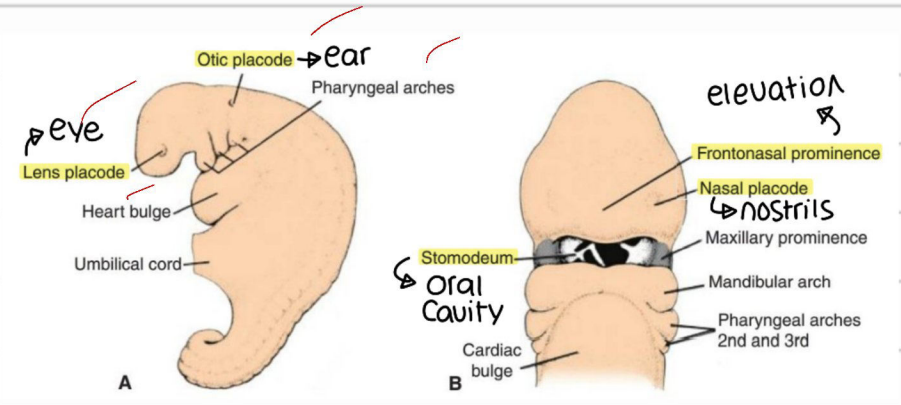
RS EMBRYOLOGY

NOSE AND PALATE

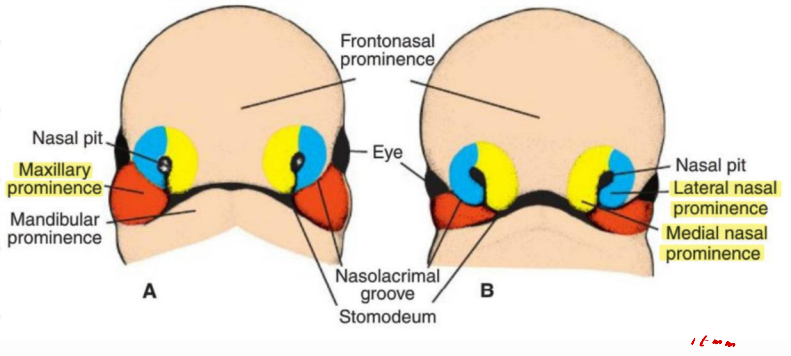


* at the end of 4th week
  - facial prominences begin to develop (mainly of neural crest mesenchyme & first pair of pharyngeal arches)
- prominence: an elevation that happens due to increased proliferation in a certain area

prominence	direction of proliferation	involves in forming:
① frontonasal	ventral to brain vesicle (bony)	upper part of stomedeum & nasal septum
	on both sides, ectoderm cells proliferate (induced by ventral fore brain)	olfactory placodes (nasal)
② maxillary	internally	jaw, upper lip, nose
③ mandibular		mandible, lower lip

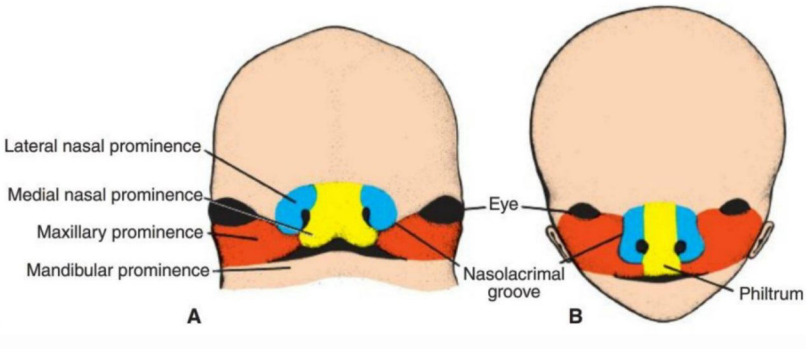
---

* during 5th week:
  - nasal placodes invaginate inwards → form nasal pits (nostril) & nasal prominences (lateral & medial) → dilation of structure forms vestibule



---

* during the following 2 weeks:
  - maxillary prominence grows medially → pushes medial nasal prominences → fusion of maxillary & nasal prominences



* Structures that form nose

① frontonasal → septum
② medial nasal (x2) → tip
③ lateral nasal (x2) → alae
④ olfactory pit → nostril & vestibule

→ 5 prominences

TABLE 17.3 Structures Contributing to Formation of the Face

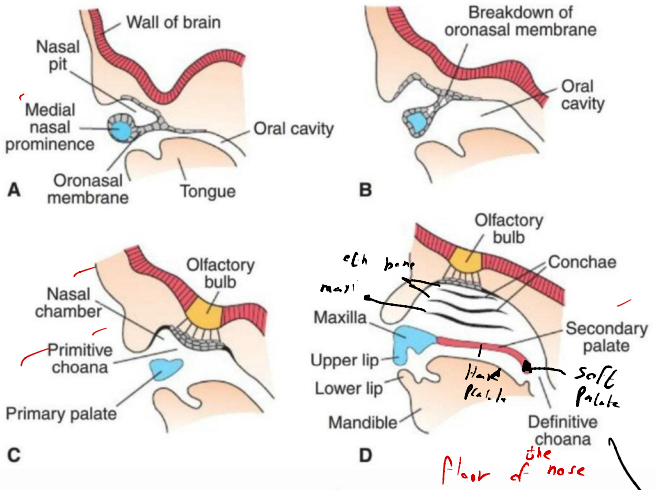
Prominence	Structures Formed
Frontonasal[a]	Forehead, bridge of nose, and medial and lateral nasal prominences
Maxillary	Cheeks, lateral portion of upper lip
Medial nasal	Philtrum of upper lip, crest, and tip of nose
Lateral nasal	Alae of nose
Mandibular	Lower lip

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

---

* during 6th week

A) nasal pits canalize due to:
① growth of nasal prominences
② their penetration into underlying mesenchyme (due to signaling of fibroblast growth factors)



B) nasal pits are seperated from oral cavity by oronasal membrane by way of forming primitive choanae (foramina) which lie on each side of midline & behind 1° palate

D) then 2° palate forms & development of nasal chambers (further seperation of oral & nasal cavities → definitive choanae lie at junction of nasal cavity & pharynx (lateral wall)

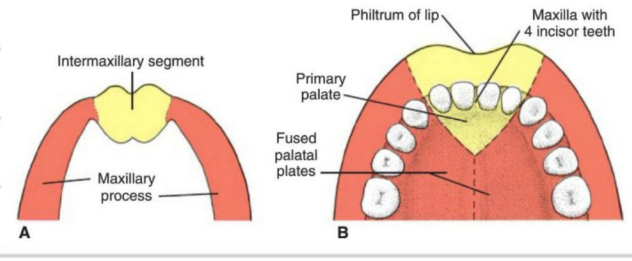
---

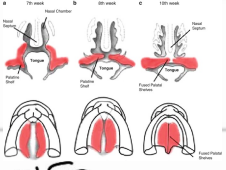
* paranasal sinuses → develop as diverticula (canalization) from lateral wall to target skull bone (frontal, maxillary, esthmoidal, sphenoidal) / max size at puberty

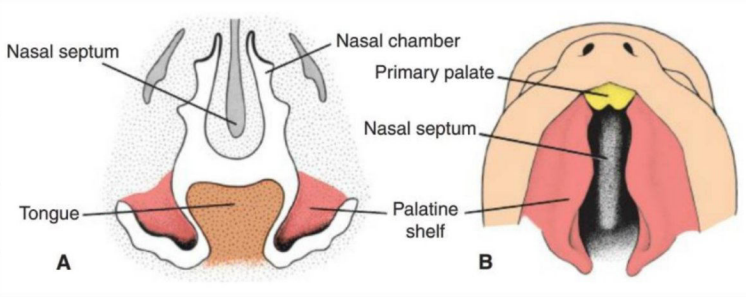
---

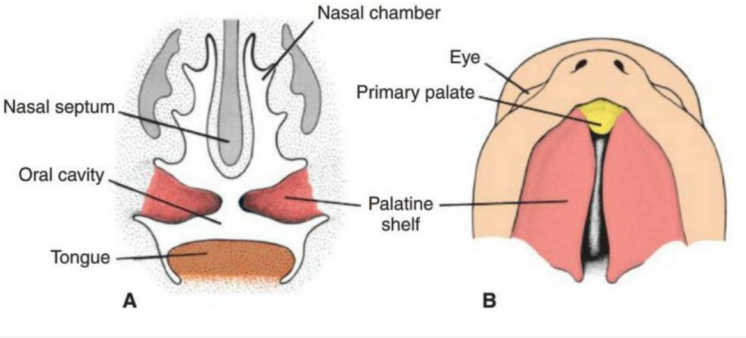
* 1° palate

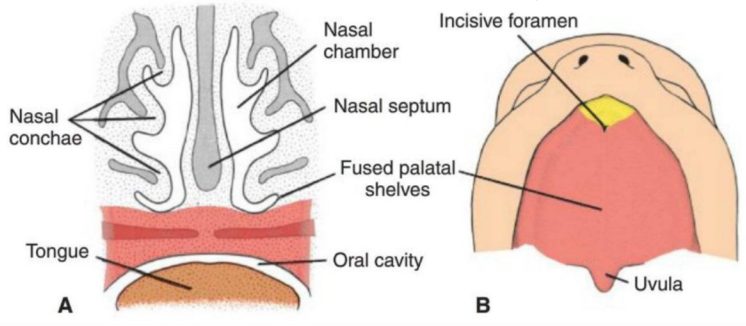
medial growth of maxillary prominence → merge & form intermaxillary segment (continous with rostral portion of nasal septum (formed by frontal prominence) / the segment has:
① labial component → forms philtrum / ② upper jaw → carries 4 incisors / ③ palatal component → forms triangular 1° palate











* 2° palate
- at 6th week palatine shelfs appear as oblique & downward directed outgrowths from maxillary prominences (on sides of tounge)
- during 7th week
  ① palatine shelfs assend horizontally above tounge & fuse medially forming 2° palate
  ② anteriorly, the shelves fuse with triangular 1° palate (midline is incisive foramen)
  ③ nasal septum grows & joins cephalic aspect of 2° palate
- the 2 folds grow posterior from edge of palatine process to form soft palate & uvula:
  ① soft palate folds unite → during 8th week
  ② uvula folds unite → during 11th week

---

* developmental anomalies
  ① no fusion of maxillary & medial nasal prominences → uni/bilateral cleft lip (unilateral cleft can reach nose)
  ② no fusion of 1° & 2° palate → uni/bi lateral cleft palate (can involve soft palate & uvula)

---

* embryo layers:
  ① endoderm → inner lining
  ② mesoderm → bone, muscle, CVS, internal sexual organs
  ③ ectoderm → skin, nervous system

PRIMITIVE GUT

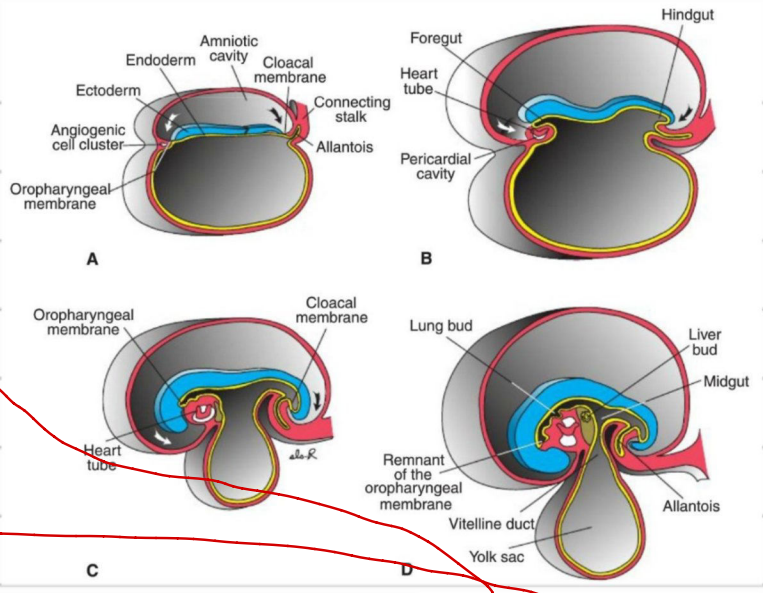
* 4 Sections:

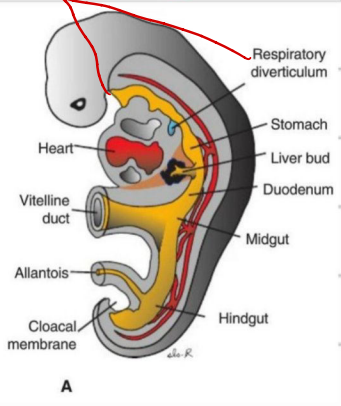
① pharyngeal gut / Pharynx
P.18 us ant Jeac
from buccopharyngeal membrane (between primitive mouth & pharynx / will rupture later) to tracheobronchial diverticulum

② foregut
caudal to pharyngeal tube & extends to liver bud

③ midgut
caudal to liver & extends to 2/3 transverse colon
junction P. 2/3 and L. 1/3 of)

④ hind gut
from left 1/3 transverse colon to cloacal membrane

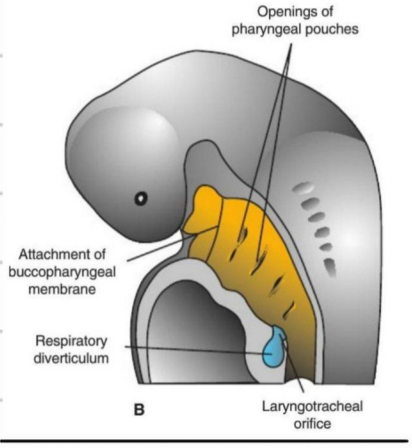




---

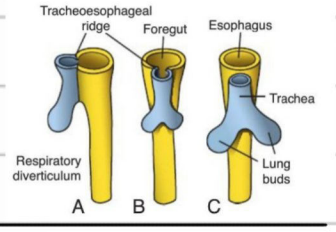
* during 4th week: appearance of respiratory diverticulum (lung bud) from ventral wall of foregut induced by fibroblast growth factor (FGFs) because the embryo has a gene box that controls signals of growth of several systems.

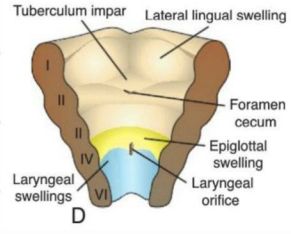
* respiratory tract embryonic origin: Bronch- / Lary-
① endoderm → lining epithelium (Trach-
② mesoderm → cartilage, muscle, CT
(splanchnic mesoderm surrounding foregut)
③ ectoderm → outer surface



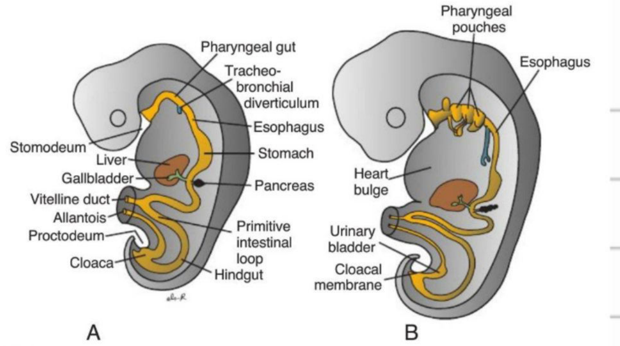
* initially lung bud has open communication with foregut → when bud expands caudally it's seperated from foregut by tracheoesophageal ridges → ridges fuse into a septum

* respiratory primordium maintains communication with pharynx by laryngeal slit → T-shaped → opening





ESOPHAGUS



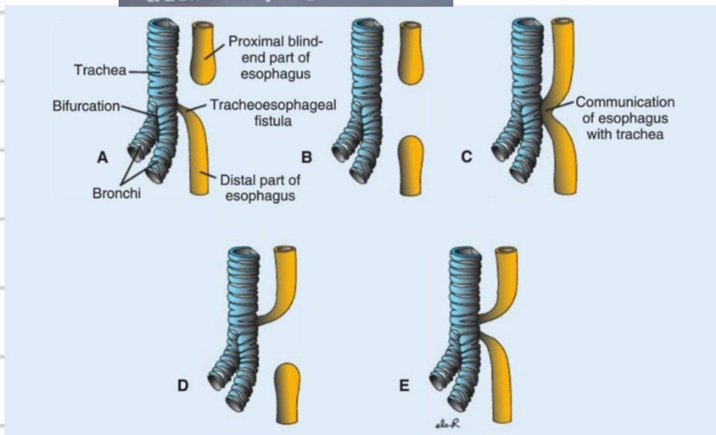
- at beginning it's very short → elongates rapidly with desending heart *and lungs*
- upper 1/3 → *muscular coat* striated / vagus
- lower 2/3 → *muscle coat* smooth / splancnic plexus

esofo - upper skilital / middle mix / lower smooth)

---

* anomalies in trachea & esophagus:

> Abnormalities in partitioning of the esophagus and trachea by the tracheoesaphageal septum result in **esophageal atresia** with or without **tracheoesaphageal fistulas**



1 tracheoesophageal fistula (TEF)

A → proximal atresia / distal fistula / most common (1/3000) / 90% of cases

B → double atresia (not TEF) (isolated / 4%)

C → H type fistula without atresia (4%) *(X) shape*

D → distal atresia & proximal fistula (1%)

E → atresia & double tracheoesophageal fistula (1%)

- TEF is most common anomaly in lower respiratory tract & causes:
  1. infants cough & choke due to ↑ saliva in mouth
  2. can't swallow milk
     Polyhydramnios (↑ amniotic fluid around baby) *← الطبيعي السائل من oral ← urine (mom) ليس بالحالة هاي لا ما بنزله ، السائل حوالين الطفل*
  3. food enters trachea → pneumonitis & pneumonia *(انو الاكل يطلع من المعدة ويفوت ال lung)*

- TEF is associated with other abnormalities (VACTERL)
  V → vertebral / A → anal / C → cardiac (33%) / T → TEF / E → esophageal atresia / R → renal / L → limb
  - the cause of these abnormalities is unknown / ♂ > ♀ *(Male infants تصيب الغالب)*
  - Most common associated cardiac abnormalities: ASD, VSD, fallot

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

Uncommon anomalies ↓

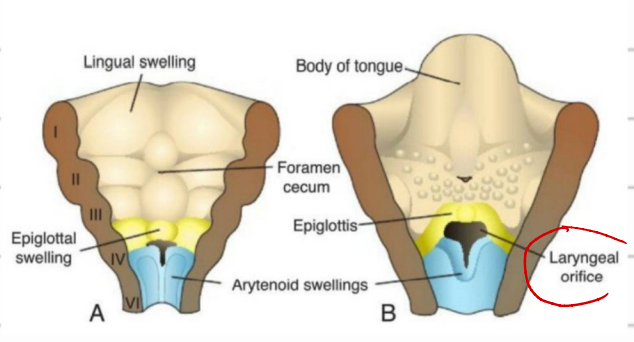
2 tracheal atresia & stenosis

→ usually associated with TEF *(one of the verities of)*

3 incomplete tracheal atresia

→ obstruction of airways by web tissue

LARYNX



* origin:
  ① endoderm → lining epithelium
  ② mesoderm → cartilage, muscle (mesenchyme of 4th & 6th arches)

* formation:
  . 4th & 6th arches form thyroid, arytenoid, cricoid cartilages giving characteristic (adult) shape of laryngeal orifice which is bound anteriorly by epiglottis & laterally by aryepiglottic folds
  ▸ As a result of rapid proliferation of this mesenchyme, the laryngeal orifice changes in appearance from a sagittal slit to a T-shaped opening
  . rapid proliferation growth → occlusion of lumen → recanalization & vacuolization → forming lateral recesses (laryngeal ventricles) in glottic area of larynx between true & false vocal cords.
  ▸ These recesses are bounded by folds of tissue that differentiate into the **false** and **true vocal cords.**

* innervation:
  vagus branches:
  · superior laryngeal (external) → 4th arch structures (cricothyroid muscle)
  · recurrent laryngeal → 6th arch structures (other intrinsic muscles)

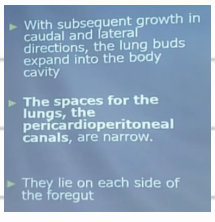
---

* anomalies:
  · laryngeal atresia → rare, may cause CHAOS (congenital high airway obstruction syndrome) → lung enlargement & echoes (echogenic) (sono)
  (distal to the atresia)
  · anomalies that accompany CHAOS:
    ① diaphragm (flattened/inverted)
    ② fetal ascitis & hydrops (↑ serous fluid (in abdom.) / diagnosed by prenatal ultrasonography)

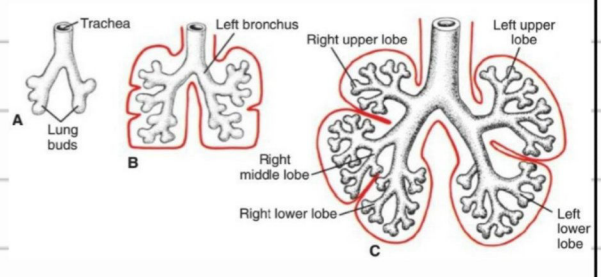
LUNGS AND BRONCHIAL TREE

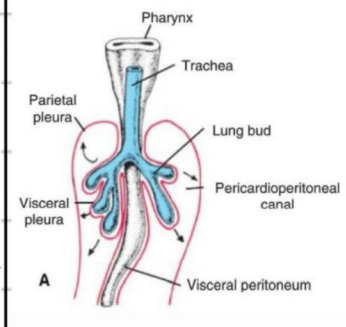
- lung bud → forms trachea → elongates till T_4,T_5 (angle of Louis) → bifurcates to bronchial buds → at beginning of 5th wk: buds enlarge into rt & lt main bronchi → give lobar bronchi (3 rt, 2 lt) → give segmental bronchi (10 rt & 8 lt) → then reach alveoli

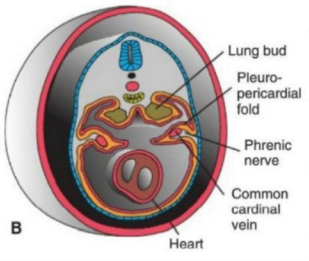
- as bronchi grow distally pericardioperitoneal canals are developing → later on, pleuroperitoneal & pleuropericardial folds seperate pericardioperitoneal canals from peritoneal & pericardial cavities & the remaining spaces form primitive pleural cavities → forming of parietal & viseral pleura surrounding pleural cavity

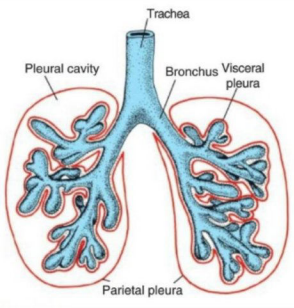


* bronchial tree:
  - trachea → 1° bronchi → 2° bronchi → 3° bronchi → + 14 generations of dicotomus divisions (each one divides to 2) → at end of 6th month we have 17 generations → + 6 gens after birth (adult has 23 gens)
  - branching is regulated by epithelial mesenchymal interactions between endoderm of lung buds & surrounding splanchic mesoderm (signalled by fibroblast growth factor)
  - branching is associated with caudal descending of trachea to reach 4th thoracic vertebrae at birth
- branching of 3° bronchi forms terminal & respiratory bronchiols marks the beginning of maturation of alveolar ducts, sacs & alveoli









MATURATION AND DEVELOPMENT OF LUNGS

* development of respiratory bronchials

Stage 1: pseudo glandular period

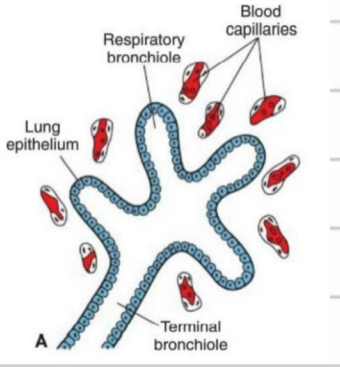
- in weeks 5-16 (half of 4th mo.) → terminal bronchials only (conducting) / simple cuboidal epithelium

Stage 2: canalicular period (pic A)

- Up to the seventh prenatal month, the bronchioles divide continuously into more and smaller canals (canalicular phase)

- in weeks 16-26 (6 & half mo.) → alveolar ducts (canaliculi)
- 1 terminal bronchiole → 2 respiratory bronchials → 3-6 ducts (x2)
- changes:
  1. simple cuboidal epithelium → simple squamous
  2. ↑ vascular supply (formation of alveolar capillaries) but no gas exchange (no connection) → baby born in this stage (≤ 7th mo.) can survive (with adequate treatment to enhance alveoli & capillary growth + O_2 & surfactant)

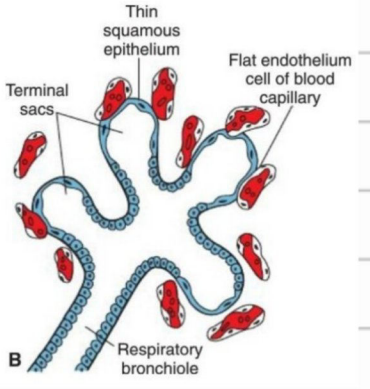
- Respiration becomes possible when some of the cells of the cuboidal **respiratory bronchioles** change into thin, flat cells



Stage 3: terminal sac period (pic B)

- These cells are intimately associated with numerous blood and lymph capillaries, and the surrounding spaces are now known as **terminal sacs** or **primitive alveoli**

- in weeks 26-birth → terminal sacs or primitive alveoli (immature) / from respiratory bronchials
- connection between squamous epithelium & blood capillaries → gas exchange is possible → baby born at >7 mo. can survive without support



Stage 4: alveolar period

- During the last 2 months of prenatal life and for several years thereafter, the number of terminal sacs increases steadily

- from 8th mo. to 10th year of age → mature alveoli (not before birth)
- thining of type I alveolar cells (sac lining) allowing capillaries to protrude into alveolar sacs → fusion → complete contact (respiratory memb. / blood-air barrier)
- connection of lymph to walls

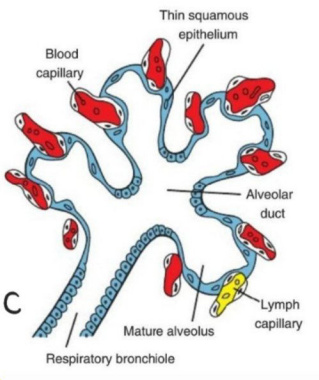


TABLE 14.1 Maturation of the Lungs

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

* Notes:

- Only 1/6 of total adult alveoli are present at birth / increase in number of alveoli & bronchials is more important than increase in size
- type II surfactant alveolar cells (from end of 6th to 8th mo.) → peak surfactant production (9th mo. / 2 wks before delivery) / importance: less pressure needed to keep alveoli open after expiration / missing → atelectasis / collapse (next inspiration is hard)

* lungs

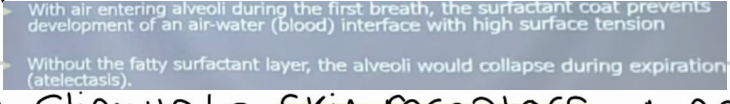
- before birth

lungs filled with fluid (↑Cr, ↓protein, some mucus of bronchial glands, surfactant) / breathing (aspiration) of amniotic fluid
Stimulates growth of respiratory muscles needed after birth

- at/after birth

blood & lymph resorb lung fluid, a small amount of fluid leaves through trachea during delivery → lungs are left with liquid-air interface at sacs + phospholipid surfactant

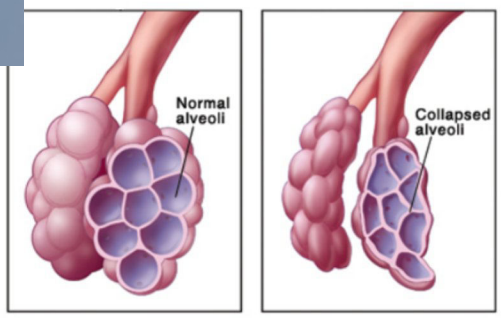
- after birth



Dr. slaps baby's back to stimulate skin receptors → nerve impulses to respiratory centers → brain sends impulses (phrenic motor nerve) → stimulate diaphragm to contract → air flow from nose to lung → breathing starts & baby cries

*anomalies:

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



① RDS (respiratory distress Syndrome)
- missing surfactant at birth (premature birth) → loss of compliance → collapse of alveoli → need high pressure to open
- 30% of neonatal diseases / 20% of neonatal deaths
- Common complication: intrauterine asphyxia (suffocation due to debrivation of O_2) → irreversible damage of type II cells → no survival even with treatment)
- treatment: ⊕ surfactant production by:
  - ↳ glucocorticoids (betamethazone)
  - ↳ thyroxine (most important stimulator / for mothers with hypothyroidism)

It Also allowed survival of some babies as young as 5.5 months of gestation

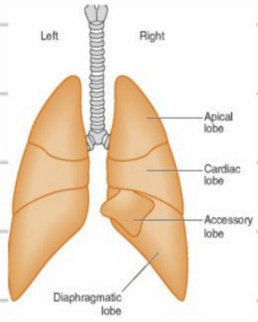
- RDS can also be called: hyaline membrane disease (↑ protein content & lamellar bodies derived from surfactant layer)

② blind ending trachea (atresia) + agenesis of one of lungs
- rare / if led to ↓ O_2 → death / can be caused by a teratogenic drug the mother used.

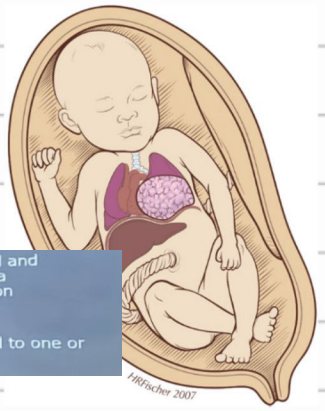
Abnormal divisions of the bronchial tree are more common; some result in supernumerary lobules.

These variations of the bronchial tree have little functional significance, but they may cause unexpected difficulties during bronchoscopies.

③ Supernumerary lobules & ectopic (accessory) lobes
- excessive branching of bronchial tree → 3-4 lobes in left lung / no functional significance
- additional respiratory buds by foregut → lobes from trachea, esophagus or in mediastinum independent on respiratory system



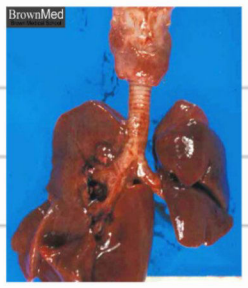
④ Congenital Cysts of lung
- most important clinically
- formed by dilation of large or terminal bronchi (uni/multi) → restrict inflation → ↓ O_2
- honey comb appearance in radiograph
- Cysts drain poorly → Chronic infxns
- treat by surgical removement (can be intrauterine)



These cysts may be small and multiple, giving the lung a honeycomb appearance on radiograph

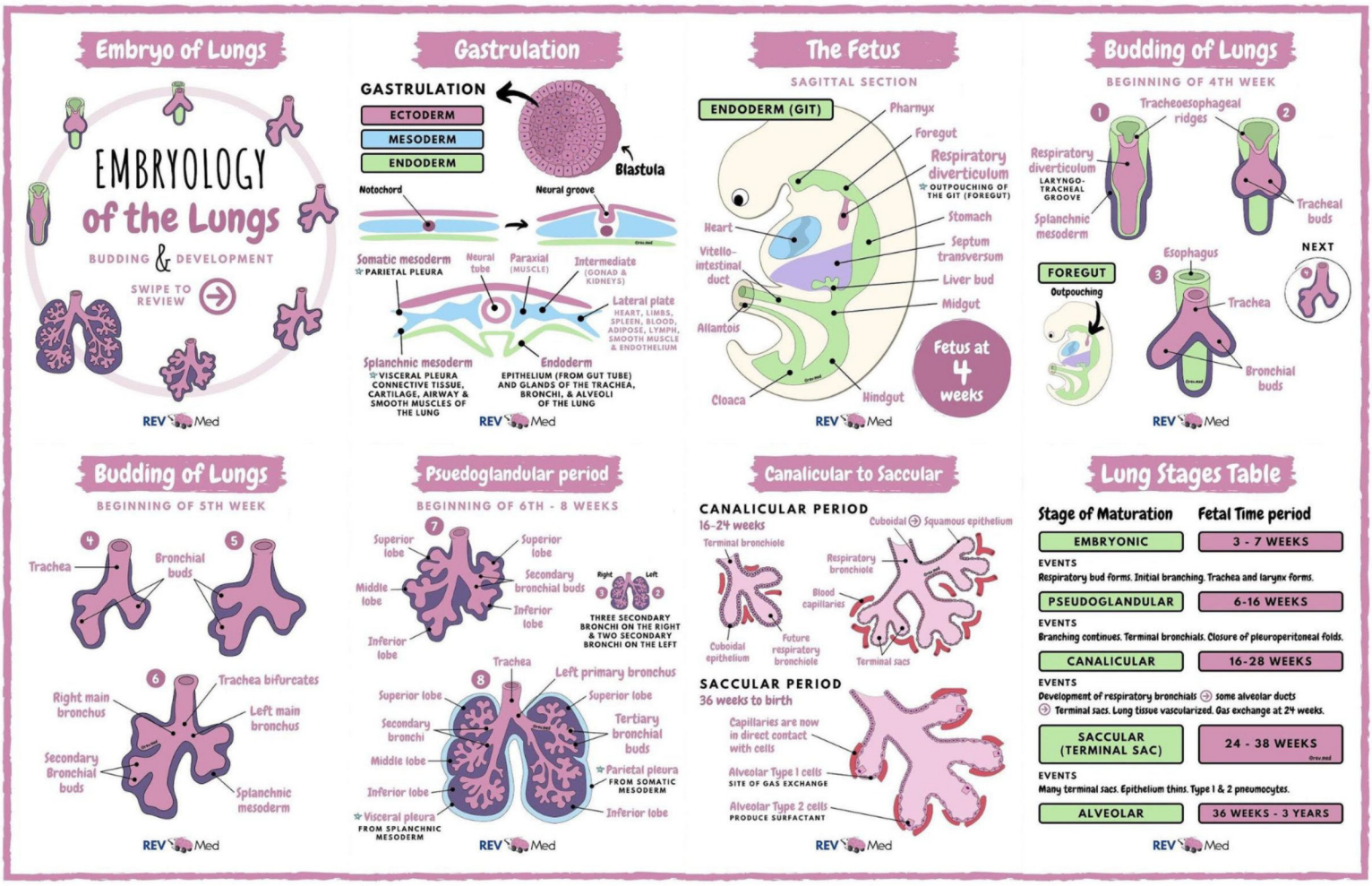
Or they may be restricted to one or more larger ones

⑤ lung hypoplasia



- most common cause : congenital diaphragmatic hernia (CDH) → hernia pushes some abdominal structures to thoracic cavity → lung is unable to develop normally (compressed by abdominal viscera) → ↓ lung volume (left side more common)
- infants with CDH usually die of pulmonary insufficiency
- oligohydramnios (↓ amniotic fluid) → severe lung hypoplasia

* if the newborn was found dead after delivery → possibilities :
  ① air filled lung → float on water (slipped from dr's hands)
  ② fluid filled lung → sink in water (baby is already dead in womb / still born)



by INSAF IYAD