

DEVELOPMENT OF THE RESPIRATORY SYSTEM

Andrea Heinzlmann

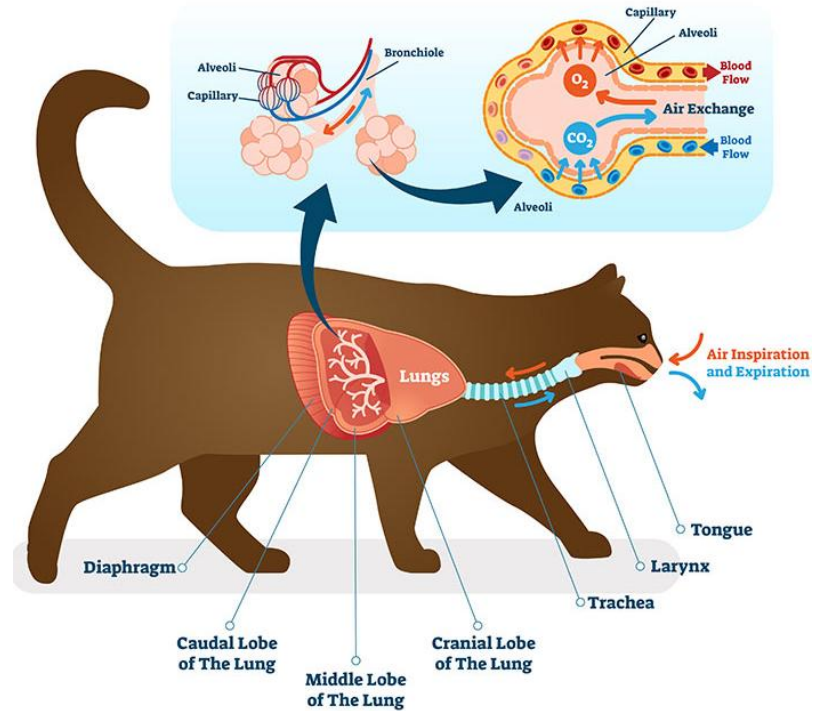
University of Veterinary Medicine, Budapest

Department of Anatomy and Histology

Embryology Course

RESPIRATORY SYSTEM

- the development of the respiratory system is closely related to the development of the face and pharynx
- 1. the upper respiratory system composed of:
 - a. nasal cavity
 - b. pharynx (nasopharynx and interpharyngeal ostium)
 - c. larynx



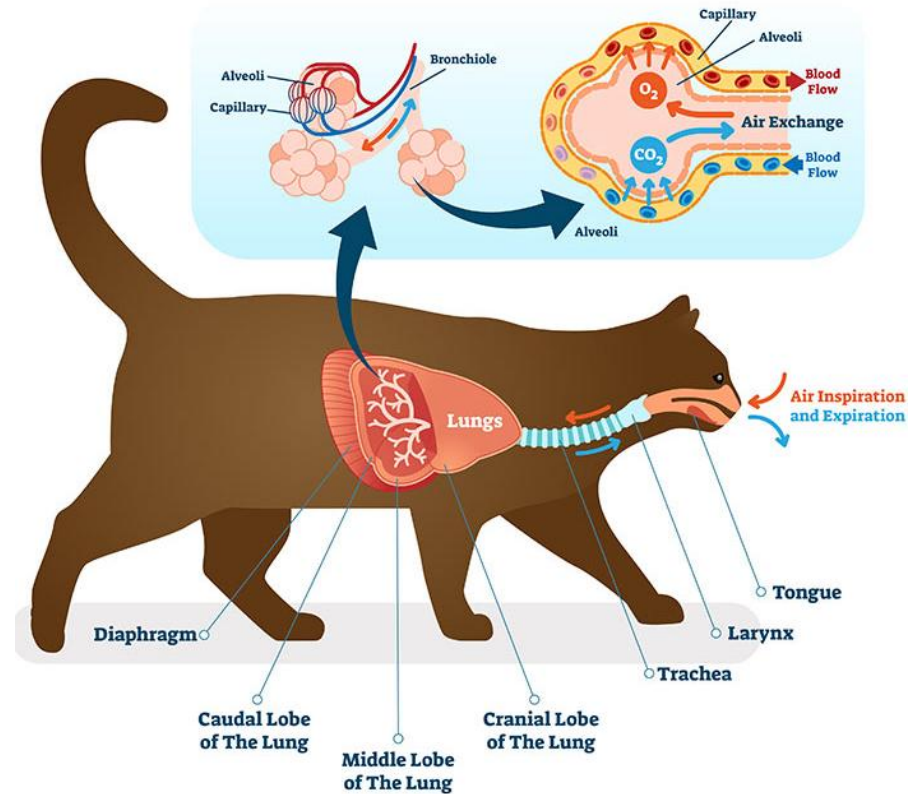
RESPIRATORY SYSTEM

2. the lower respiratory system composed of:

a. trachea

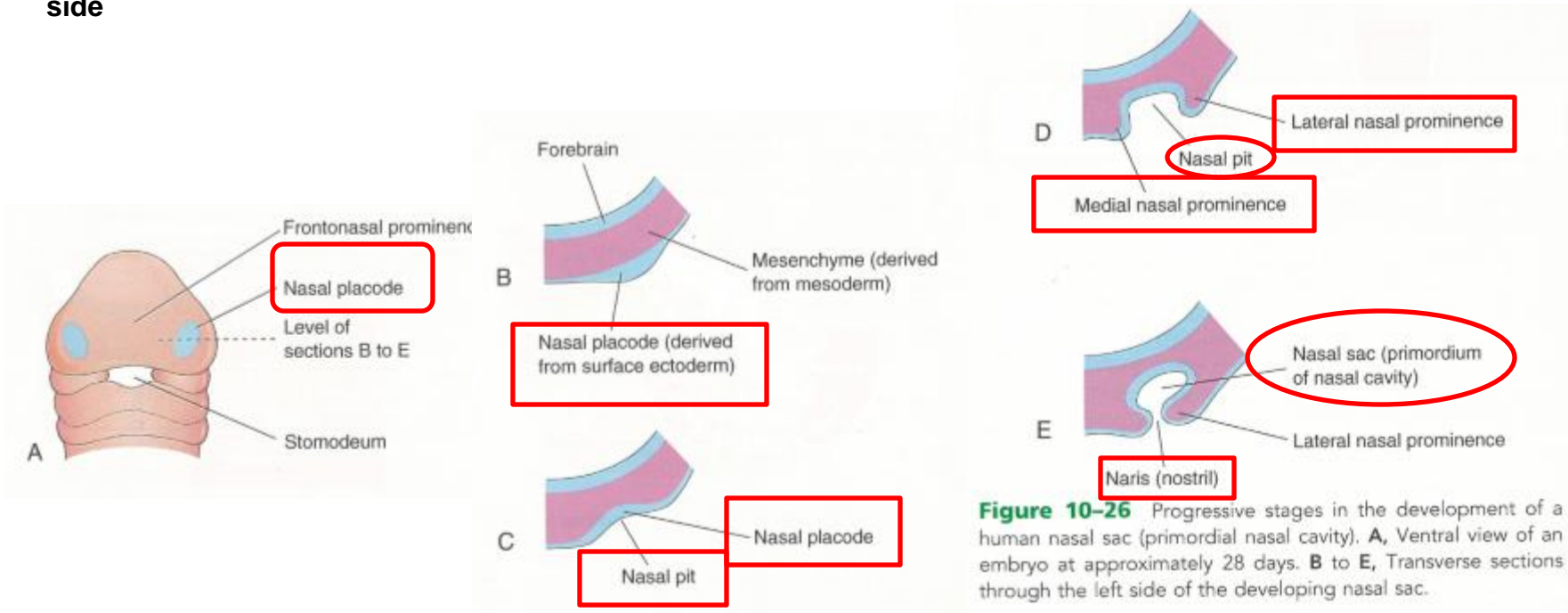
b. lungs

- is an indirect derivative of the embryonic pharynx



NASAL CAVITY

1. formed from the olfactory (nasal) placodes
2. the olfactory placodes become indented and deeper by the formation and growth of the mesenchyme of the medial and lateral nasal prominences – they become the nasal pits
3. the nasal pits remain open ventrally via the nasal groove
4. the rostralmost part of the nasal groove closed by fusion of the medial and lateral nasal prominences
5. the caudal part of the nasal groove closed by the fusion of the maxillary and medial nasal prominence of each side



NASAL CAVITY

6. with the closure of the nasal groove – a blind sac - like cavity is formed – this is the primitive nasal cavity (nasal sac)
7. the rostral openings of the nasal sacs will be the external nares (nostrils) in the adult
8. the nasal sacs become deeper

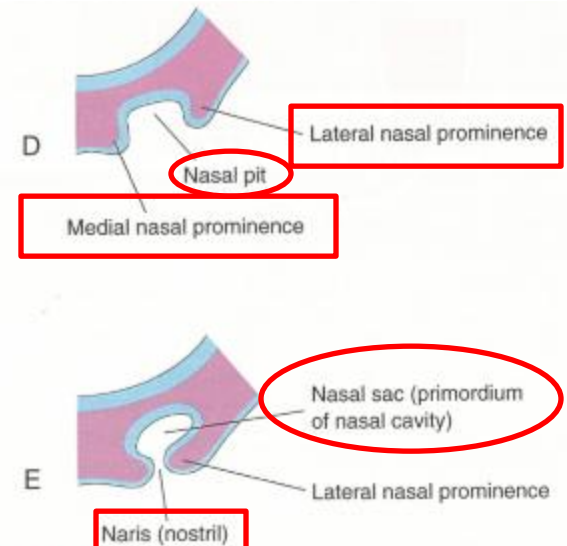
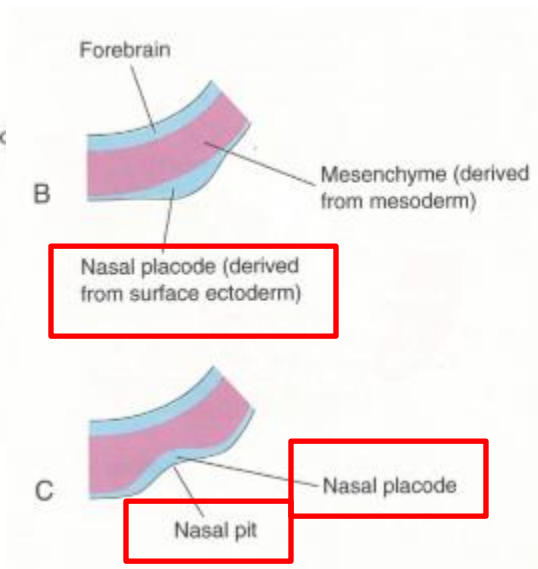
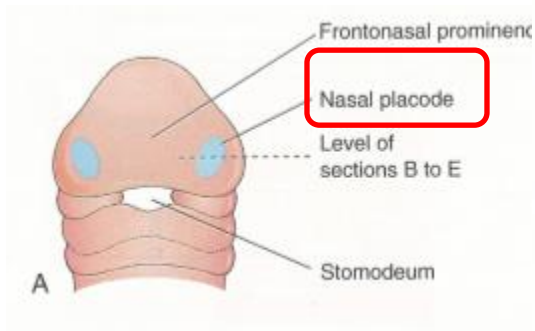


Figure 10-26 Progressive stages in the development of a human nasal sac (primordial nasal cavity). **A**, Ventral view of an embryo at approximately 28 days. **B** to **E**, Transverse sections through the left side of the developing nasal sac.

NASAL CAVITY

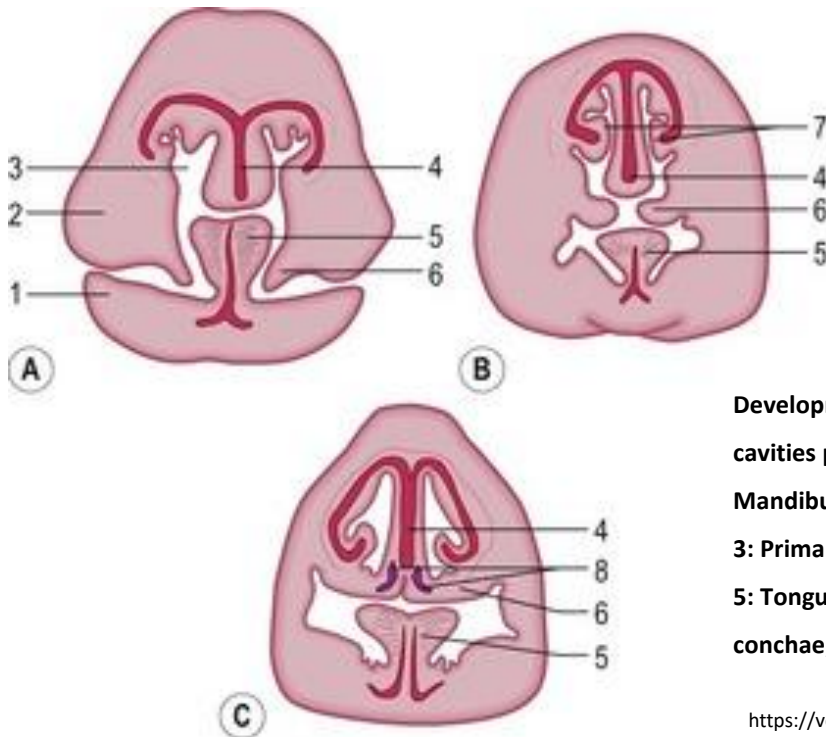
9. **the two medial nasal prominences fuse** to each other to form the basis of the nasal septum

the ventral part of the septum:

- formed by the vomer and the perpendicular part of the ethmoid bone,

the rostral part of the septum:

- formed by the cartilage



Development of the secondary oral and nasal

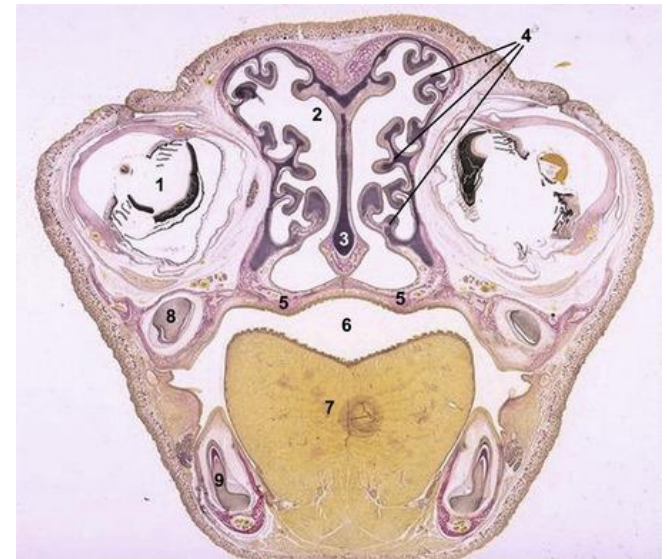
cavities presented as cross sections (A-C). 1:

Mandibular prominence; 2: Maxillary prominence;

3: Primary nasal cavity; 4: Developing nasal septum;

5: Tongue; 6: Palate process; 7: Developing

conchae; 8: Developing vomeronasal organ.



Cross section of fetal cat head. 1: Eye; 2:

Secondary nasal cavity; 3: Developing

nasal septum; 4: Developing conchae; 5:

Palatine processes; 6: Secondary oral

cavity; 7: Tongue; 8: Dental primordium

in the maxilla; 9: Dental primordium in

the mandible.

FORMATION OF THE PALATE (PALATOGENESIS)

the palate develops from two primordia:

a. the primary palate

b. the secondary palate

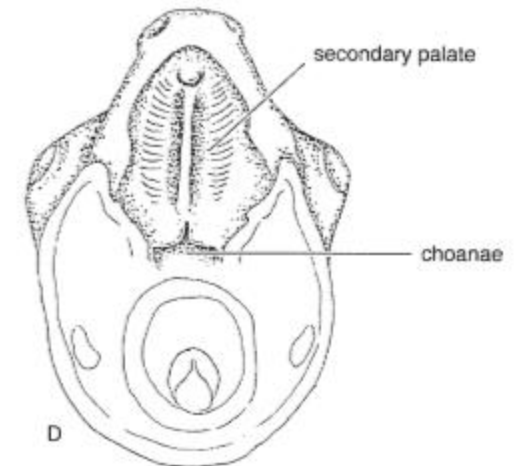
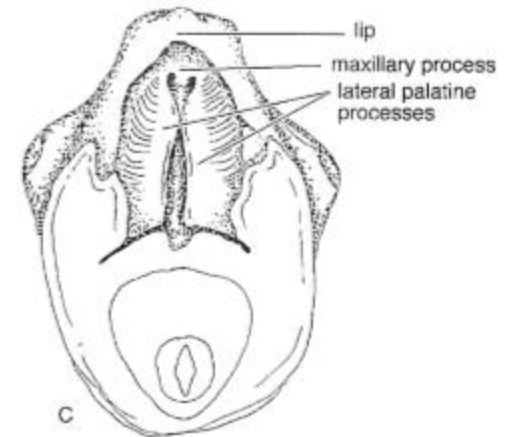
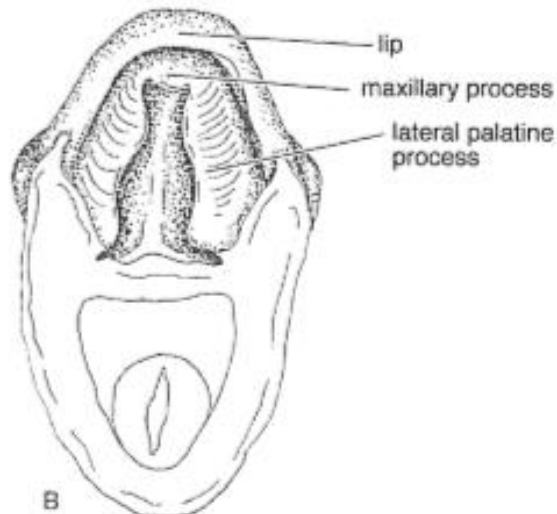
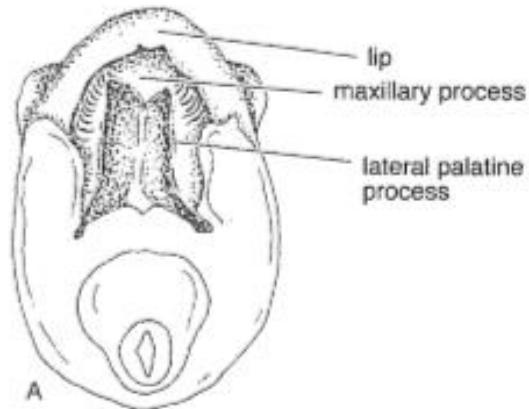
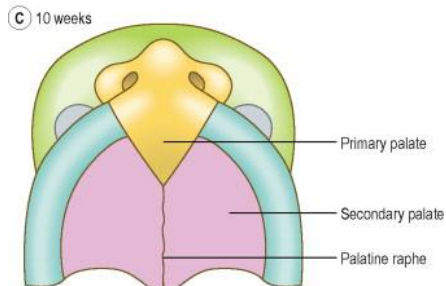
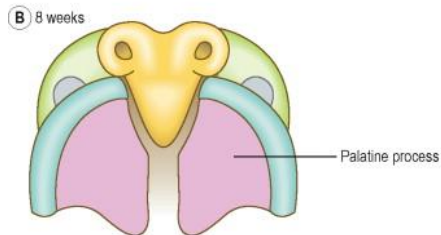
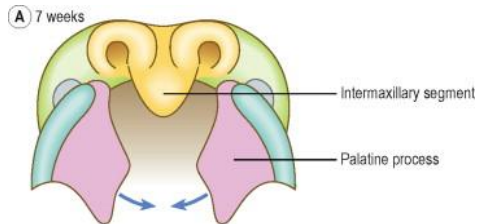
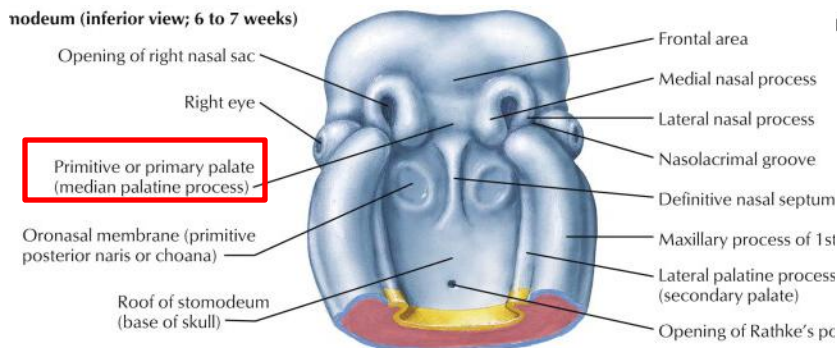


Figure 19.6 Ventral views of the developing porcine palatine processes showing progressive formation of the secondary palate.

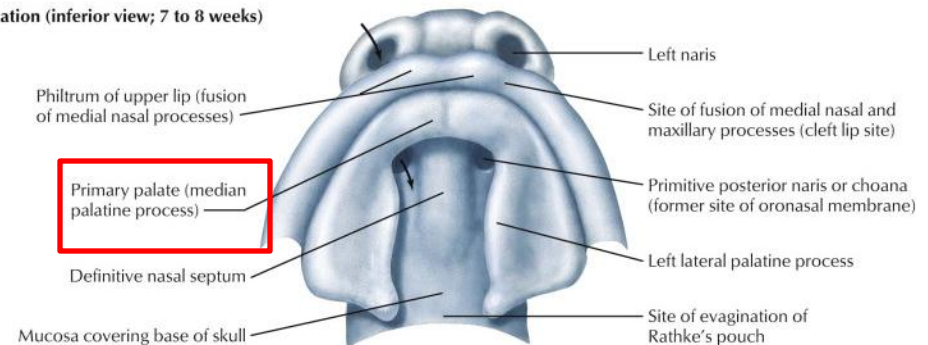
FORMATION OF THE PALATE

PRIMARY PALATE:

1. the primary palate (median palatine process) begins to develop from the deep part of the intermaxillary segment of the maxilla
 - the intermaxillary segment is a wedge – shaped mass of mesenchyme between the internal surface of the maxillary prominences of the developing maxillae
 - the primary palate forms the premaxillary part of the maxilla
 - when the premaxillary parts fuse – the results is the union of the primordia of the palatine portions of the incisive bones - this union forms the rostral part of the hard palate in the adult



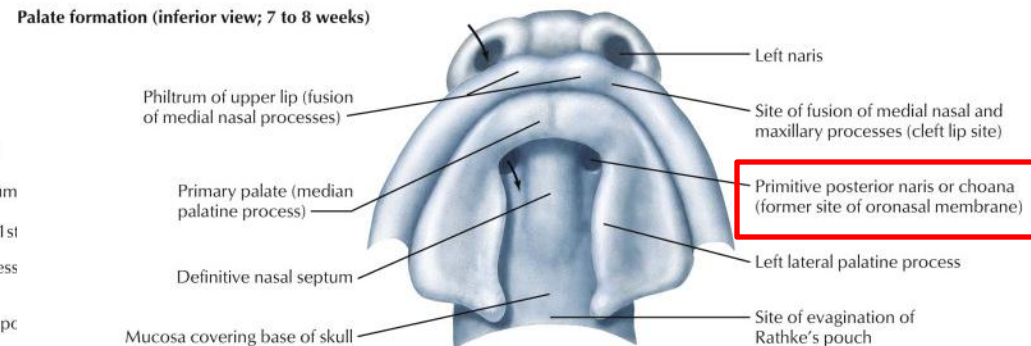
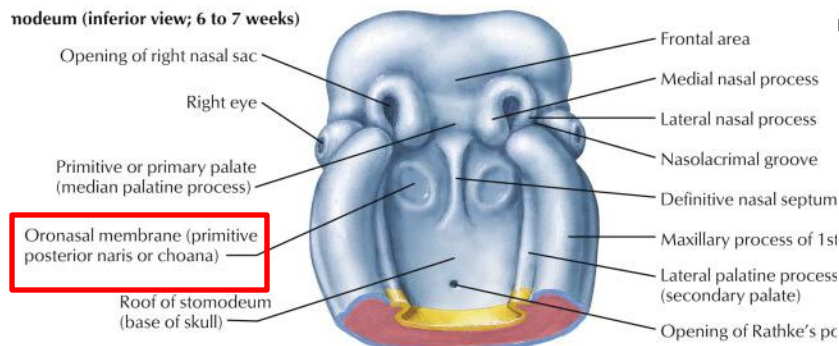
Palate formation (inferior view; 7 to 8 weeks)



FORMATION OF THE PALATE

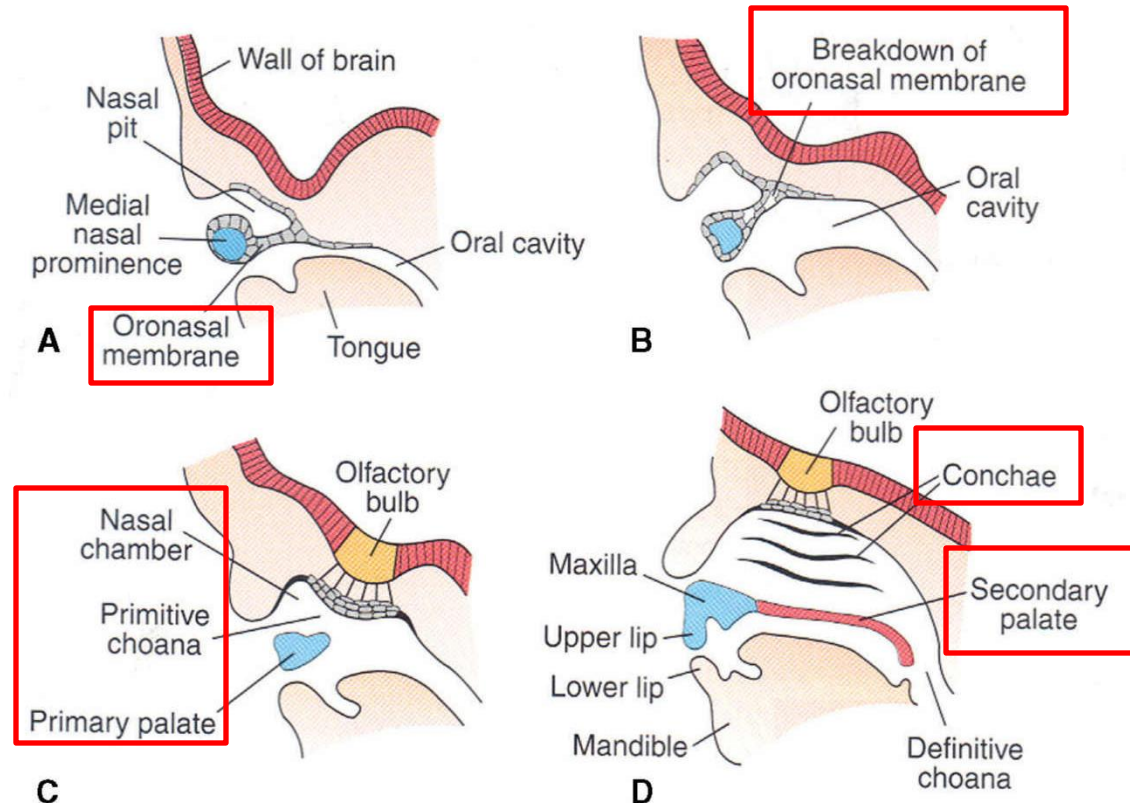
ORONASAL MEMBRANE:

1. after the formation of the primary palate, the floor of the midcaudal part of the nasal sac becomes thinned ventromedially - the oronasal membrane is formed
2. this membrane separates the lumen of the nasal sac from the oral cavity
3. the oronasal membrane becomes perforated
4. than the oronasal membrane ruptures – bringing the nasal and oral cavities into communication
5. the regions of the continuity between the nasal and oral cavities are the primordial (primitive) choanae



FORMATION OF THE PALATE

ORONASAL MEMBRANE



Development of the maxilla is influenced by contiguous structures—the skull base, the breakdown of the oronasal membrane, and the nasomaxillary complex. (A) 5 weeks, the primitive nasal cavity is separated from the oral cavity by an intact oronasal membrane; (B) 6 weeks, with breakdown of the oronasal membrane; (C) 7 weeks, with nasal and oral cavity communication; (D) 12 weeks, with an intact primary and secondary palate and patency of an appropriately developed choanal aperture

FORMATION OF THE PALATE

SECONDARY PALATE:

- the partitioning of the oral cavity from the nasal cavity is necessary
- this partitioning is brought about by the formation of the secondary palate

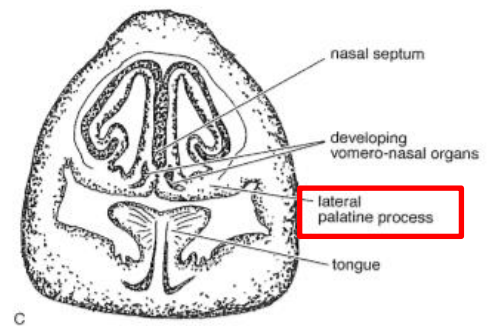
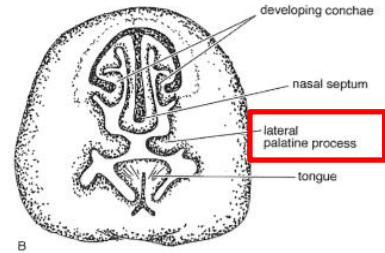
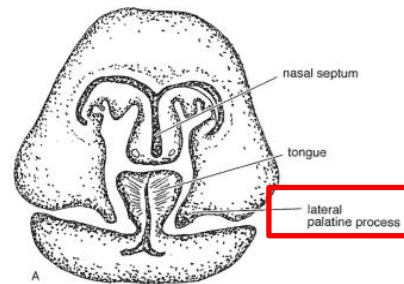
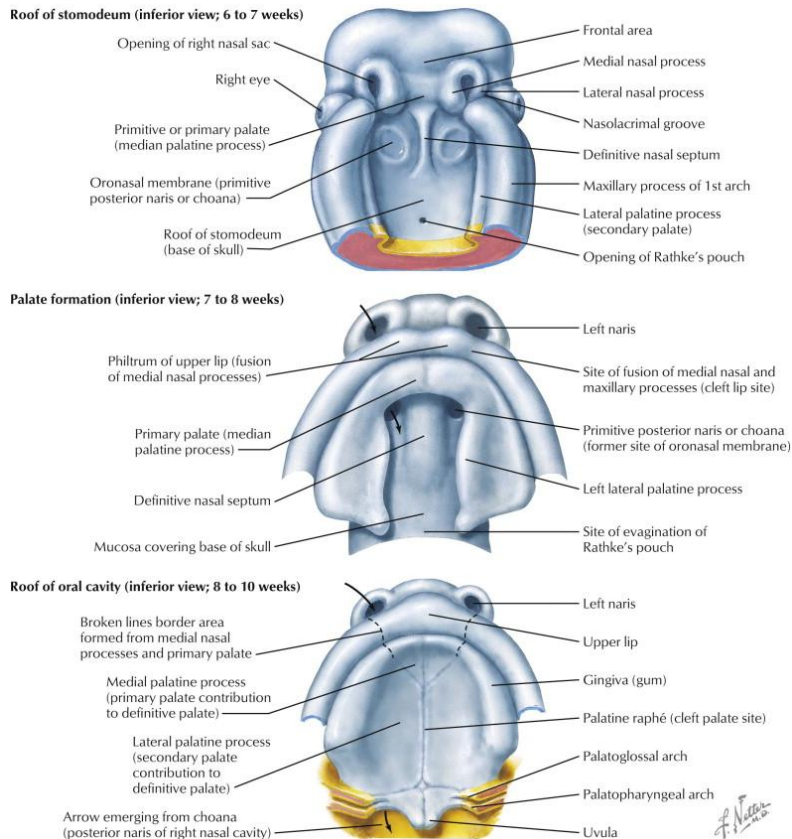


Figure 19.5 Cross-sections through the developing nasal and oral cavities in the pig showing the formation of the secondary palate, nasal septum and conchae.

FORMATION OF THE PALATE

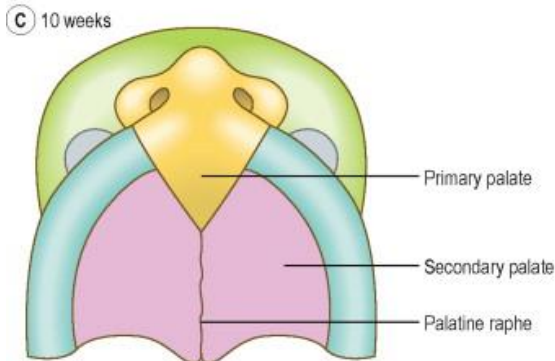
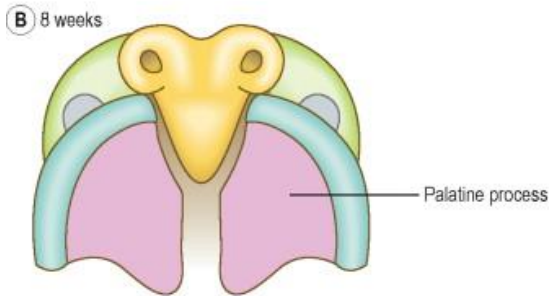
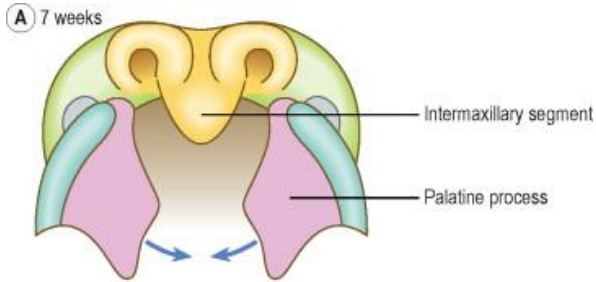
SECONDARY PALATE:

- **the secondary palate is the primodium of the hard and soft part of the palate**

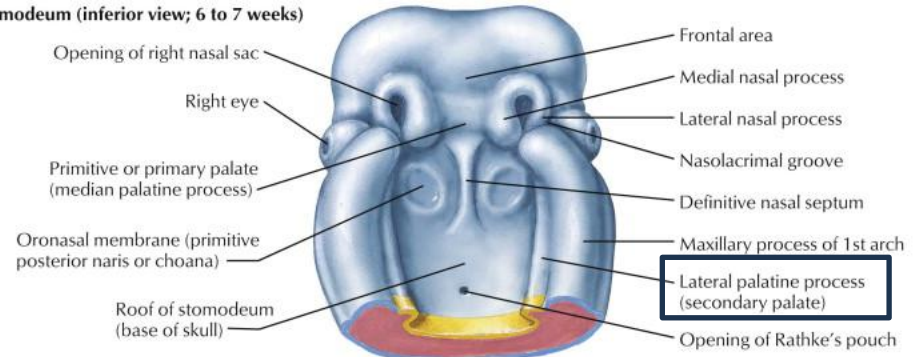
1. **the secondary palate begins to develop from two mesenchymal projections that extend from the internal aspects of the maxillary processes**
2. **these mesenchymal projections are the lateral palatine processes – they project on each side of the tongue – when the palatine processes first appear, the tongue completely fills the oral cavity**
3. **as the jaws develop and the oral cavity enlarges – the tongue becomes smaller and moves inferiorly**
4. **the lateral palatine processes elongate and ascend to a horizontal position above to the tongue**
5. **the lateral palatine processes approach each other and fuse in the median plane**
6. **the lateral palatine processes fuse with the nasal septum and the caudal part of the primary palate**

FORMATION OF THE PALATE

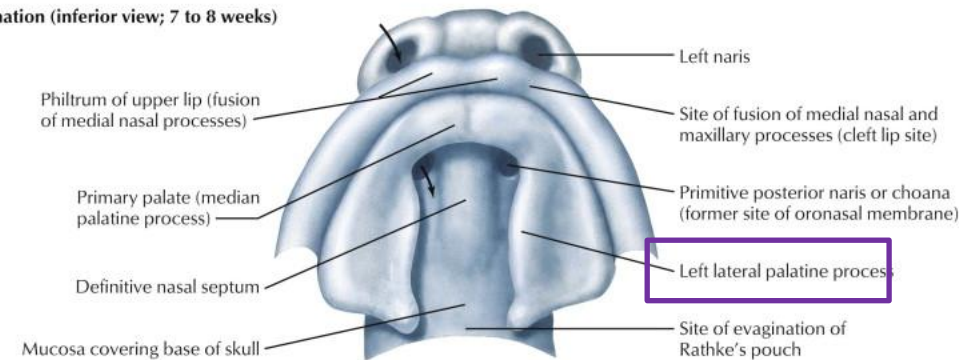
SECONDARY PALATE:



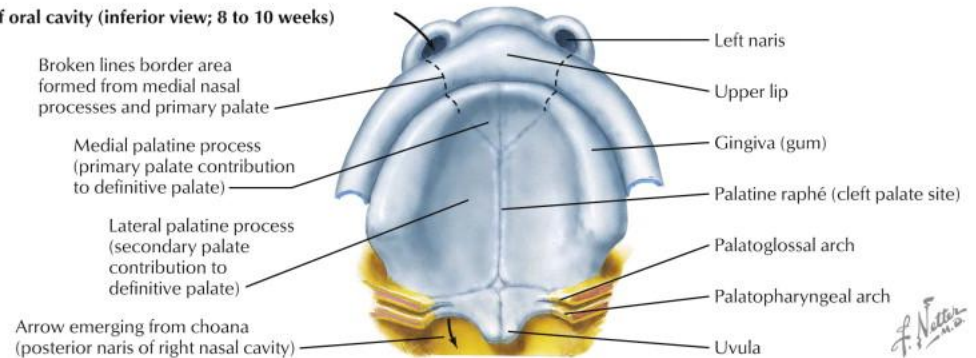
Roof of stomodeum (inferior view; 6 to 7 weeks)



Palate formation (inferior view; 7 to 8 weeks)



Roof of oral cavity (inferior view; 8 to 10 weeks)



F. Netter M.D.

FORMATION OF THE PALATE

- the formation of the secondary palate moves the position of the primitive choanae caudally

this changes in position of primitive choanae allows communication between:

- the nasal cavities and the pharynx
- the nasal cavities and the mouth

- the relocated choanae become the internal nares or choanae in adults

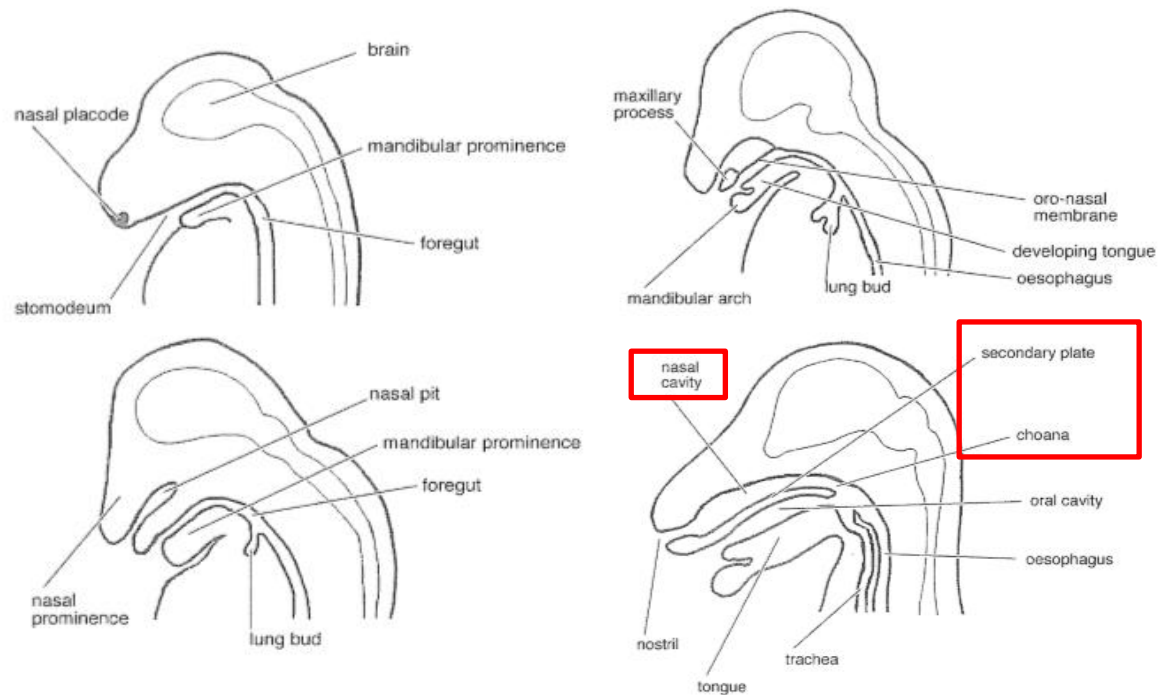


Figure 19.4 Longitudinal sections through the cranial regions of developing embryos at the level of the nasal pit showing progressive development of the nasal and oral cavities.

FORMATION OF THE PALATE

SECONDARY PALATE:

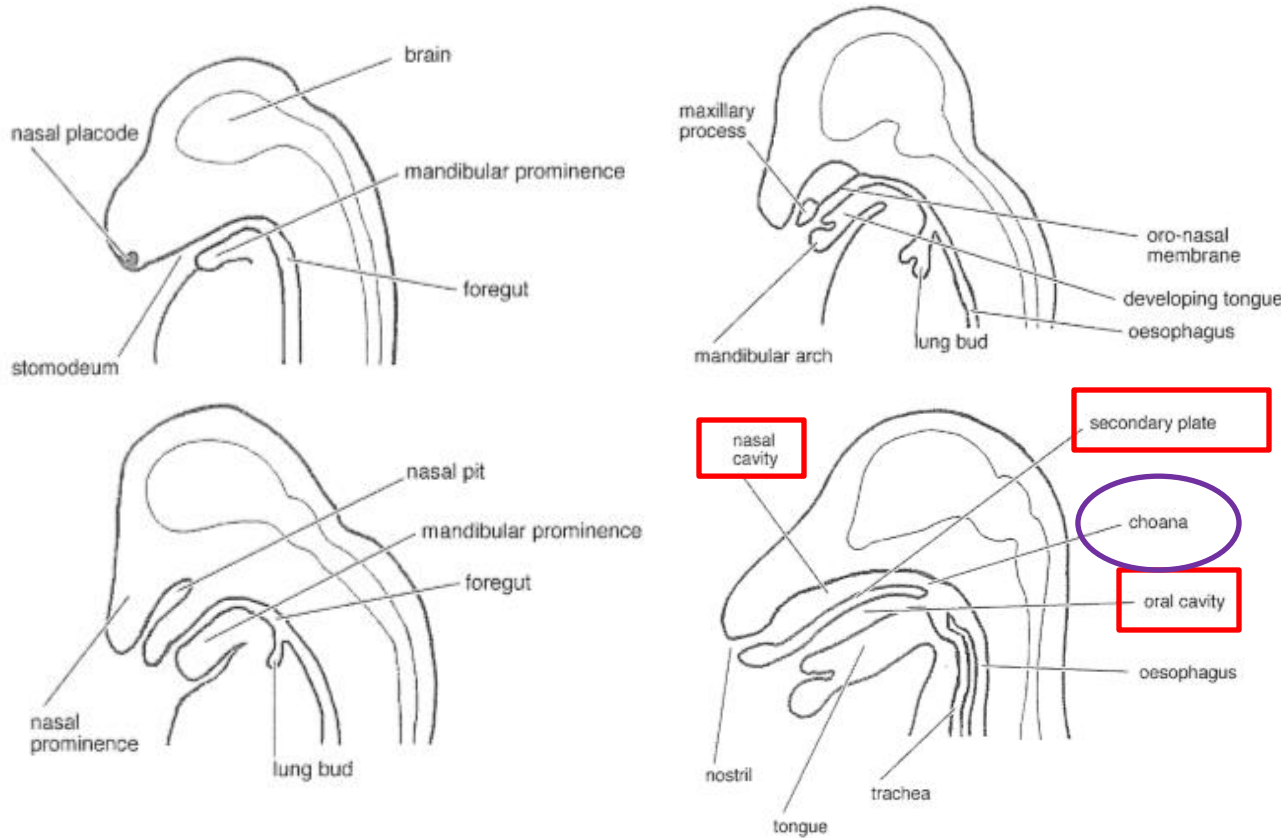


Figure 19.4 Longitudinal sections through the cranial regions of developing embryos at the level of the nasal pit showing progressive development of the nasal and oral cavities.

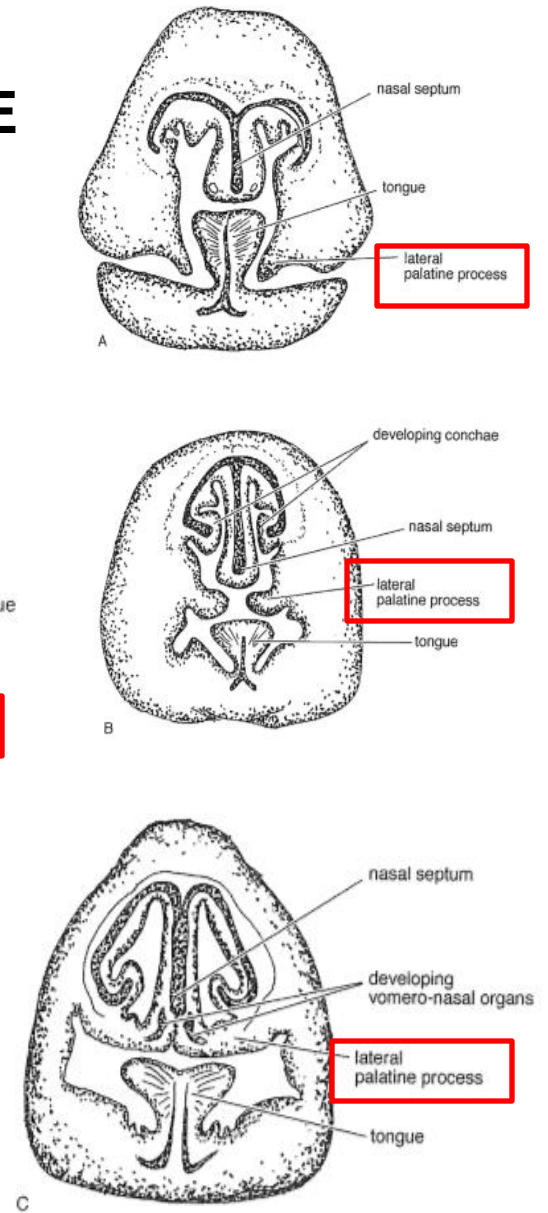


Figure 19.5 Cross-sections through the developing nasal and oral cavities in the pig showing the formation of the secondary palate, nasal septum and conchae.

FORMATION OF THE PALATE

- the rostralmost part of the palatine processes form bone that becomes:
 - palatine processes of the maxillae
 - horizontal lamina of the palatine bones in adults
- these bony structures and the derivatives of the primary palate form the adult hard palate

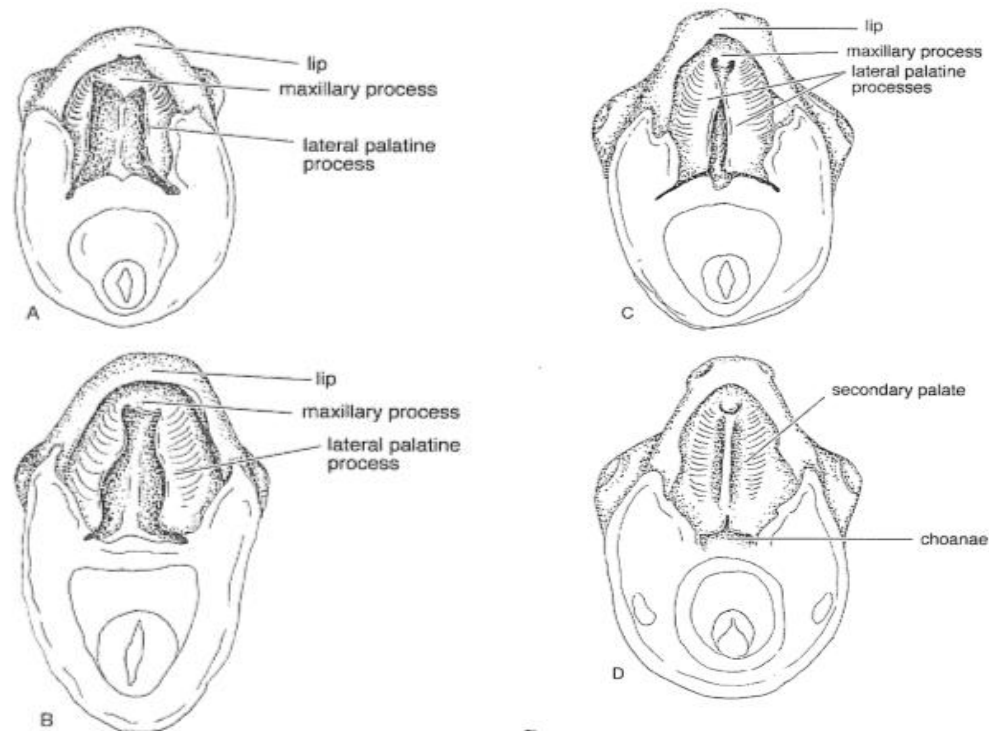


Figure 19.6 Ventral views of the developing porcine palatine processes showing progressive formation of the secondary palate.

FORMATION OF THE PALATE

SOFT PALATE:

- a portion of the caudalmost part of the hard palate do not become ossified and nor do they fuse with the embryonic nasal septum
- this partition formed caudally to the choanae, becomes the soft palate

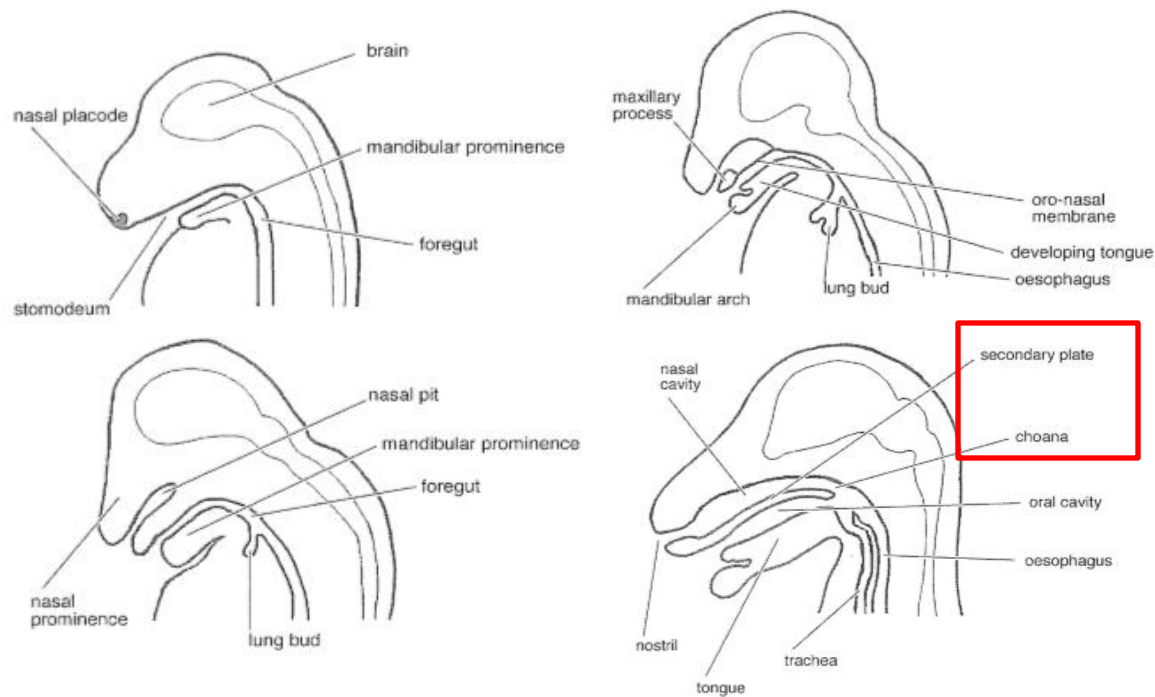


Figure 19.4 Longitudinal sections through the cranial regions of developing embryos at the level of the nasal pit showing progressive development of the nasal and oral cavities.

FORMATION OF THE PALATE

PALATINE CLOSURE:

- the primary and the secondary palates fused with each other

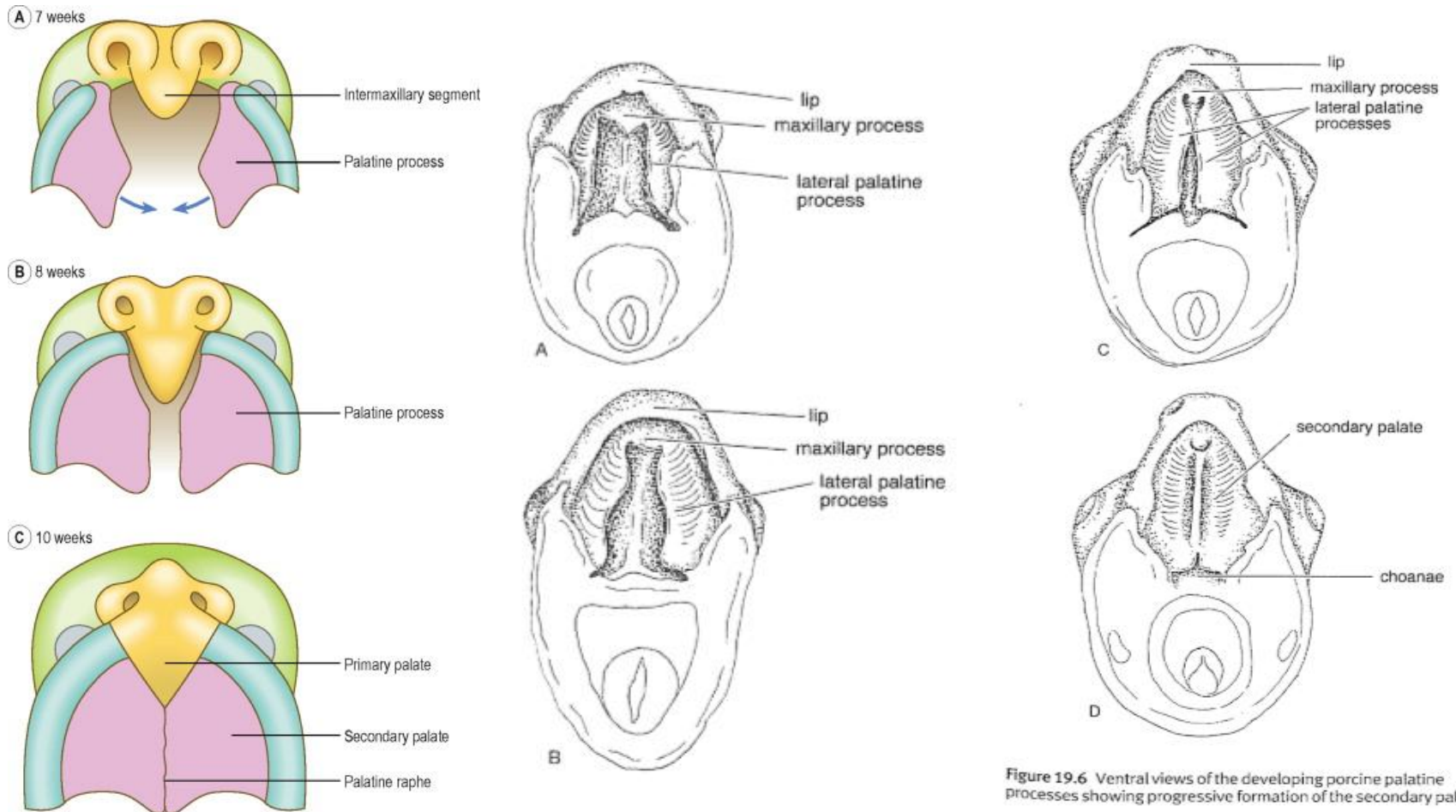


Figure 19.6 Ventral views of the developing porcine palatine processes showing progressive formation of the secondary palate.

LOWER RESPIRATORY SYSTEM

- the primordium of the lower respiratory system is the laryngotracheal groove

I. LARYNGOTRACHEAL GROOVE:

- develops caudal to the 4th pair of pharyngeal pouches

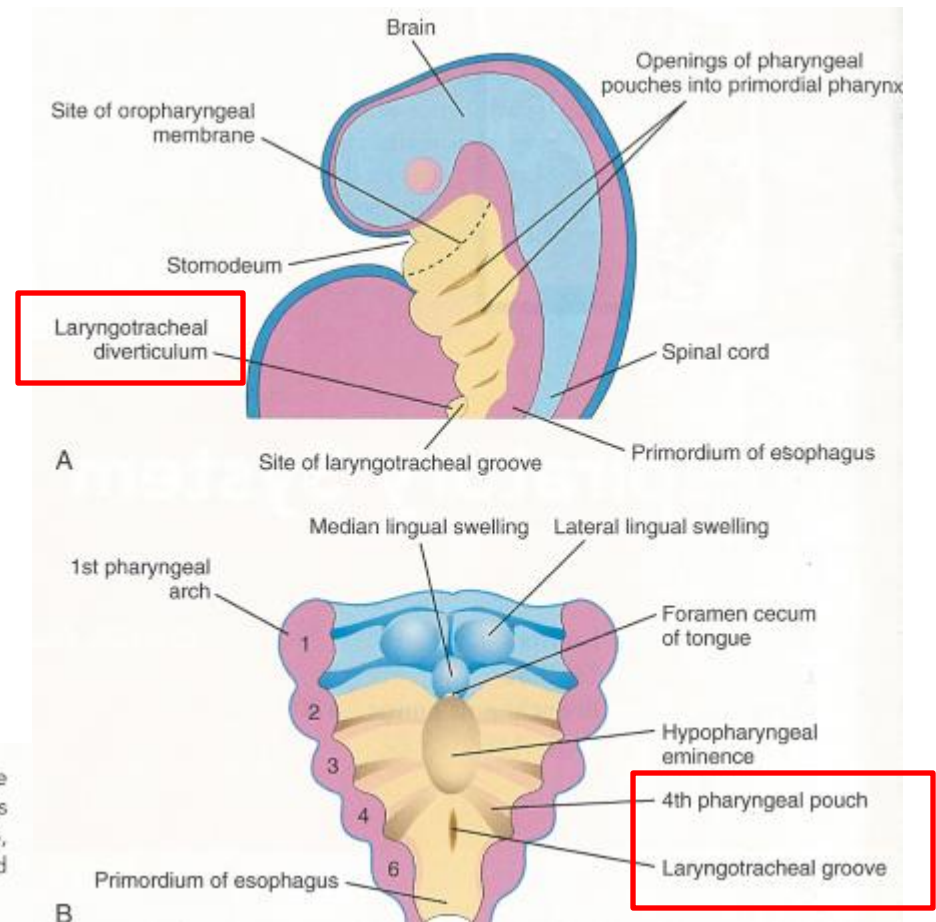


Figure 11-1 A, Sagittal section of the cranial half of the embryo. Lateral view, 4 weeks old. B, Horizontal section of the embryo, showing the floor of the primordial pharynx and the location of the laryngotracheal groove.

LOWER RESPIRATORY SYSTEM

I. LARYNGOTRACHEAL GROOVE:

the **endodermal lining of the laryngotracheal groove gives rise to the epithelium and glands of the:**

- a. larynx
- b. trachea
- c. bronchi
- d. pulmonary epithelium

- **the connective tissue, cartilage, smooth muscle in these structures develop from the splanchnic mesoderm surrounding the foregut**

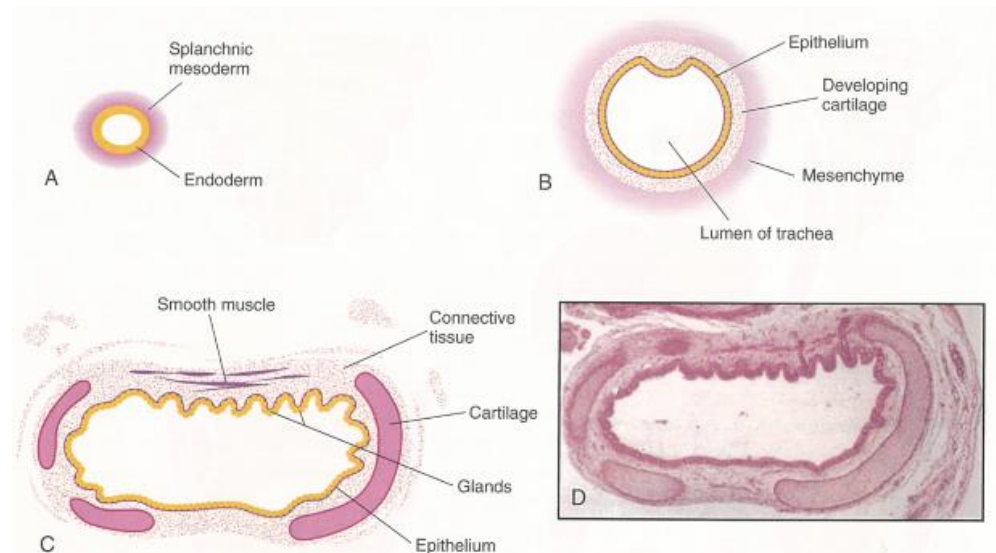
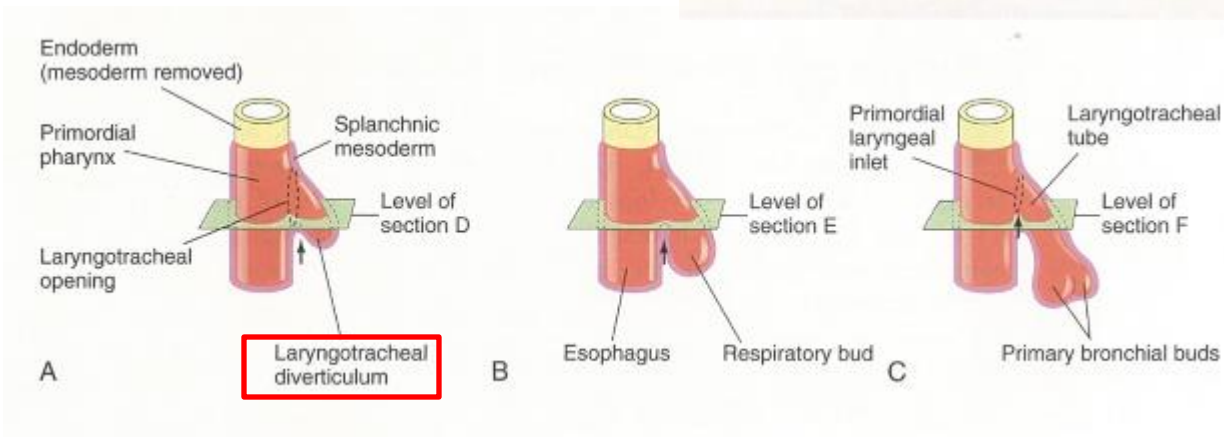
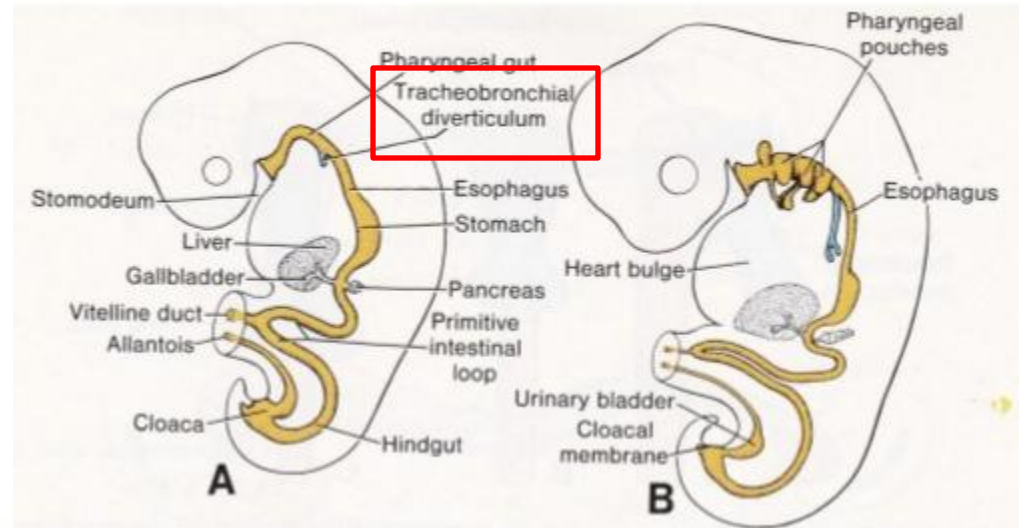


Figure 11-4 Transverse sections through the laryngotracheal tube, showing progressive stages in the development of the trachea. **A**, At 4 weeks. **B**, At 10 weeks. **C**, At 11 weeks. Note that the endoderm of the tube gives rise to the epithelium and the glands of the trachea and that the mesenchyme surrounding the tube forms the connective tissue, muscle, and cartilage (drawing of the micrograph shown in **D**). **D**, Photomicrograph of a transverse section of the developing trachea at 12 weeks. (From Moore KL, Persaud TVN, Shiota K: *Color Atlas of Clinical Embryology*, 2nd ed. Philadelphia, WB Saunders, 2000.)

LOWER RESPIRATORY SYSTEM

II. LARYNGOTRACHEAL DIVERTICULUM:

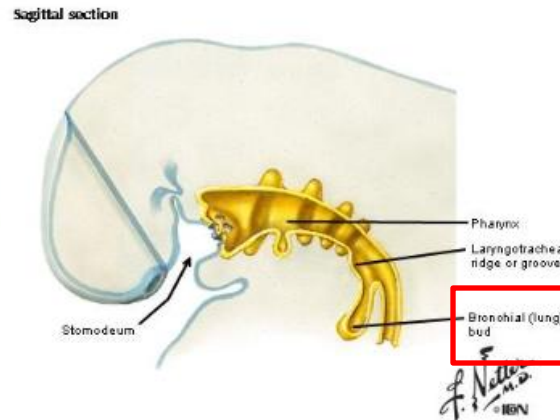
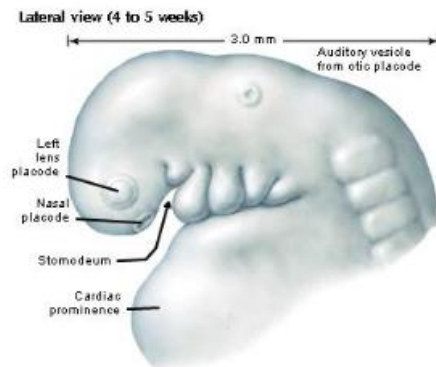
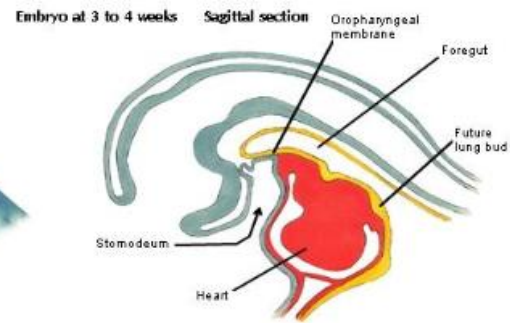
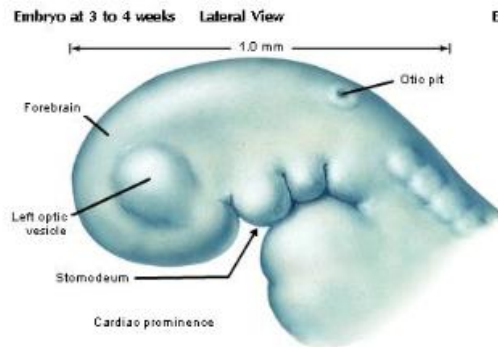
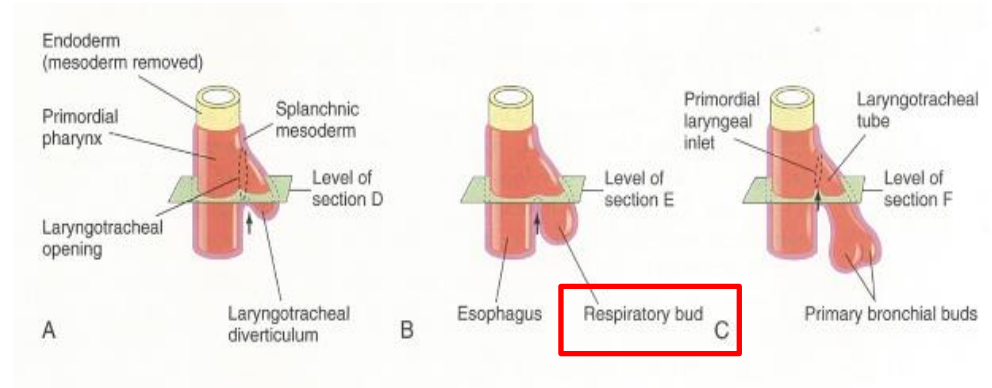
- a pouchlike laryngotracheal diverticulum has formed at the laryngotracheal groove
- located ventral to the caudal part of the foregut



LOWER RESPIRATORY SYSTEM

III. RESPIRATORY BUD:

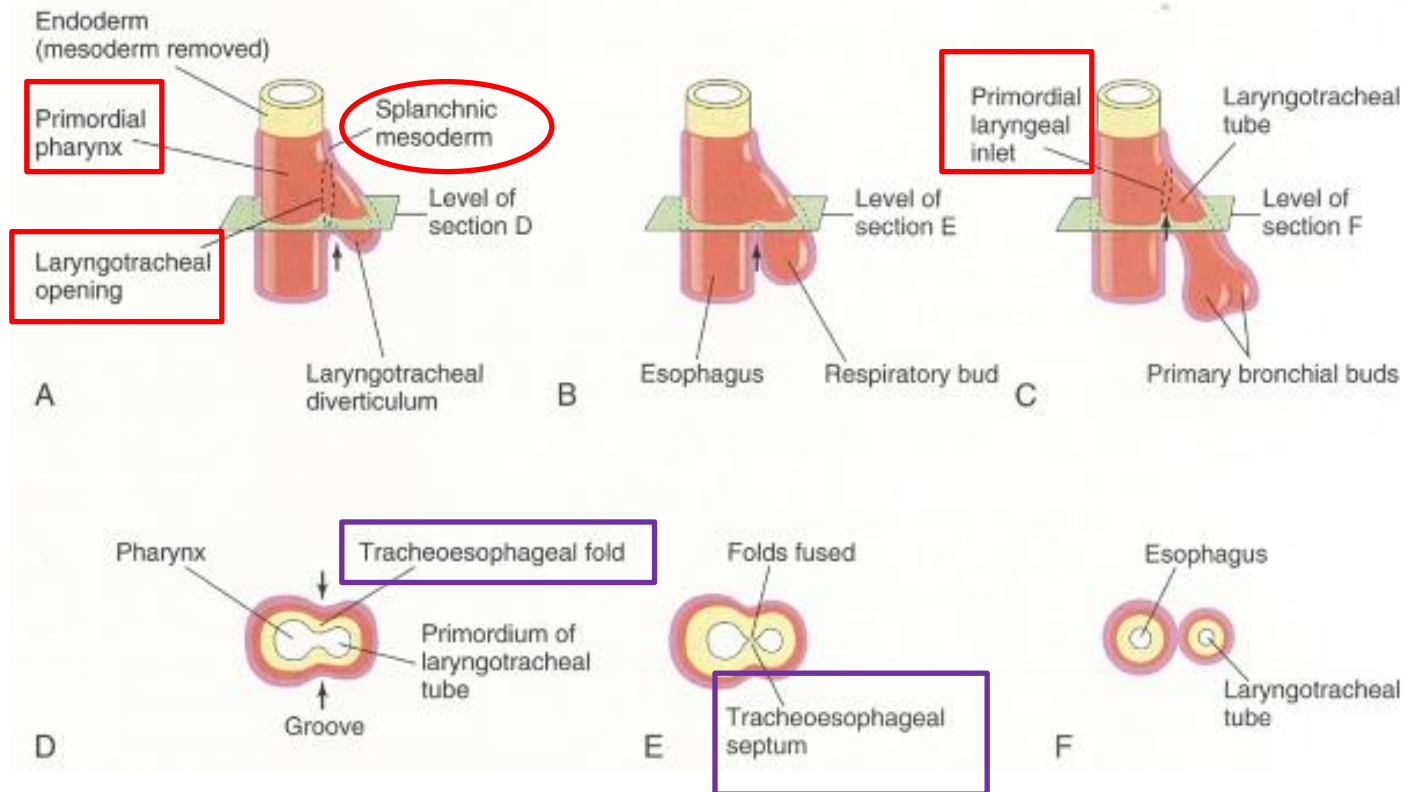
- the laryngotracheal diverticulum elongates
- distal end of the diverticulum elongates to form the globular respiratory bud



LOWER RESPIRATORY SYSTEM

II. LARYNGOTRACHEAL DIVERTICULUM:

- a. the laryngotracheal diverticulum soon separates from the primordial pharynx
- b. maintains communication with the primordial pharynx through the primordial laryngeal inlet
- c. as the laryngotracheal diverticulum elongates – it is invested with splanchnic mesoderm

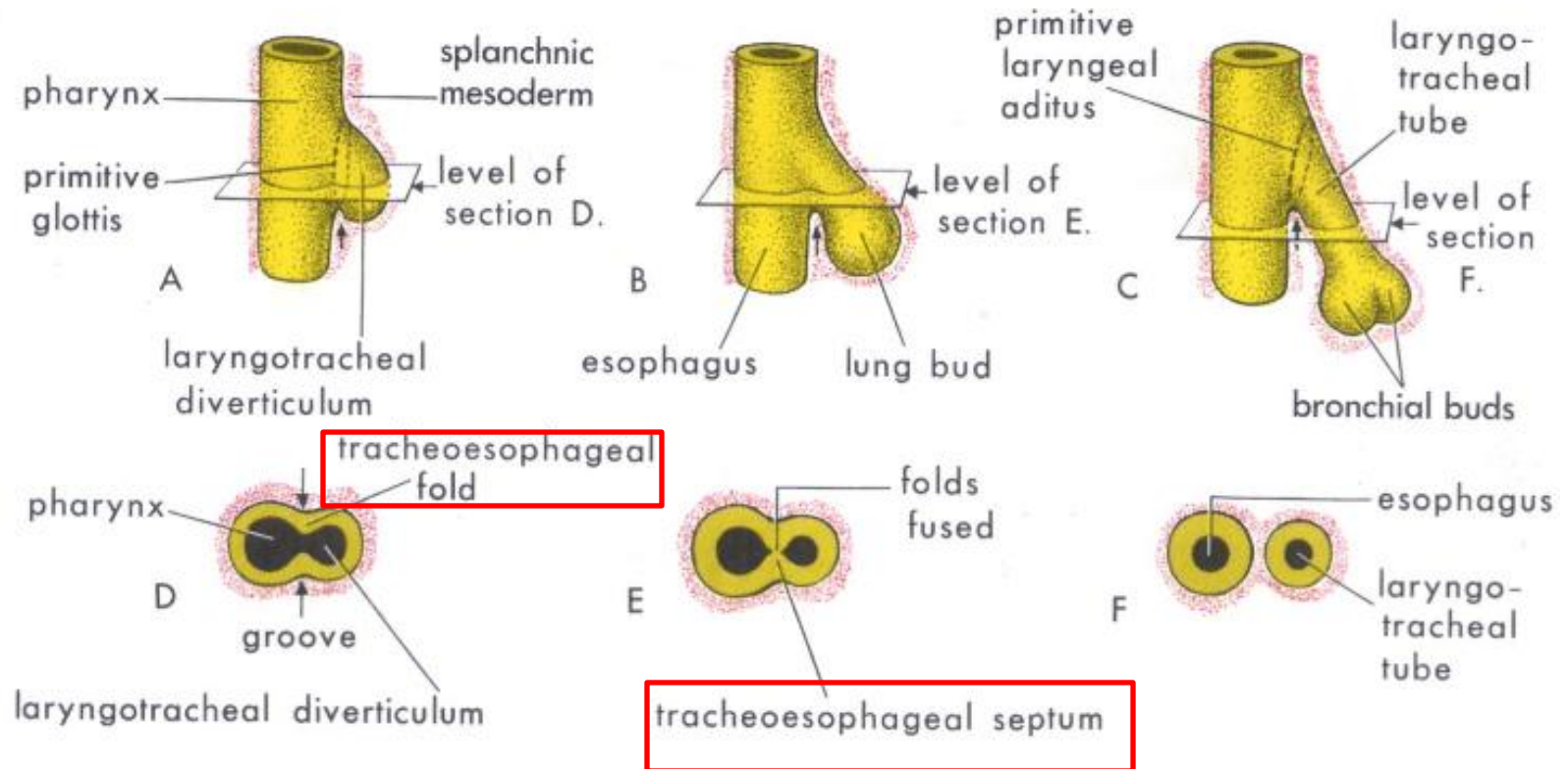


LOWER RESPIRATORY SYSTEM

II. LARYNGOTRACHEAL DIVERTICULUM:

d. longitudinal tracheoesophageal folds develop in the laryngotracheal diverticulum

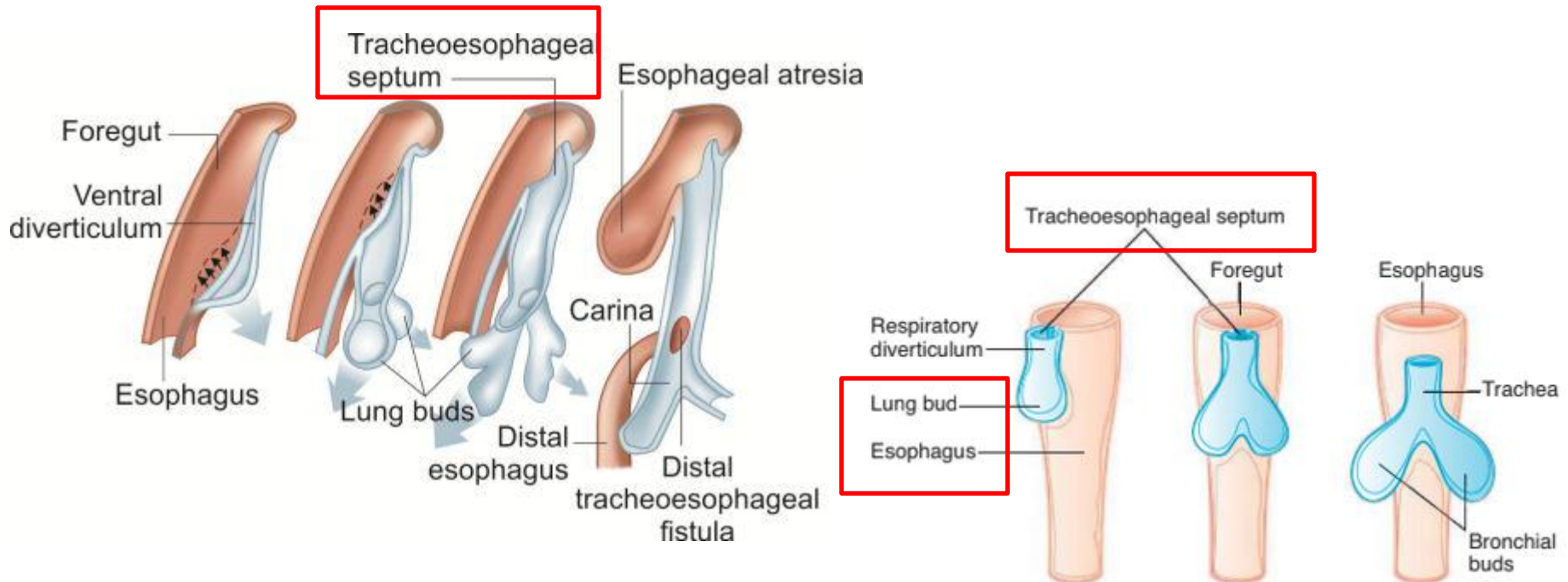
e. the folds approach each other – and fuse to form a partition the tracheoesophageal septum



LOWER RESPIRATORY SYSTEM

TRACHEOESOPHAGEAL SEPTUM:

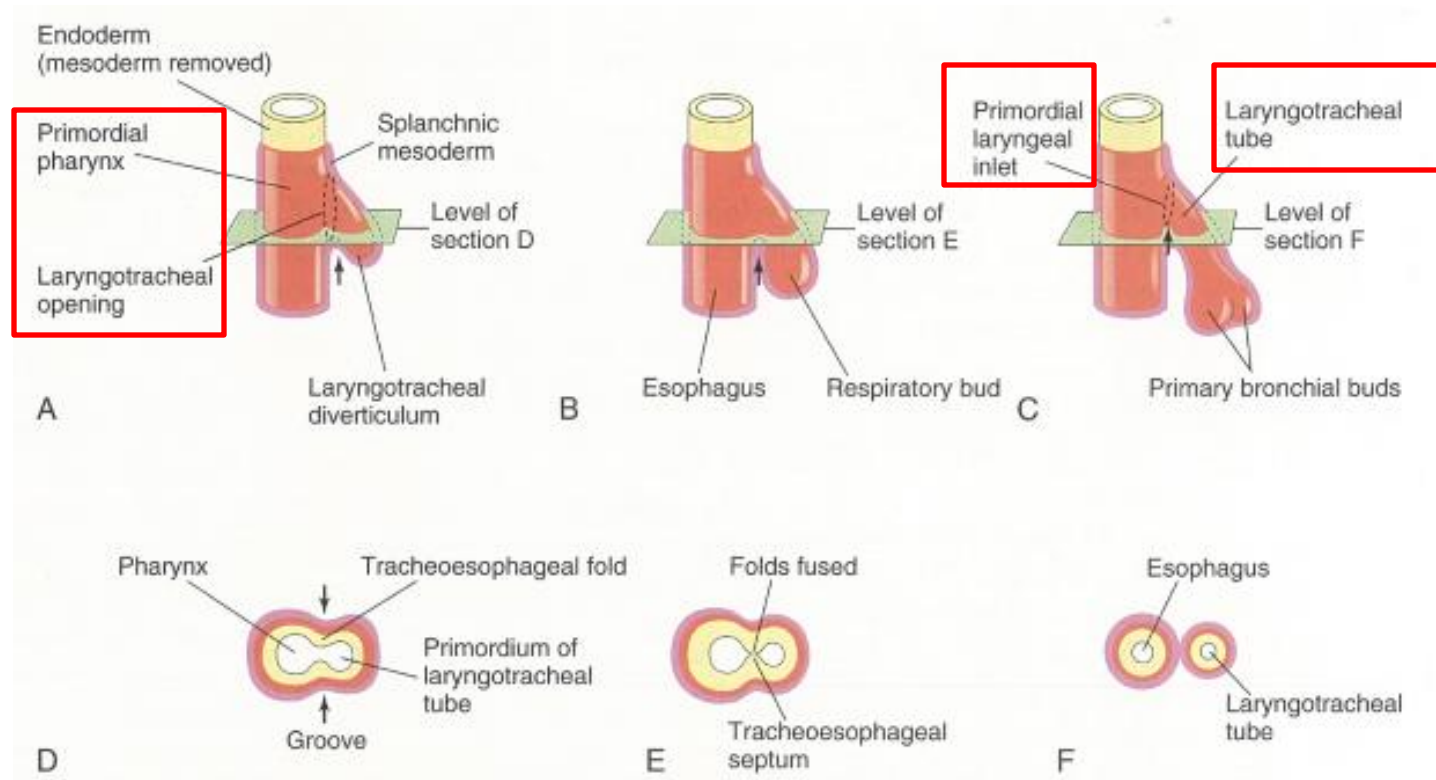
- **divides the cranial part of the foregut into:**
 - a ventral part – the laryngotracheal tube (primordium of the larynx, trachea, bronchi, lungs)
 - a dorsal part – primordium of the oropharynx, esophagus



LOWER RESPIRATORY SYSTEM

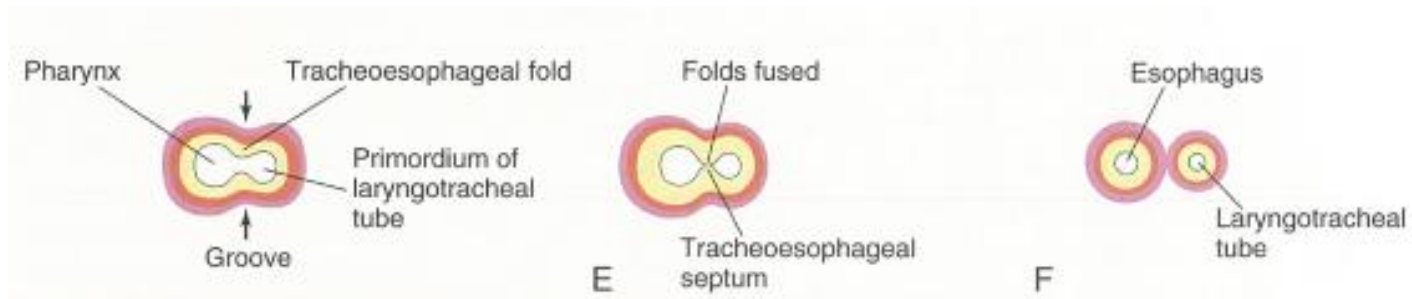
PRIMORDIAL LARYNGEAL INLET:

- is the opening of the laryngotracheal tube into the pharynx



DEVELOPMENT OF LARYNX

- a. the epithelial lining of the larynx develops from the endoderm of the cranial end of the laryngotracheal tube
- b. cartilages of the larynx develop from cell populations in the 4th and 6th pairs of pharyngeal arches
 1. the laryngeal cartilages develop from mesenchyme that derived from neural crest cells
 2. the mesenchyme at the cranial end of the laryngotracheal tube proliferates – producing paired arytenoid swellings
 3. these swellings grow toward the tongue converting the primordial glottis into a T – shaped laryngeal inlet
 4. the laryngeal epithelium proliferates rapidly – resulting a temporary occlusion of the laryngeal lumen
 5. the lumen of the larynx undergoes recanalization
 6. the laryngeal ventricles form during this recanalization



DEVELOPMENT OF LARYNX

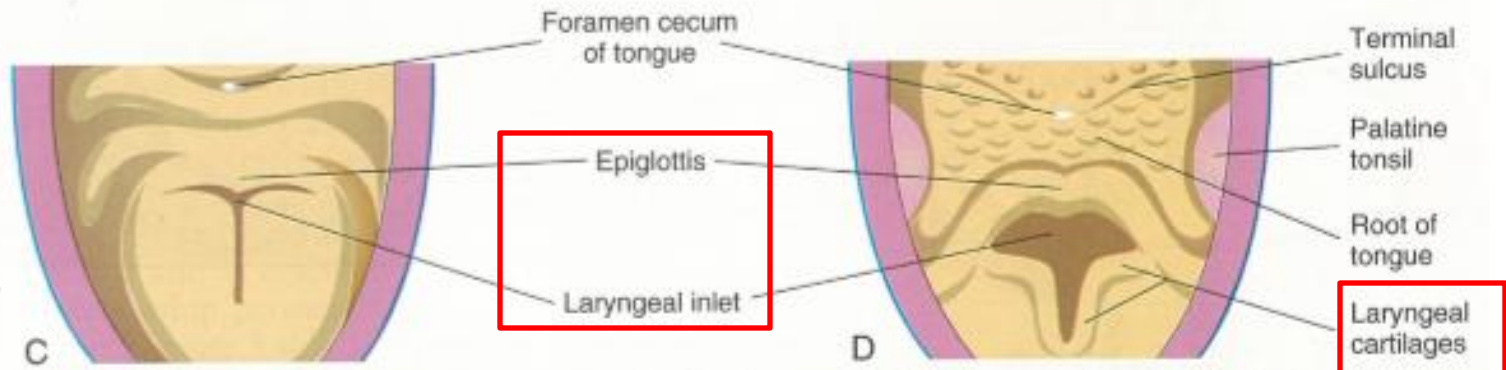
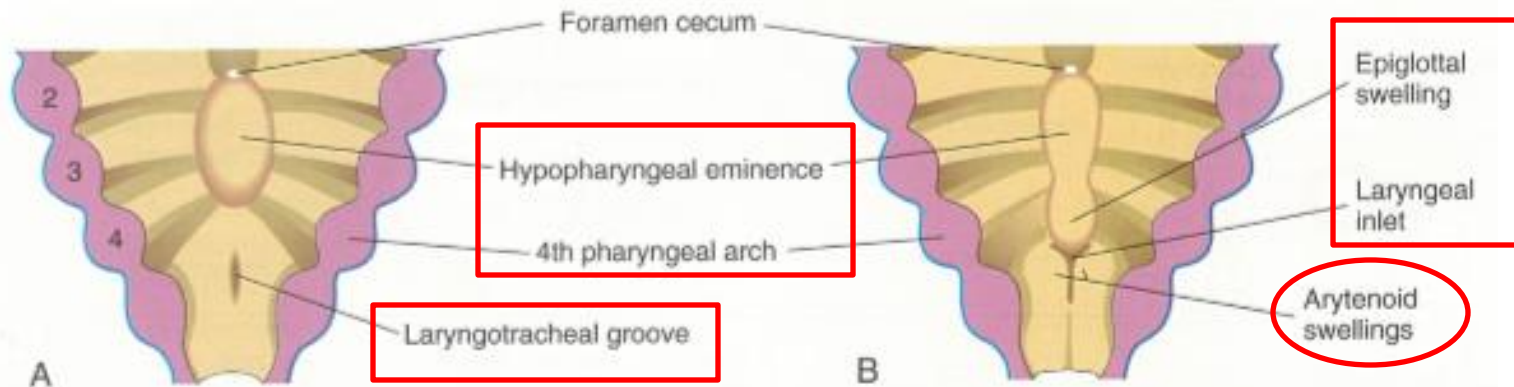
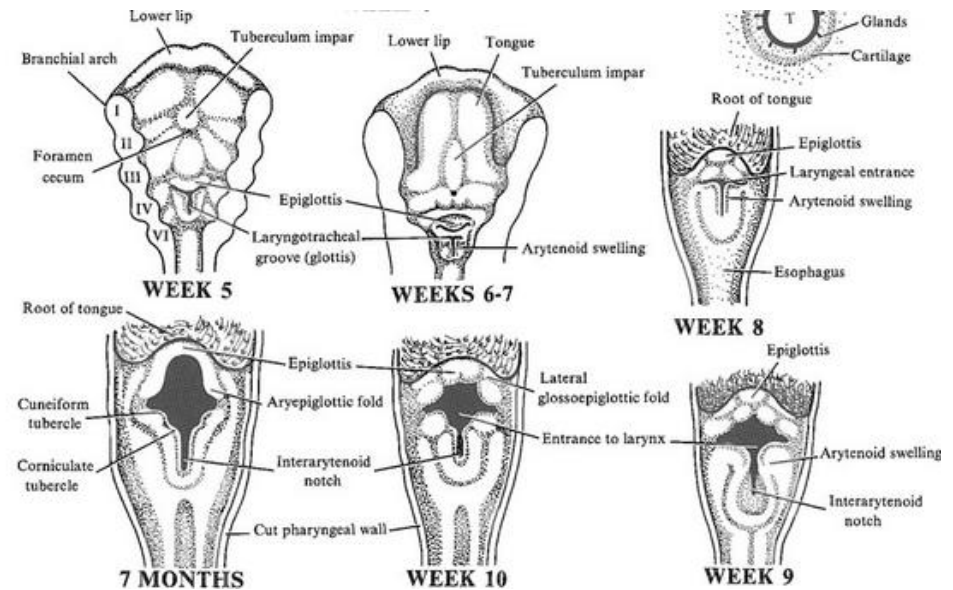
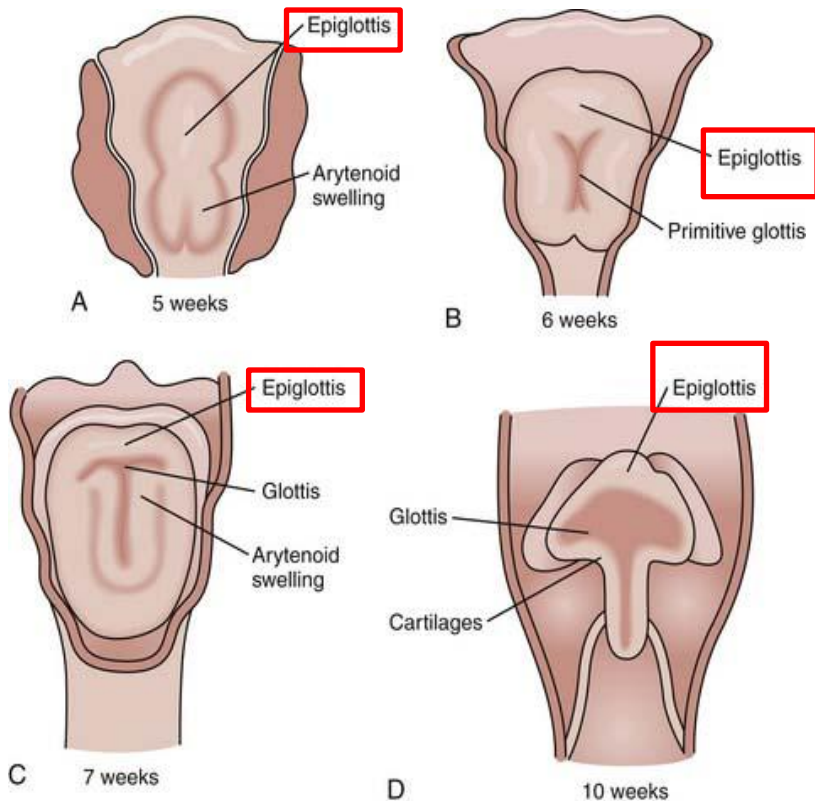


Figure 11-3 Successive stages in the development of the larynx. **A**, At 4 weeks. **B**, At 5 weeks. **C**, At 6 weeks. **D**, At 10 weeks. The epithelium lining the larynx is of endodermal origin. The cartilages and muscles of the larynx arise from the mesenchyme in the fourth and sixth pairs of pharyngeal arches. Note that the laryngeal inlet changes in shape from a slitlike opening to a T-shaped inlet as the mesenchyme surrounding the developing larynx proliferates.

DEVELOPMENT OF LARYNX

7. the epiglottis develops from the caudal part of the hypopharyngeal eminence (produced by the proliferation of mesenchyme in the ventral ends of the 3rd and 4th pharyngeal arches)

8. the larynx and epiglottis grow after birth – and the epiglottis and larynx descent to reach their position



<https://discovery.lifemapsc.com/library/review-of-medical-embryology/chapter-58-development-of-the-lower-respiratory-system-larynx-and-trachea>

<https://aneskey.com/structure-and-development-of-the-upper-respiratory-system-in-infants-and-children/>

DEVELOPMENT OF LARYNX

9. the laryngeal muscles develop from the myoblasts in 4th and 6th pairs of pharyngeal arches

- the muscles are innervated by the laryngeal branches of the vagus nerves

EMBRYOLOGICAL DEVELOPMENT OF LARYNX

Structure	Source
Laryngeal mucosa	Endoderm of cephalic part of foregut
Laryngeal cartilages	Mesenchyme
Epiglottis	Hypobranchial eminence
Upper part of thyroid cartilage	4th branchial arch
lower part of thyroid cartilage, cricoid, corniculate, and cuneiform cartilages	6th branchial arch
Intrinsic muscles of larynx	6th branchial arch

DEVELOPMENT OF TRACHEA

- the endodermal lining of the laryngotracheal tube distal to the larynx differentiates into:

- a. the epithelium and the glands of the trachea
- b. the pulmonary epithelium

- the cartilage, connective tissue, muscles of the trachea derived from the splanchnic mesoderm surrounding the laryngotracheal tube

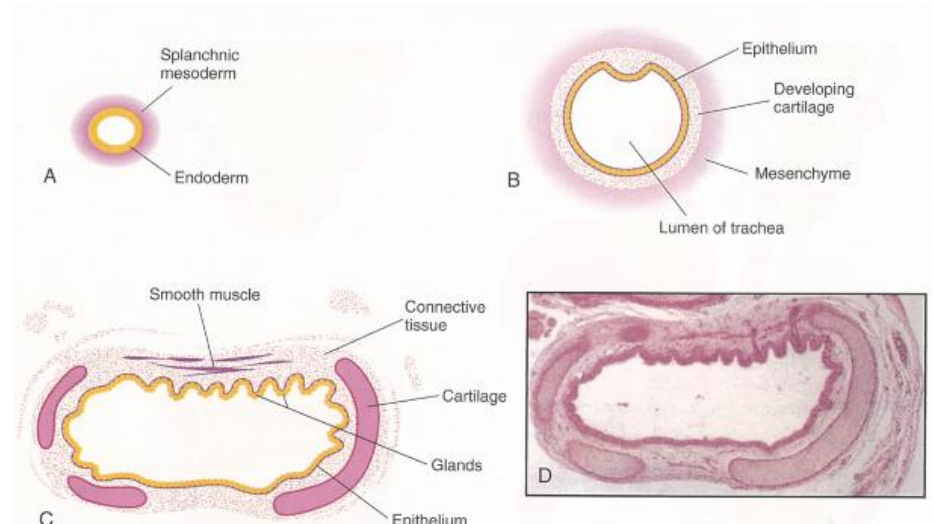
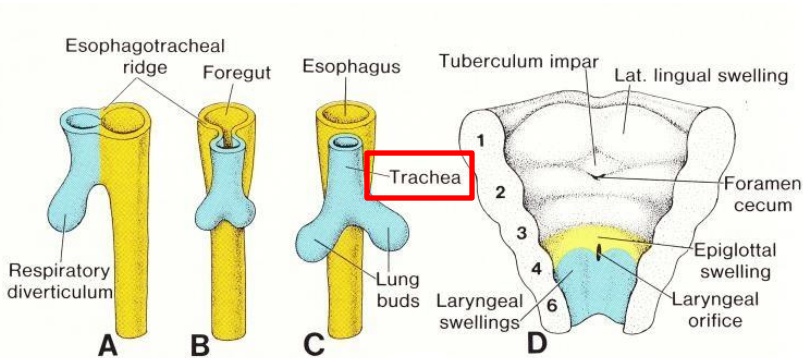


Figure 11-4 Transverse sections through the laryngotracheal tube, showing progressive stages in the development of the trachea. **A**, At 4 weeks. **B**, At 10 weeks. **C**, At 11 weeks. Note that the endoderm of the tube gives rise to the epithelium and the glands of the trachea and that the mesenchyme surrounding the tube forms the connective tissue, muscle, and cartilage (drawing of the micrograph shown in **D**). **D**, Photomicrograph of a transverse section of the developing trachea at 12 weeks. (From Moore KL, Persaud TVN, Shiota K: *Color Atlas of Clinical Embryology*, 2nd ed. Philadelphia, WB Saunders, 2000.)

DEVELOPMENT OF BRONCHI AND LUNGS

1. the respiratory bud (lung bud) developed at the caudal end of the laryngotracheal diverticulum
2. the respiratory bud divides into two outpouching – primary bronchial buds
3. later secondary and tertiary bronchial buds form and grow into the pericardioperitoneal canals
4. together with the surrounding splanchnic mesoderm, the bronchial buds differentiate into :
 - a. the bronchi and their ramifications in the lungs

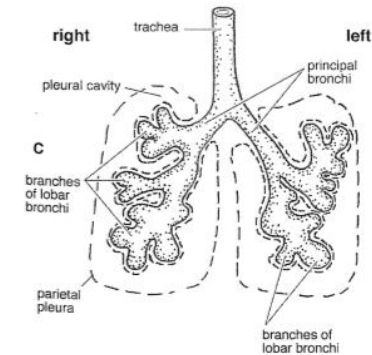
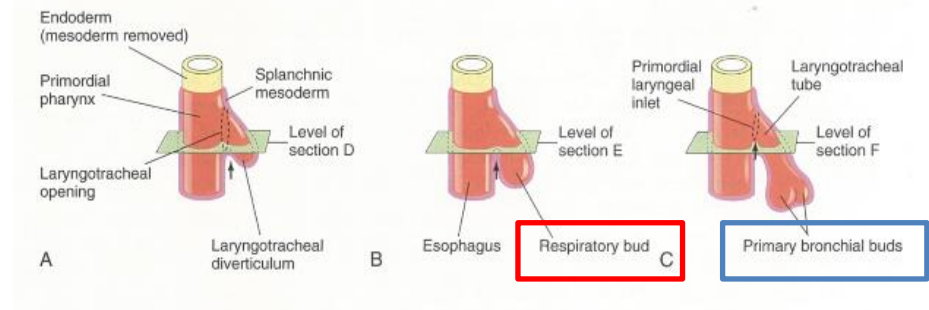
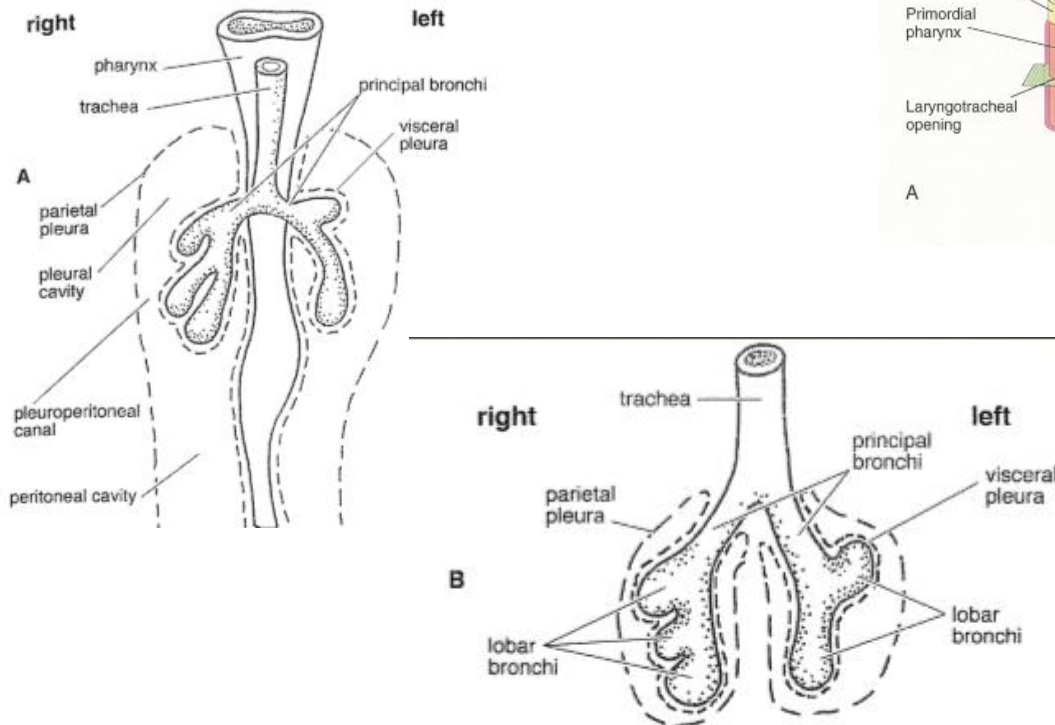
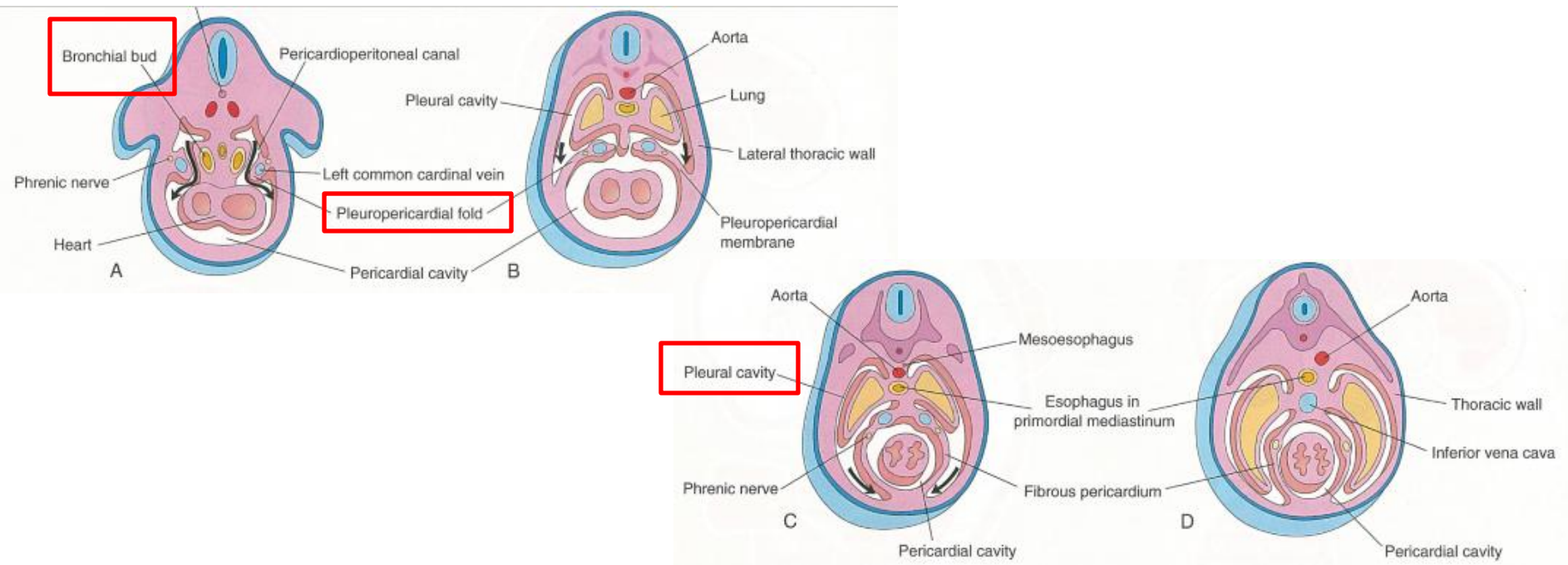


Figure 16.2 Ventral views of sequential stages in lung development showing the formation of the principal bronchi and the origins of lobar bronchi and their branches.

DEVELOPMENT OF BRONCHI AND LUNGS

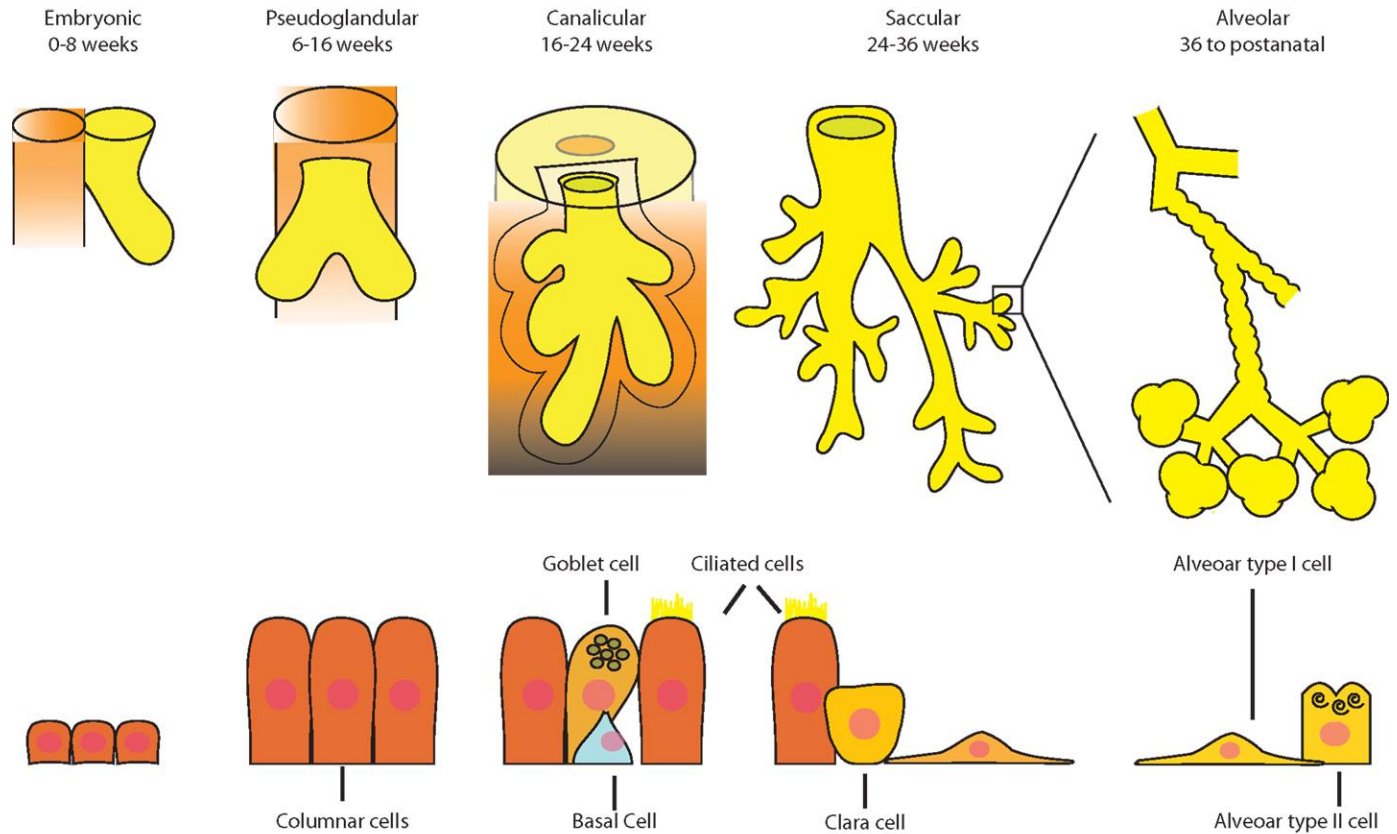
7. as the bronchi develop, **cartilaginous plates are formed from the surrounding splanchnic mesenchyme**
8. **the bronchial smooth muscle, connective tissue, capillaries, pulmonary connective tissue formed by the splanchnic mesenchyme**
9. as the lungs develop they acquire a layer of visceral pleura from the splanchnic mesoderm
10. the thoracic bodywall becomes lined by a layer of parietal pleura derived from the somatic mesoderm
11. the lungs and the pleural cavity grow caudally into the mesenchyme of the body wall and lie close to the heart



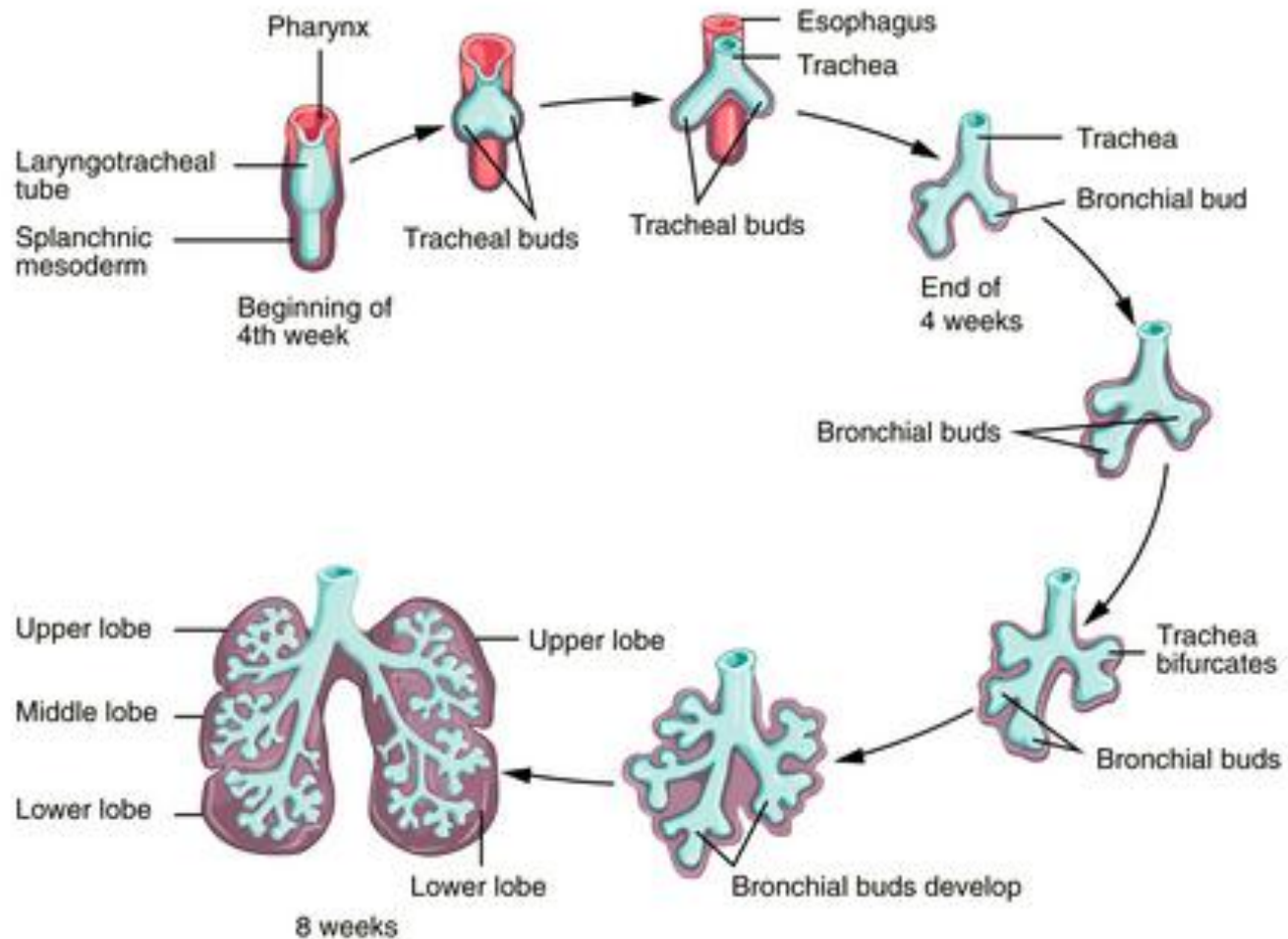
MATURATION OF LUNGS

the maturation of the lungs divided into four stages:

1. pseudoglandular stage
2. canalicular stage
3. terminal stage
4. saccular stage



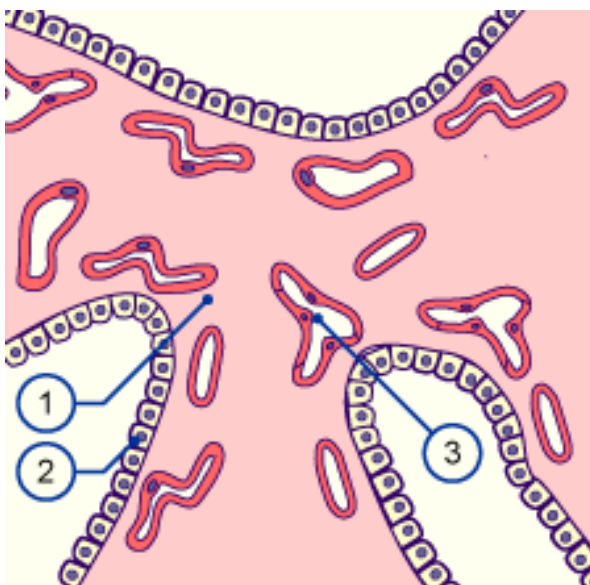
MATURATION OF LUNGS



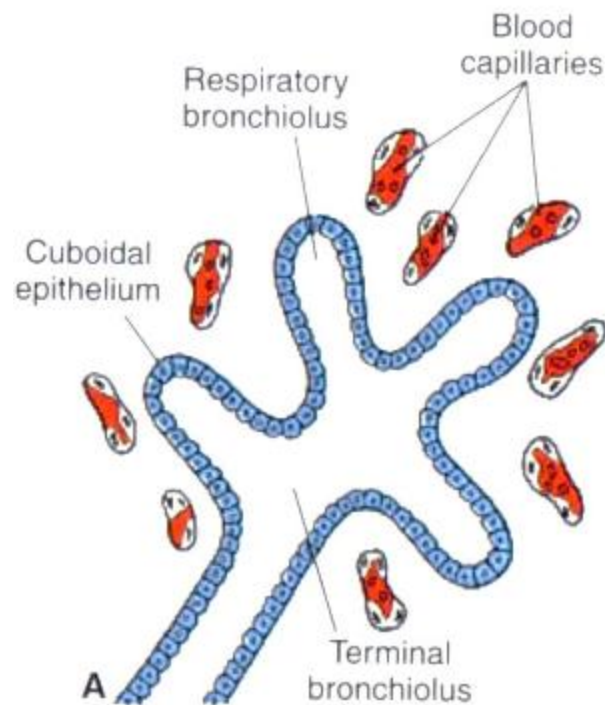
MATURATION OF LUNGS

PSEUDOGLANDULAR STAGE (PERIOD):

- **the developing lungs resemble** on a histological basis **an exocrine gland** during the early part of this period
- **all of the major elements of the lung have formed except those involved in gas exchanges**
- **respiration is not possible**



- 1 Lung mesenchyma
- 2 Type II pneumocytes
- 3 Capillaries

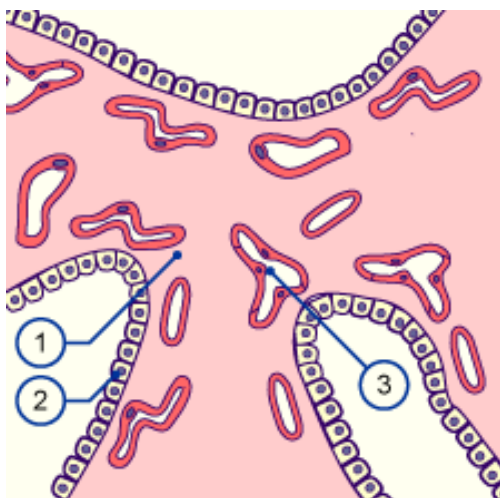


Canalicular period -
16 - 24 weeks

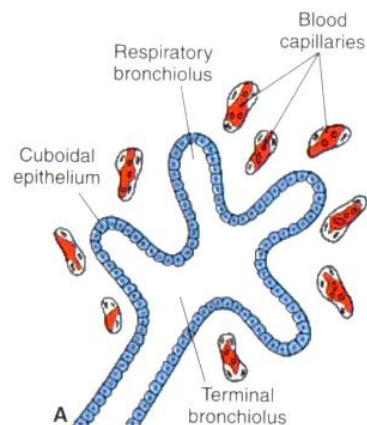
MATURATION OF LUNGS

CANALICULAR STAGE (PERIOD):

- overlaps the pseudoglandular stage, because the cranial segments of the lung mature faster than the caudal ones
- during this period **the lumina of the bronchi and the terminal bronchioli become larger**
- during this period **the lung tissue becomes highly vascular**
- **each terminal bronchioli give rise to respiratory bronchioles**
- **each respiratory bronchioles divide into alveolar ducts**
- **some thin – walled terminal sacs (primordial alveoli) developed at the end of the respiratory bronchioles**



- 1 Lung mesenchyma
- 2 Type II pneumocytes
- 3 Capillaries

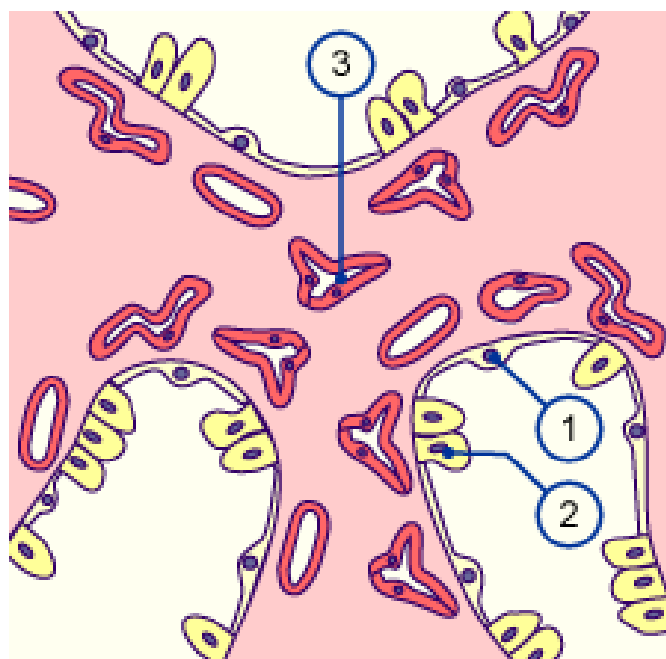


Canalicular period -
16 - 24 weeks

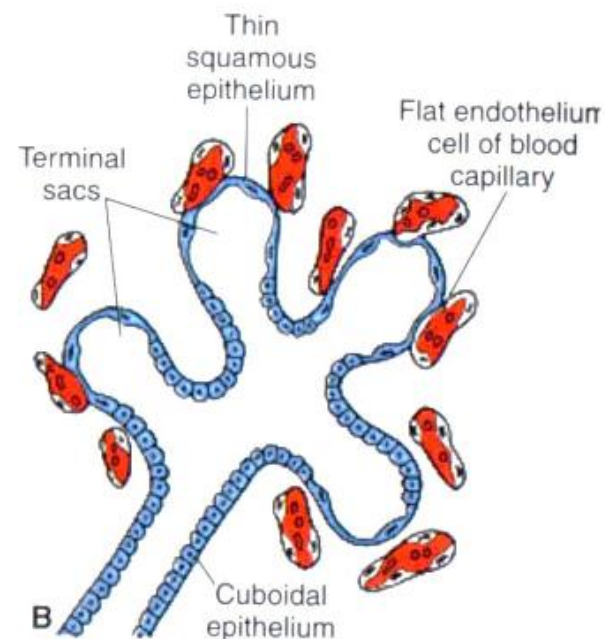
MATURATION OF LUNGS

TERMINAL SAC STAGE (SACCULAR STAGE) :

- many more terminal sacs develop
- the terminal sacs are lined by type I pneumocytes – across which gas exchanges occurs
- the capillary network proliferates rapidly in the mesenchyme around the developing alveoli
- type II pneumocytes scattered among type I pneumocytes
- type II pneumocytes secrete pulmonary surfactant



- 1 Type I pneumocytes
- 2 Type II pneumocytes
- 3 Capillaries

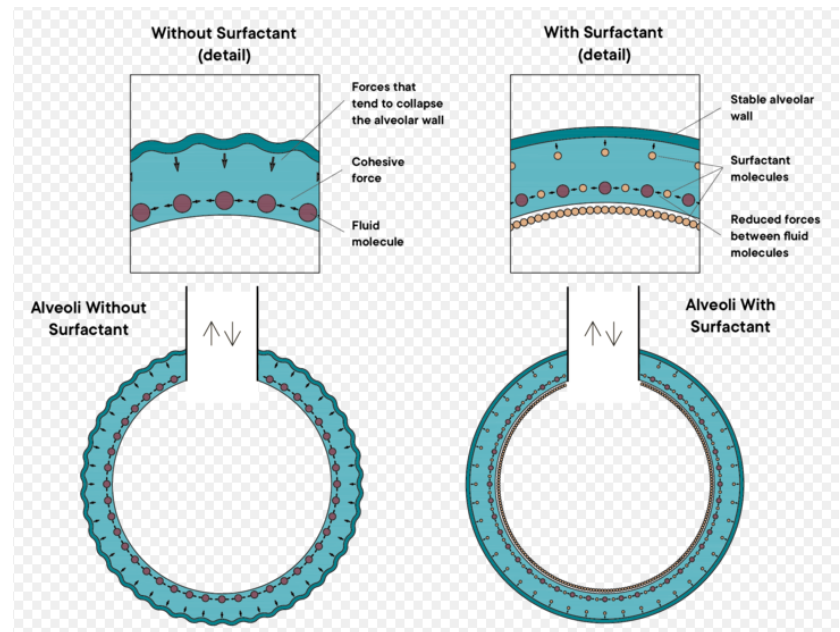


Terminal sac Period
24 weeks - birth

MATURATION OF LUNGS

SURFACTANT:

- produced by type II pneumocytes
- complex mixture of phospholipids and proteins
- forms a monomolecular film over the interior walls of the alveolar sacs
- counteracts surface tension forces at the air – alveolar interface
- facilitates expansion of the terminal sacs (primordial alveoli)

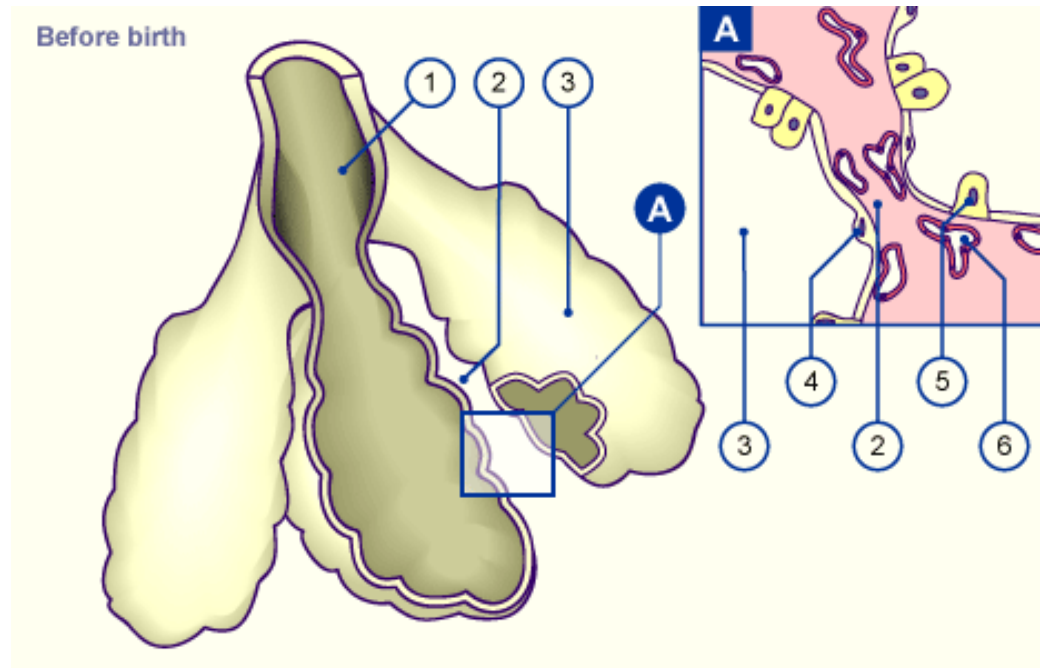


MATURATION OF LUNGS

ALVEOLAR PERIOD:

- at the beginning of the alveolar period , **each respiratory bronchiole terminates in a cluster of thin walled terminal sacs these are separated from one another by loose connective tissue**
- **these terminal sacs represent future alveolar ducts**
- **the alveolocapillary membrane (pulmonary diffusion barrier or respiratory membrane) is sufficiently thin to allow gas exchange**

- 1 Alveolar duct
- 2 Primary septum
- 3 Alveolar sac
- 4 Type I pneumocyte
- 5 Type II pneumocyte
- 6 Capillaries

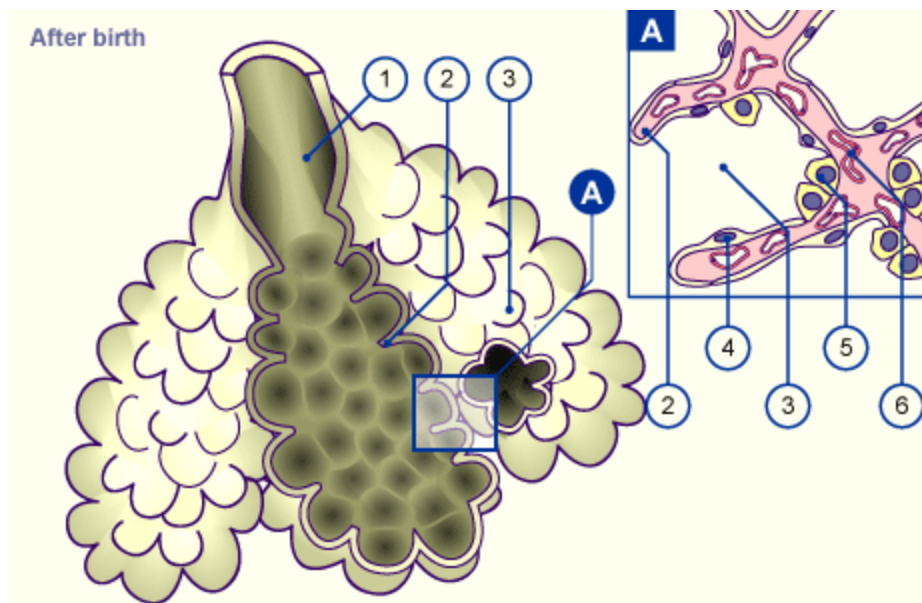


MATURATION OF LUNGS

ALVEOLAR PERIOD:

- all mammals form alveoli postnatally
- the increase in the number of alveoli after birth accounts for the major part of the early postnatal growth of the lung
- later the growth of lung is primarily due to an increase in alveolar size
- little or no branching of the respiratory tree occurs postnatally but the major air passage (bronchi) do increase in size

- 1 Alveolar duct
- 2 Secondary septum
- 3 Alveoli
- 4 Type I pneumocyte
- 5 Type II pneumocyte
- 6 Capillaries



MATURATION OF LUNGS

three factors essential for normal lung development:

- a. adequate thoracic space for lung growth**
- b. adequate amniotic fluid volume**
- c. fetal breathing movements**

MATURATION OF LUNGS

FETAL BREATHING MOVEMENTS:

<https://www.youtube.com/watch?v=QvTnX4e279k>

- occur before birth
- a) exerts sufficient force to cause aspiration of amniotic fluid into the lungs
- b) these movements stimulate lung development creating pressure gradient between the lungs and the amniotic fluid
- c) by birth the fetus has had the advantage of several months of breathing exercise
- d) fetal breathing movements increase as the time of delivery approaches

MATURATION OF LUNGS

FETAL BREATHING MOVEMENTS:

e. at birth the lungs are approx. half – filled with amnionic fluid derived from amnionic cavity, the lungs and the tracheal glands

f. Aeration of the lungs at birth occurs - the intra – alveolar fluid will be replaced rapidly by air

the fluid in the lungs is cleared at birth by three routes:

- 1. through the mouth and nose by pressure on the thorax during vaginal delivers**
- 2. into the pulmonary capillaries and pulmonary arteries and veins**
- 3. into lymphatics**

BIBLIOGRAPHY

William K. Latshaw: Veterinary Developmental Anatomy, A Clinically Oriented Approach, 1987

T.A. Mcgeady, P.J. Quinn, E.S. FitzPatrick and M.Z. Ryan: Veterinary Embryology, Blackwell Publishing, 2006

Keith L. Morre, T.V.N. Persaud, Mark G. Torchia: before we were Born, Essentials of Embryology and Birth defects, 8th Edition, Elsevier