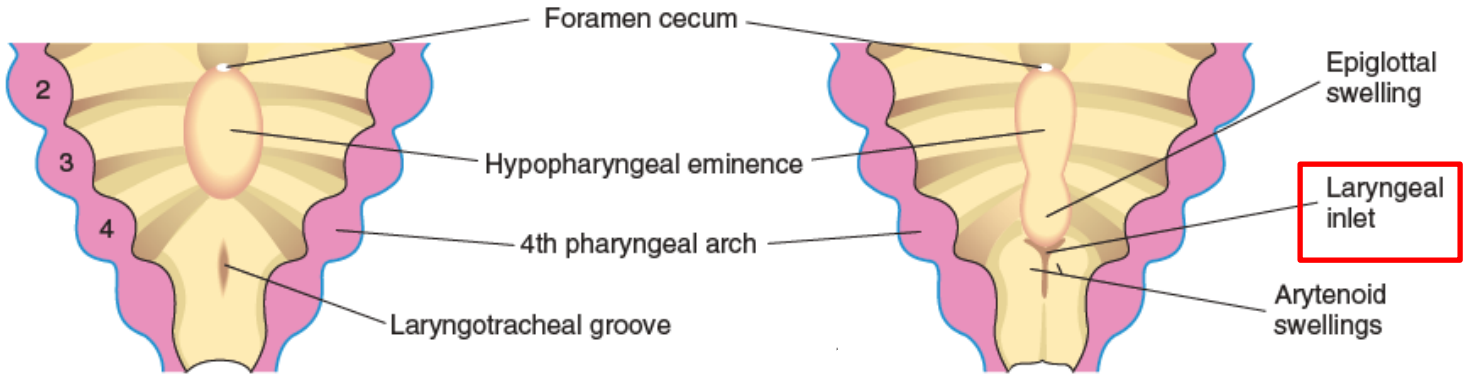
In some case a web tissue may obstructs the airflow (incomplete tracheal atresia).

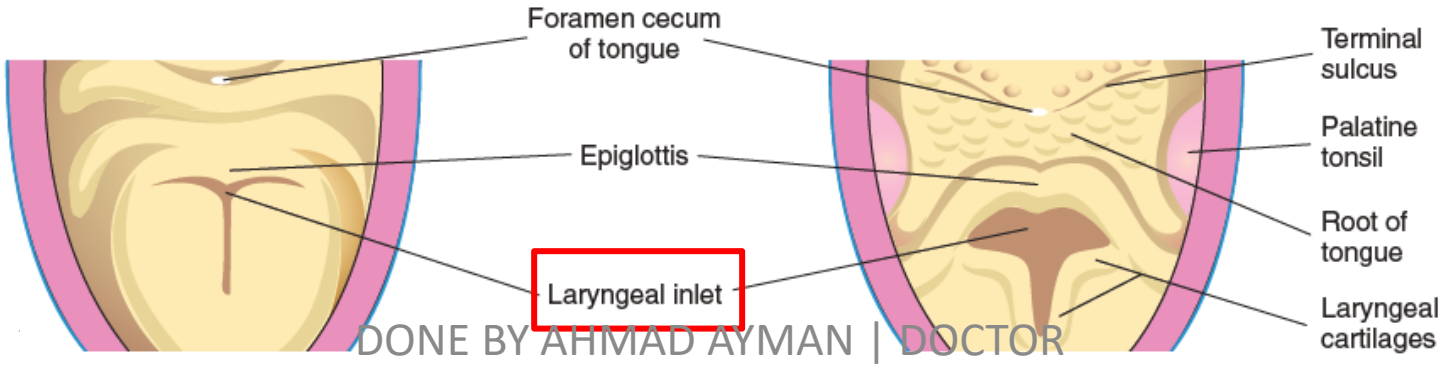


DEVELOPMENT OF THE LARYNX

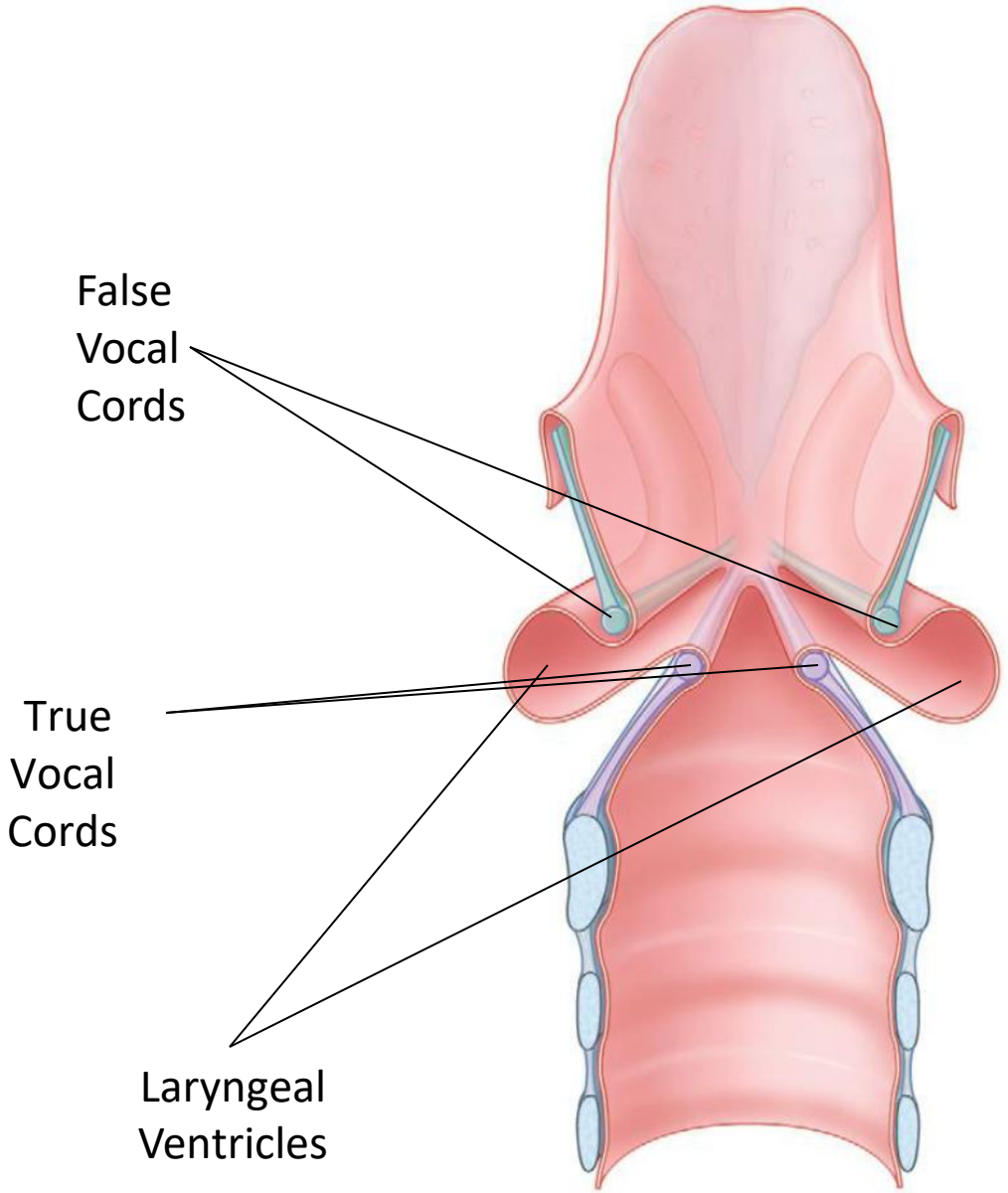
The internal lining of the larynx originates from endoderm, but the cartilages and muscles originate from mesenchyme (mesoderm) of the fourth and sixth pharyngeal arches.

As a result of rapid proliferation of this mesenchyme, the laryngeal orifice changes in appearance froma sagittal slit to a T-shaped opening. Subsequently, when mesenchyme of the two arches transforms into the thyroid, cricoid, and arytenoid cartilages, the characteristic adult shape of the laryngeal orifice can be recognized.

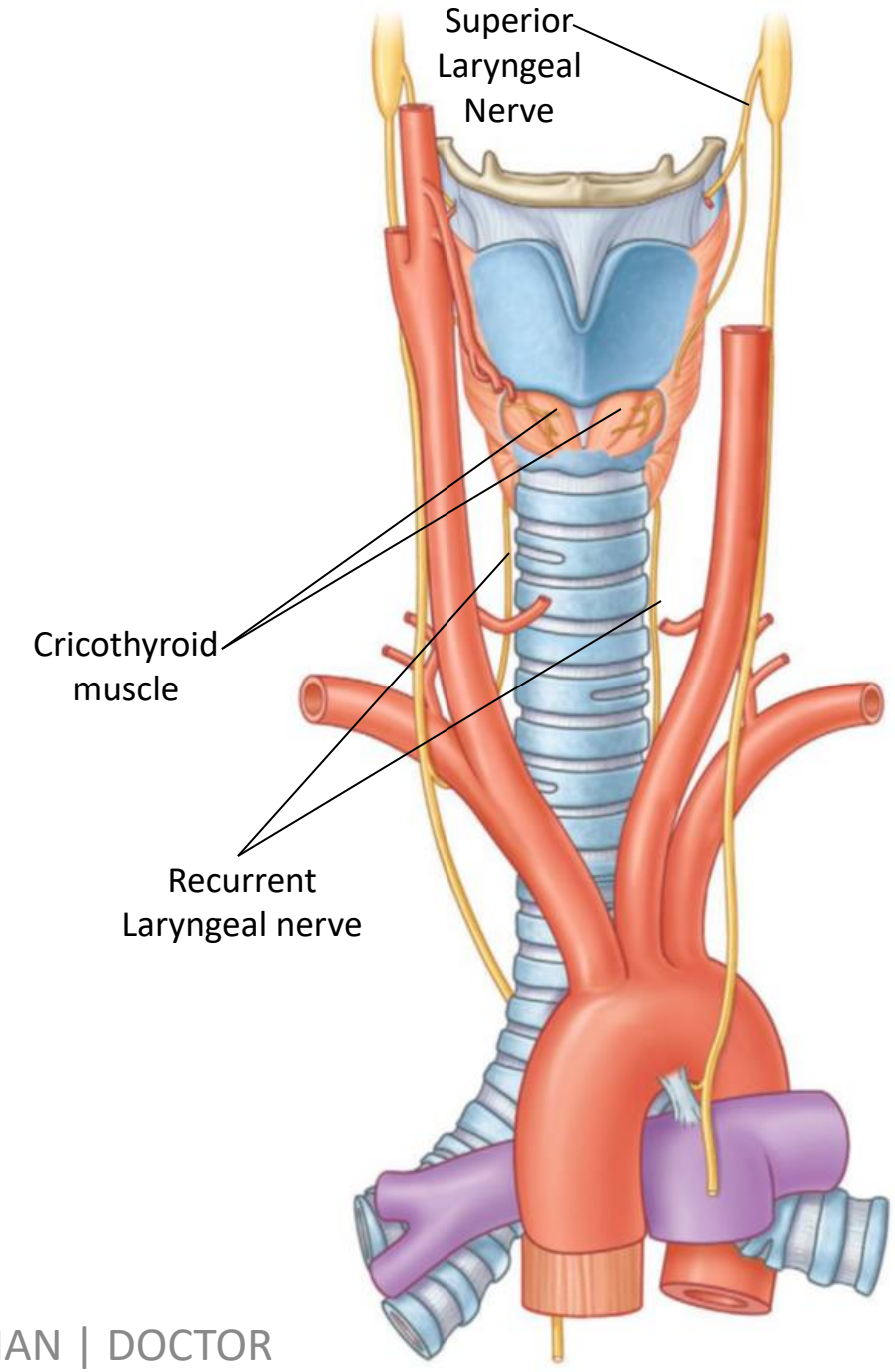




- At about the time that the cartilages are formed, the laryngeal epithelium also proliferates rapidly resulting in a temporary occlusion of the lumen.
  - Subsequently, vacuolization and recanalization produce a pair of lateral recesses, the laryngeal ventricles.
- These recesses are bounded by folds of tissue that differentiate into the false and true vocal cords.

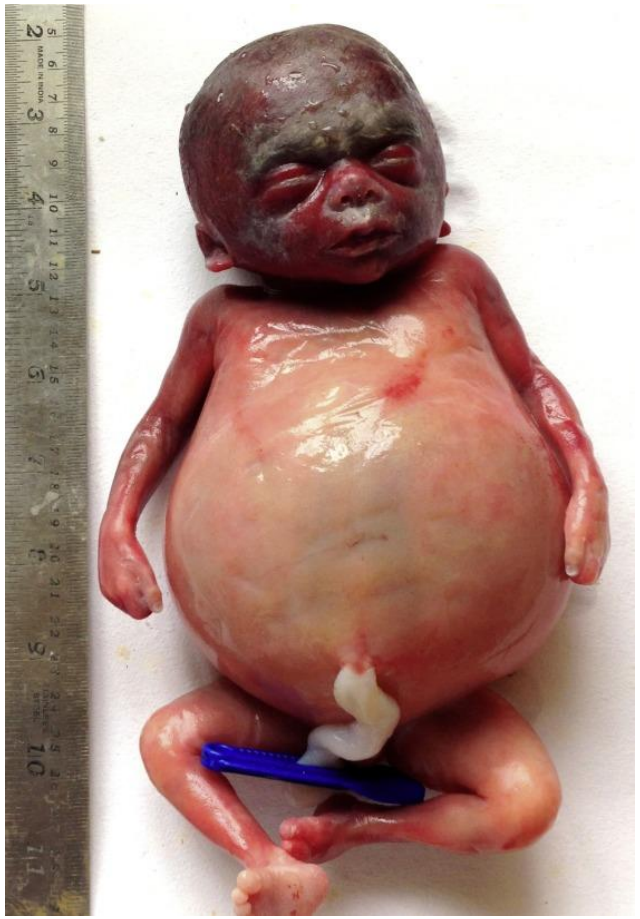


- Since musculature of the larynx is derived from mesenchyme of the fourth and sixth pharyngeal arches, all laryngeal muscles are innervated by branches of the tenth cranial nerve, the vagus nerve
- The superior laryngeal nerve innervates derivatives of the fourth pharyngeal arch including cricothyroid muscle, and the recurrent laryngeal nerve innervates derivatives of the sixth pharyngeal arch including all other laryngeal muscles.



ANOMALIES OF THE LARYNX: LARYNGEAL ATRESIA

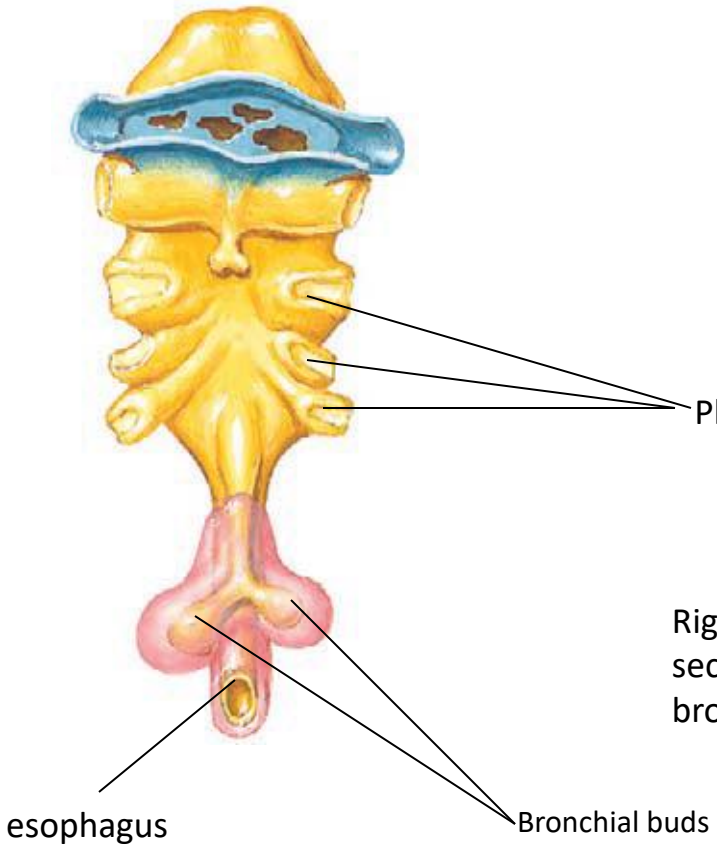
- Laryngeal atresia is a rare anomaly and cause obstruction of the upper fetal airway
- Also known as congenital high airway obstruction syndrome (CHAOS)
- Distal to the atresia or stenosis the lung are enlarged and capable of producing echoes (echogenic)
- Also the diaphragm is flattened or inverted and fetal ascites and hydrops (accumulation of serous fluid) is present
- Prenatal ultra-sonograpghy permits diagnosis.

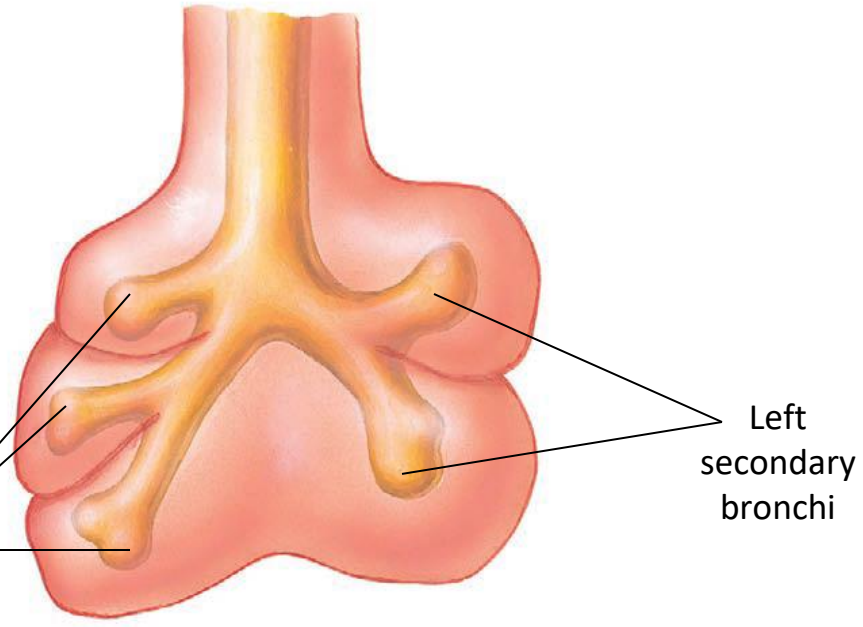


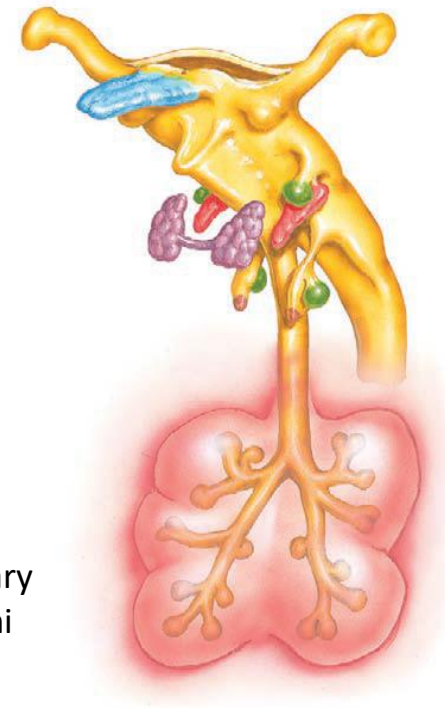
Notice the enlarged abdomen due to ascites.

LUNGS, TRACHEA AND BRONCHIAL TREE DEVELOPMENT

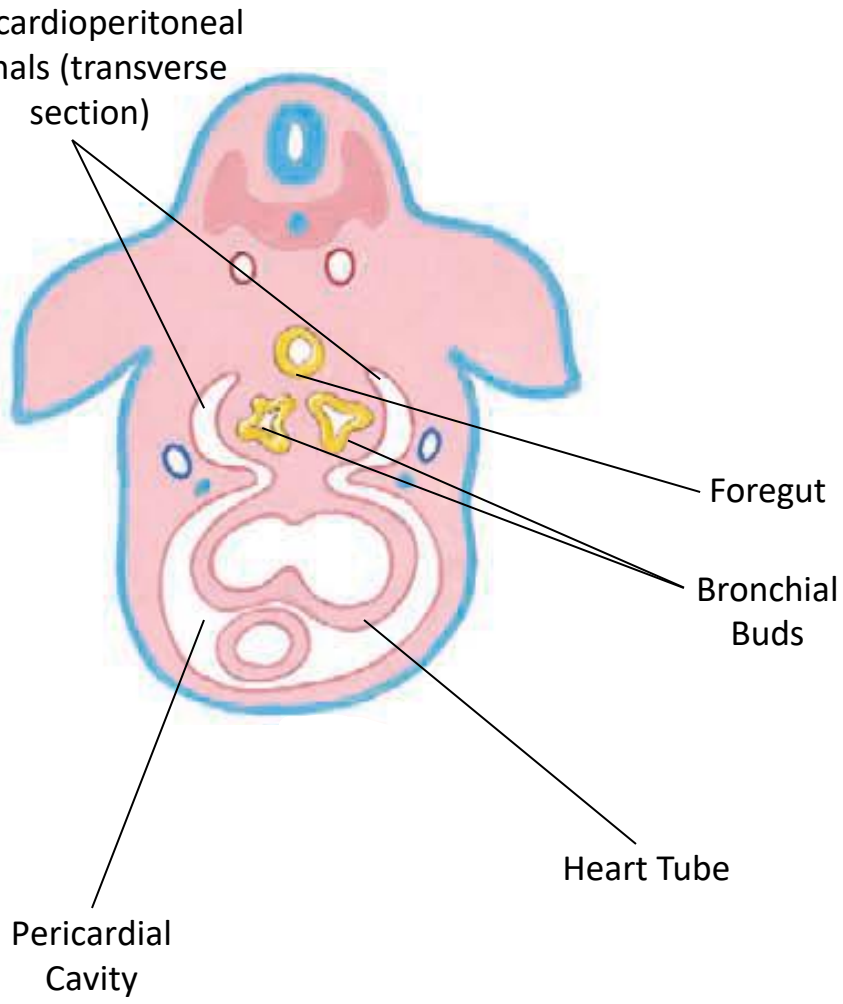
- During its separation from the foregut, the lung bud forms the trachea and two lateral outpocketings, the bronchial buds that occur at the level of T4
  - At the beginning of the fifth week, each of these buds enlarges to form right and left main bronchi
- The right bronchial bud then forms three secondary bronchi, and the left bronchial buds forms two secondary (lobar) bronchi, thus foreshadowing the three lobes on the right side and two on the left side, then, the tertiary (segmental) bronchi are formed, then the bronchioles and so on.

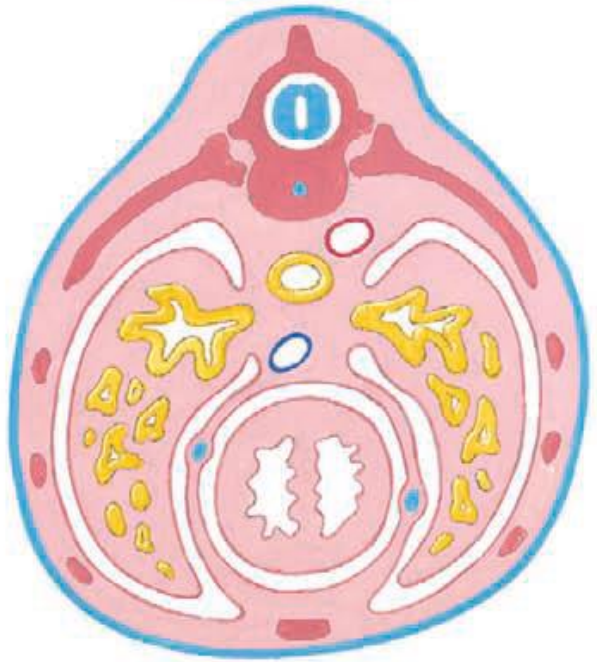






- With subsequent growth in caudal and lateral directions, the lung buds expand into the body cavity.
- The spaces for the lungs, the pericardioperitoneal canals, are narrow, they lie on each side of the foregut.

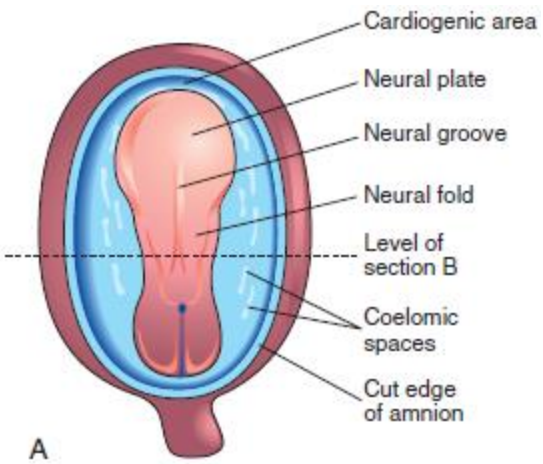


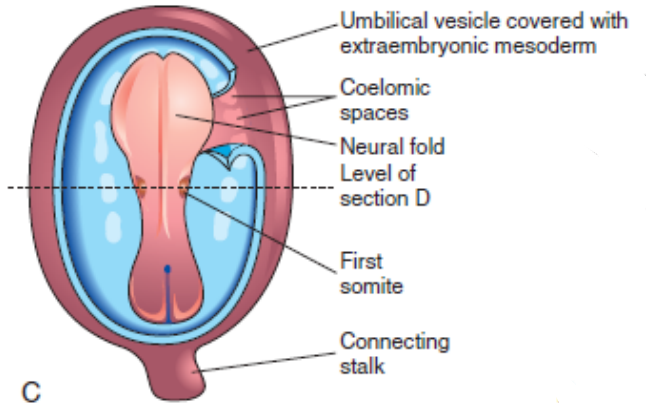


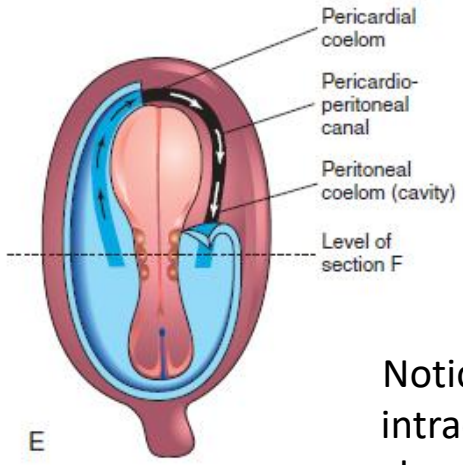
Note: these are transverse sections

Note: to understand the next slides, I’ll explain in the few slides the development of the body cavity, until the next notification, this is not an exam material.

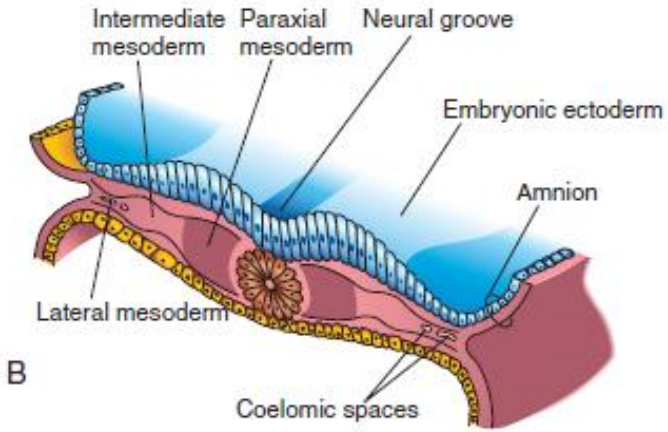
Till the third week of development, the embryo is just a trilaminar disc, it is a disc literally, it has no cavities within, after that, a small cavity called the intraembryonic coelom appears in this trilaminar disc, it appears within the middle layer that is the mesoderm, separating it into somatic mesoderm and splanchnic mesoderm.

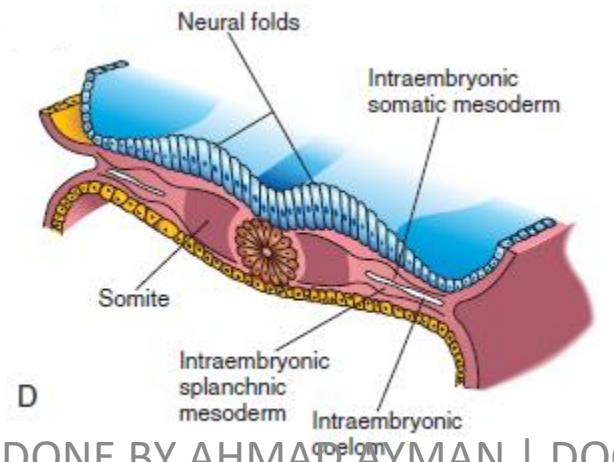


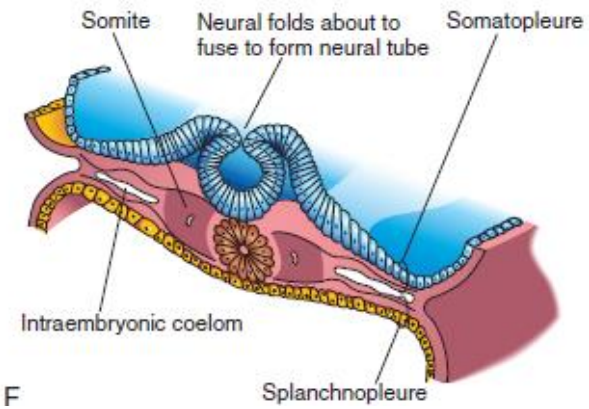




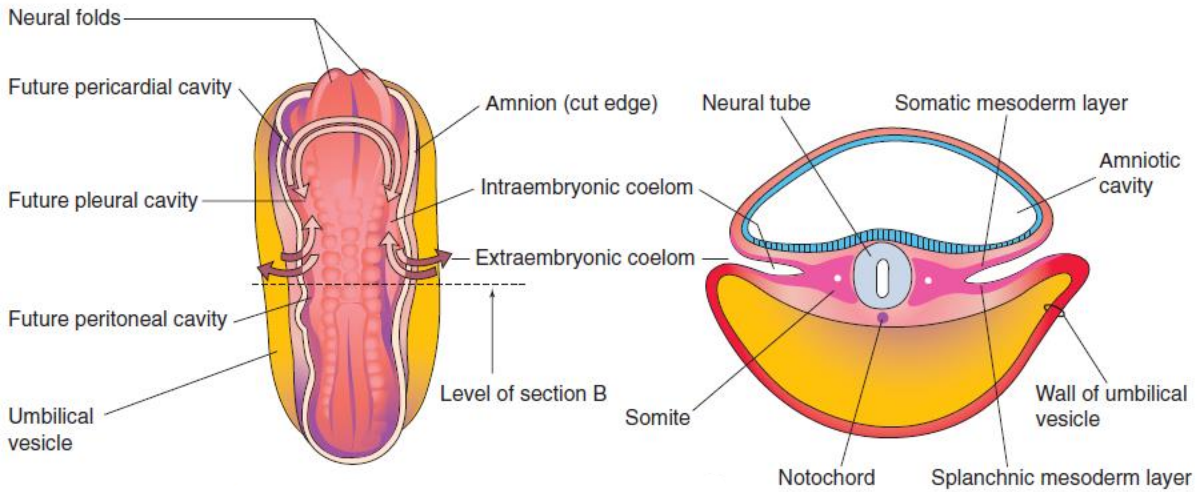
Notice that the intraembryonic coelom is U-shaped.

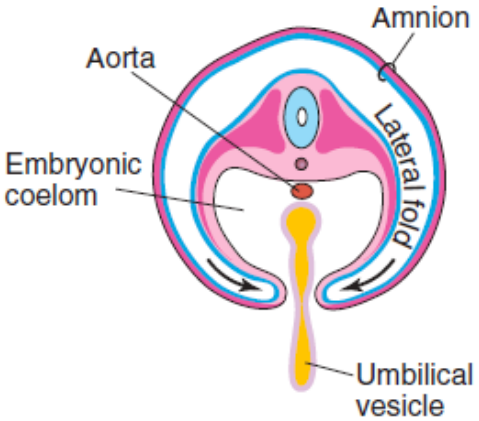


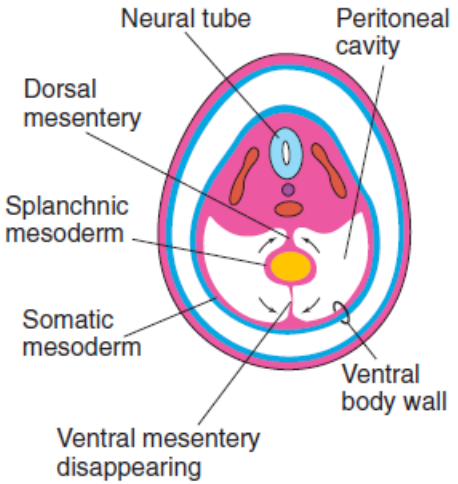


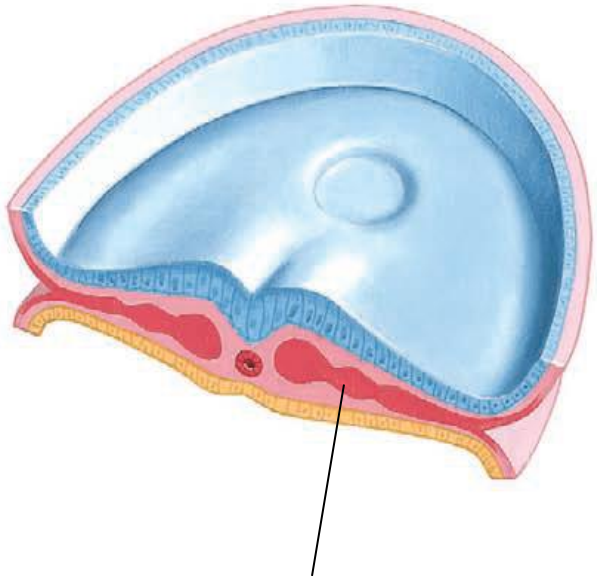


As you can see above, the intra embryonic coelom is U shaped, and it is divided into pericardial cavity (the bottom of the U), peritoneal cavities (the tips of the U), and the pericardioperitoneal canals (what links the pericardial cavity to the peritoneal cavity), at first, these divisions are continuous with each other, what happens then that the intraembryonic coelom enlarges, and it establishes a connection with the extraembryonic coelom (the cavity around the embryo, then as the embryo folds, the arms of the U unite, and the connection with the extraembryonic coelom is lost.

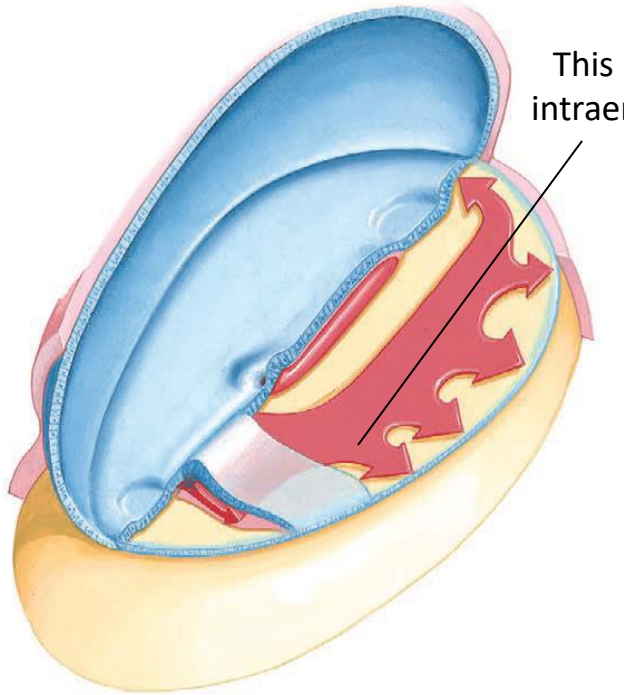




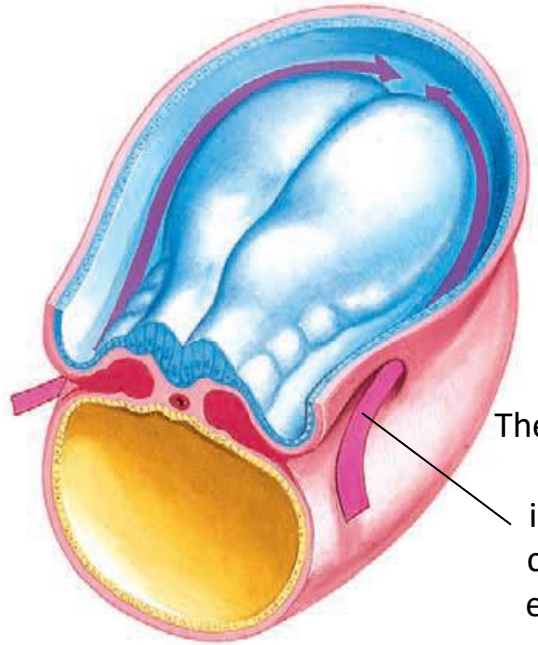




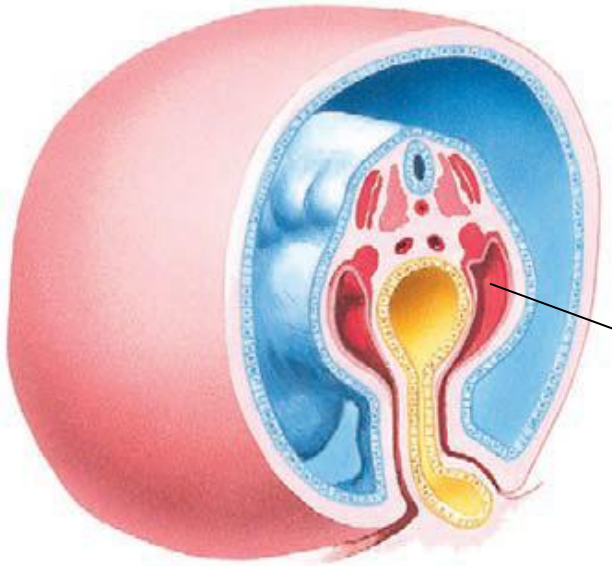
Mesoderm



This red arrow is the intraembryonic coelom

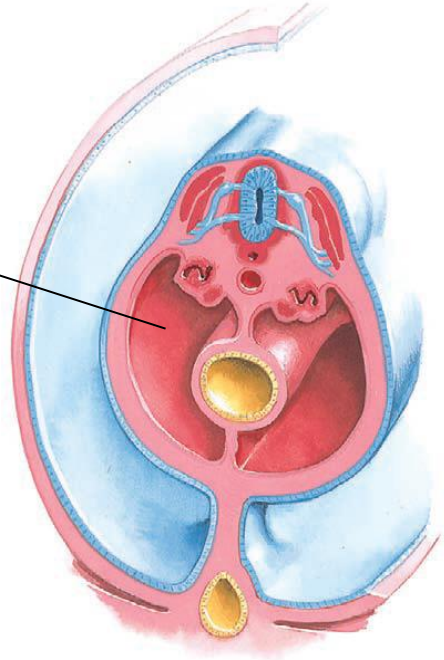


The communication between the intraembryonic coelom and the extraembryonic coelom.

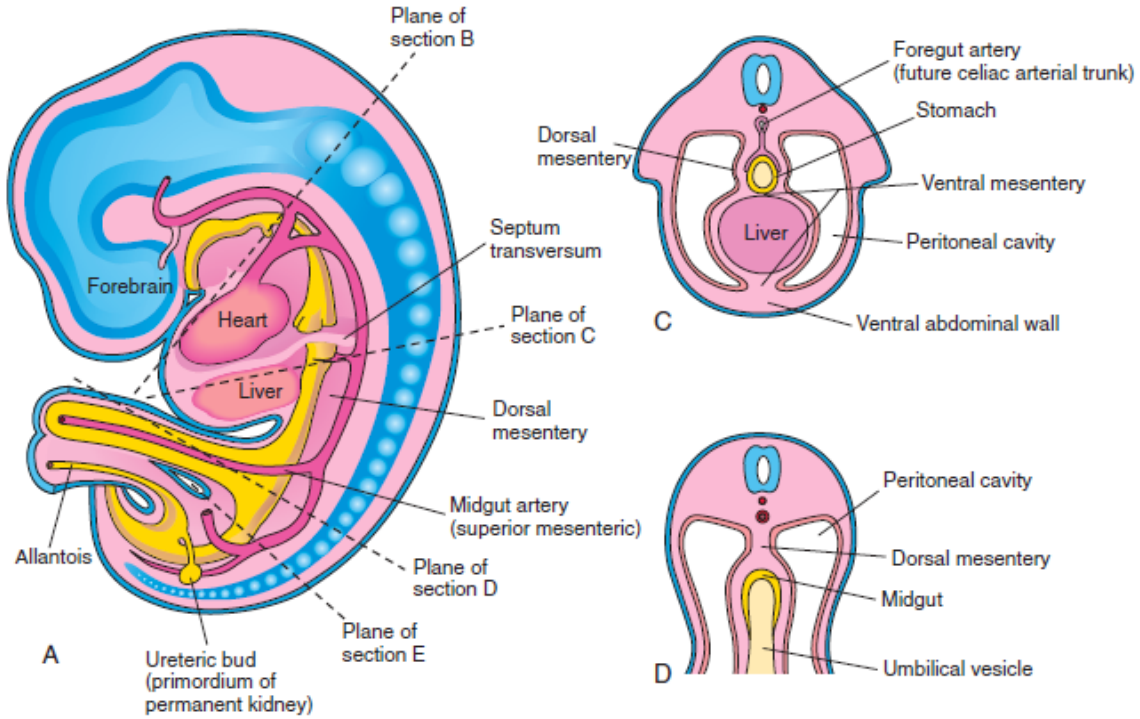


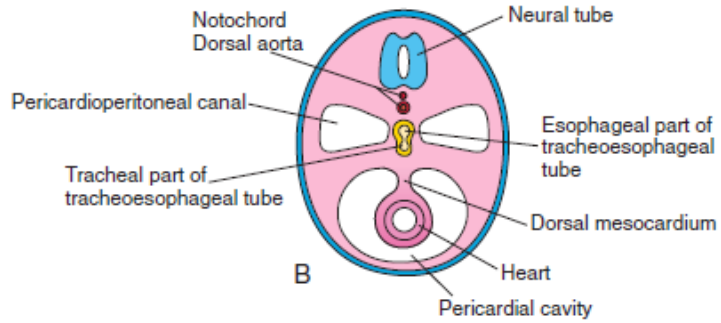
The intraembryonic coelom upon folding

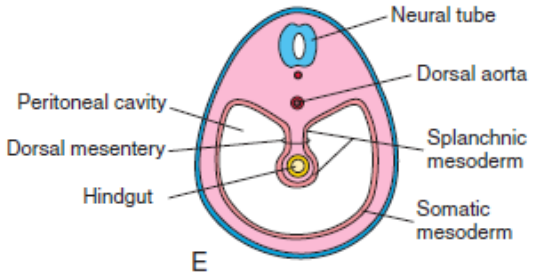
Final shape of the intraembryonic coelom



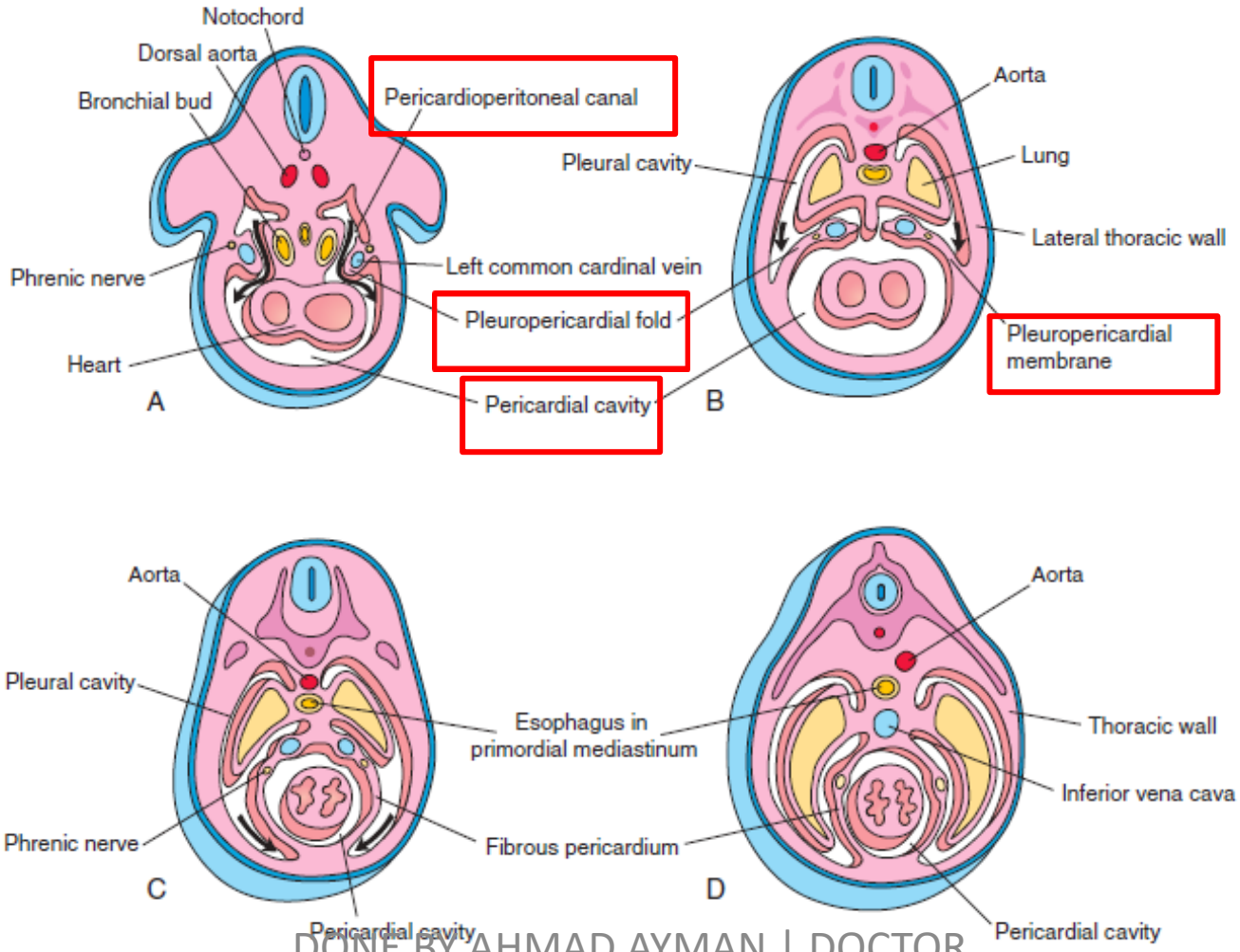
The shape of the intraembryonic coelom at different planes, note that in addition to lateral folding, cranial to caudal folding also occurs so what is cranial becomes anterior, therefore, you can see the pericardial cavity and the pericadioperitoneal canal in the same plane in figure B







Finally, folds called the pleuropericardial folds grow and seal the pericardial cavity from the peicardioperitoneal canals, moreover, folds called the pleuroperitoneal folds seal the pericadioperitoneal canals from the peritoneal cavities, so that we have now three distinct cavities, the pericardial cavity which houses the heart, two pleural cavities (pericardioperitoneal canals) which houses the lungs, and one peritoneal cavity which houses abdominal organs.

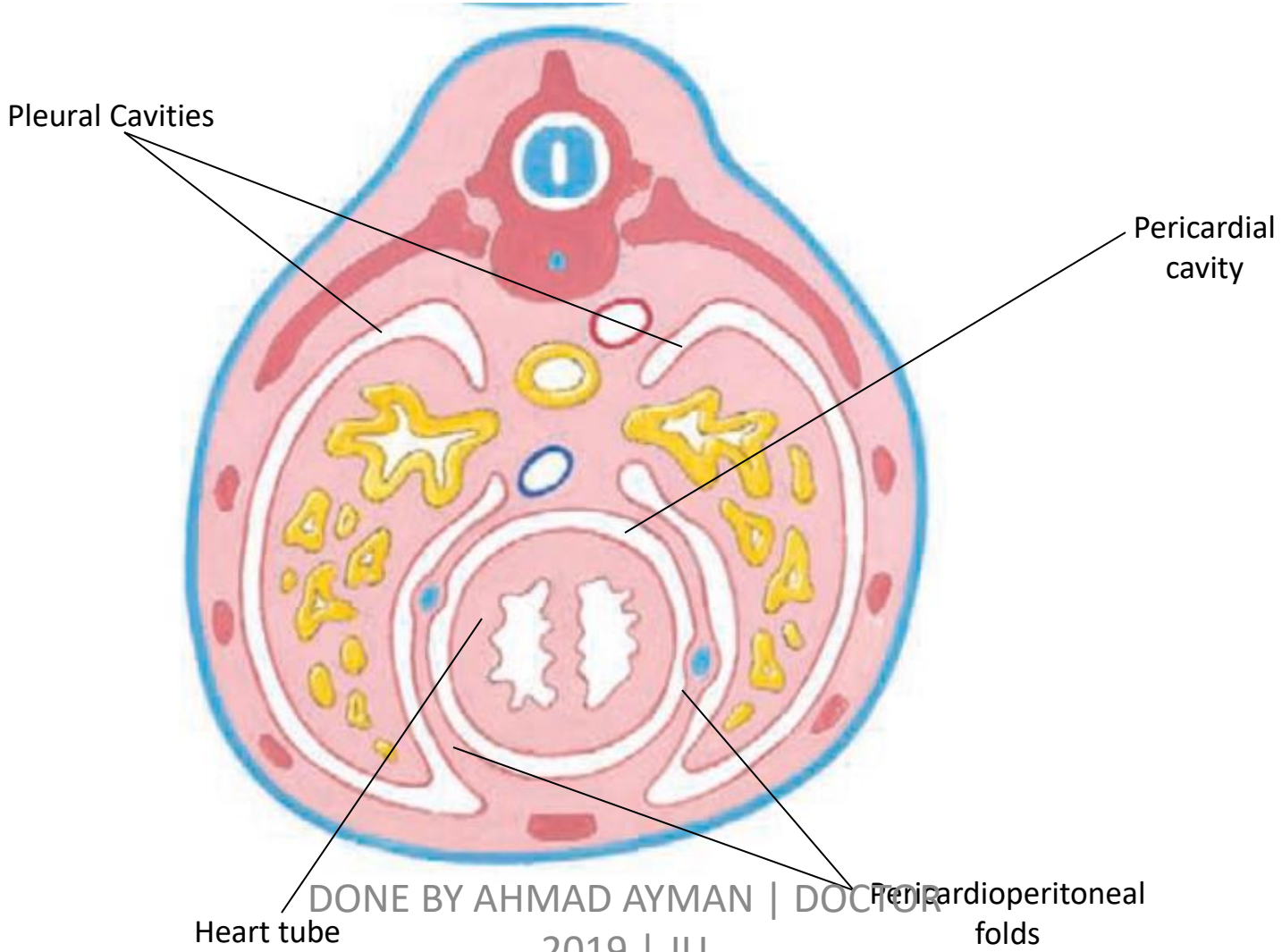


Now we're done 🙃

Please check out this video: https://youtu.be/_sS9JesO_ZA

DEVELOPMENT OF THE PLEURA

The pleuroperitoneal and pleuropericardial folds separate the pericardioperitoneal canals from the peritoneal and pericardial cavities, and the remaining spaces (the pericardioperitoneal canals) form the primitive pleural cavities.

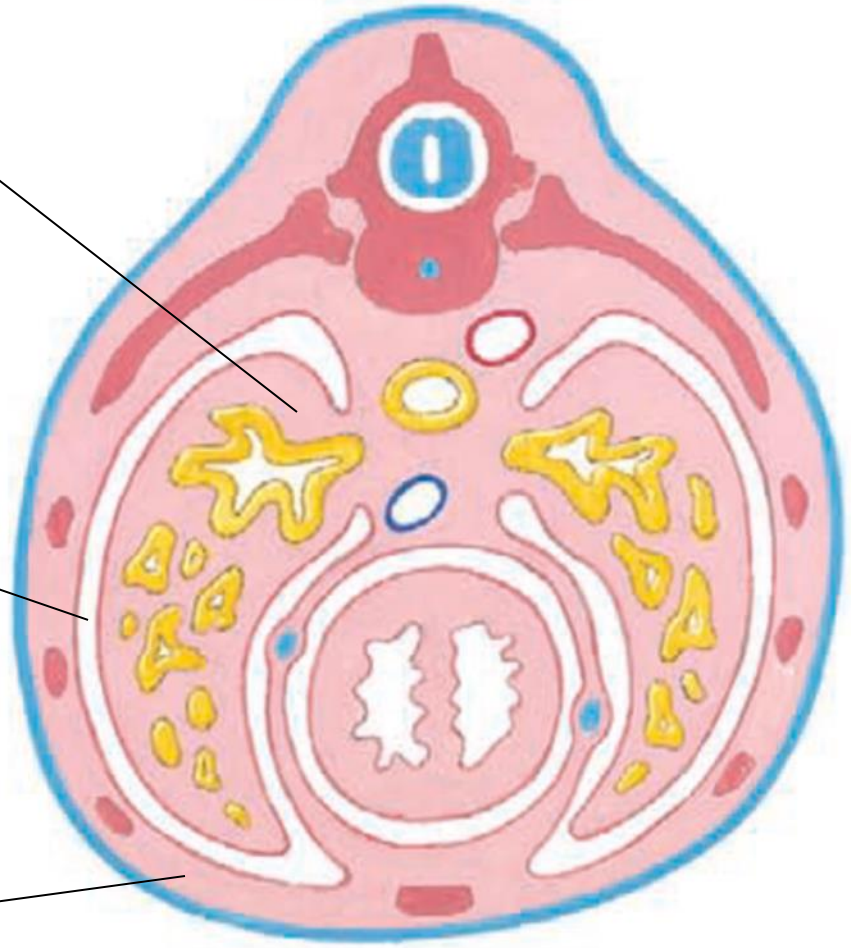


The splanchnic mesoderm layer, which covers the outside of the lung, develops into the visceral pleura.
The somatic mesoderm layer, covering the body wall from the inside, becomes the parietal pleura.
The space between the parietal and visceral pleura is the pleural cavity.

The pink color surrounding the yellow lung is the splanchnic mesoderm

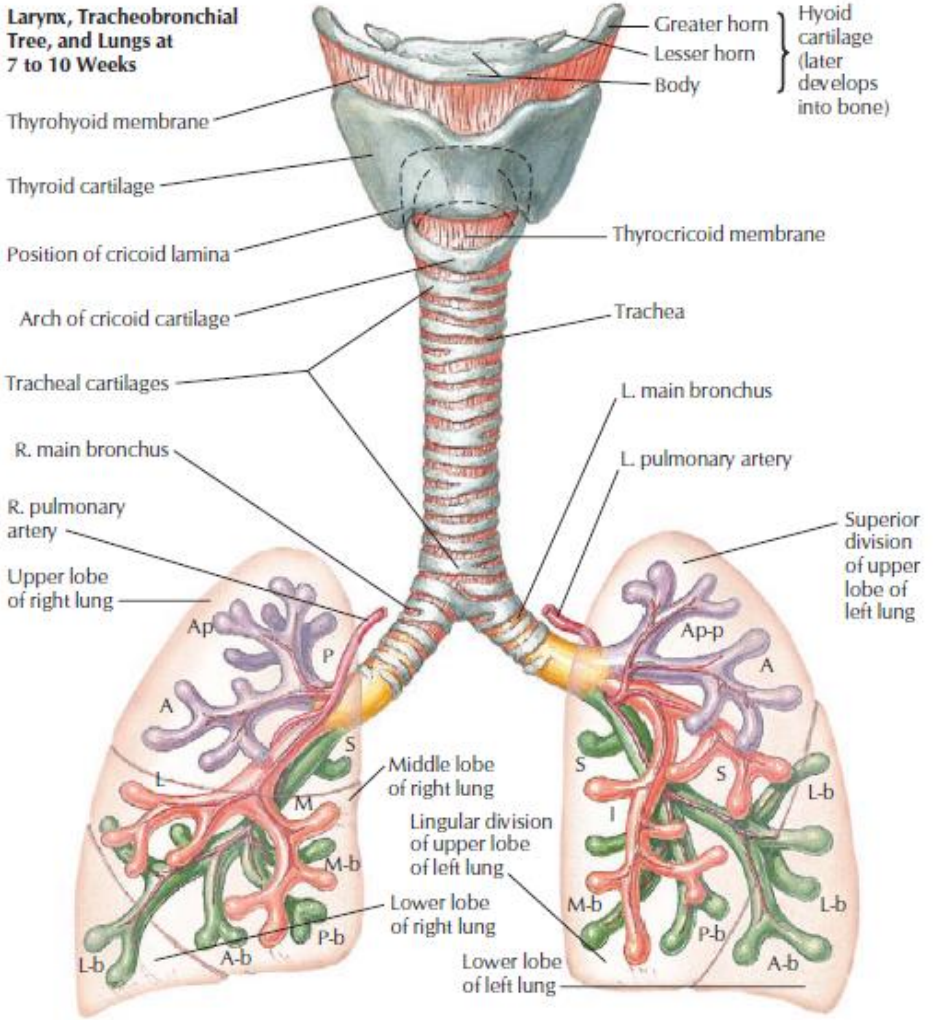
Pleural Cavity

The pink color lining the blue body wall is the somatic mesoderm



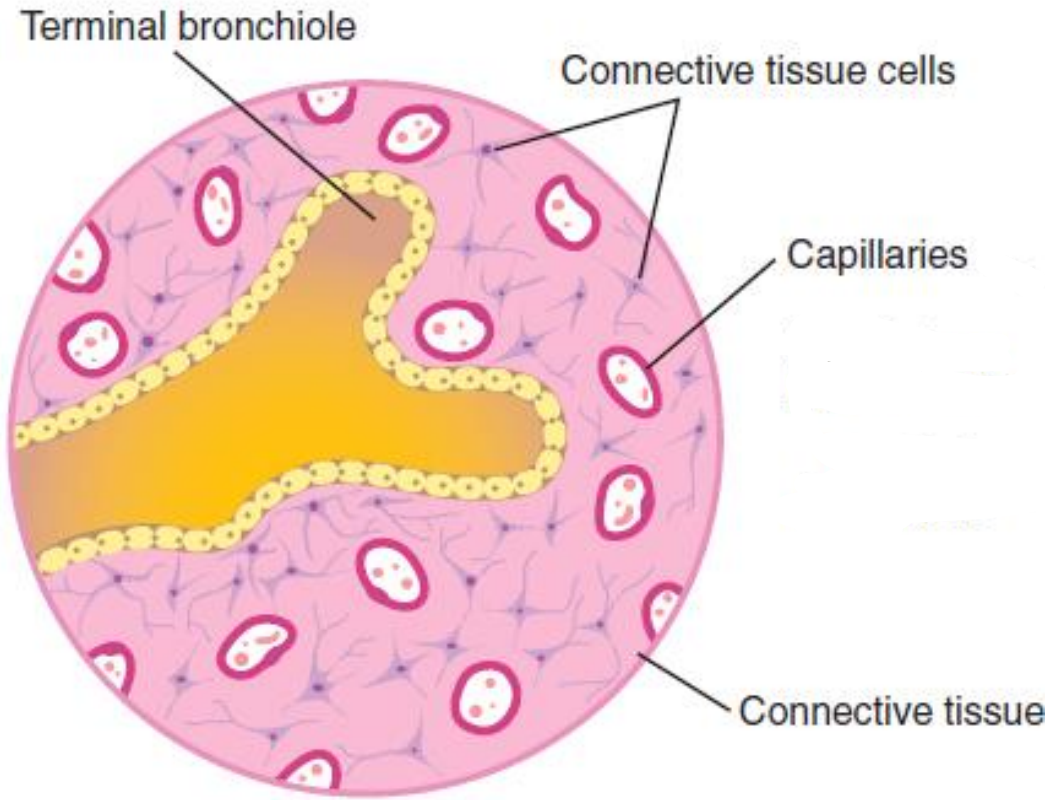
DEVELOPMENT OF LUNG SEGMENTS

- During further development, secondary bronchi divide repeatedly in a dichotomous fashion, forming ten tertiary (segmental) bronchi in the right lung and eight in the left lung, creating the bronchopulmonary segments of the adult lung.
- By the end of the sixth month, approximately 17 generations of subdivisions of the bronchial tree have formed.
- Before the bronchial tree reaches its final shape, however, an additional six divisions form during postnatal life.
- Branching is regulated by epithelial-mesenchymal interactions between the endoderm of the lung buds and splanchnic mesoderm that surrounds them
- Signals for branching, which emit from the mesoderm, involve members of the fibroblast growth factor (FGF) family.
- While all of these new subdivisions are occurring and the bronchial tree is developing, the lungs assume a more caudal position, so that by the time of birth the bifurcation of the trachea is opposite the fourth thoracic vertebra.



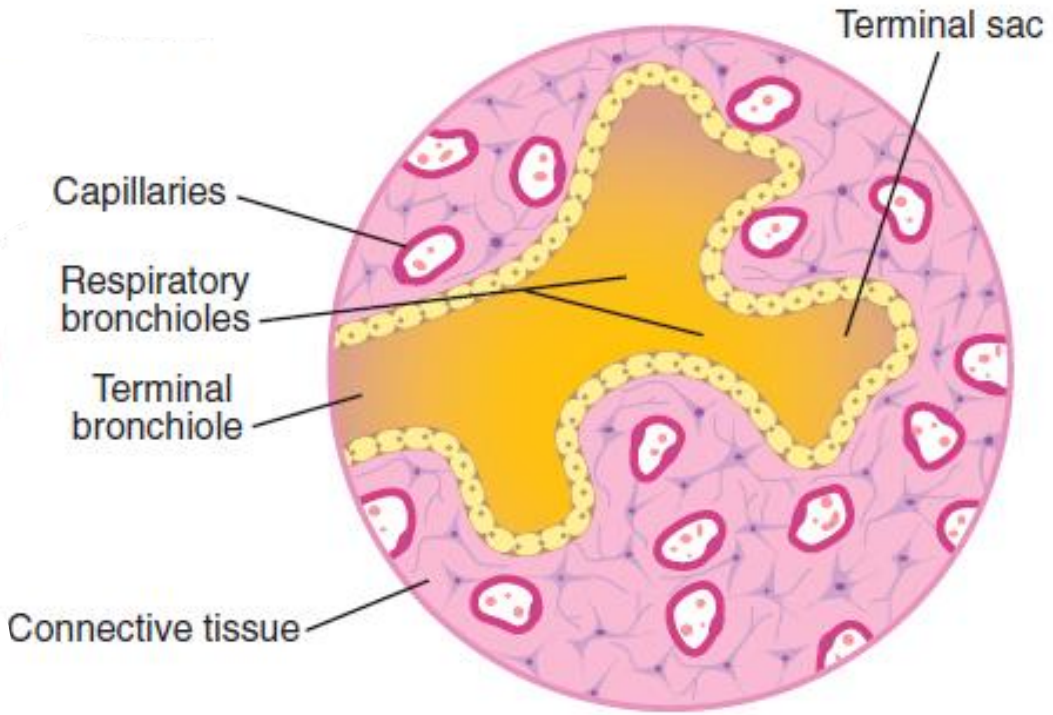
MATURATION OF THE LUNGS

In-utero maturation of the lung occurs on four stages, the first stage is referred to as the psuedoglandular stage period, then we have the canalicular period, terminal sac period and the alveolar period, we are concerned in the changes that occur in each developmental period, the pseudoglandular period lasts between the 5th and the 16th week of gestation, in this period, branching of the bronchial tree occurs, this period extends until the terminal bronchioles (the 16th generation of the bronchial tree) are formed, but there is no respiratory bronchioles or alveoli, so if you take a biopsy from the lung at this stage, you'll see that it is similar histologically to glands (e.g. salivary glands), that's why it is called the pseudogranular period.



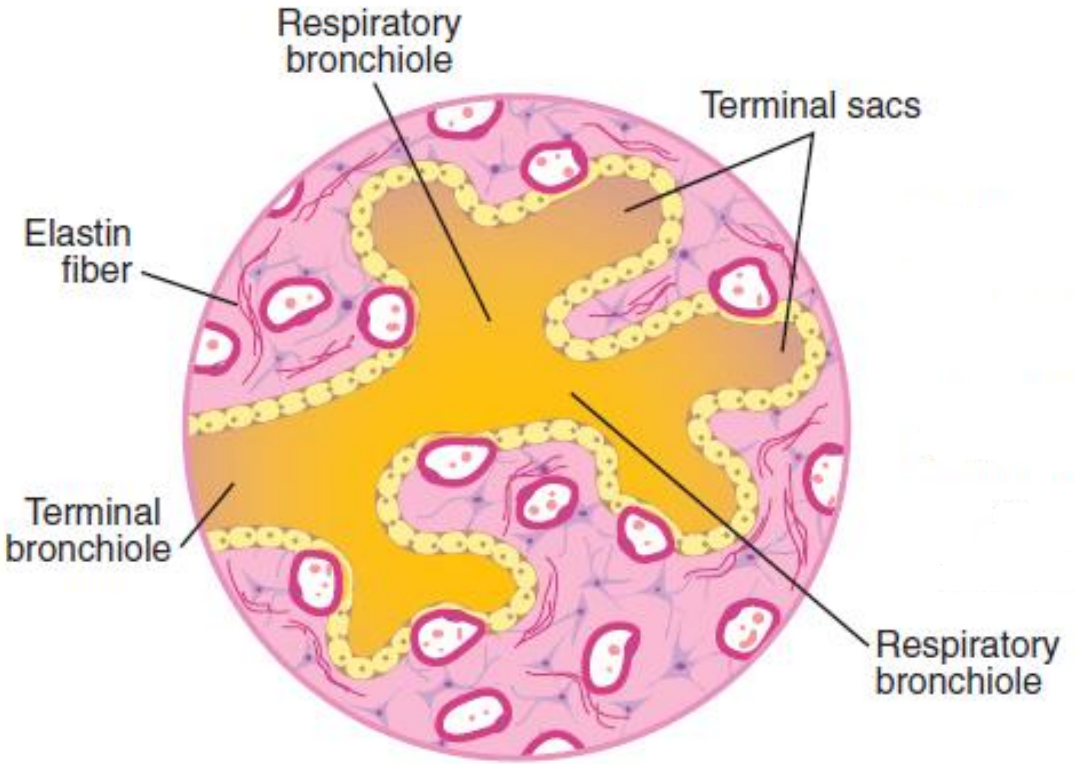
A lung in the pseudogranular period.

During the canalicular period of lung maturation, which lasts during the 16th-26th weeks of gestation, in this period, the respiratory bronchioles and the alveolar ducts are formed by branching of the terminal bronchioles, however, the respiratory membrane (the connection between the capillaries and the alveoli) is not yet established, because the capillaries are not yet adherent to the alveoli.



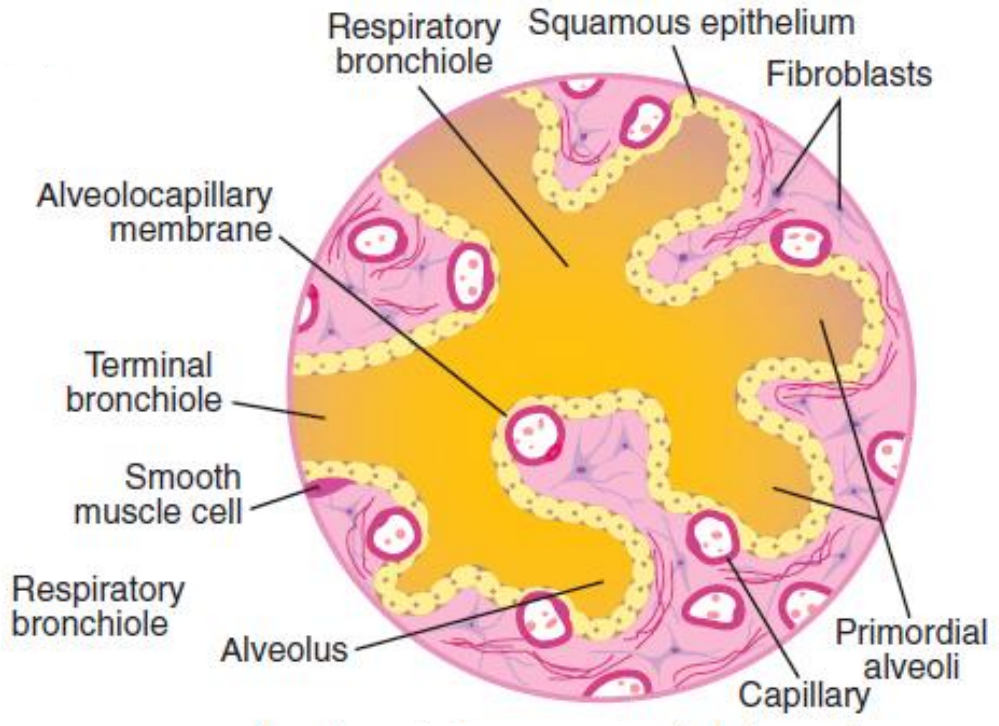
The lungs in the canalicular period.

In the terminal sac period, the respiratory membrane (that is the contact between the capillaries and the alveoli) is established, this period lasts from the 26thof pregnancy till birth, and a baby can survive if it was born in this period. In this period, the primitive alveoli (terminal sac) has established a contact with the pulmonary capillaries.



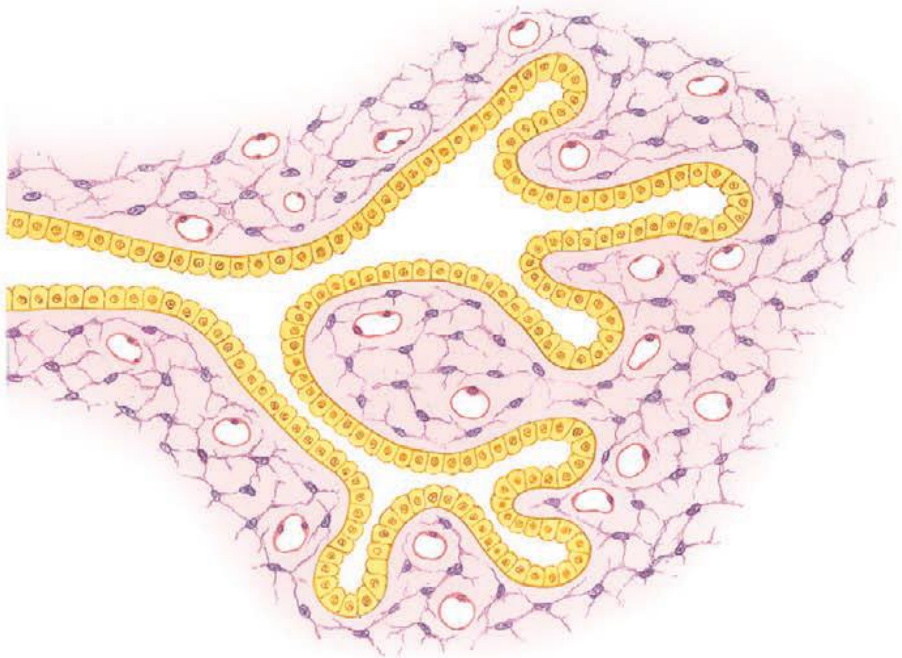
This is what a lung looks lac during the terminal sac period.

The alveolar period is the last stage of alveolar maturation, this stage starts at the 32th week of pregnancy (so it overlaps the terminal sac period) and extends to the first eight years of life, in this period, the primitive alveoli undergo structural changes to become mature, moreover, the number of alveoli increases greatly, and the surface are of contact between the alveoli and the capillaries reach its maximum.

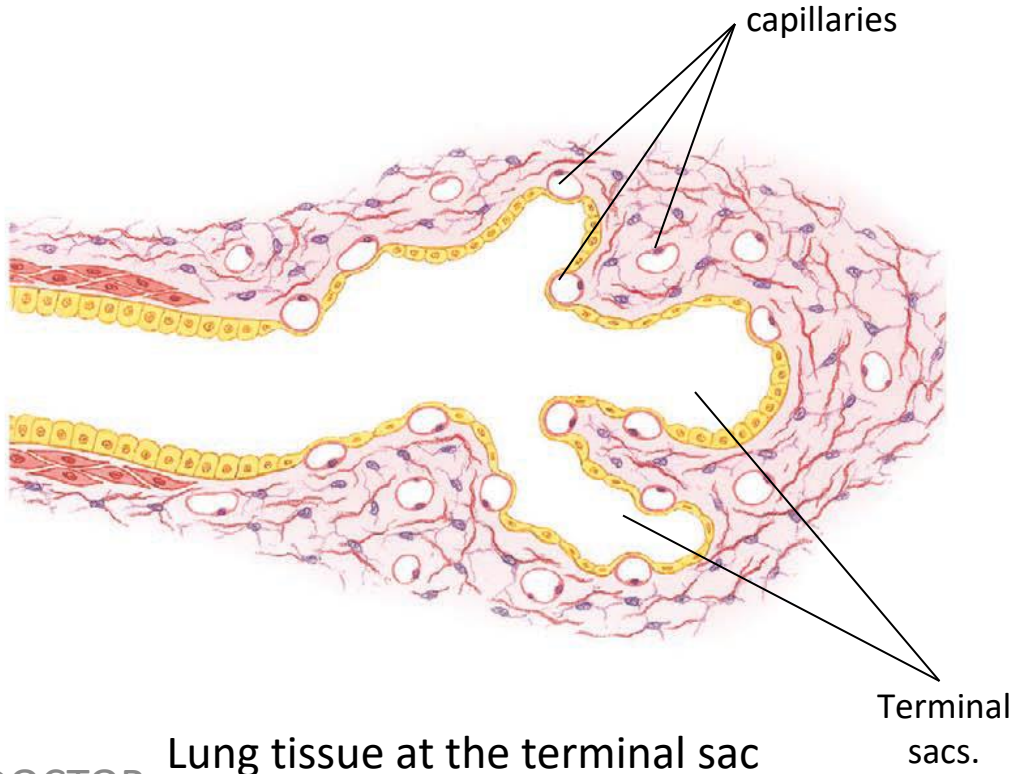


A lung in the alveolar period.

- Up to the seventh prenatal month, the bronchioles divide continuously into more and smaller canals, this is the canalicular phase of maturation, in this phase, the vascular supply increases steadily.
- Respiration becomes possible when some of the cells of the cuboidal respiratory bronchioles change into thin, flat cells (so in the terminal sac period).
- in the terminal sac period, these cells are intimately associated with numerous blood and lymph capillaries, and the surrounding spaces are now known as terminal sacs or primitive alveoli
- During the seventh month, sufficient numbers of capillaries are present to guarantee adequate gas exchange, and the premature infant is able to survive.

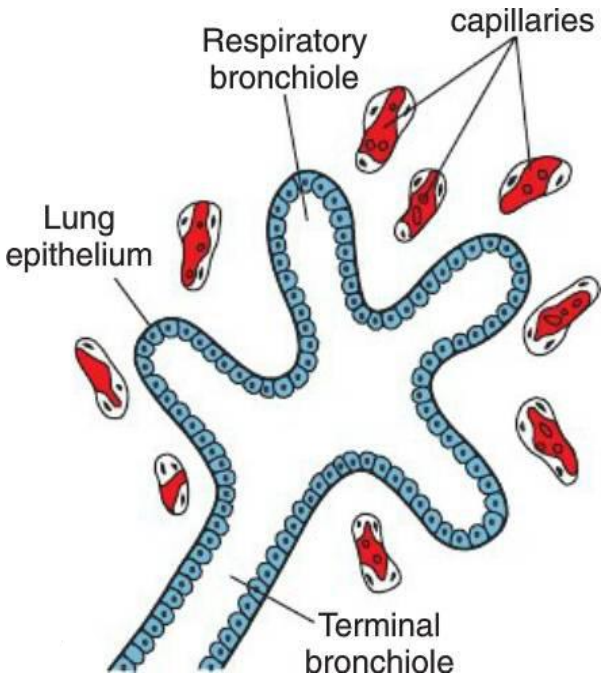


Lung tissue at the early canalicular period.

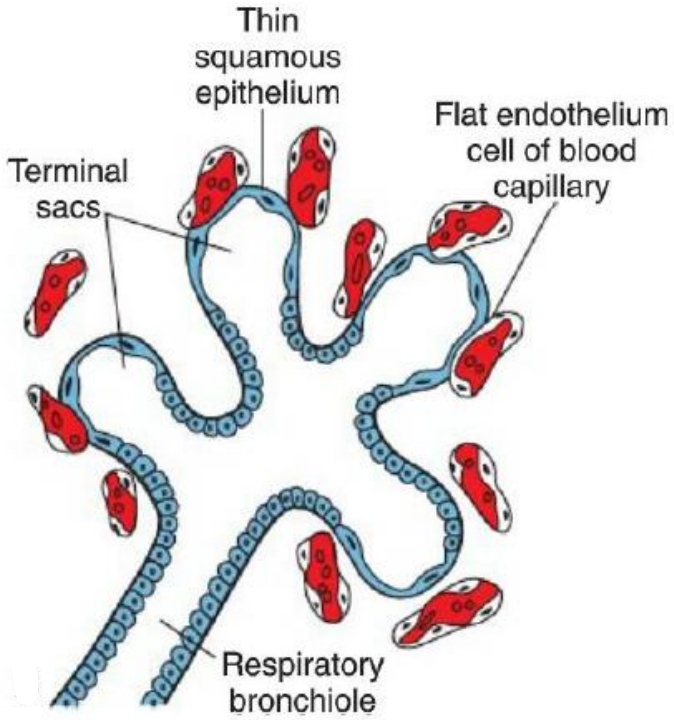


Lung tissue at the terminal sac period.

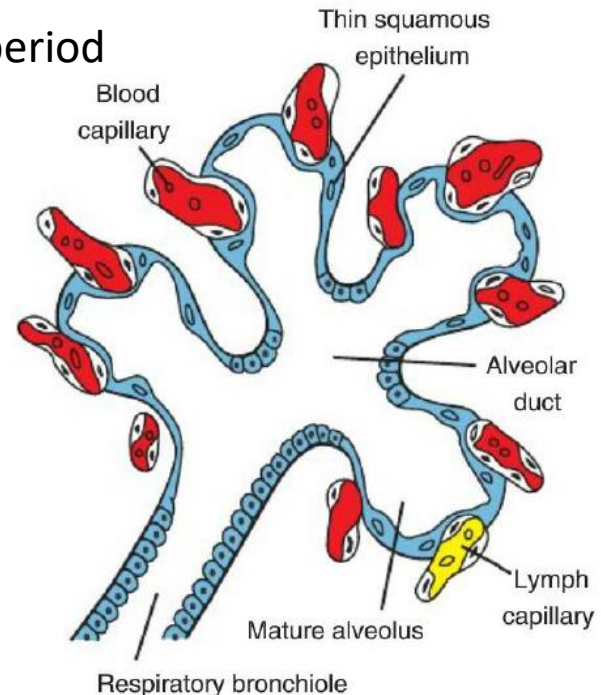
- in the alveolar phase, which lasts during the last two months of prenatal life and for several years thereafter, the number of terminal sacs increases steadily.
- In addition, cells lining the sacs, known as type I alveolar epithelial cells, become thinner, so that surrounding capillaries protrude into the alveolar sacs. (they become squamous instead of cuboidal)
- This intimate contact between epithelial and endothelial cells makes up the blood-air barrier.
- Mature alveoli are not present before birth, as most maturation occurs after birth
- In addition to endothelial cells and flat alveolar epithelial cells, another cell type develops at the end of the sixth month. These cells, type II alveolar epithelial cells, produce the pulmonary surfactant.
- Before birth the lungs are full of fluid that contains a high chloride concentration, little protein, some mucus from the bronchial glands, and surfactant from the alveolar epithelial cells (type II). (this fluid must be sucked upon birth).
- The amount of surfactant in the fluid increases, particularly during the last two weeks before birth.
- The production of the pulmonary surfactant begins at the 6th month, but the peak of its rate of production is at the end of the 8th month and the beginning of the 9th month



Canalicular period



Terminal Sac period

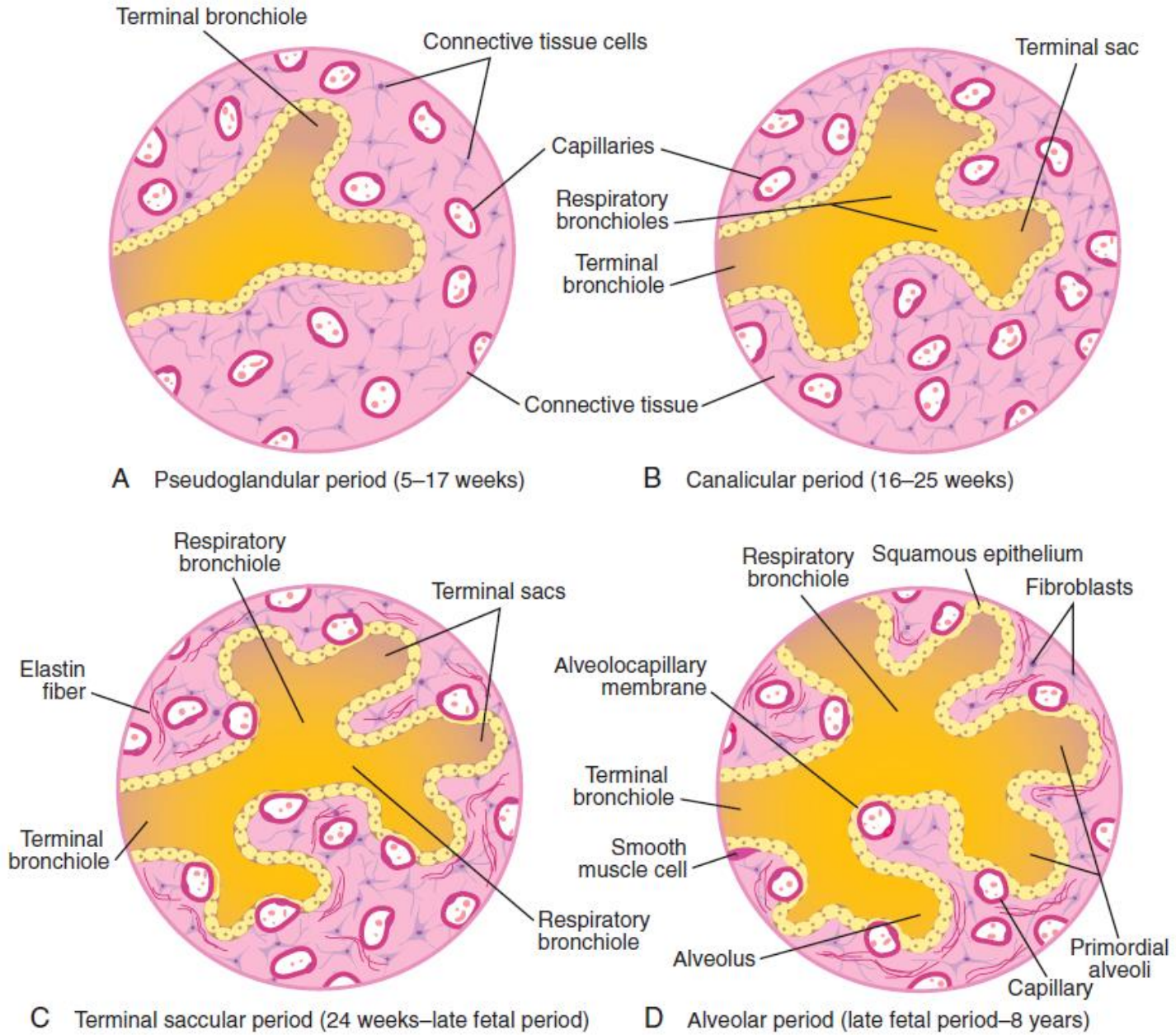


Alveolar Period

- Fetal **breathing movements** begin before birth and cause aspiration of amniotic fluid, these movements are important for stimulating lung development and conditioning respiratory muscles
- When respiration begins at birth, most of the lung fluid is rapidly resorbed by the blood and lymph capillaries, and a small amount is probably expelled via the trachea and bronchi during delivery, when the fluid is resorbed from alveolar sacs, surfactant remains deposited as a thin phospholipid coat on alveolar cell membranes.
- With air entering alveoli during the first breath, the surfactant coat prevents development of an air-water (blood) interface with high surface tension, Without the fatty surfactant layer, the alveoli would collapse during expiration (atelectasis).
- Respiratory movements after birth bring air into the lungs, which expand and fill the pleural cavity.
- Although the alveoli increase somewhat in size, growth of the lungs after birth is due primarily to an increase in the number of respiratory bronchioles and alveoli.
- It is estimated that only one-sixth of the adult number of alveoli are present at birth
- The remaining alveoli are formed during the first 10 years of postnatal life through the continuous formation of new primitive alveoli.
- The doctor slaps the baby's back upon birth to make him cry, crying would stimulate the respiratory centers in the brain, which sends efferent neurons to the diaphragm through the phrenic nerve, contraction of diaphragm widens the thorax, which in turn causes inflation of the lung and respiration, so crying is an evidence of good respiration.

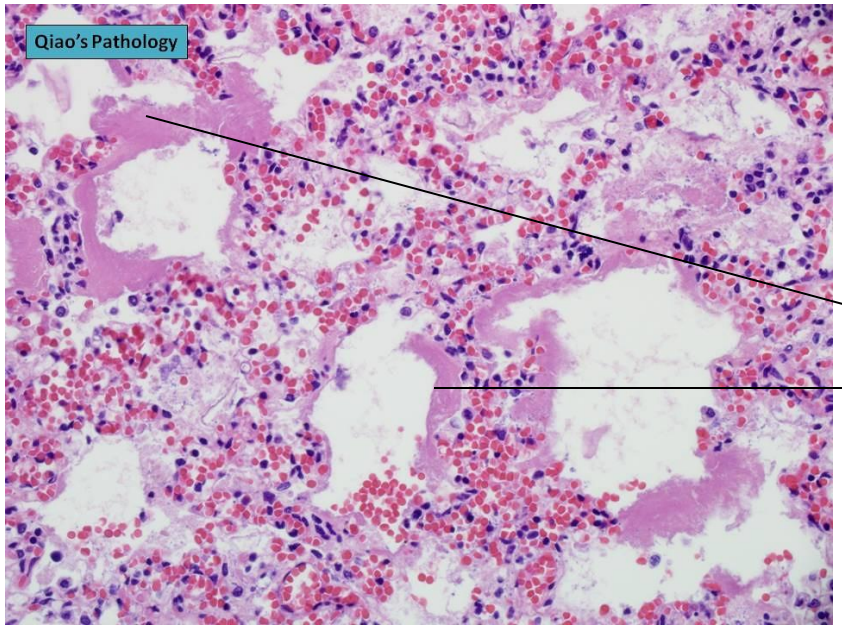
TABLE 12.1 Maturation of the Lungs

Pseudoglandular period	5-16 weeks	Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli are present.
Canalicular period	16-26 weeks	Each terminal bronchiole divides into 2 or more respiratory bronchioles, which in turn divide into 3-6 alveolar ducts.
Terminal sac period	26 weeks to birth	Terminal sacs (primitive alveoli) form, and capillaries establish close contact.
Alveolar period	8 months to childhood	Mature alveoli have well-developed epithelial endothelial (capillary) contacts.

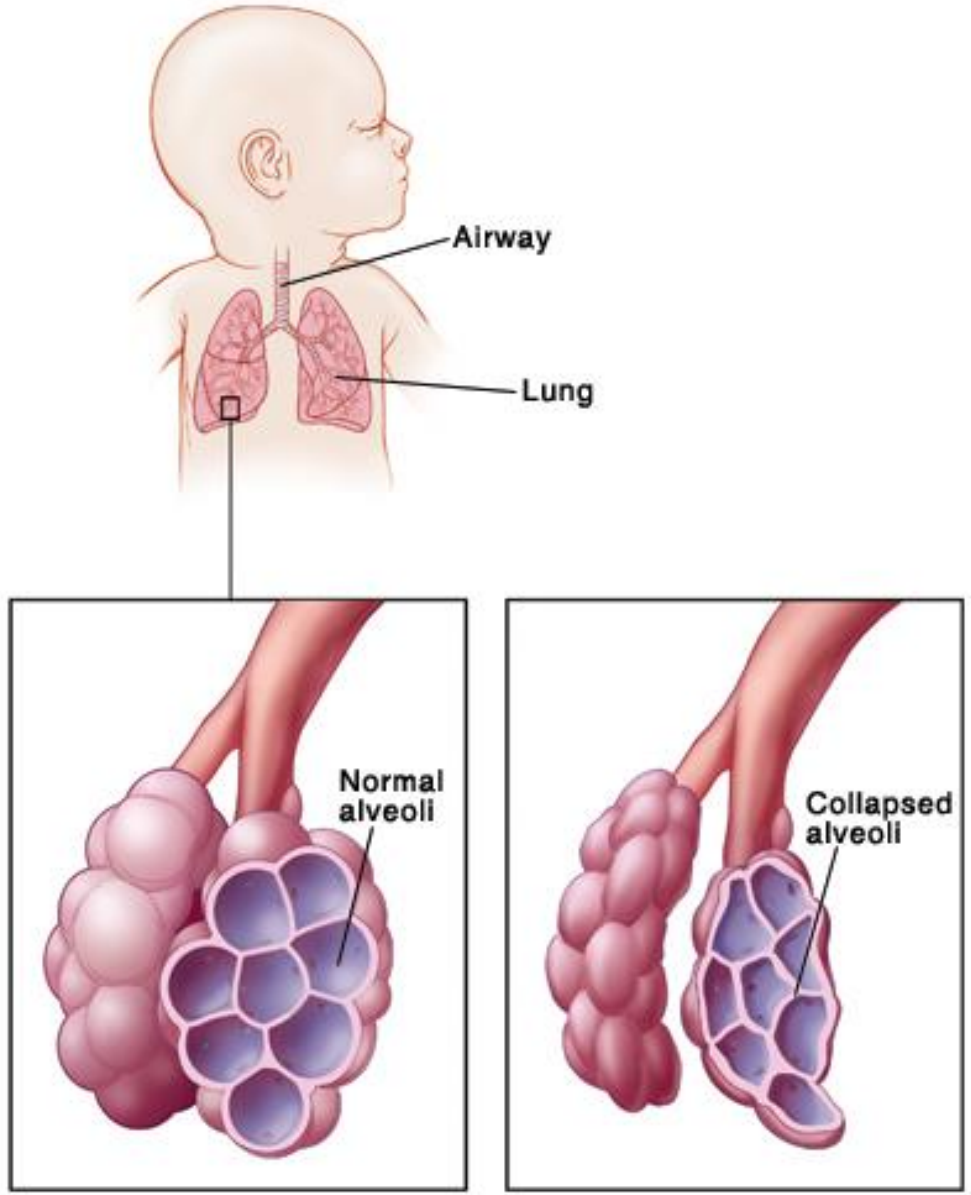


ANOMALIES OF THE LUNG: INFANT RESPIRATORY DISTRESS SYNDROME

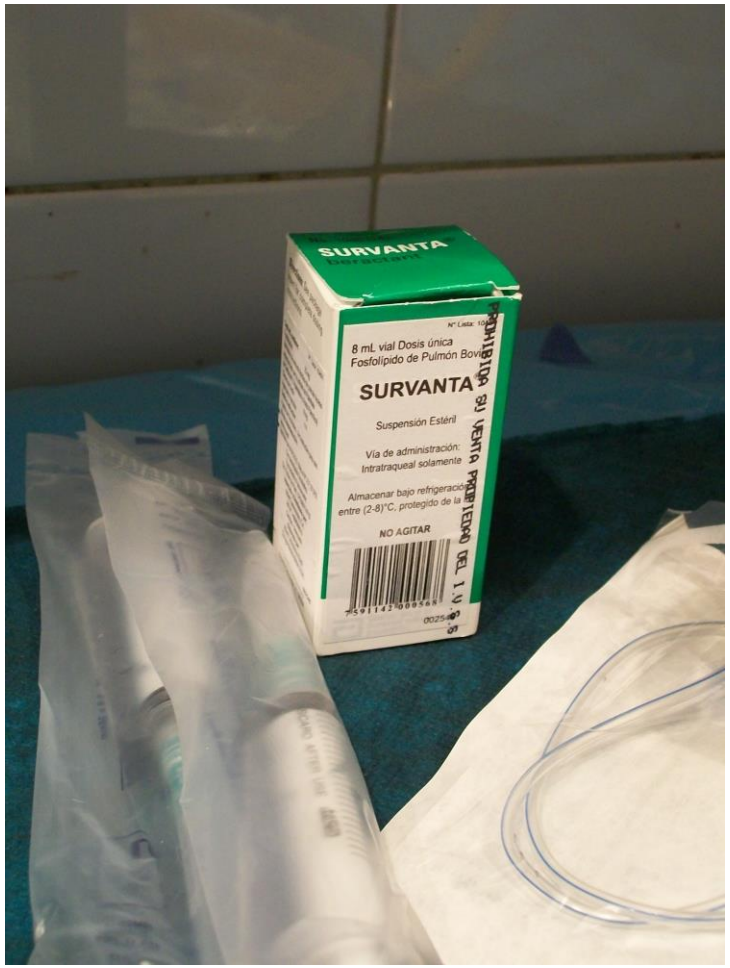
- The pulmonary surfactant is particularly important for survival of the premature infant.
- When the surfactant is insufficient, the air-water (blood) surface membrane tension becomes high, bringing great risk that alveoli will collapse during expiration.
- As a result, infant **respiratory distress syndrome** (RDS) develops, it is a common cause of death in the premature infant (30% of all neonatal diseases).
- In these cases the partially collapsed alveoli contain a fluid with a high protein content, many hyaline membranes, and lamellar bodies, probably derived from the surfactant layer.



These hyaline membranes are seen upon histopathologic examination



- RDS, is therefore also known as **hyaline membrane disease,** accounts for approximately 20% of deaths among newborns
- Intrauterine Asphyxia (lack of oxygen) may produce irreversible changes in type II cells.
- Recent development of artificial surfactant and treatment of premature babies with glucocorticoids (betamethasone) to stimulate surfactant production have reduced the mortality associated with RDS.
- It Also allowed survival of some babies as young as 5.5 months of gestation.
- Thyroxine is the most important stimulator for surfactants production, thyroxine is secreted by the thyroid gland, so anomalies of thyroid gland might also result in IRDS.

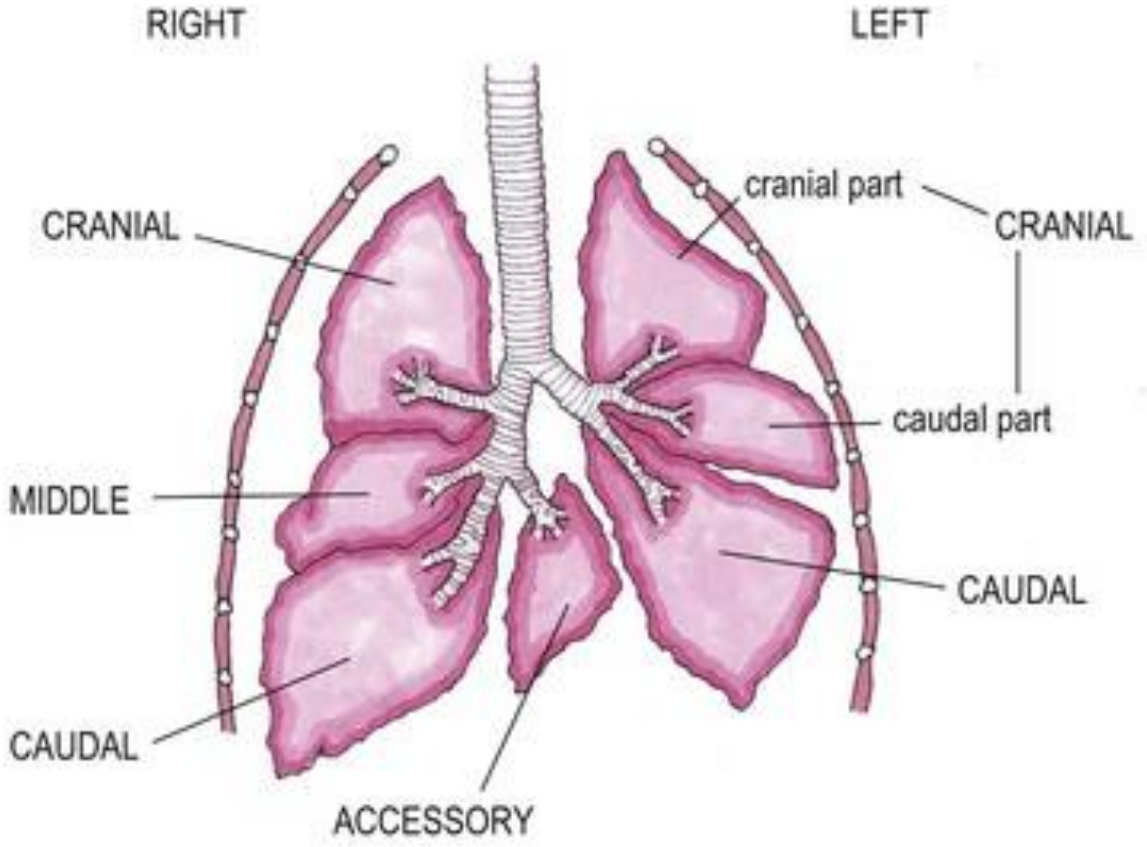


RARE LUNG ANOMALIES

- Although many abnormalities of the lung and bronchial tree have been found (e.g., blind-ending trachea with absence of lungs and agenesis (the word agenesis means absence) of one lung) most of these gross abnormalities are rare.
- Bilateral lung agenesis is of course incompatible with life, but unilateral agenesis might be compatible, because the remaining lung might undergo hypertrophy to ensue adequate function.
- Abnormal divisions of the bronchial tree are more common; some result in supernumerary lobules (like having three lungs, having four lobes of the right lung, three lobes of the left lung, etc.)
- These variations of the bronchial tree have little functional significance, but they may cause unexpected difficulties during bronchoscopies.

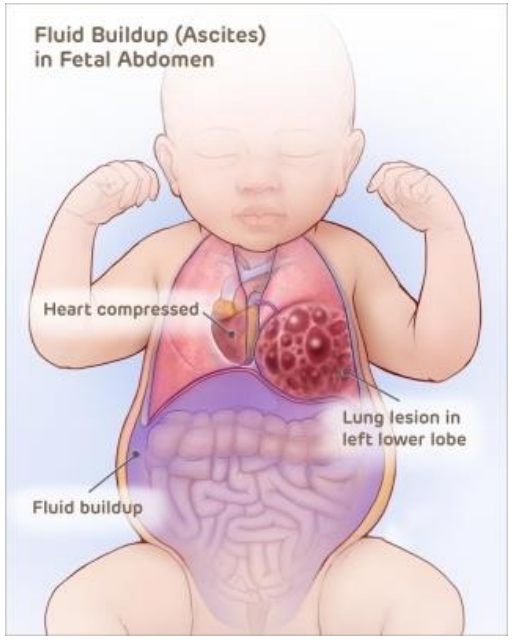
ECTOPIC LUNG LOBES

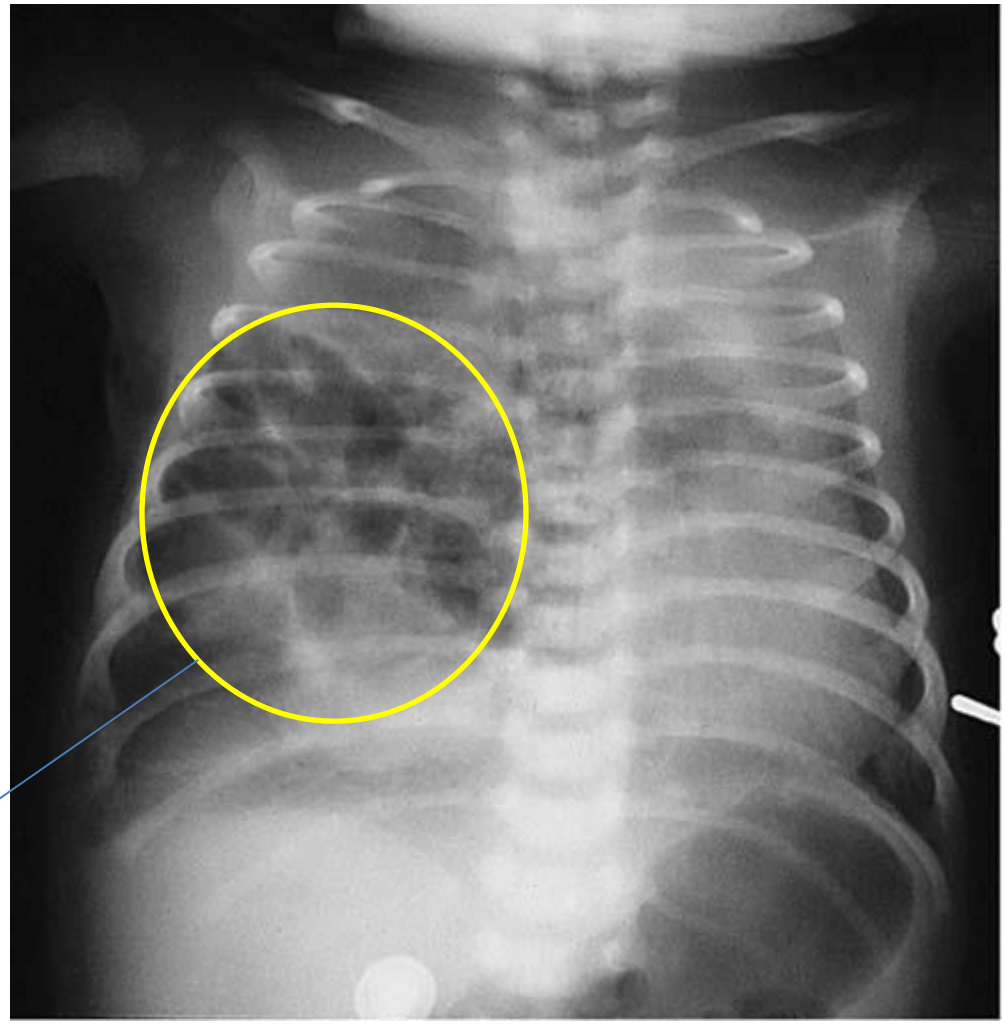
- ectopic lung lobes are inappropriately placed lung lobes arising from the trachea or esophagus.
- It is believed that these lobes are formed fromadditional respiratory buds of the foregut that develop independently of the main respiratory system.
- Theses ectopic lobes might be in peculiar sites, like the abdomen or the root of the neck.



CONGENITAL LUNG CYSTS

- Most important clinically are congenital cysts of the lung, which are formed by dilation of terminal or larger bronchi.
- These cysts may be small and multiple, giving the lung a honeycomb appearance on radiograph, or they may be restricted to one or more larger ones.
- Cystic structures of the lung usually drain poorly and frequently cause chronic infections.
- Remember: a cyst means a ball filled with fluid usually, but in this case it is filled with air.





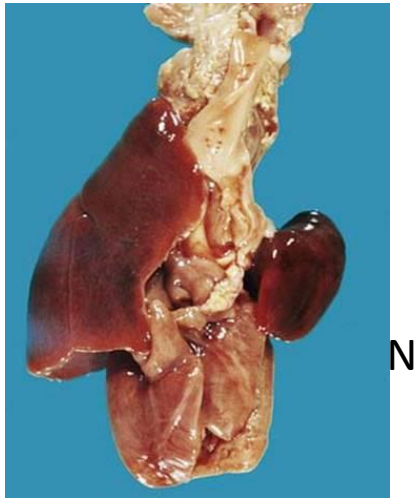
This honeycomb is due to multiple lung cysts

LUNG HYPOPLASIA نقص تنسّج رئويّ

•In infants with congenital diaphragmatic hernia (CDH) the lung is unable to develop normally, Because it is compressed by the abnormally positioned abdominal viscera

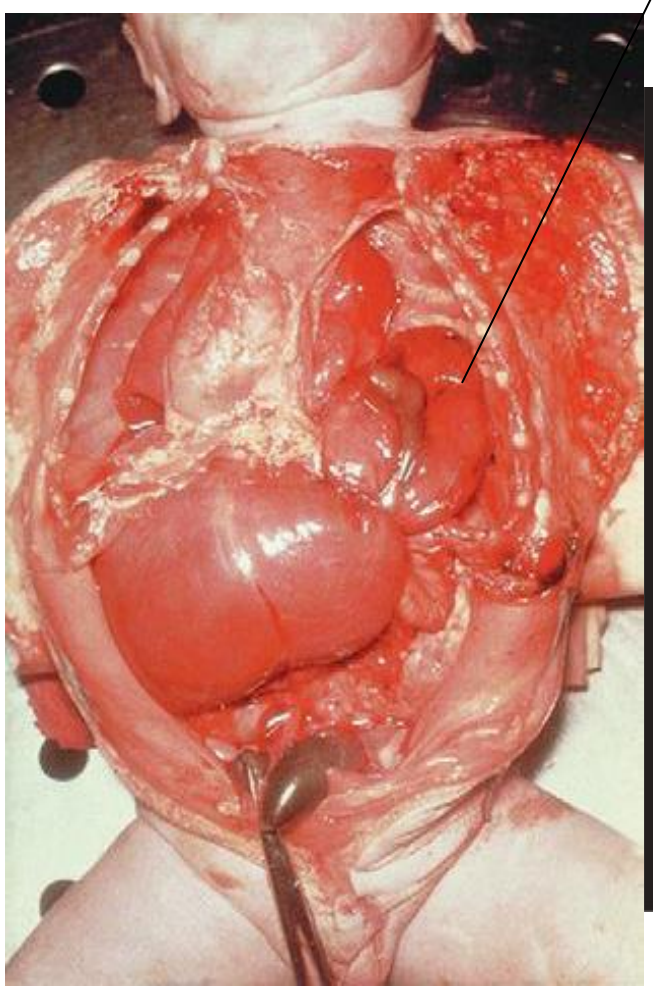
• lung hypoplasia is characterized by reduced lung volume, most infants with CDH die of pulmonary insufficiency as their lungs are too hypoplastic to support life.

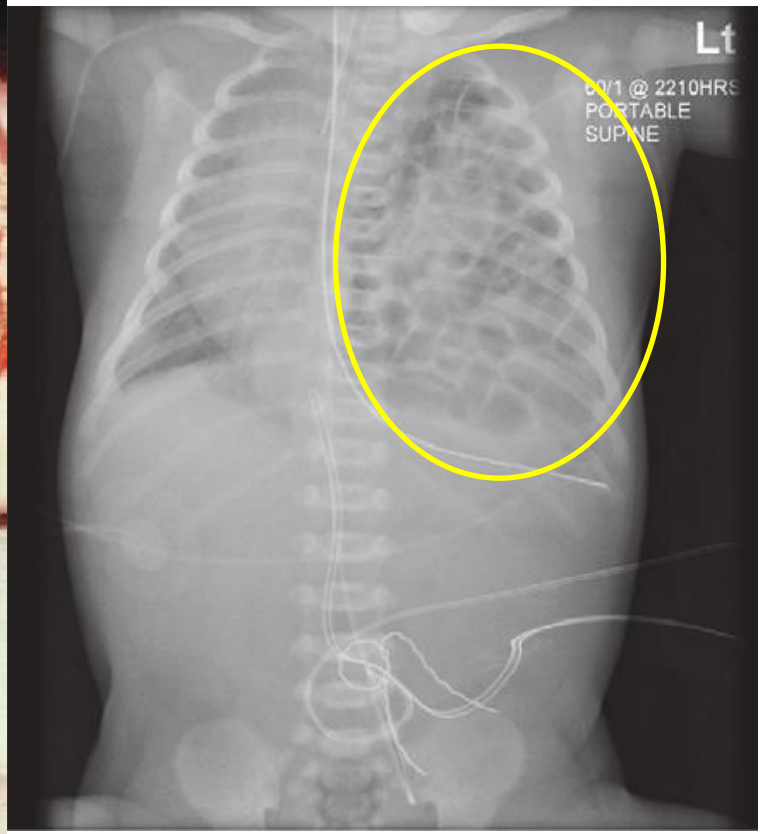
•Pulmonary hypoplasia may also result from oligohydramnios. (reduced amount of amniotic fluid)



Note how small they are !!!

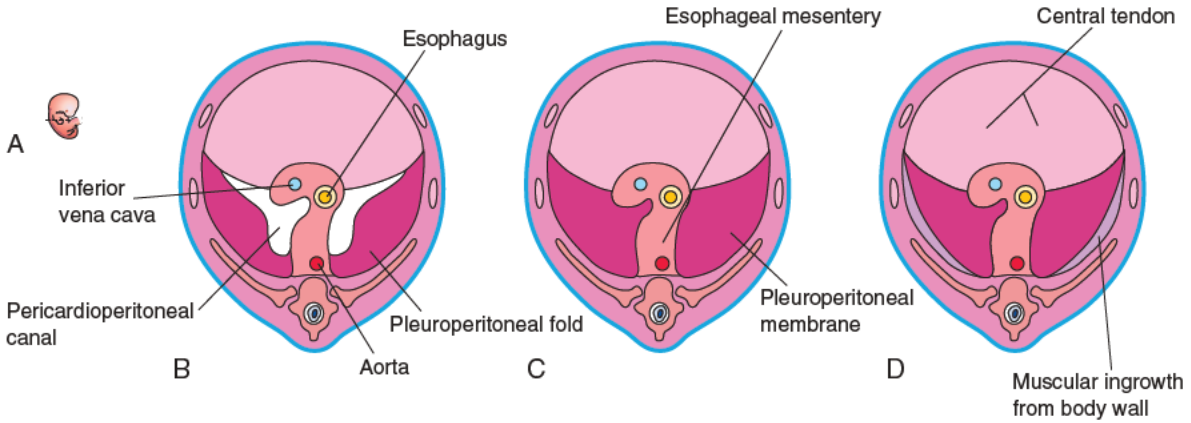
Abdominal viscera in the chest

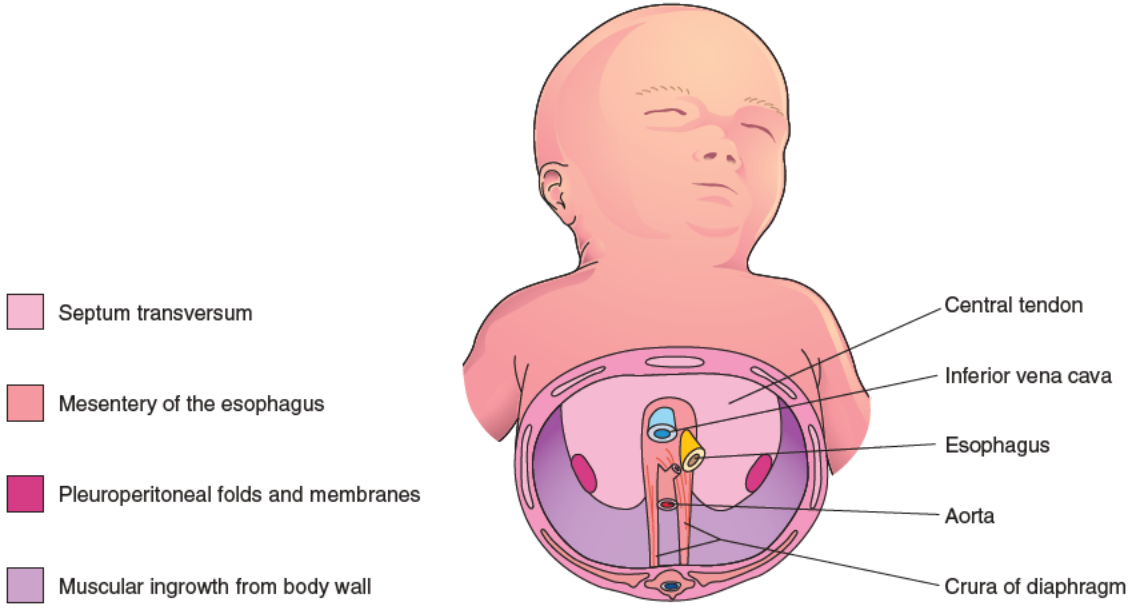




Congenital diaphragmatic hernia

Because the diaphragm is formed by fusion of three primordia: the septum transversum, and the two pleuroperitoneal folds, congenital diaphragmatic hernias are common because they result when two of these fail to fuse, resulting in abdominal organs herniating into the thoracic cavity, and they interfere with normal lung development CHDs most commonly occur on the left side.





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LUNGS OF THE NEWBORN INFANT.

- Fresh and healthy lungs contain some air so pulmonary samples float in water.
- The lungs of the stillborn infants are firm and sink in water because they contain fluids not air, this piece of information is useful to know if the baby was born dead or died after birth, if it was born dead, then there no is air in his lungs and the sample would sink, if he died after birth, then the lung would be filled with air and the sample would float, this is particularly useful when doctors kill the baby because of bad practices, and state that the baby was born dead.