

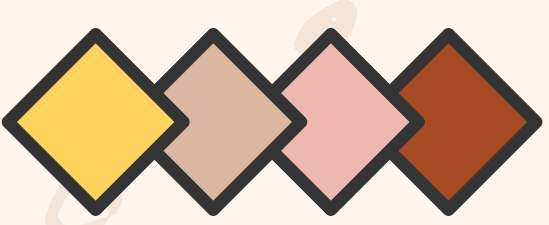


Development and Physiology of cells in Respiratory system

Basic science in pediatrics

R2 Nattapat Keawkaew
Col.Asst.Prof. Sanitra Sirithangkul





Outline

”

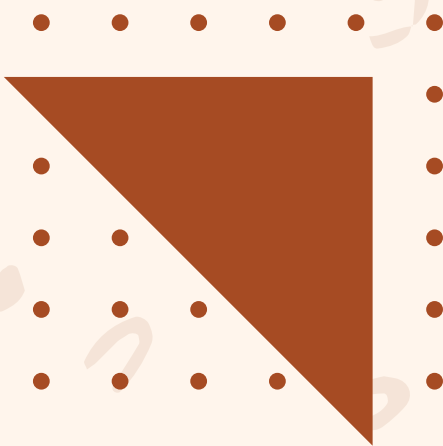
Development of Lung

”

Normal lung anatomy and cell function

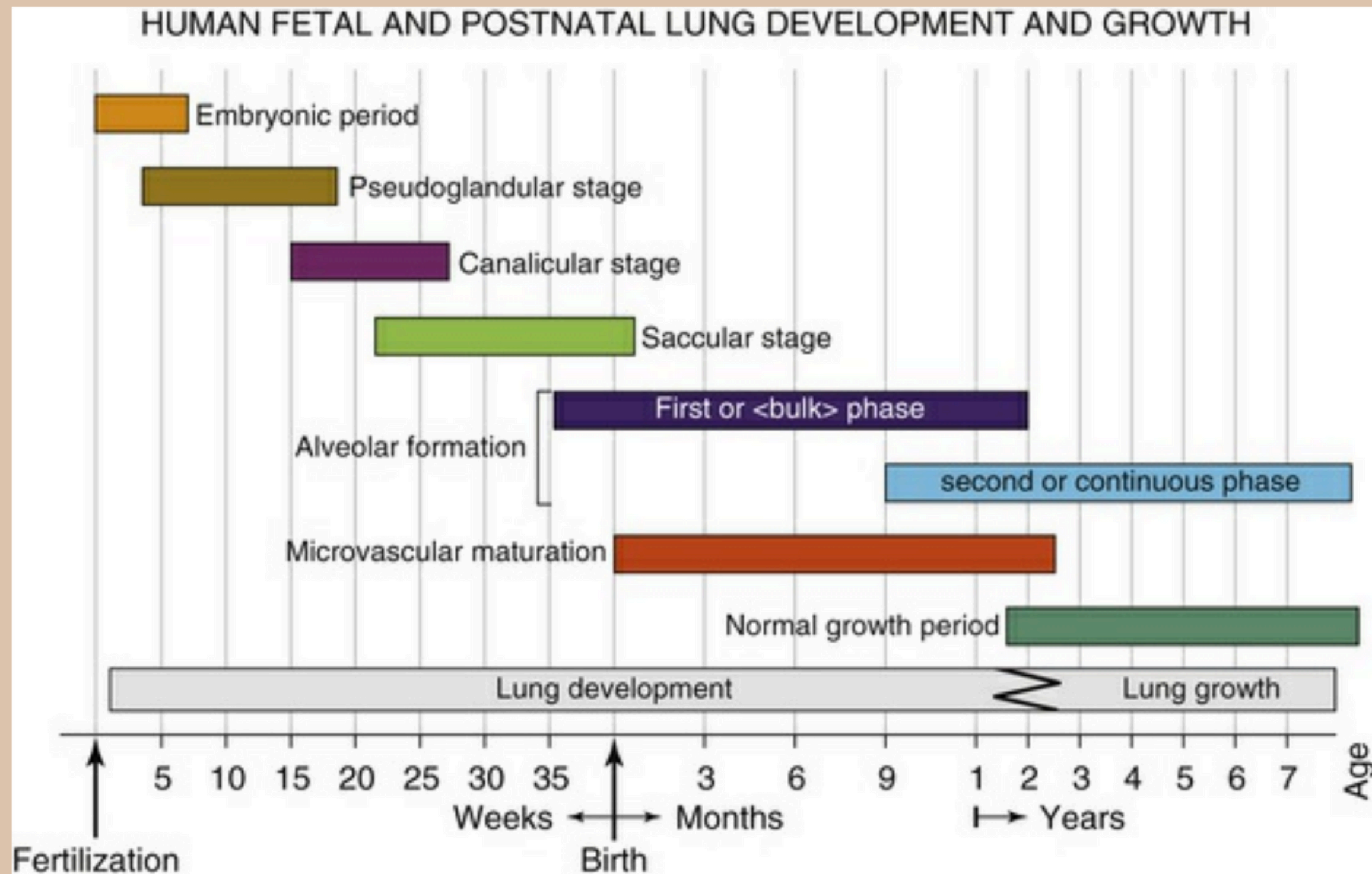
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Case study of
abnormal lung development



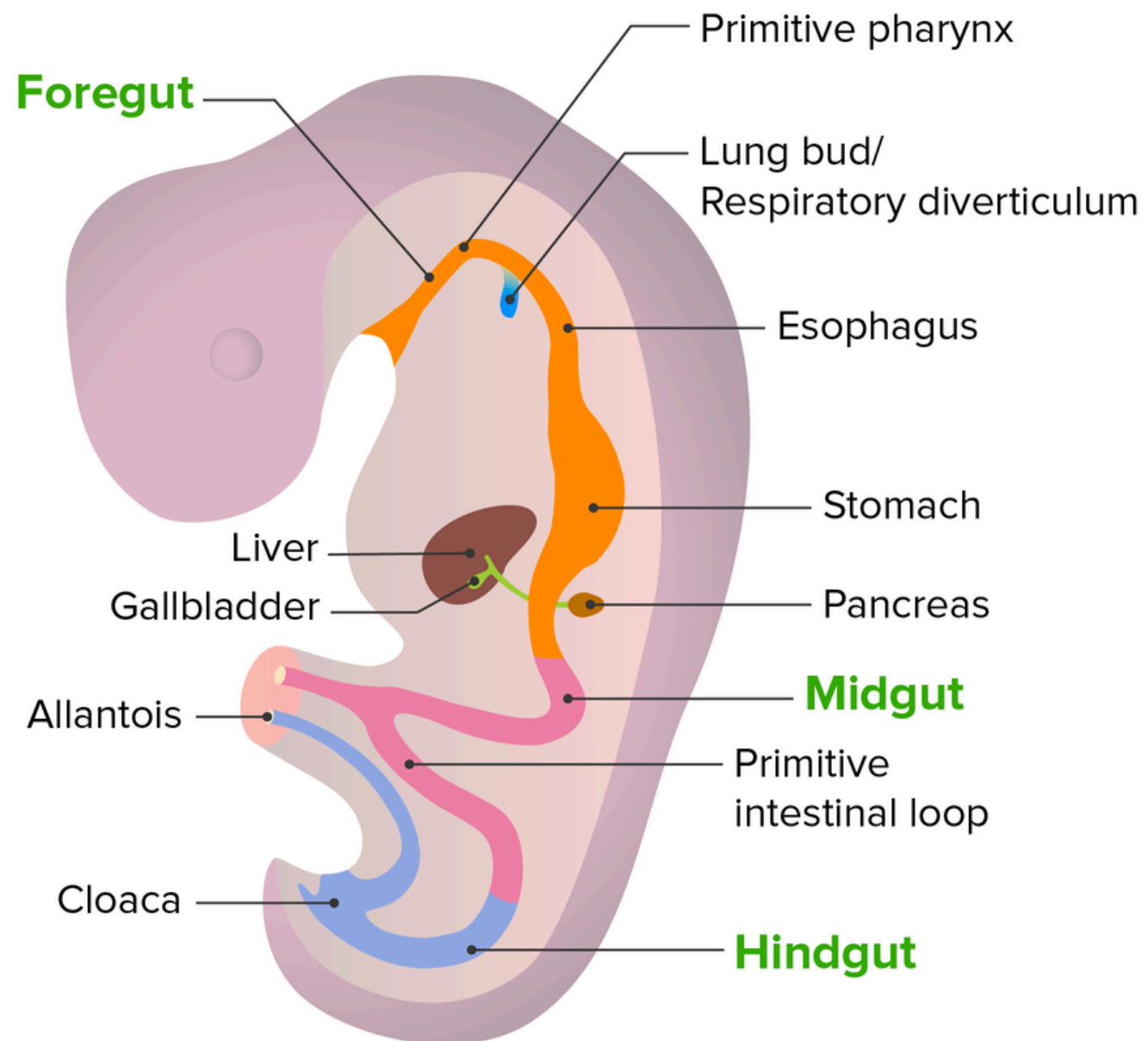
Development of Lung

Sequences of lung development



Development of Lung

Embryonic stage



Embryonic stage 3 to 6 weeks' GA

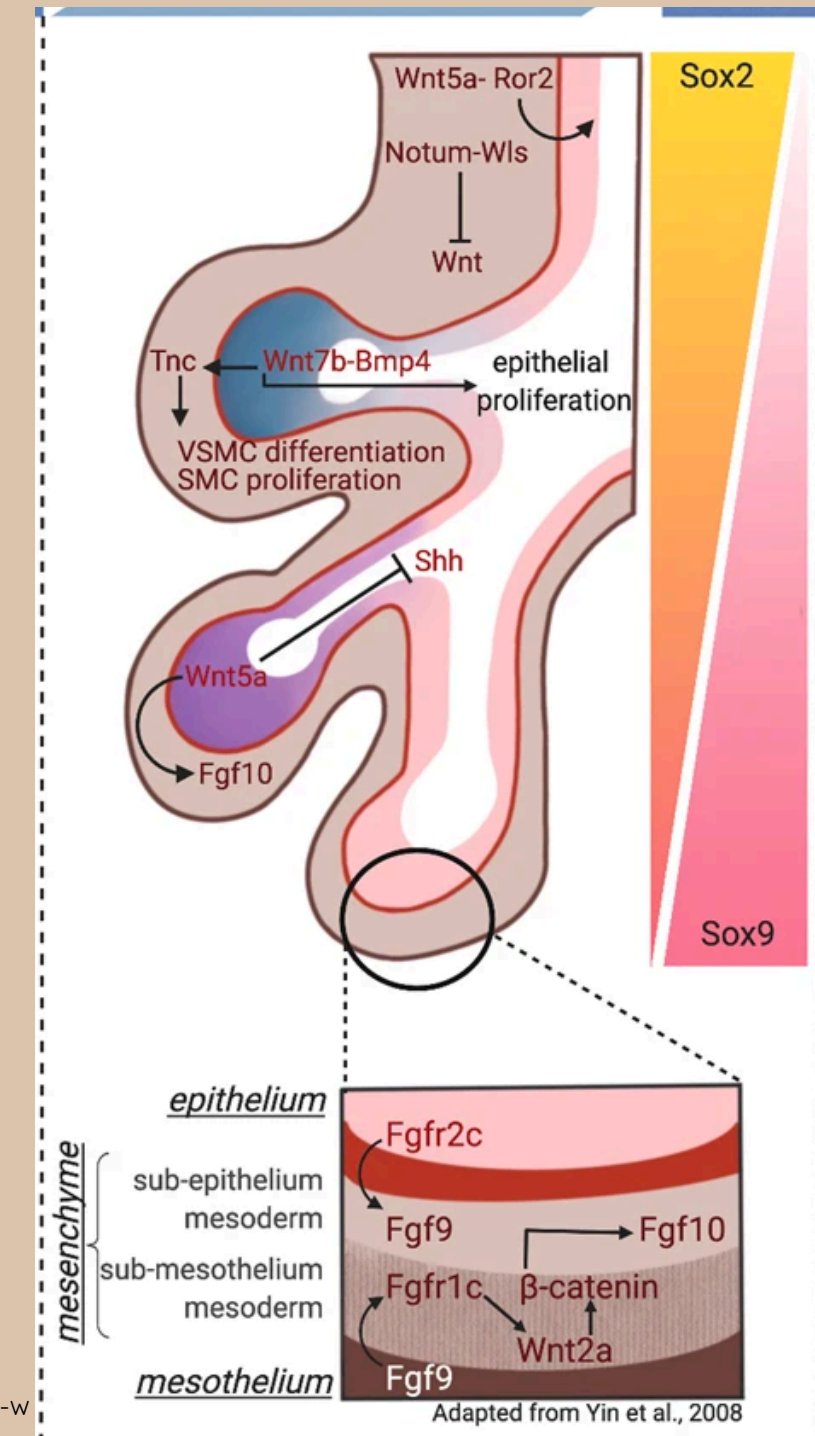
- **Ventral outpouching of the primitive gut**
- Primary bronchi elongate into the mesenchyme and divide into the two main bronchi
- Main pulmonary artery arises from the sixth pharyngeal arch
- **Abnormal: lung agenesis, tracheobronchial fistula**

Growth and Development of Lung

Pseudoglandular stage

Pseudoglandular stage 6 to 16 weeks' GA

- Mesenchyme differentiates into cartilage, smooth muscle, and connective tissue around the epithelial tubes
- **End at terminal bronchioles**
- All preacinar arterial branches formed
- **Abnormal: bronchopulmonary sequestration, cystic adenomatoid malformation, tracheo-esophageal fistula and congenital diaphragmatic hernia**



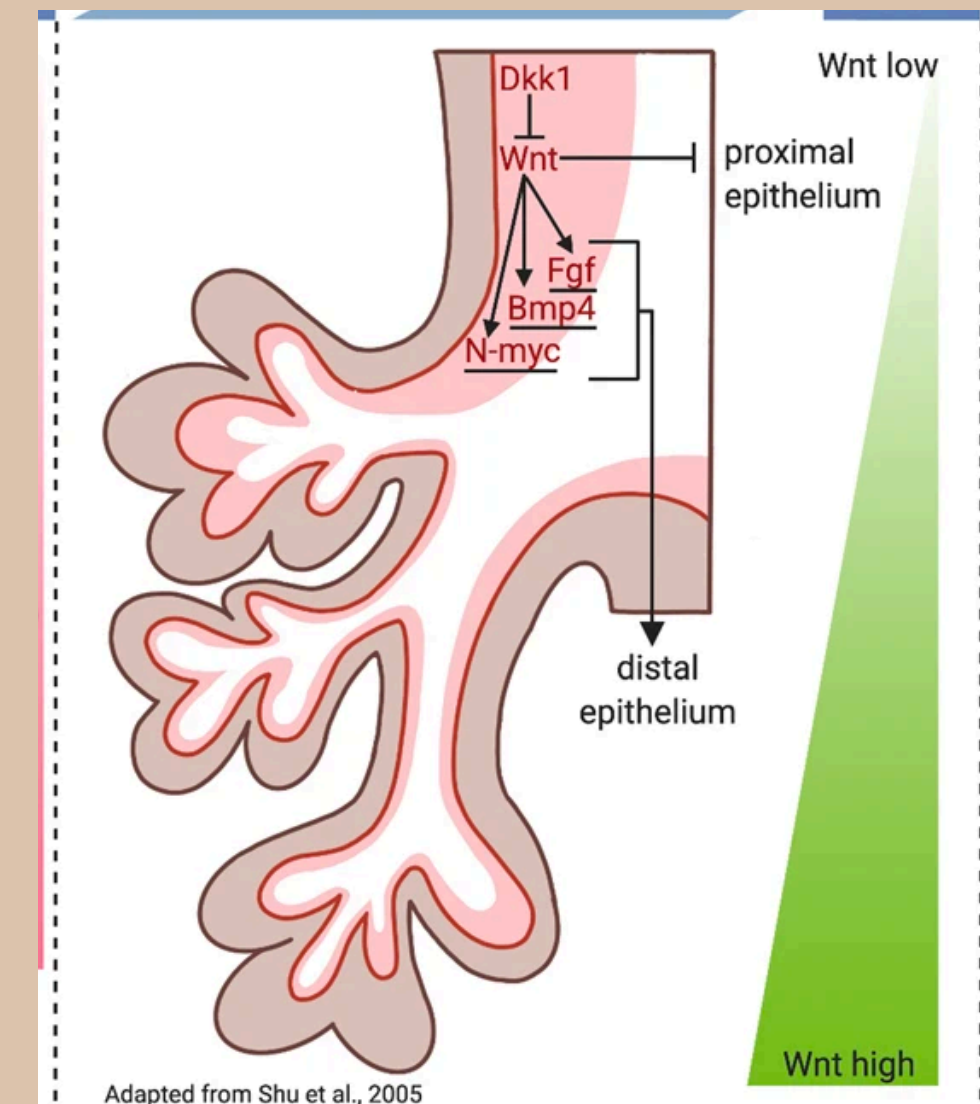
Development of Lung

Canalicular stage

Canalicular stage

16 to 26 weeks' GA

- Respiratory bronchioles develop
- **End at terminal sac formed**
- Glandular appearance is lost as the interstitium has less connective tissue and the lung develops a rich vascular supply
- **Abnormal: pulmonary hypoplasia**



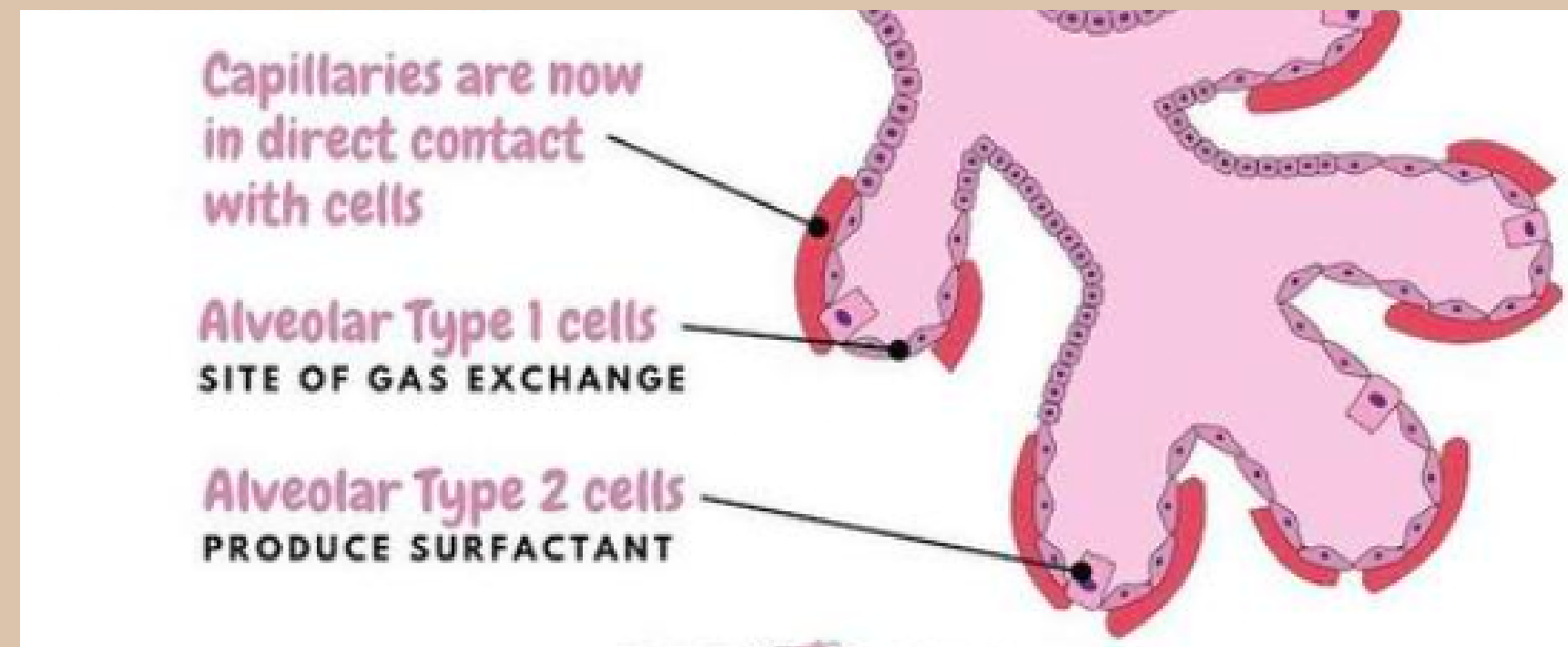
Development of Lung

Saccular stage

Saccular stage

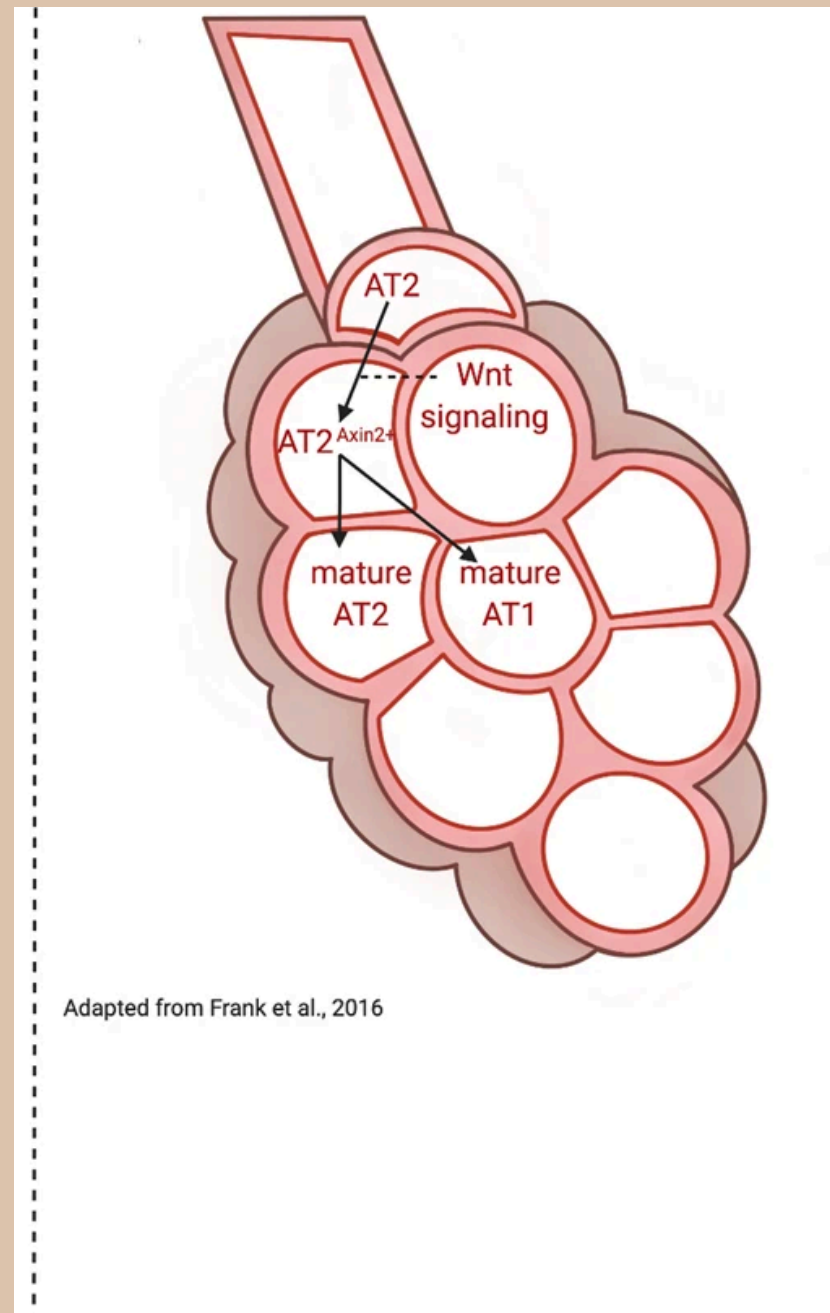
26 to 36 weeks" GA

- Capillary proliferation and thinning of the epithelium => enabling gas exchange
- cuboidal (type II) and thin (type I) epithelial cells begin to line the airspace
- **Abnormal: respiratory distress syndrome**



Development of Lung

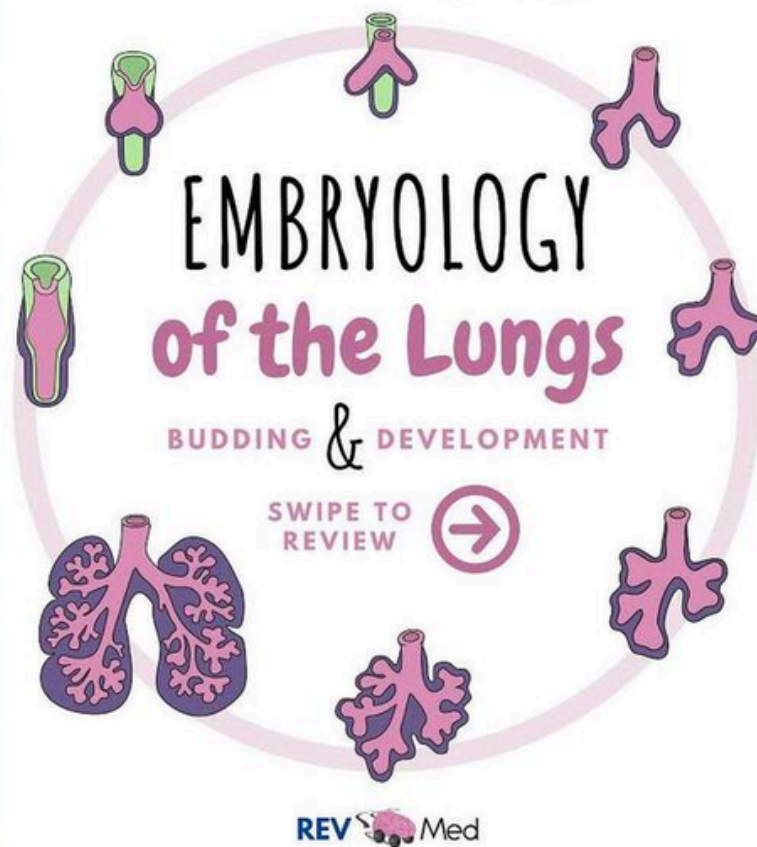
Alveolar stage



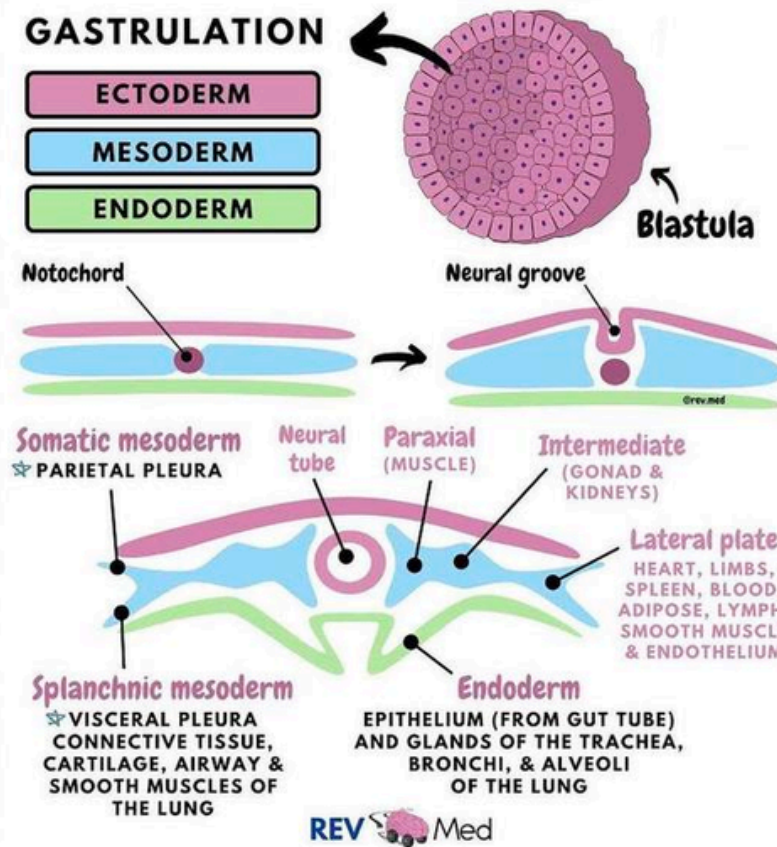
Alveolar stage since 36 weeks' GA through adult

- Secondary septa form the walls and collateral airway between alveoli
- Estimated alveolar units **at birth are 20-150 million units**
- Increased numbers of alveolar unit **until 3 years of age**
=> Total 200-300 million units
- Increasing volume during childhood til adulthood
- **Abnormal: congenital lobar emphysema, acquired diseases**

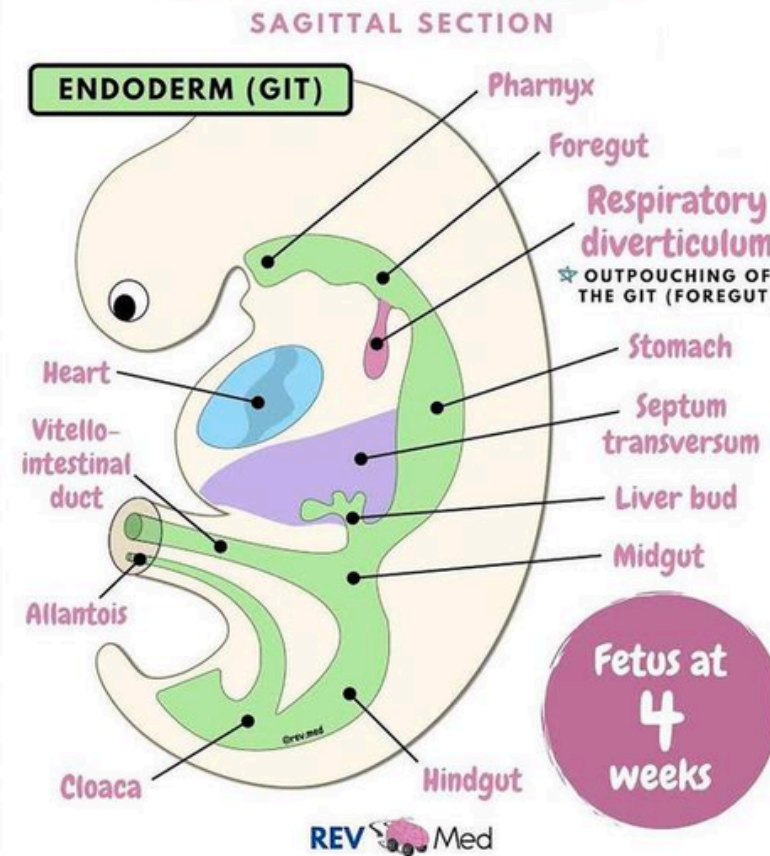
Embryo of Lungs



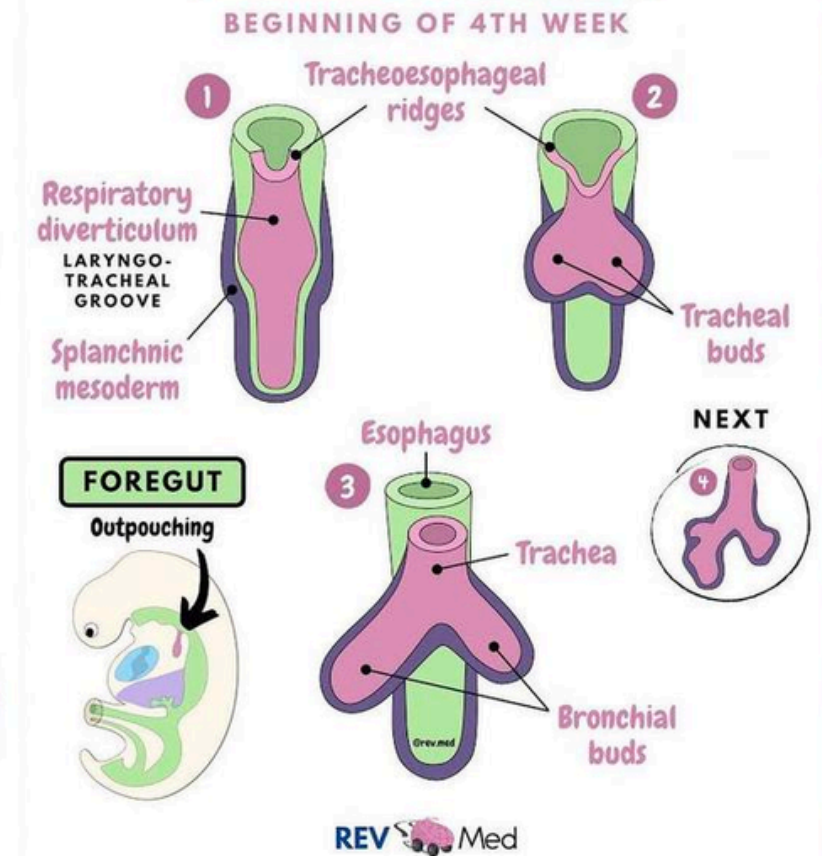
Gastrulation



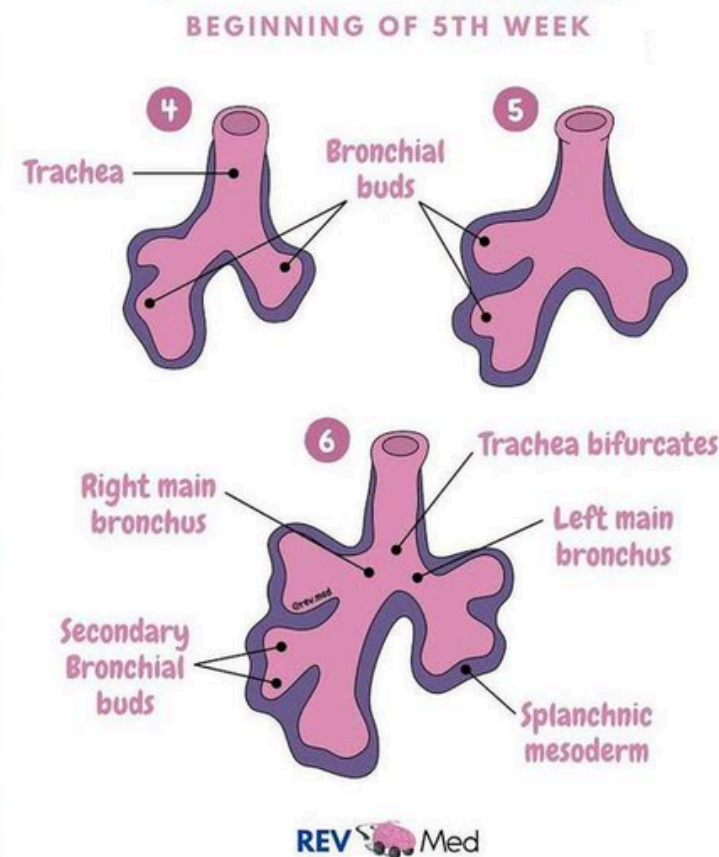
The Fetus



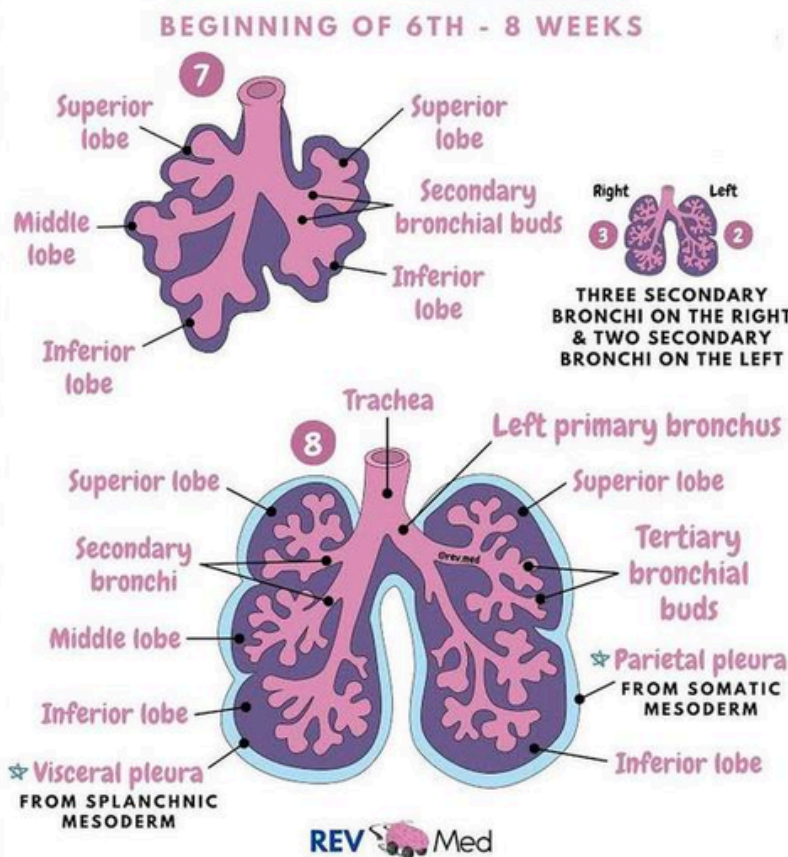
Budding of Lungs



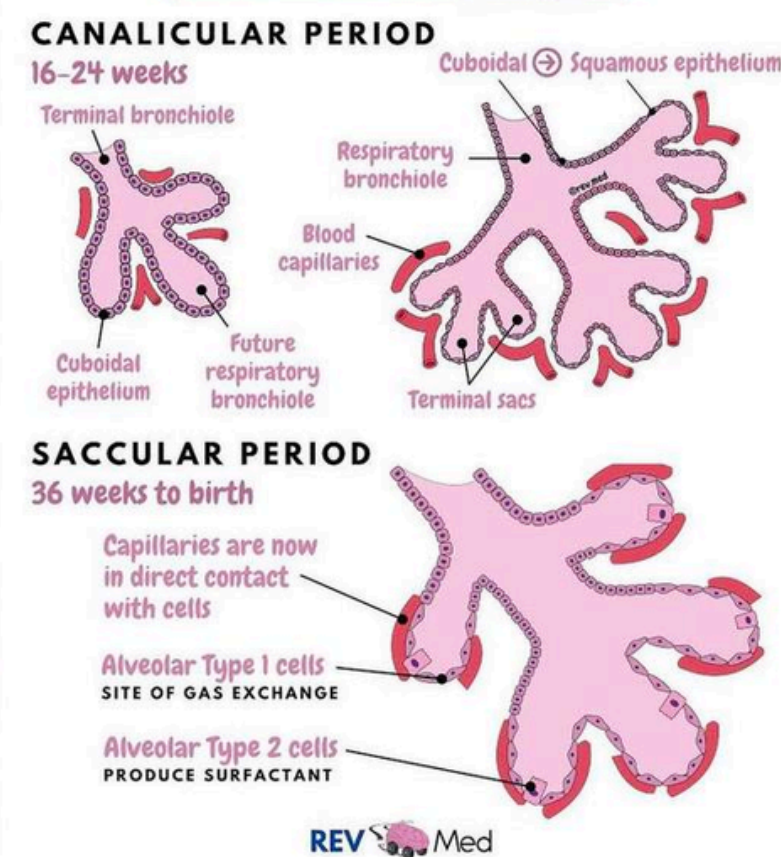
Budding of Lungs



Pseudoglandular period



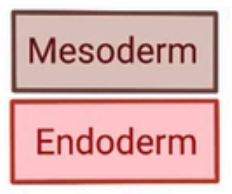
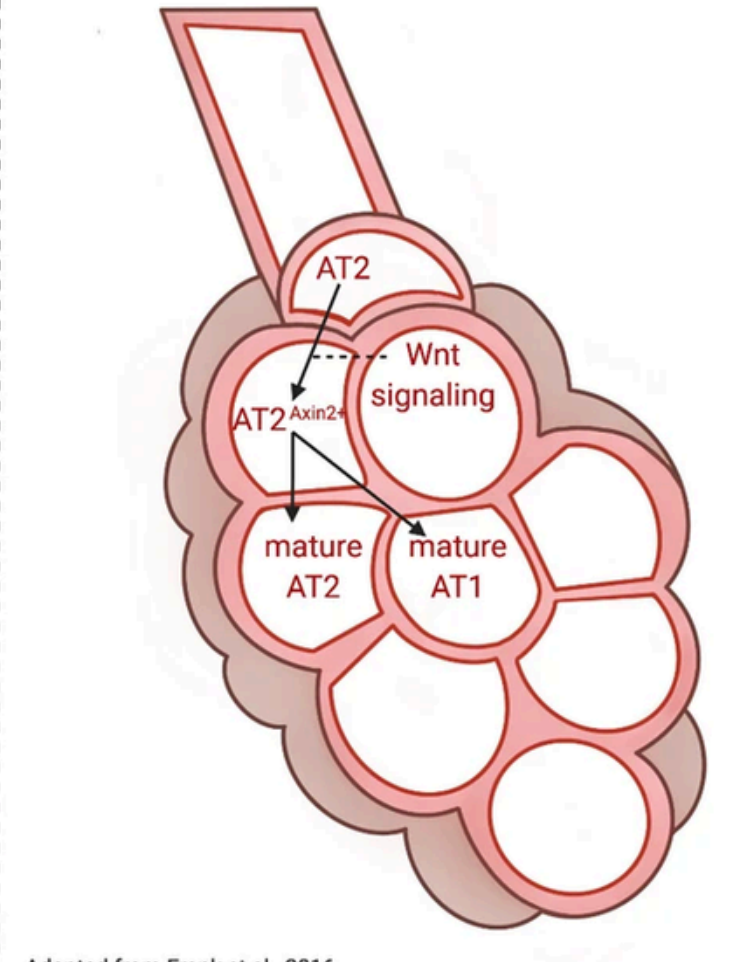
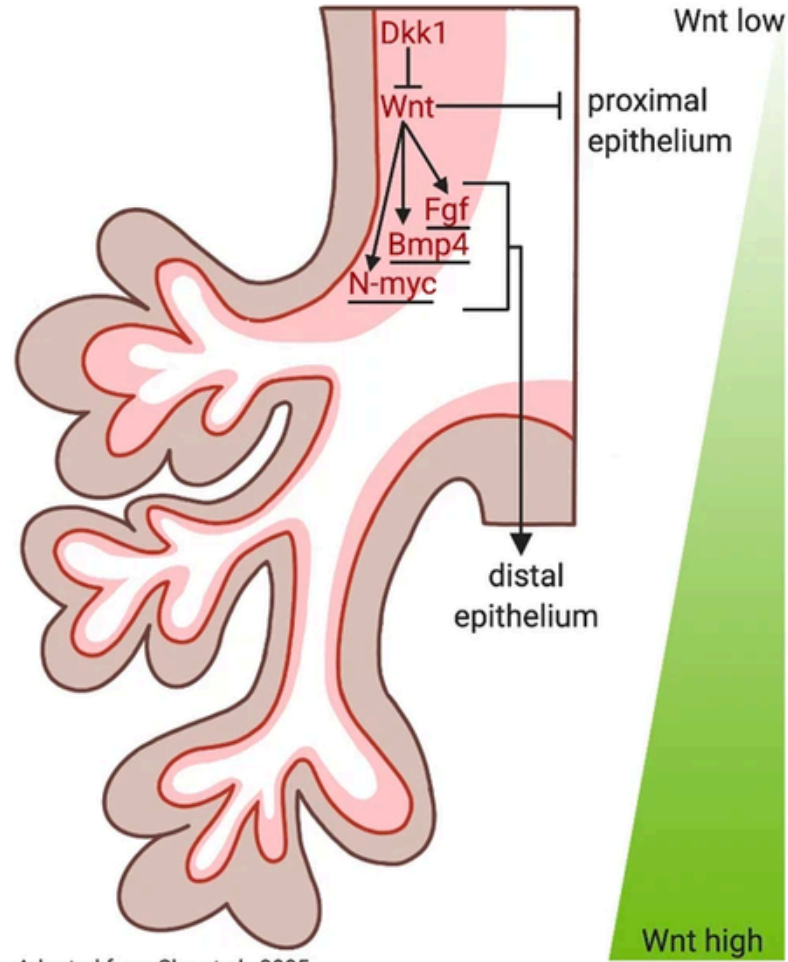
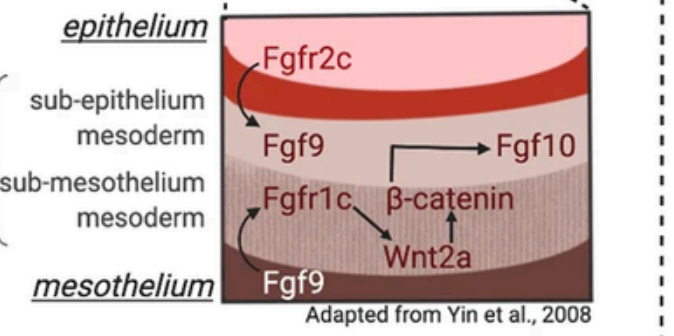
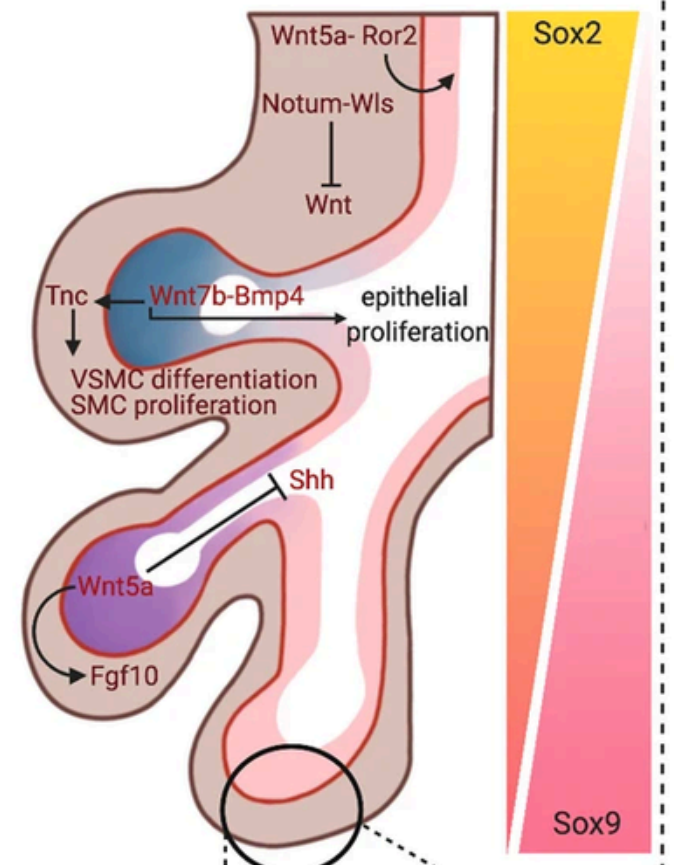
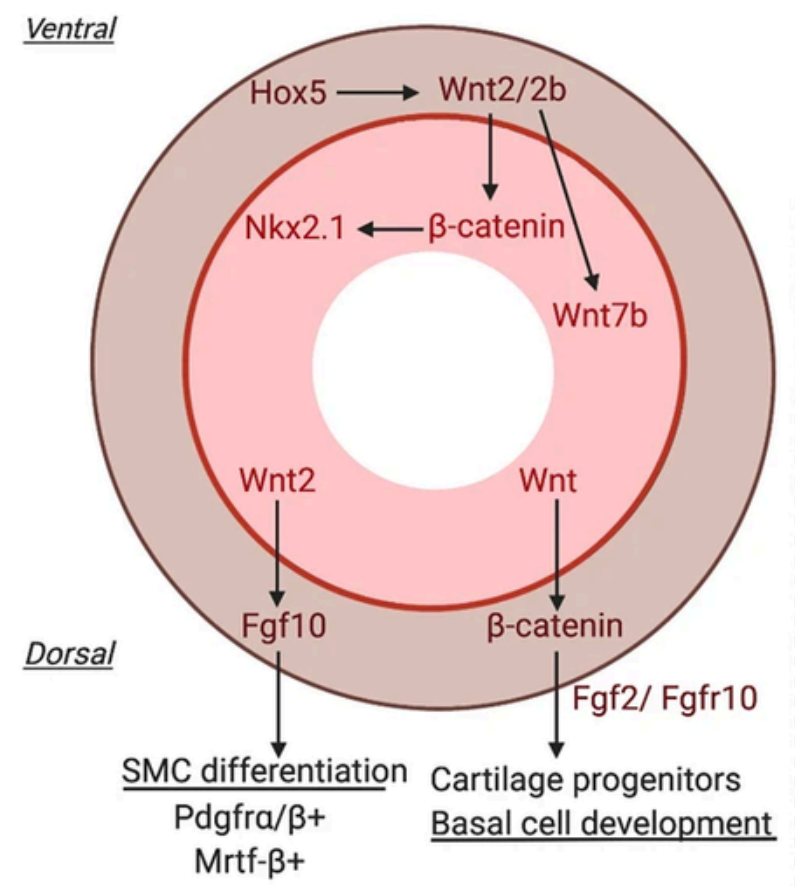
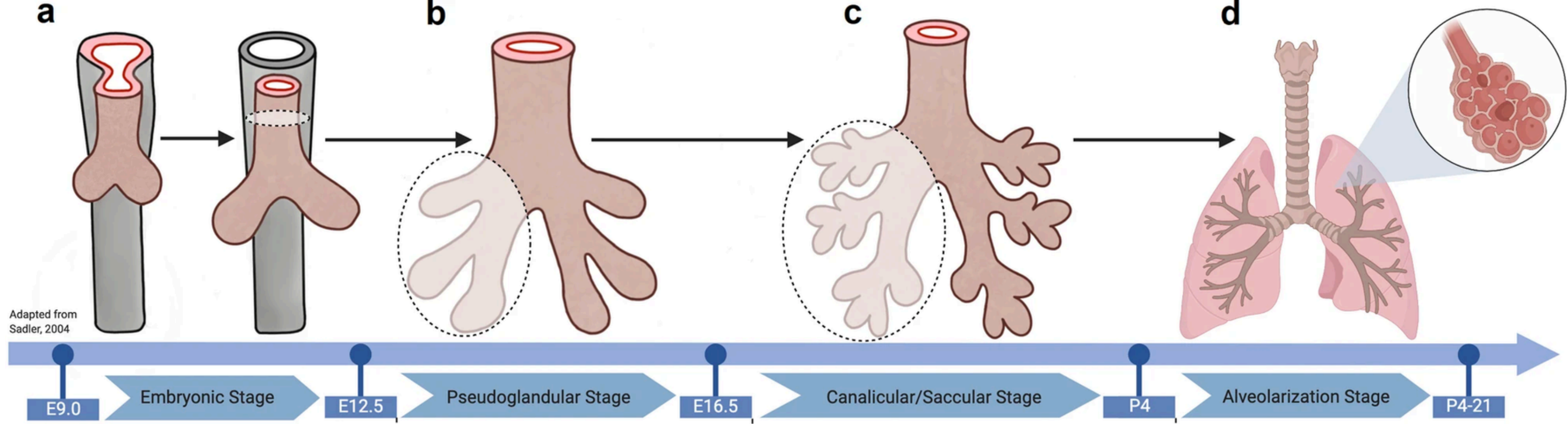
Canalicular to Saccular



Lung Stages Table

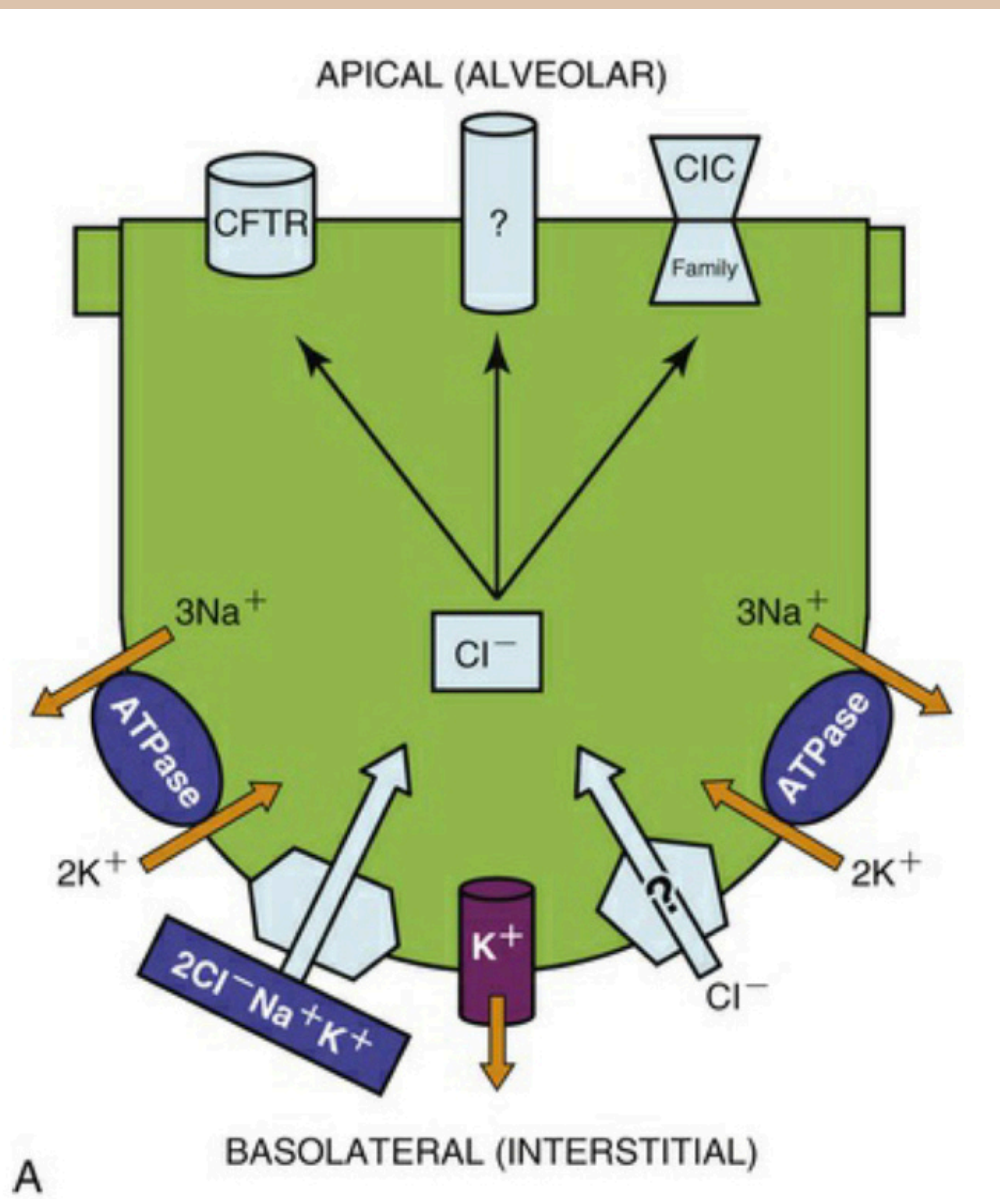
Stage of Maturation	Fetal Time period
EMBRYONIC	3 - 7 WEEKS
EVENTS Respiratory bud forms. Initial branching. Trachea and larynx forms.	
PSEUDOGLANDULAR	6-16 WEEKS
EVENTS Branching continues. Terminal bronchials. Closure of pleuroperitoneal folds.	
CANALICULAR	16-28 WEEKS
EVENTS Development of respiratory bronchials → some alveolar ducts → Terminal sacs. Lung tissue vascularized. Gas exchange at 24 weeks.	
SACCULAR (TERMINAL SAC)	24 - 38 WEEKS
EVENTS Many terminal sacs. Epithelium thins. Type 1 & 2 pneumocytes.	
ALVEOLAR	36 WEEKS - 3 YEARS

REV Med



Development of Lung

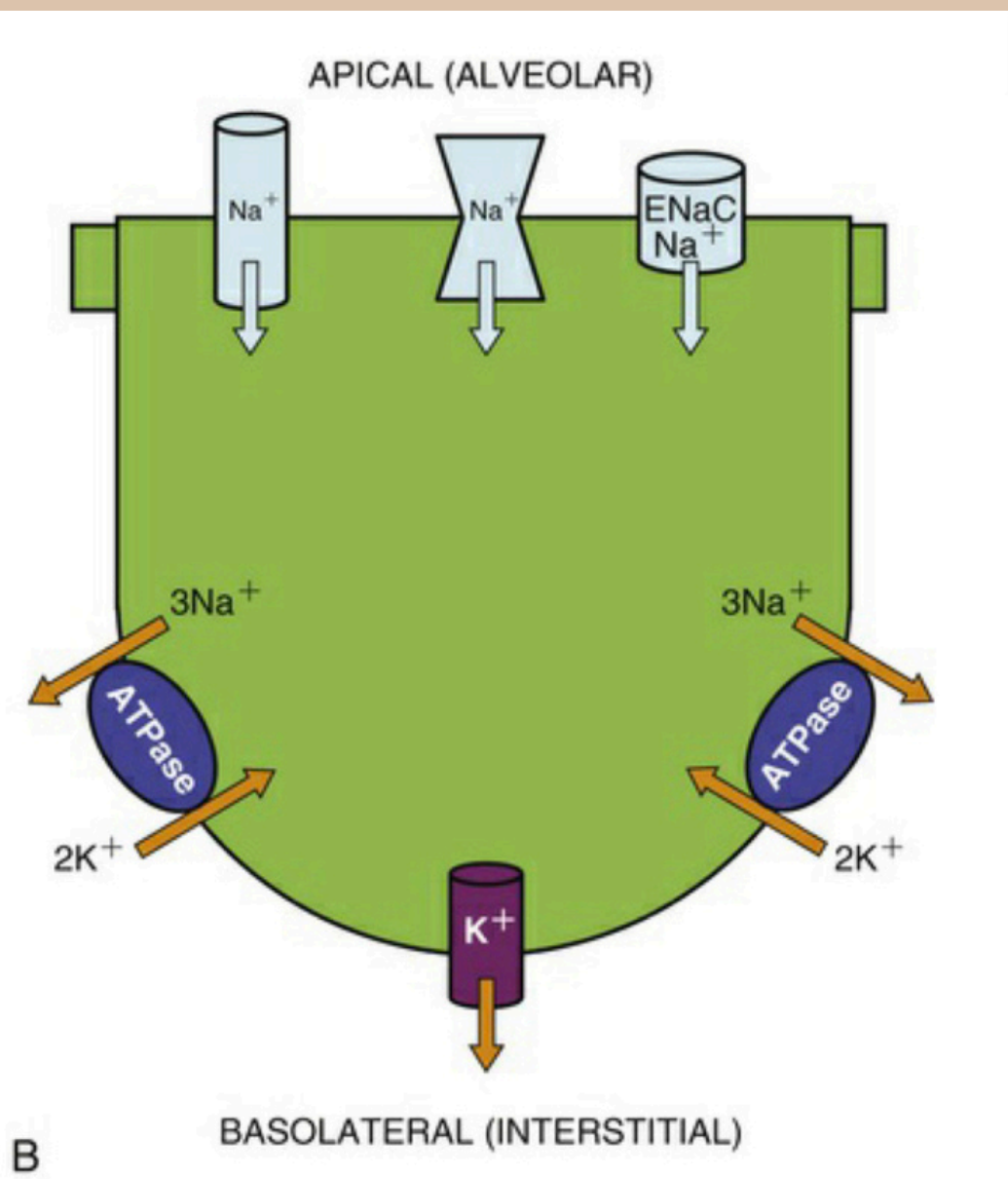
Chloride channel and fluid excretion in fetal alveoli



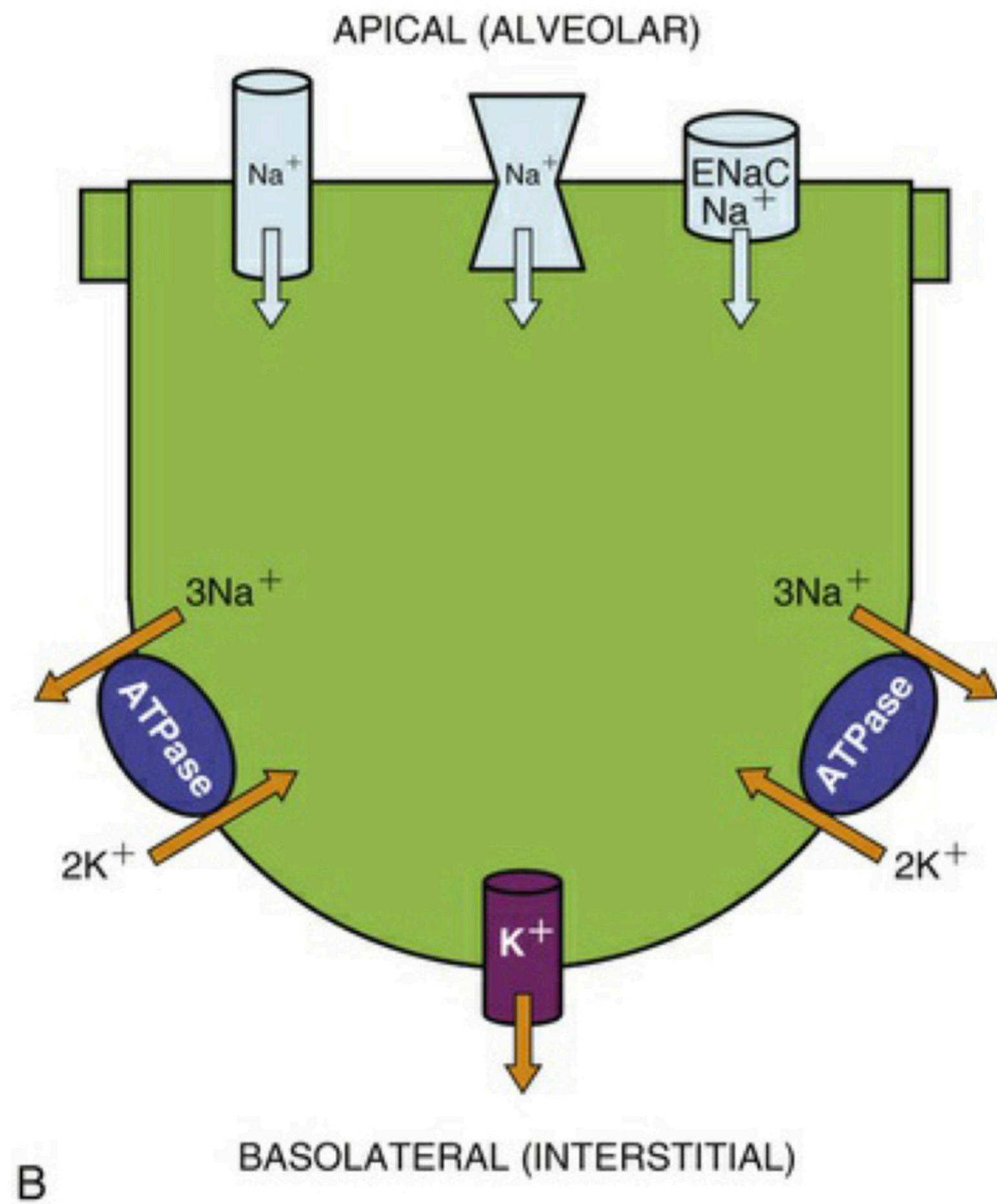
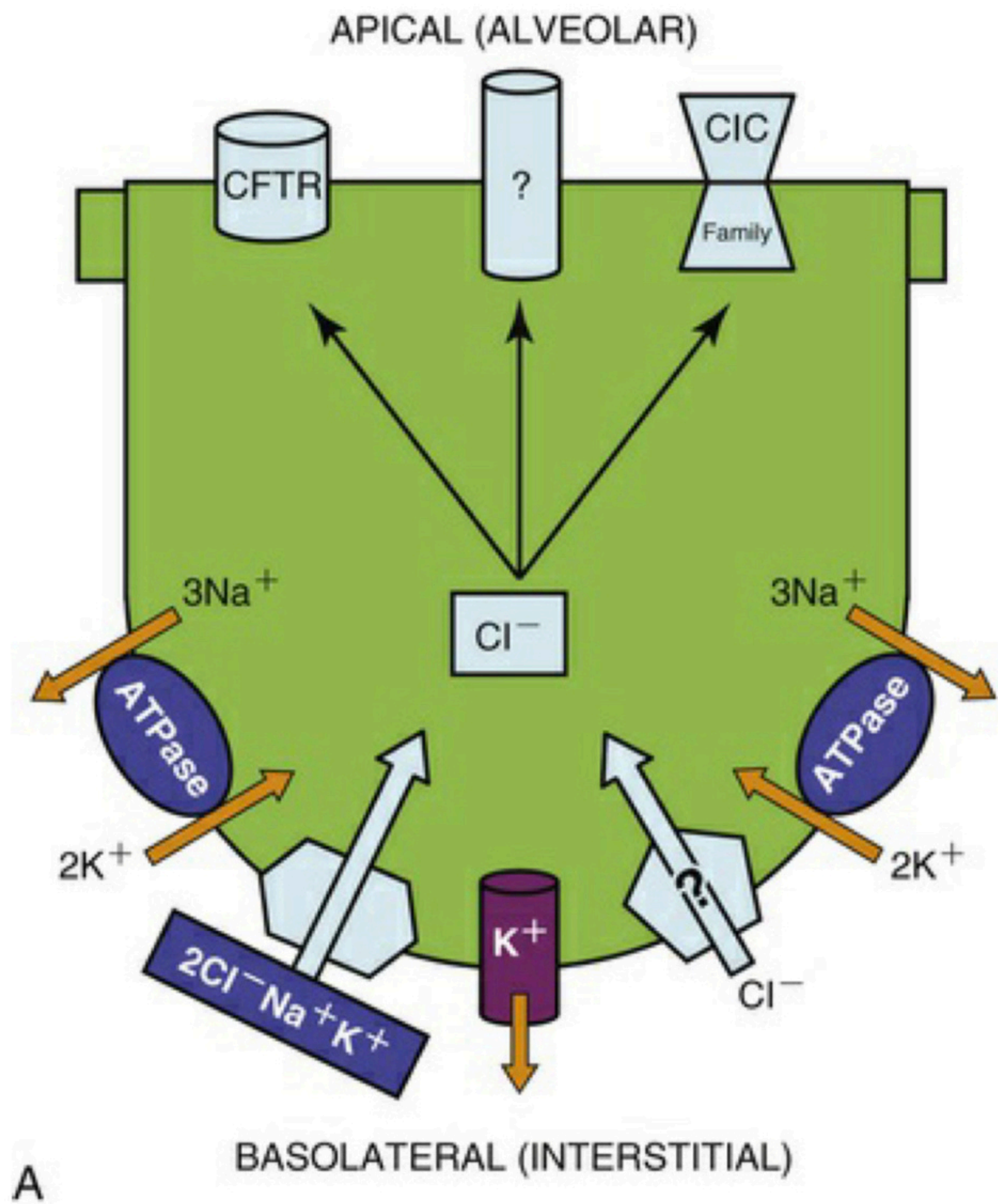
- The polarized epithelium lining the fetal lung's **lumen actively secretes Cl^-** , with Na^+ and H_2O following => **fluid distends the fetal lung.**
 - Cl^- enters on the basolateral side through membrane-bound protein transporters + secreted out the apical membrane through different chloride channels
 - one of which is the chloride channel encoded by the **cystic fibrosis transmembrane regulator (CFTR)**
- => **Abnormal CFTR: Cystic fibrosis**

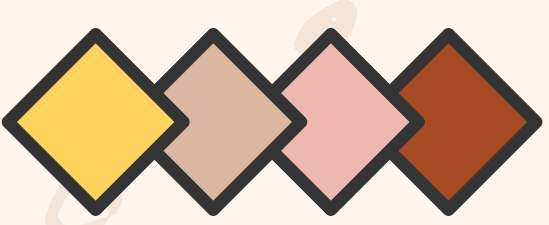
Development of Lung

Chloride channel and fluid excretion in postnatal alveoli



- **Actively absorbs Na⁺**, with Cl⁻ and H₂O following, clears the fetal lung liquid that is present at birth
- Approximately 1/3 fluid is squeezed out during a vaginal delivery
- **Catecholamines** released during labor: temporarily convert the fetal lung from a fluid-secreting organ to a fluid-absorbing organ
- Permanently converts the lung epithelium into a **sodium-absorbing mode**
- **Fluid retention in alveoli => "TTNB" due to painless labour or caesarean section**





Outline

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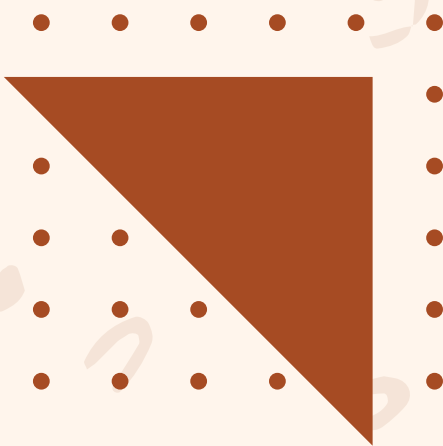
Development of Lung

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Normal lung anatomy and cell function

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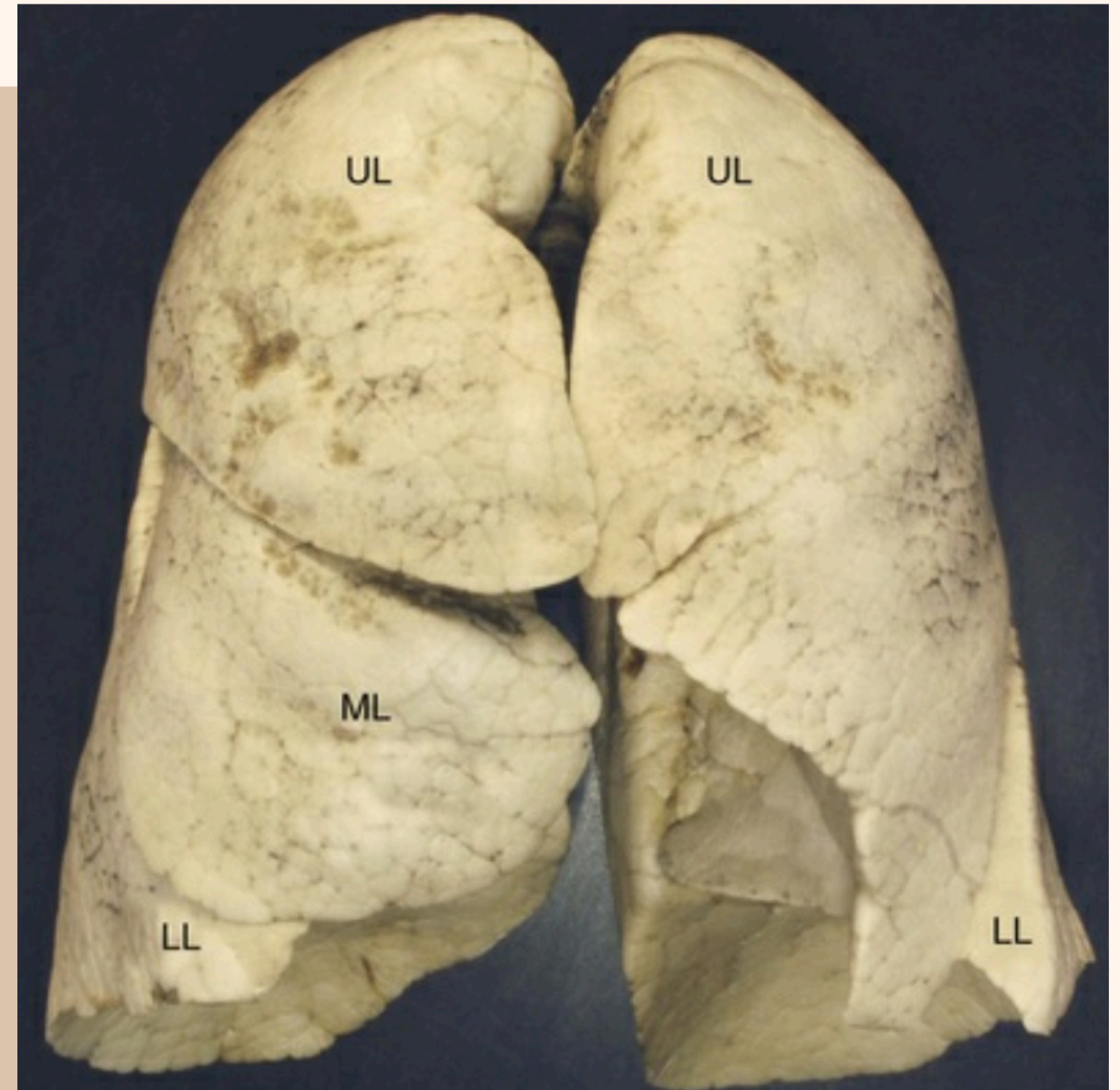
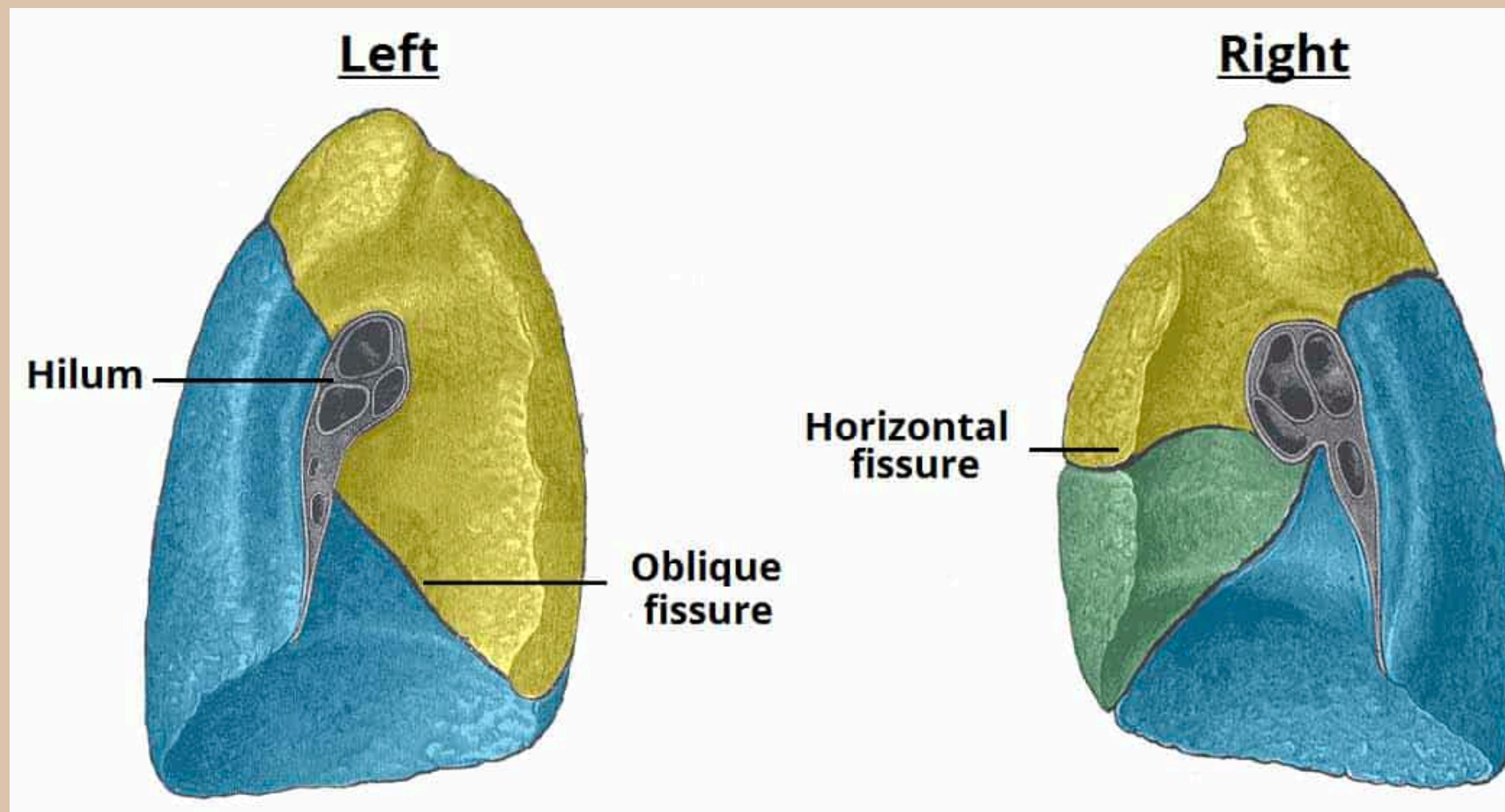
Case study of
abnormal lung development



Normal lung anatomy and cell function

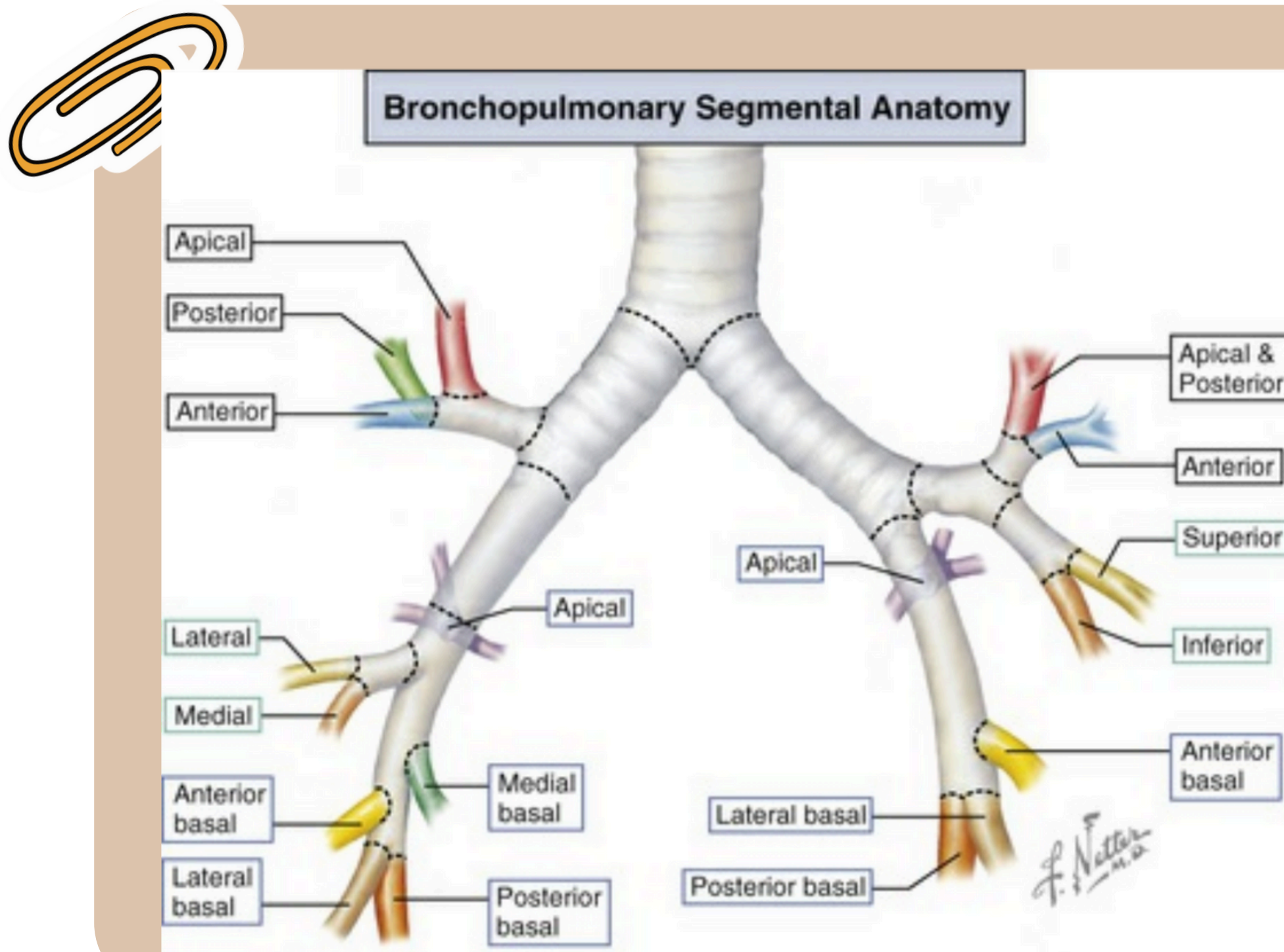
Shape and Lobe of lung

embedded in a separate pleural cavity and are separated by the mediastinum. Except at the hilum



Normal lung anatomy and cell function

Airways



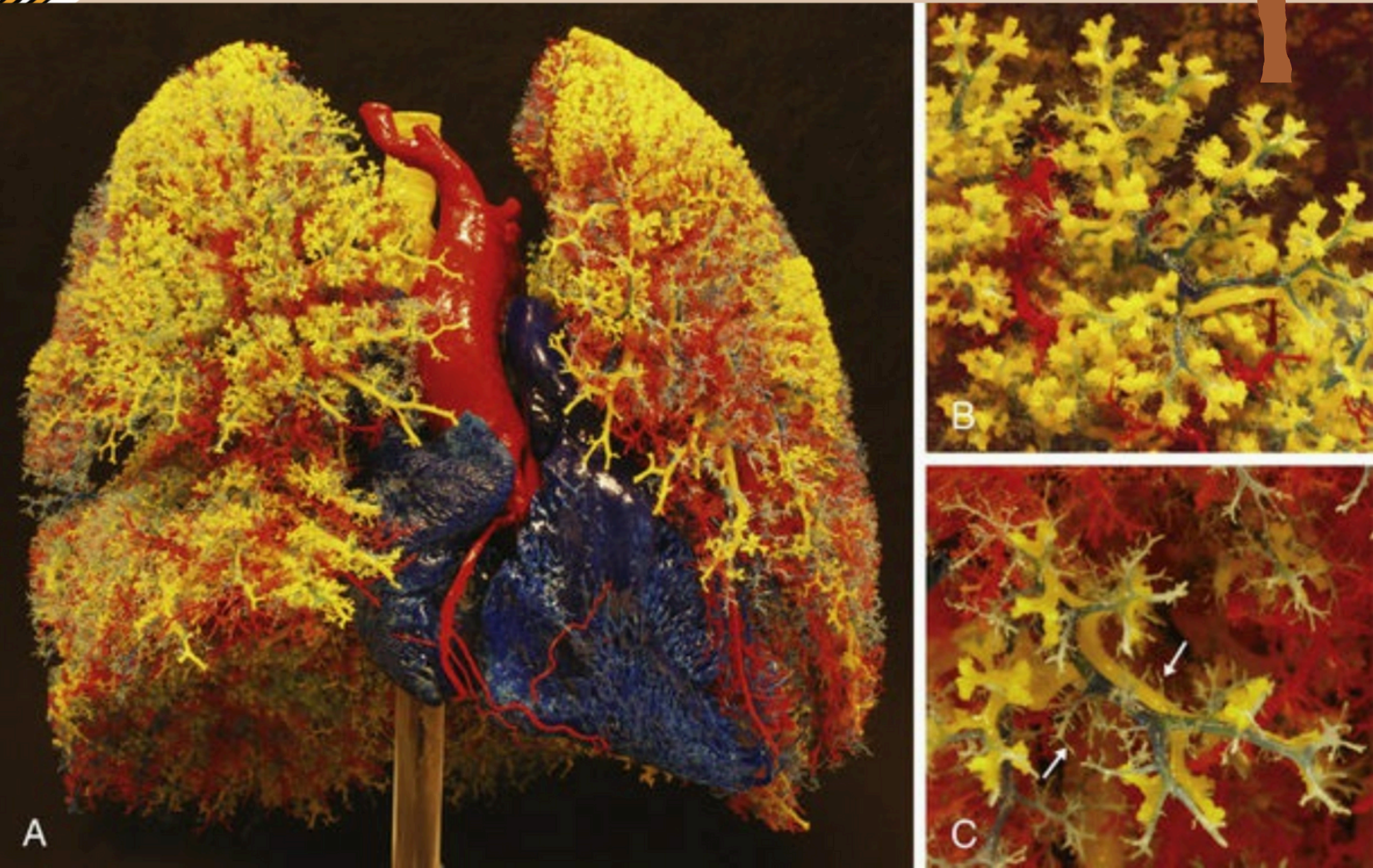
Two functional compartments

1. proximal conducting zone (the bronchial tree)
2. distal respiratory zone (the alveolar region): gas exchange

- dichotomous branching, over an average of **23 generations**

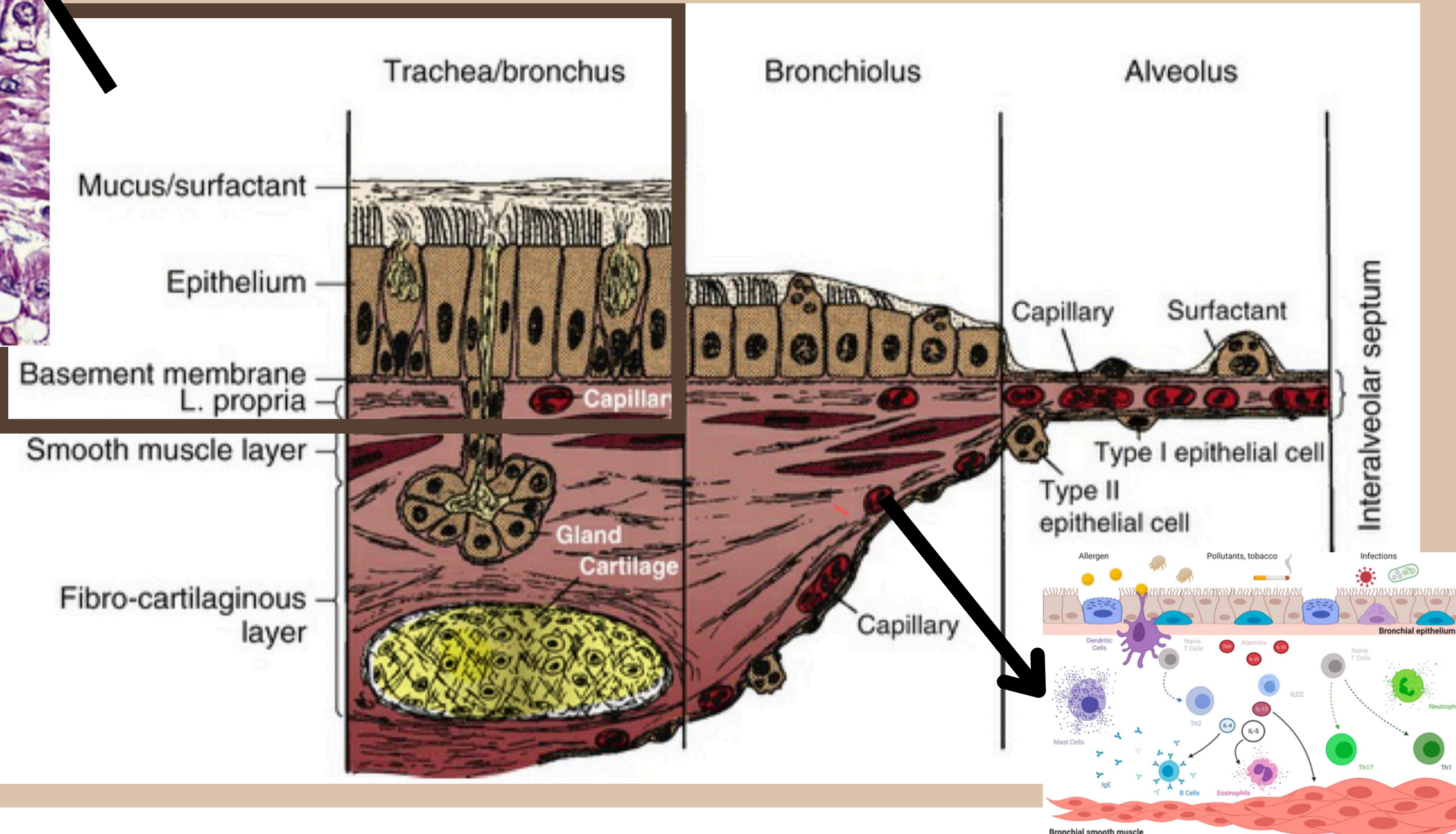
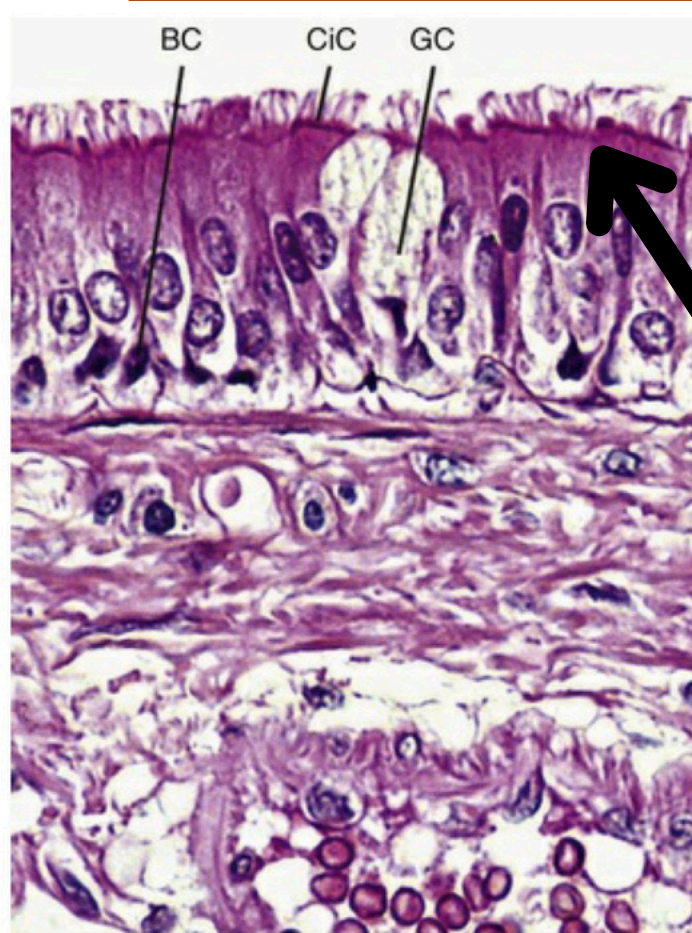
Normal lung anatomy
and cell function

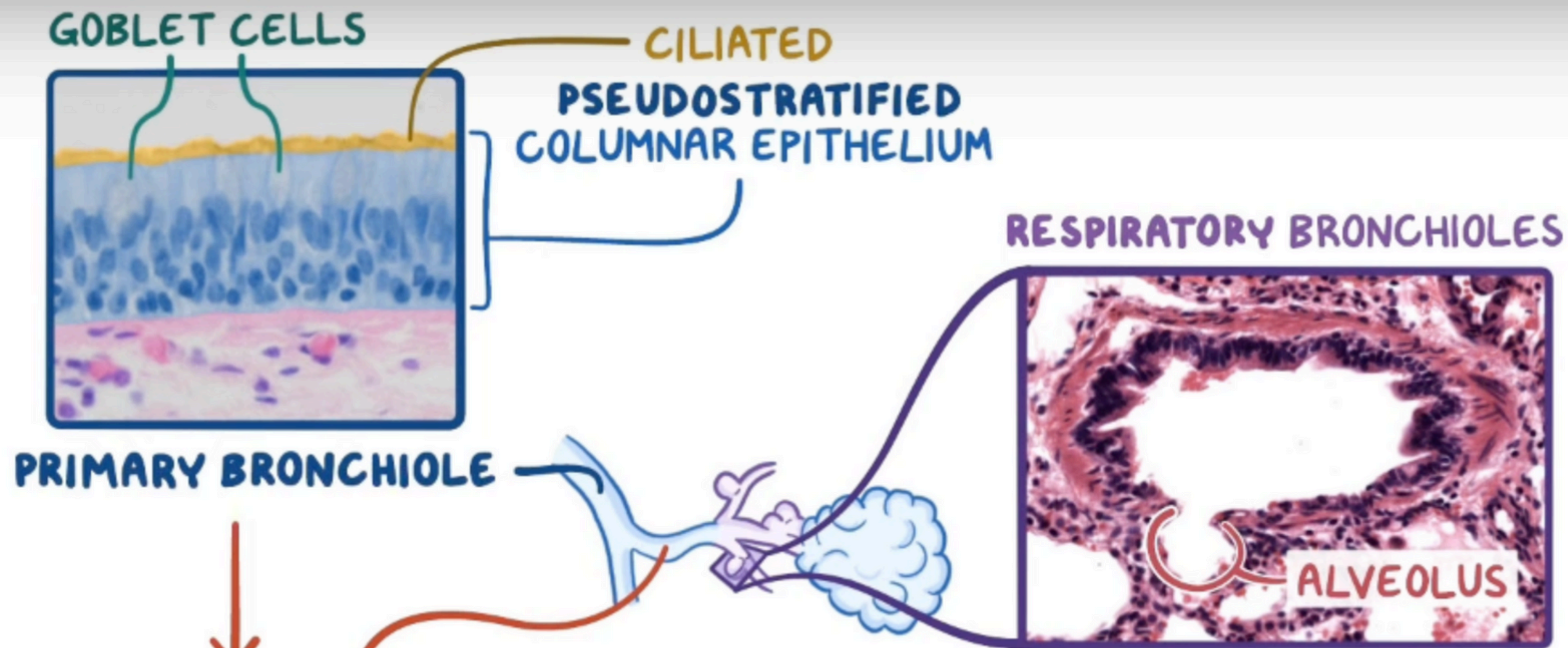
Dichotomous branching



Conducting airways	Trachea	Z	
		0	
	Bronchi	1	
		2	
		3	
Acinar airways	Bronchioles	4	
		5	
	Terminal bronchioles	14	Z'
	Transitional bronchioles	15	0
	Respiratory bronchioles	16	1
		17	2
		18	3
	Alveolar ducts	19	4
		20	5
		21	6
		22	7
	Alveolar sacs	23	8

Normal lung anatomy and cell function





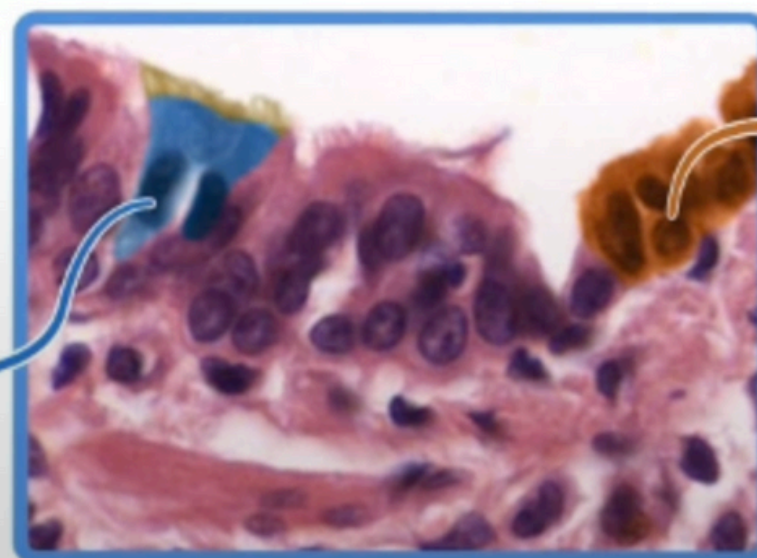
PRIMARY BRONCHIOLE

RESPIRATORY BRONCHIOLES

ALVEOLUS

MOVING DISTALLY

- * DIAMETER DECREASES
- * EPITHELIUM TRANSITIONS to **CILIATED SIMPLE COLUMNAR** & CUBOIDAL CELLS

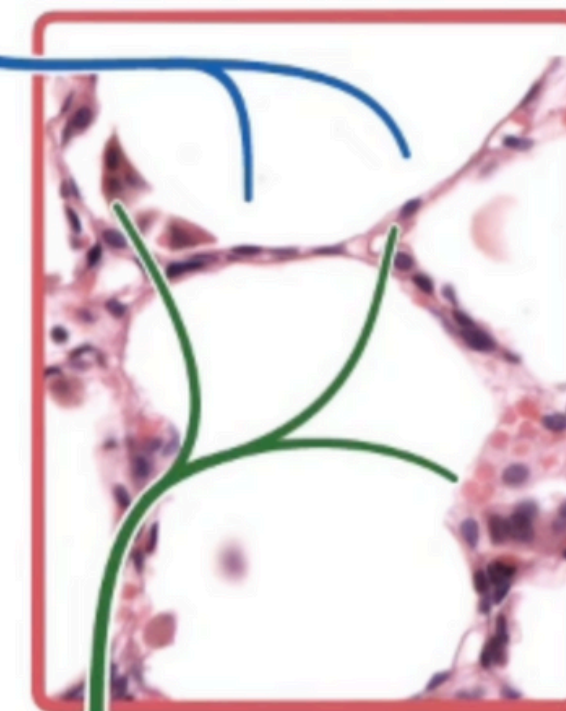


CLARA CELLS

- ~ TALL
- ~ NON-CILIATED
- ~ COLUMNAR
- ~ DOME-SHAPED APICAL ENDS

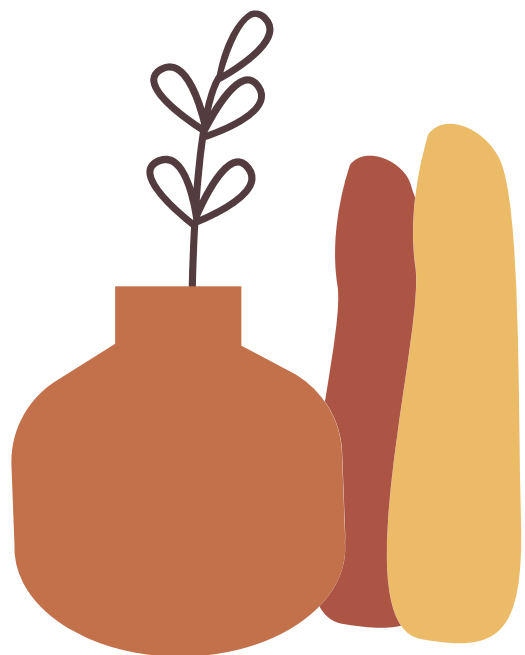
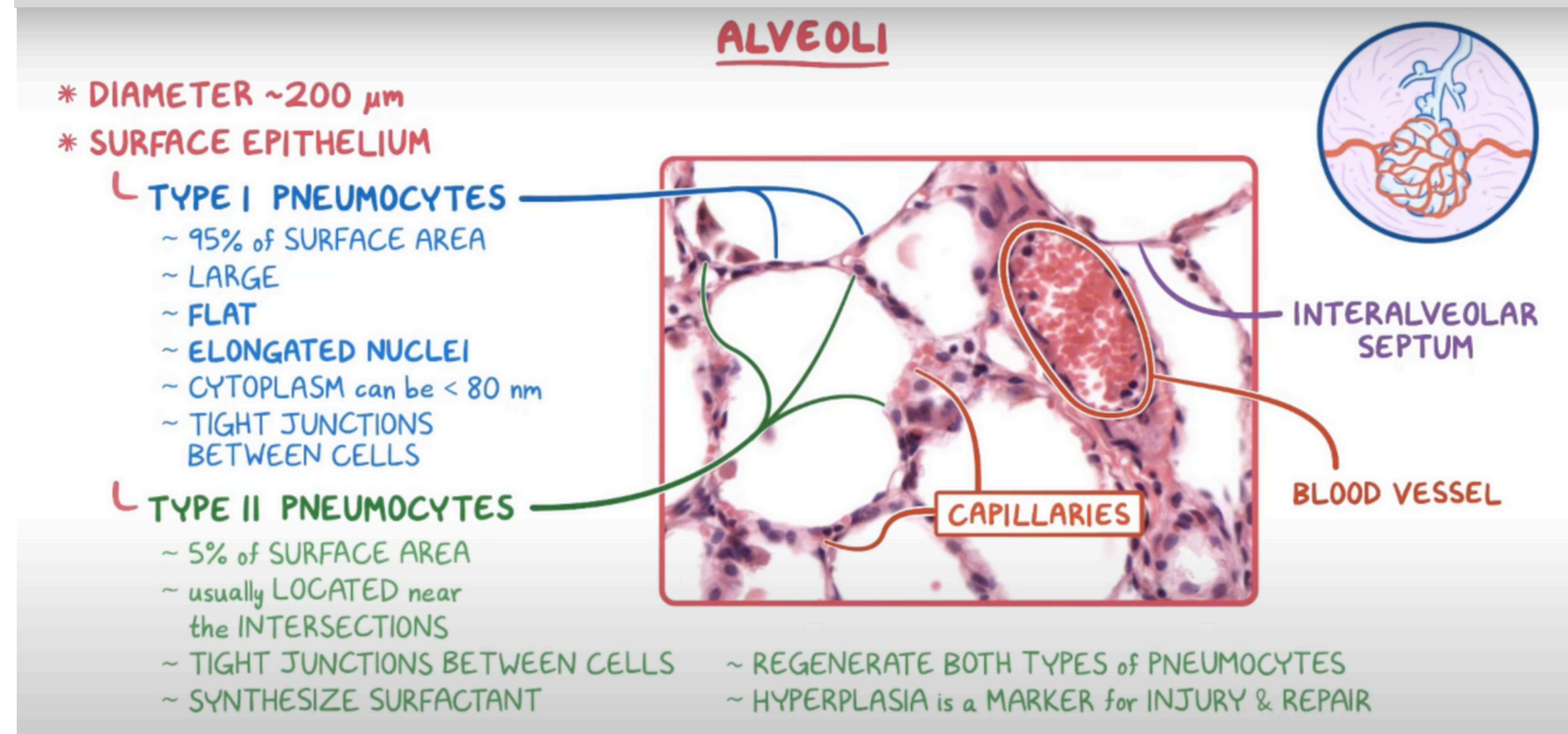
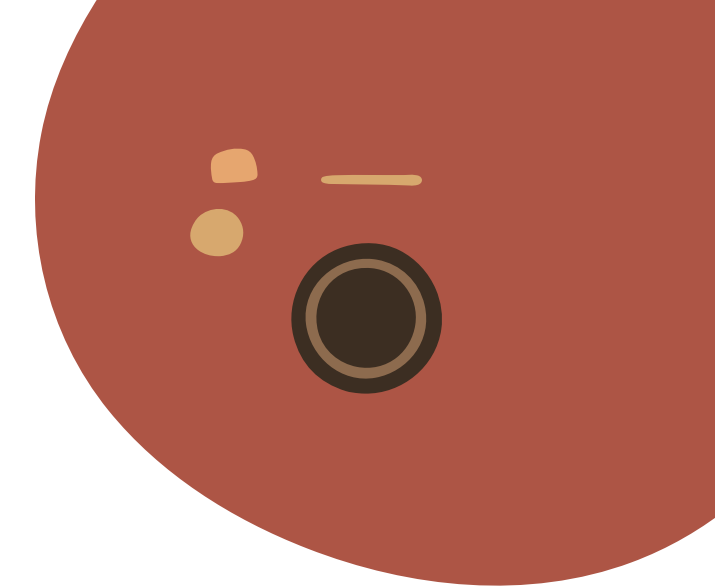
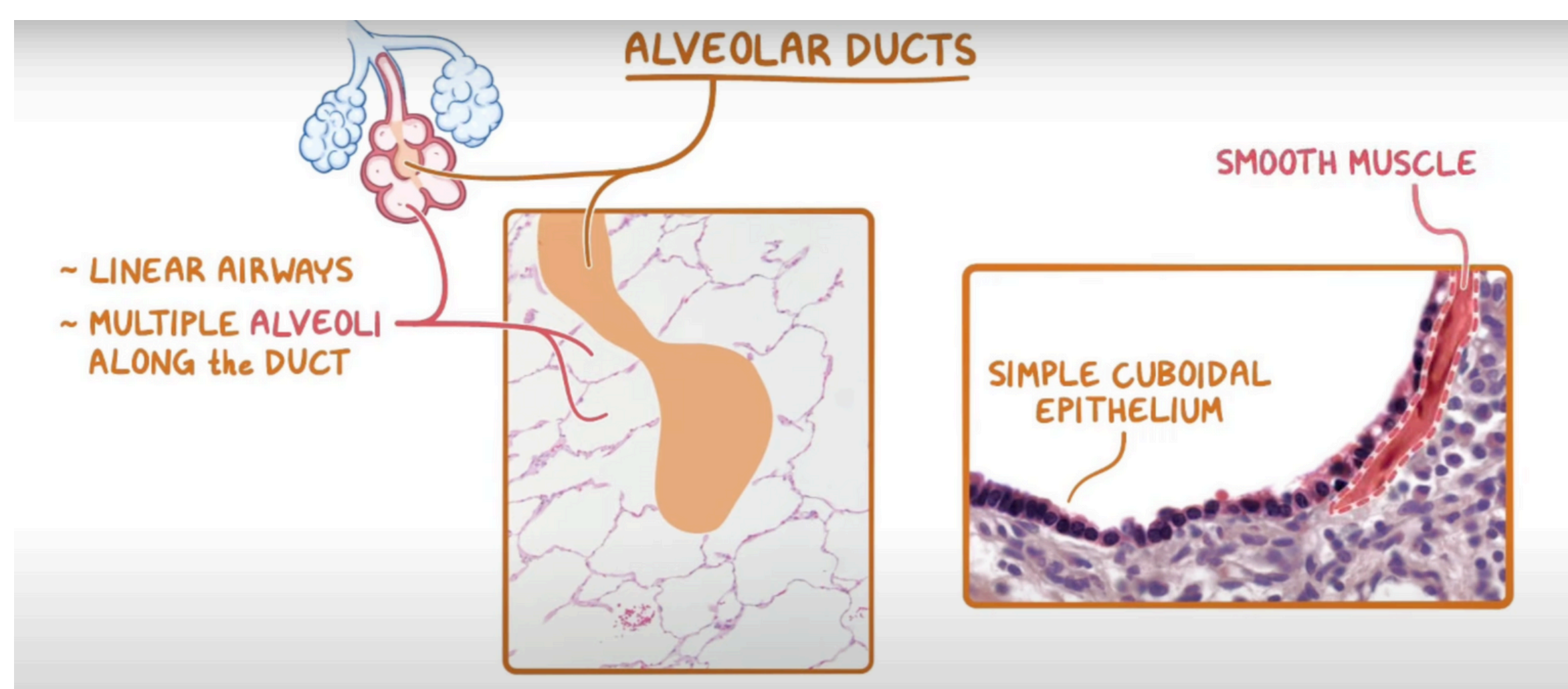
TYPE I PNEUMOCYTES

- ~ LARGE FLAT CELLS
- ~ ELONGATED NUCLEI
- ~ 95% of SURFACE AREA

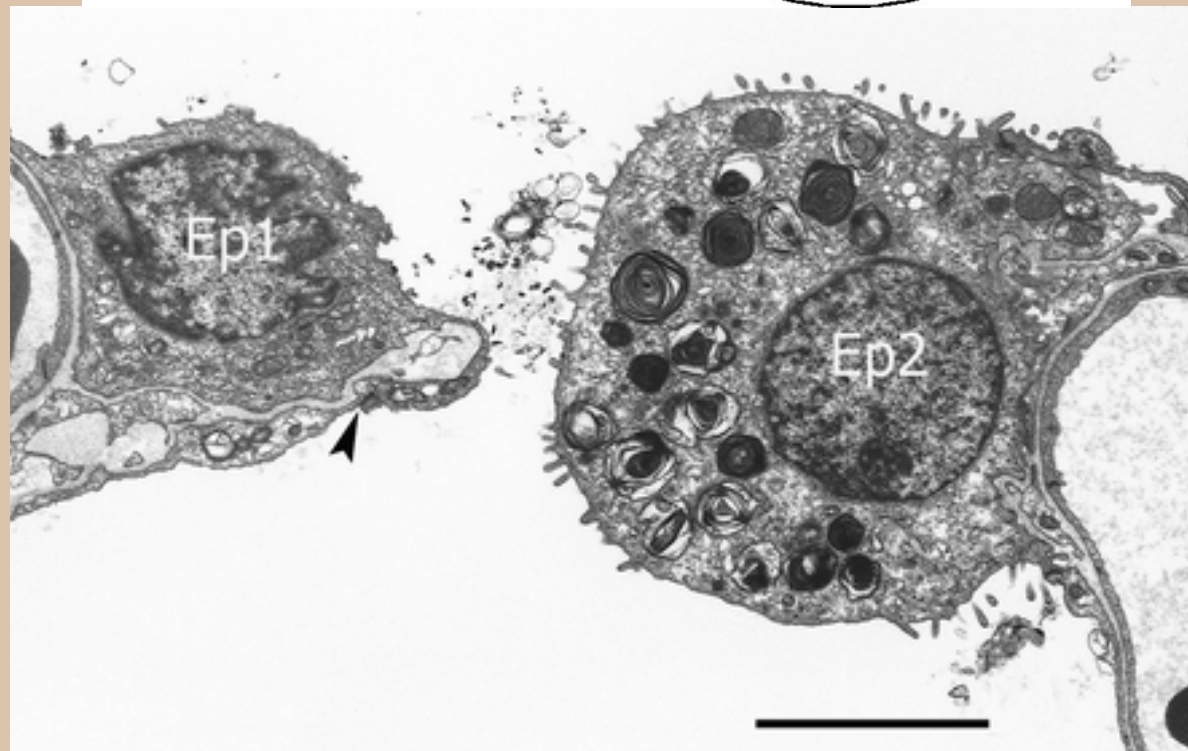
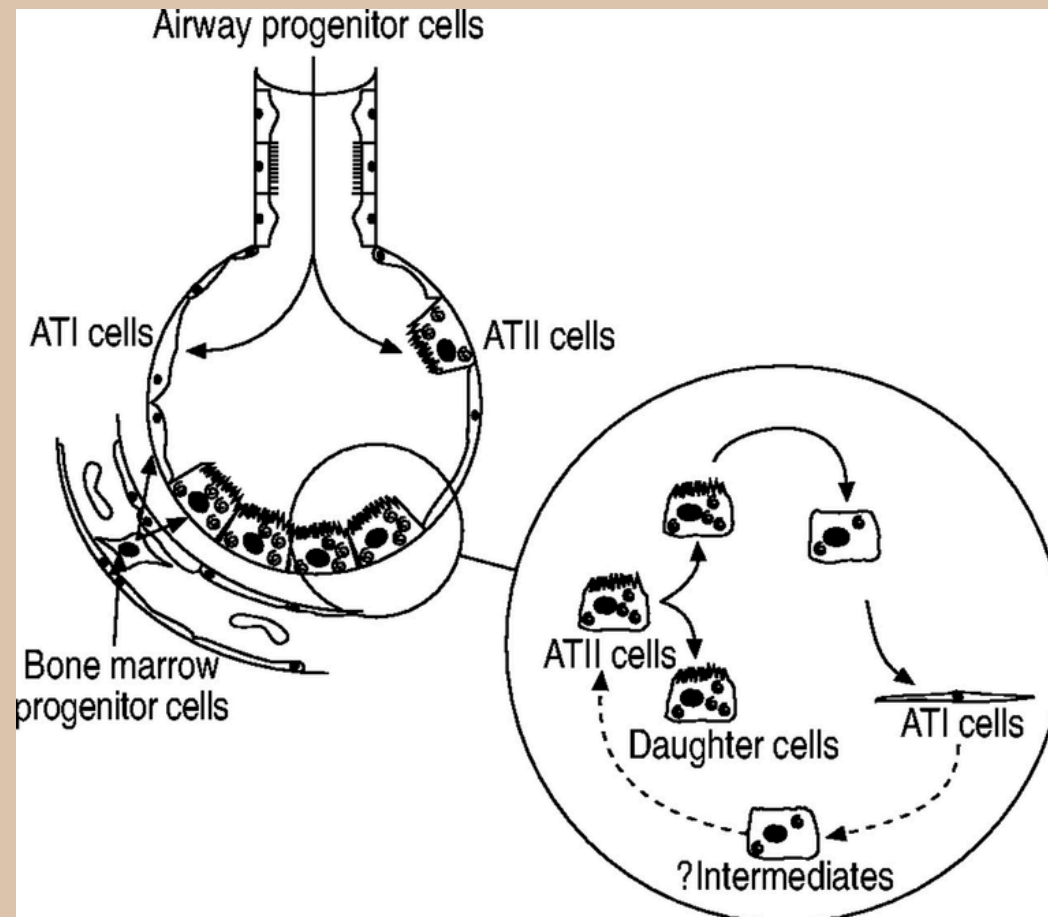


TYPE II PNEUMOCYTES

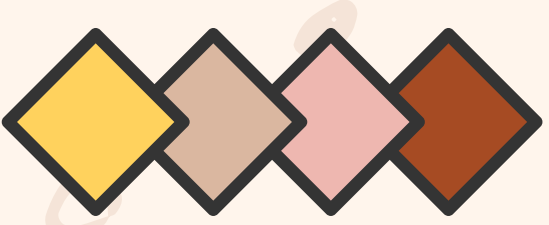
- ~ CUBOIDAL CELLS
- ~ LOCATED near INTERSECTIONS
- ~ HYPERPLASTIC when there's INJURY



Alveolars - Pneumocytes



- **Type I alveolar epithelial cells**
 - extremely broad, thin (0.1 to 0.5 micrometers) total cover about 95% of the alveolar surface
 - **Epithelial barrier** for gas exchange
 - **Actively transporting Na⁺ with Cl⁻ and water**; clearance of airspace fluid
- **Type II epithelial cells: cuboidal shape**
 - 5% of the total alveolar surface area
 - Microvilli and osmophilic inclusions => **lamellar bodies (storage sites for surfactant)**



Outline

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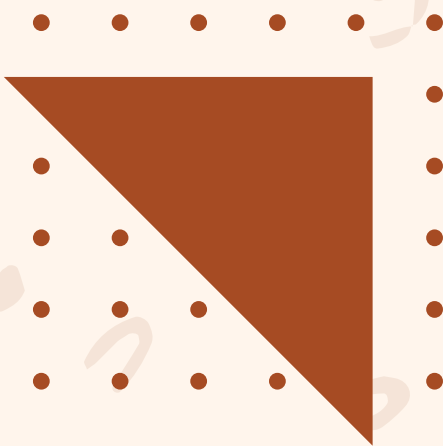
Development of Lung

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Normal lung anatomy and cell function

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Case study of
abnormal lung development



Case study of abnormal lung development



- ผู้ป่วยชาย อายุ 2 ปี
- ภูมิลำเนาเขตสายไหม กรุงเทพมหานคร
- เกิดวันที่ 27 กันยายน 2563
- ประวัติจากมารดา ความน่าเชื่อถือ: สูง

5 เดือนก่อนมาโรงพยาบาล มีอาการไอแห้งๆ เสมหะเล็กน้อย

Case study of abnormal lung development



- 5 เดือนก่อนมาโรงพยาบาล (อายุประมาณ 1 ปี 6 เดือน) ไอแห้งๆ ไม่ค่อยเสมหะ ไม่มีไข้ ไม่หอบเหนื่อย เล่นได้ดี กินได้ปกติ ไม่มีอ่อนเพลีย ไม่มีปวดกล้ามเนื้อ ปวดกระดูก ไม่มีตัวเขียว ไม่มีปวดท้องท้องเสียถ่ายเหลว ไม่มีผื่นขึ้นตามตัว
- ปฏิเสธประวัติ sick contact ในครอบครัว
- คลอด Term normal labour ไม่มีปัญหาแรกคลอด
- ได้รับการรักษาตามอาการมาตลอด แต่อาการไม่ดีขึ้น
- Physical examination ที่สำคัญ => No deformity, No rash, No abnormal HEENT, Lungs: clear, equal breath sound, Heart: regular, normal S1S2, no murmur



Case study of abnormal lung development



Case study of abnormal lung development



Middle mediastinum

Anterior: Anterior margin of the pericardium

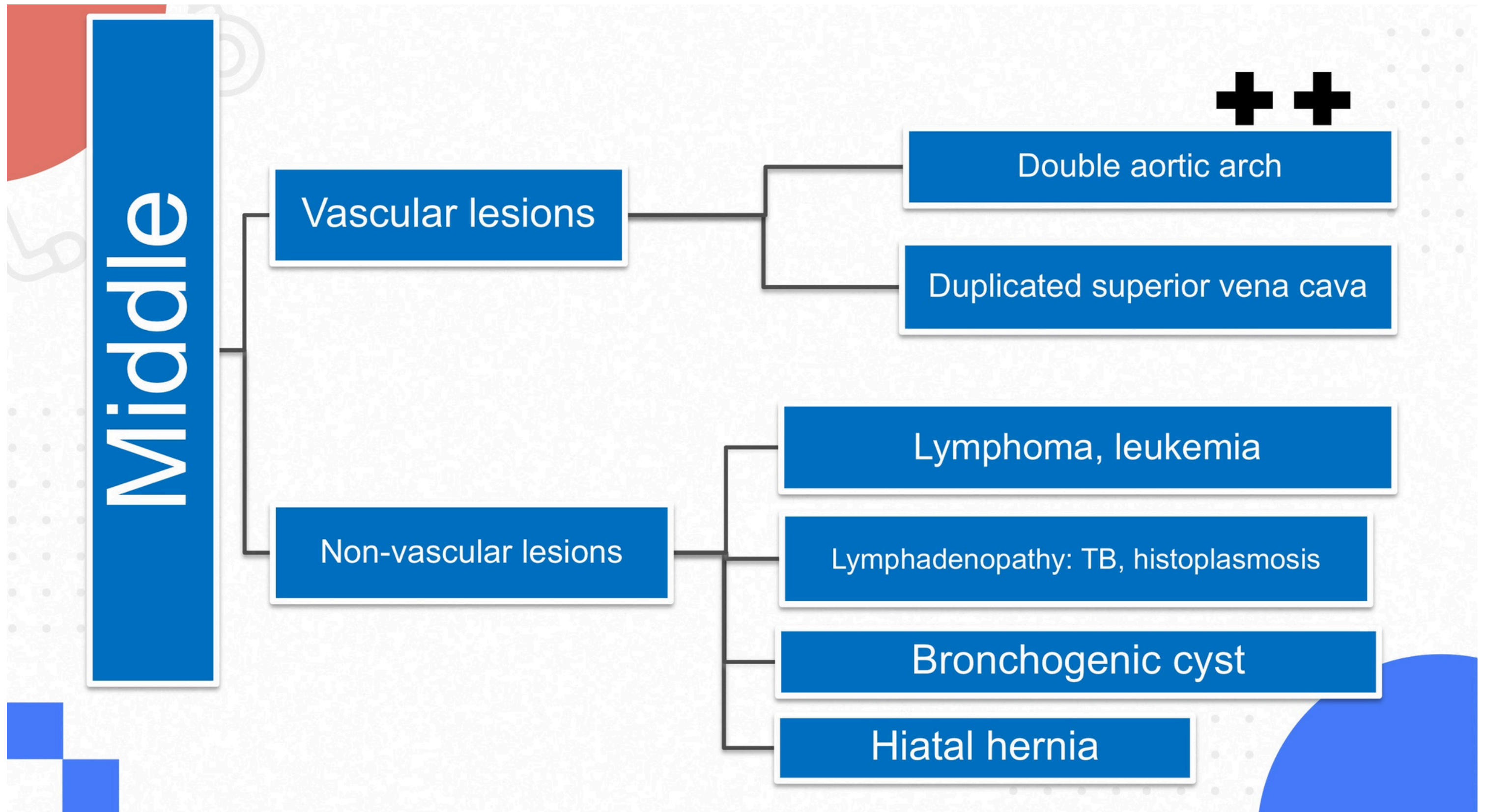
Posterior: Posterior border of the pericardium

Laterally: Mediastinal pleura of the lungs

Superiorly: Imaginary line extending between the sternal angle and the T4 vertebrae

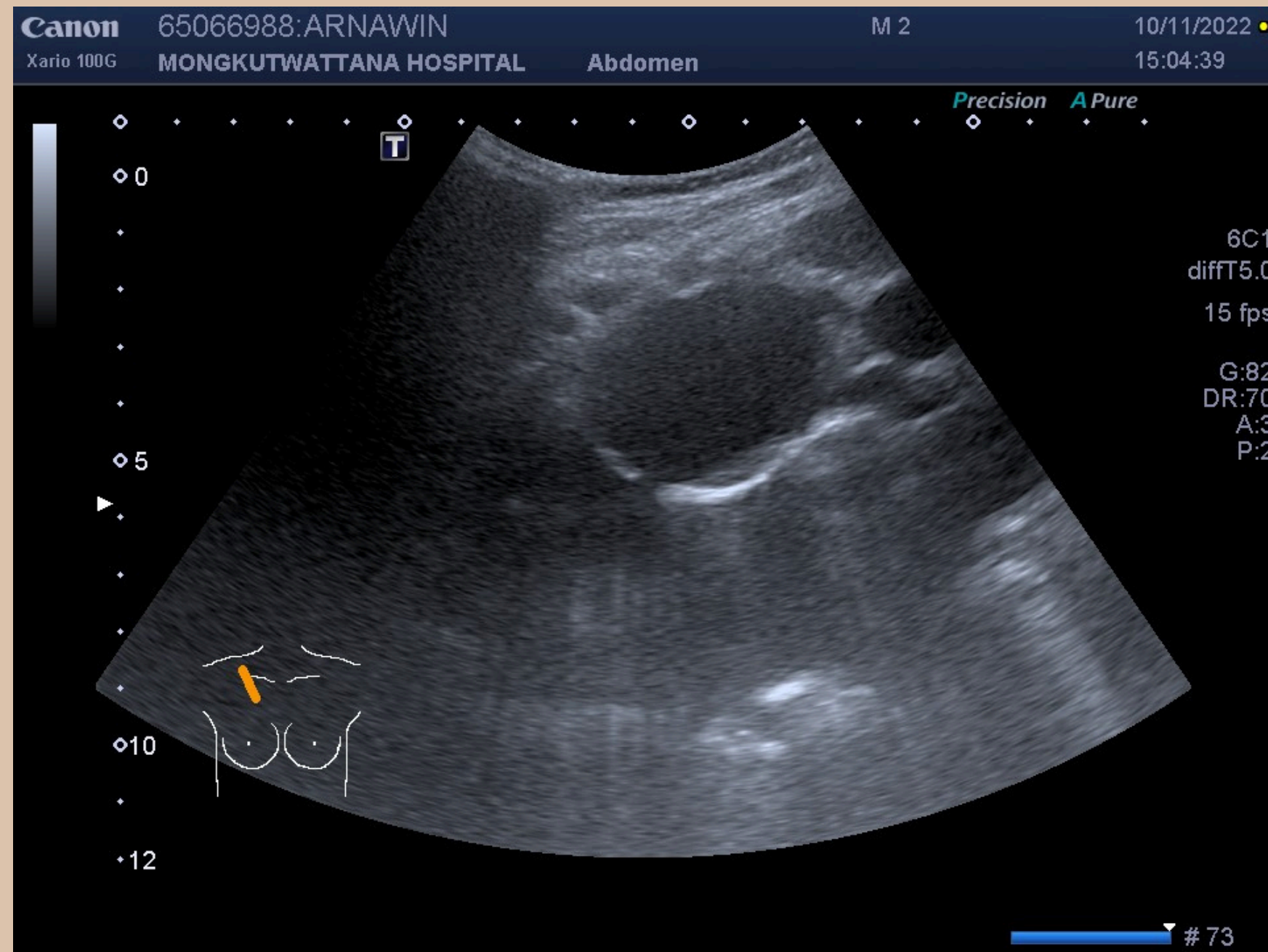
Inferiorly: Superior surface of the diaphragm

Case study of abnormal lung development



Case study of abnormal lung development

Ultrasound



Case study of abnormal lung development



Differential diagnosis

Cystic Lesions
Macrocystic adenomatoid malformation
Congenital diaphragmatic hernia
Bronchogenic cyst
Mediastinal encephalocele
Pleural and pericardial effusions

Case study of abnormal lung development



CPAM (congenital pulmonary airway malformation)

New Nomenclature	Old Terms Superseded
CLHL	Congenital lobar emphysema
	Polyalveolar lobe
CTM	Cystic adenomatoid malformation (Type 0–4 pathologically)
	Sequestration (intrapulmonary and extrapulmonary)
	Bronchogenic cyst
	Reduplication cyst
	Foregut cyst
CSL	Pulmonary hypoplasia
Absent lung, absent trachea	Agenesis of lung, tracheal aplasia
Absent bronchus	Bronchial atresia

CLHL, Congenital large hyperlucent lobe; *CSL*, congenital small lung; *CTM*, congenital thoracic malformation.

Case study of abnormal lung development



CTM (congenital thoracic malformation)

CTM	Cystic adenomatoid malformation (Type 0–4 pathologically)
	Sequestration (intrapulmonary and extrapulmonary)
	Bronchogenic cyst
	Reduplication cyst
	Foregut cyst

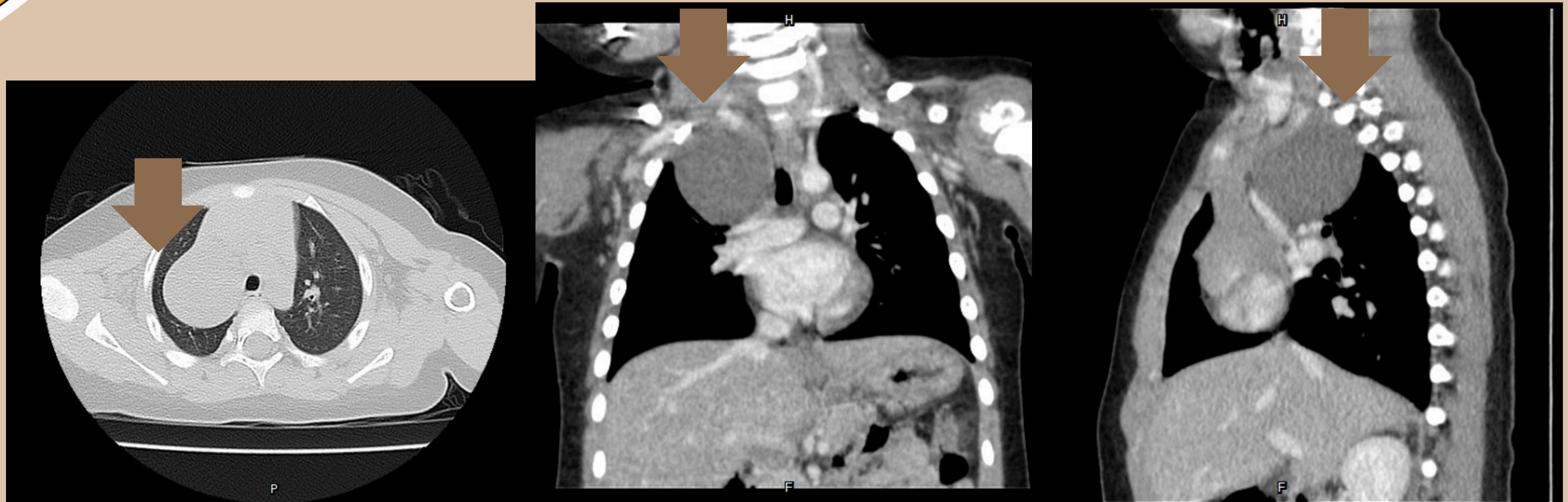
Bronchogenic cyst =>
abnormal division
foregut, not only in
lung area, **Single cyst**

CCAM => malformation
tracheobronchus
Multi-cystic lesion is
most common

Sequestration =>
Pulmonary tissue
**supply by systemic
arteries**

Case study of abnormal lung development

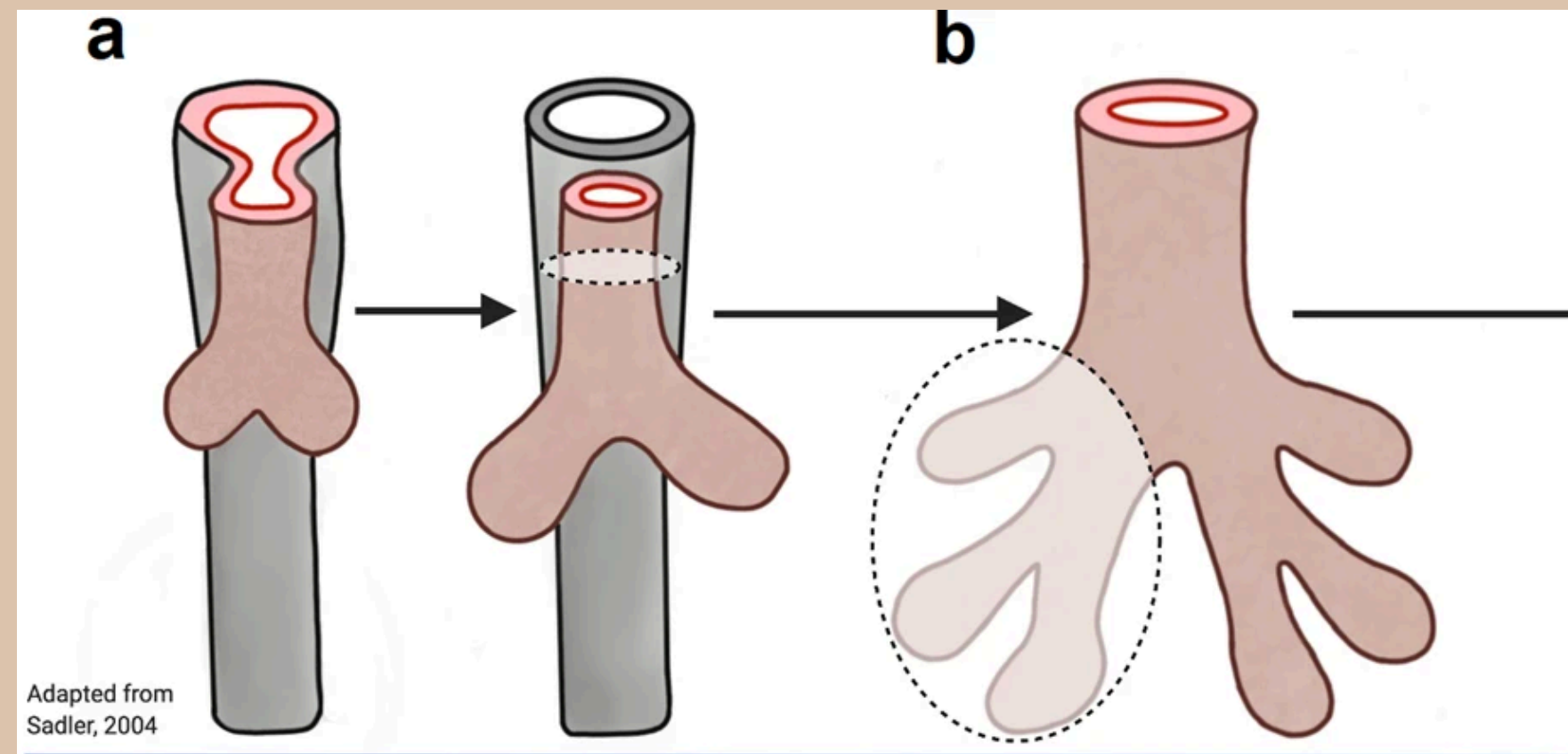
CTA



Case study of abnormal lung development

Suspected

- Bronchogenic cyst => Pseudogranular stage abnormality [6-16 weeks of Gestation]

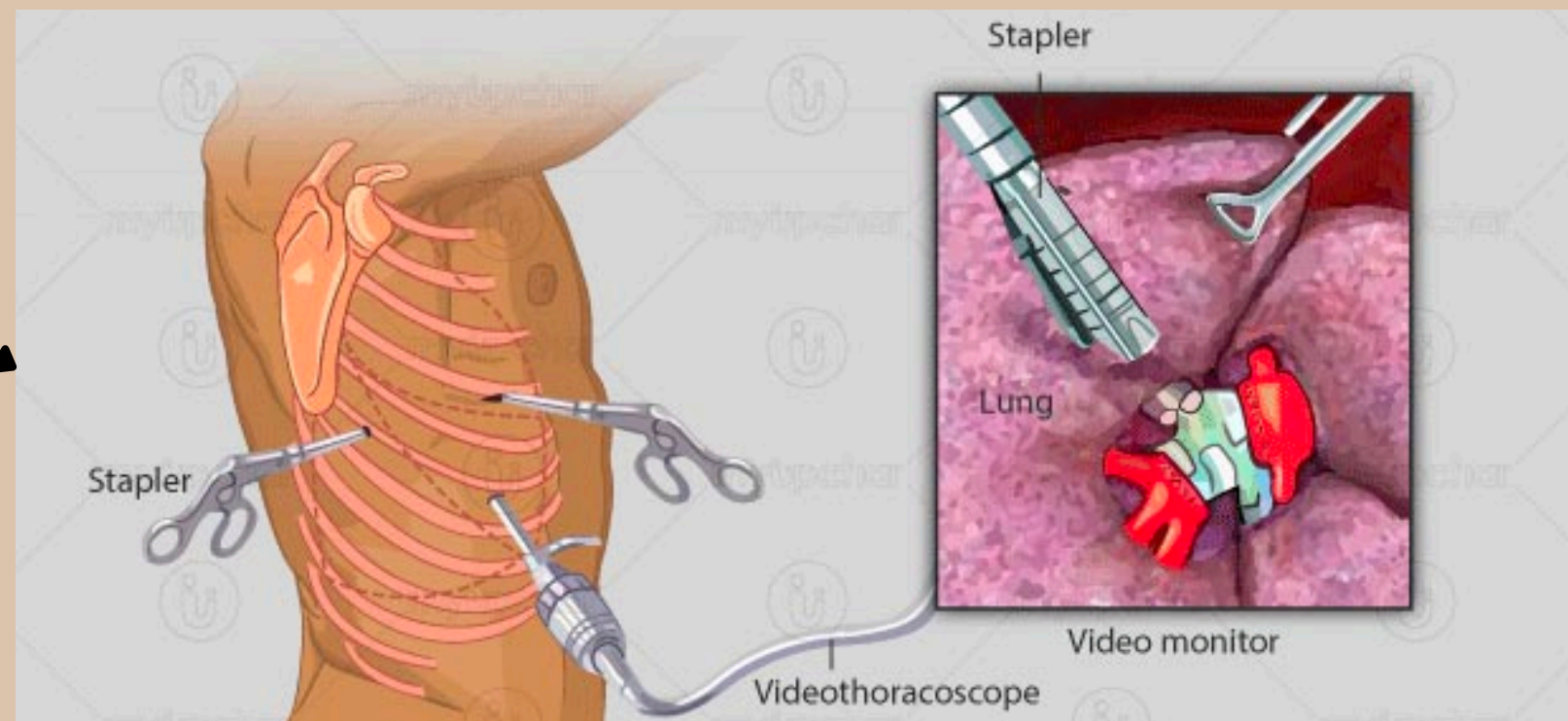


Case study of abnormal lung development

Management

Surgery - complete resection => cystectomy

- Open Thoracotomy
- Video-assisted thoracoscopy (VATS) ✓



Case study of abnormal lung development

In this case follow up

- CXR: post-op + before discharge



Case study of abnormal lung development



Pathology



Surgical Pathology Report

แผนกจักษุวิทยา กอปรวิทยา สถาบันพยาธิวิทยา
315 ถนนราชวิถี แขวงทุ่งพญาไท เขตราชเทวี กรุงเทพฯ 10400 โทร: 02-354-7600 ต่อ 85126

Diagnosis: Tissue, posterior mediastinum, removal:

- Fragments of benign cyst partially lined by benign columnar epithelium, favor bronchogenic cyst.
- No malignancy seen.

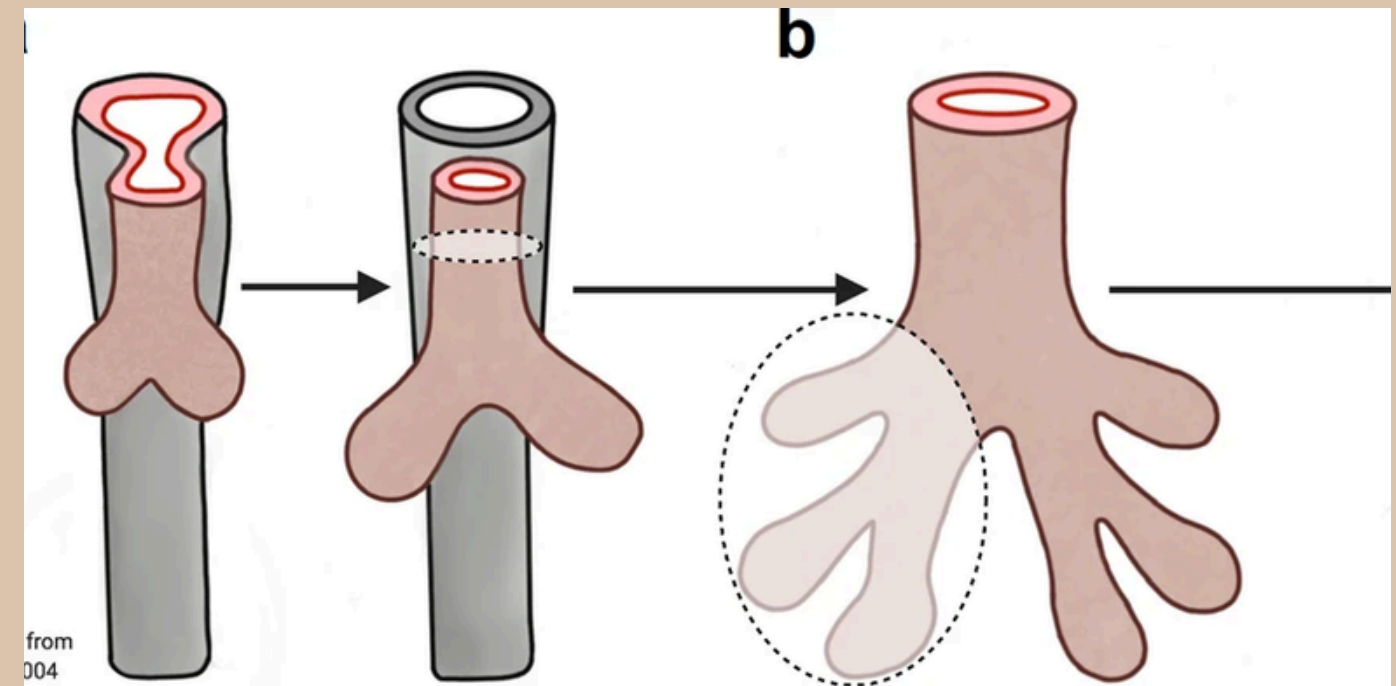
NOTE: This case was reviewed by second pathologist (Kantang Satayasoontorn, M.D.).

Case study of abnormal lung development



Bronchogenic cyst

- Abnormal budding of the tracheal diverticulum of the **foregut**
- The most common cyst in infancy
- **Late Embryonic budding to pseudogradular phase abnormality**

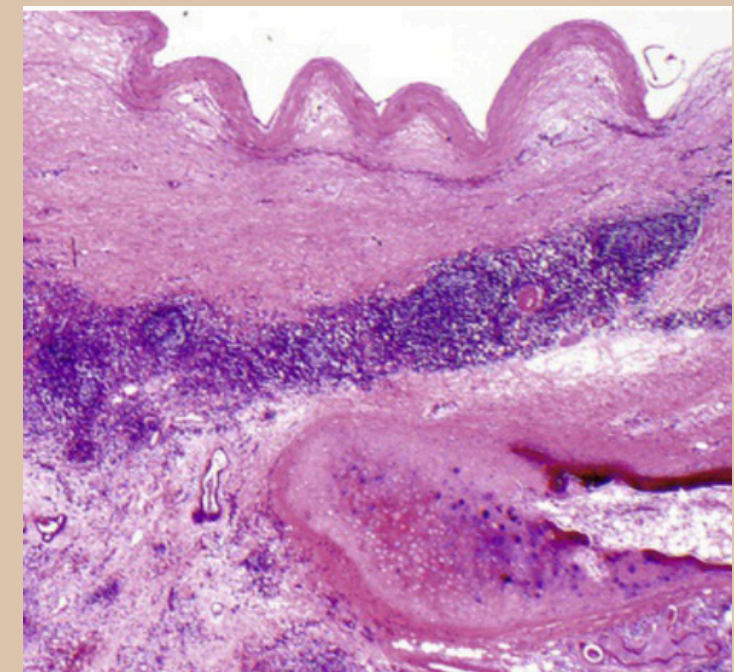
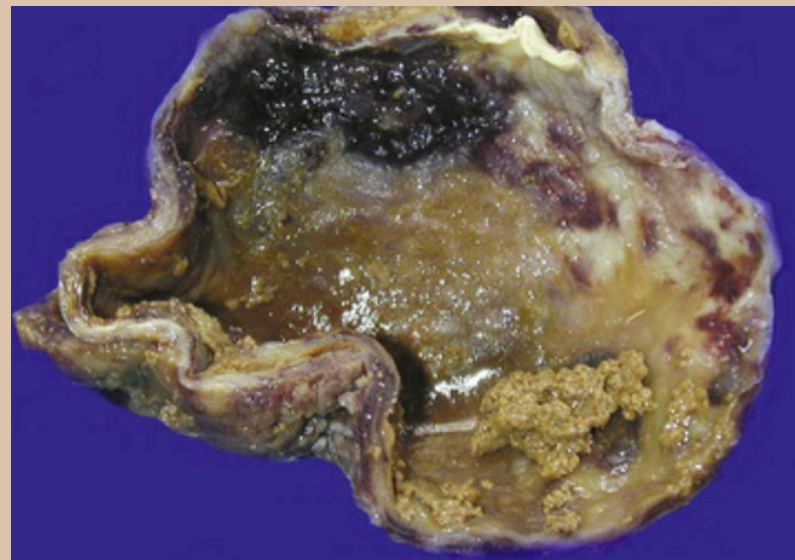


Case study of abnormal lung development



Bronchogenic cyst

- Symptoms: Recurrent infection, chest pain, productive cough, hemoptysis, dysphagia
- Pathology: Fibrous scarring, brown discoloration (chronic bleeding), purulent debris



Case study of abnormal lung development



Bronchogenic cyst

- Complication:
 - According to associated anomalies
 - Distortion and compression of mediastinal organs - Restrictive and obstructive lung disease
 - Scoliosis

Surgery - complete resection => cystectomy

- Open Thoracotomy
- Video-assisted thoracoscopy (VATS)

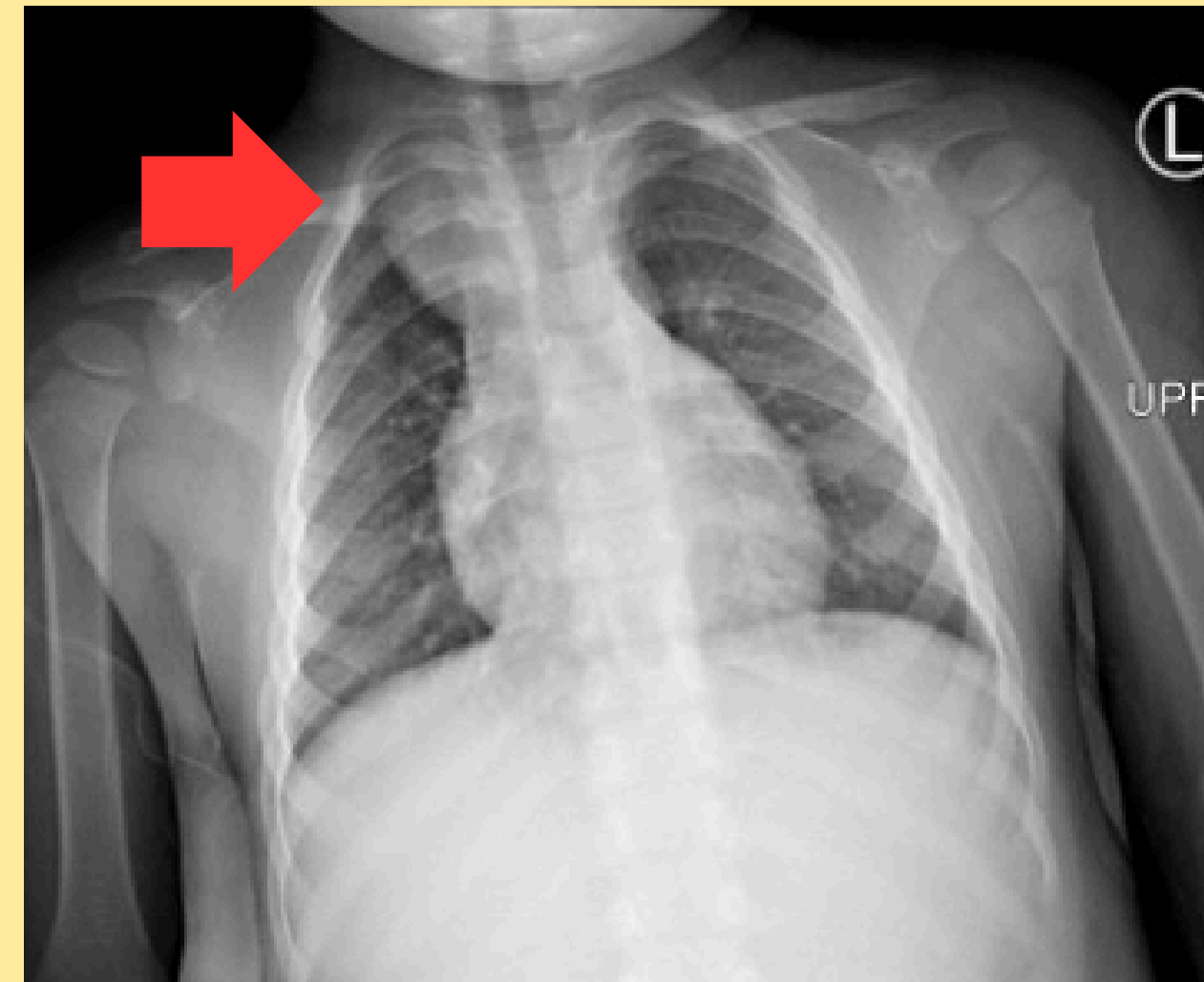
Case study of abnormal lung development



During follow up at the OPD => no abnormal symptoms, but the CXR demonstrated **abnormal mass-like opacity at the same area of previous bronchogenic cyst**



before discharge

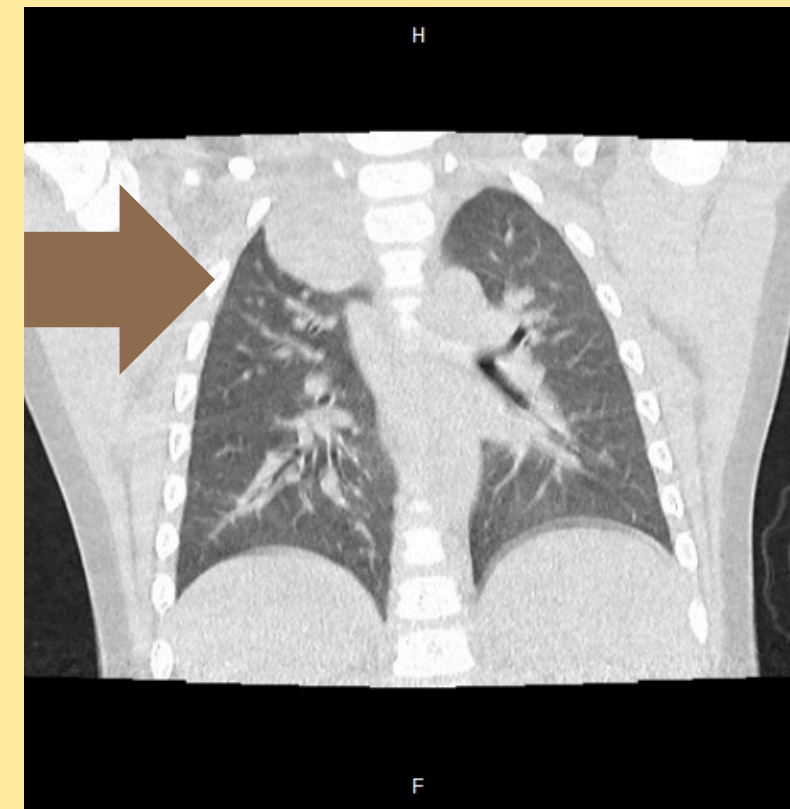
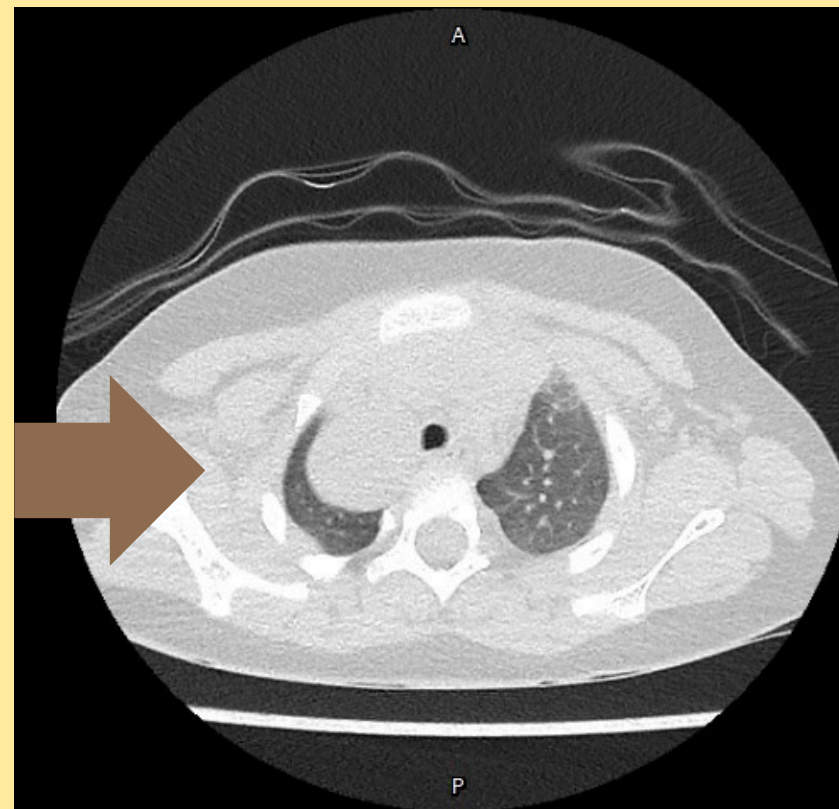


Follow-up film (3-month later)

Case study of abnormal lung development

CTA

- suspected; Recurrent bronchogenic cyst



Case study of abnormal lung development

Lung parenchyma: No discrete pulmonary nodule or mass is demonstrated.

Trachea and bronchi:

- Decrease in size of bronchogenic cyst as evident by a round shape hypodensity lesion (12-24 HU), now measured 3.0x3.2x2.6 cm in APXTRxCC dimensions (previous 4.0x4.1x4.3 cm) at right upper lung zone with adjacent to the right sided trachea.
- Trachea and main bronchi are patent.

Pleura: No abnormal pleural thickening, pneumothorax or pleural effusion is seen.

Mediastinum and lymph node:

- No mediastinal mass is seen.
- No significant size of mediastinal and hilar lymph nodes is seen.

Heart and pericardium : No cardiomegaly or pericardial effusion is noted.

Major thoracic vessels :

- Normal size of main pulmonary artery is noted.
- Normal caliber of thoracic aorta, aortic arch and abdominal aorta are noted.

The included lower neck: Normal size of thyroid gland. No abnormal enlarged supraclavicular node.

The esophagus : No esophageal dilatation or gross mass is noted.

Soft tissue and chest wall : No significant axillary node.

Bone : No osteolytic or osteoblastic lesion is detected..

The included upper abdomen : The visualized liver, stomach, bowel loops, pancreas and spleen, bilateral kidneys are unremarkable.

IMPRESSION:

- Decrease in size of bronchogenic cyst at right upper lung zone as described.
- No suspicious pulmonary nodule or enlarged intra-thoracic node.

Case study of abnormal lung development

In this case

- Management : **Open Thoracotomy** with cystectomy



Case study of abnormal lung development



Pathology from 2nd operation



Surgical Pathology Report

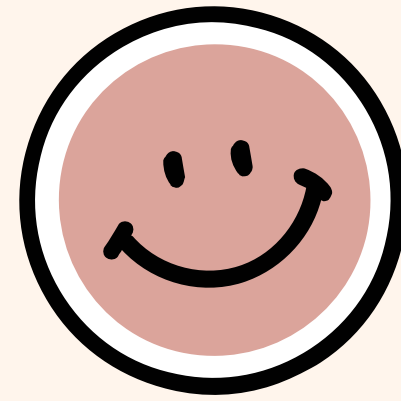
แผนกจักษุวิทยา ภาควิทยา กอภวิทยา สถาบันพยาธิวิทยา

Diagnosis: Posterior mediastinal mass, resection:

- Bronchogenic cyst
- All surgical margins are negative for tumor
- One lymph node with negative for malignancy



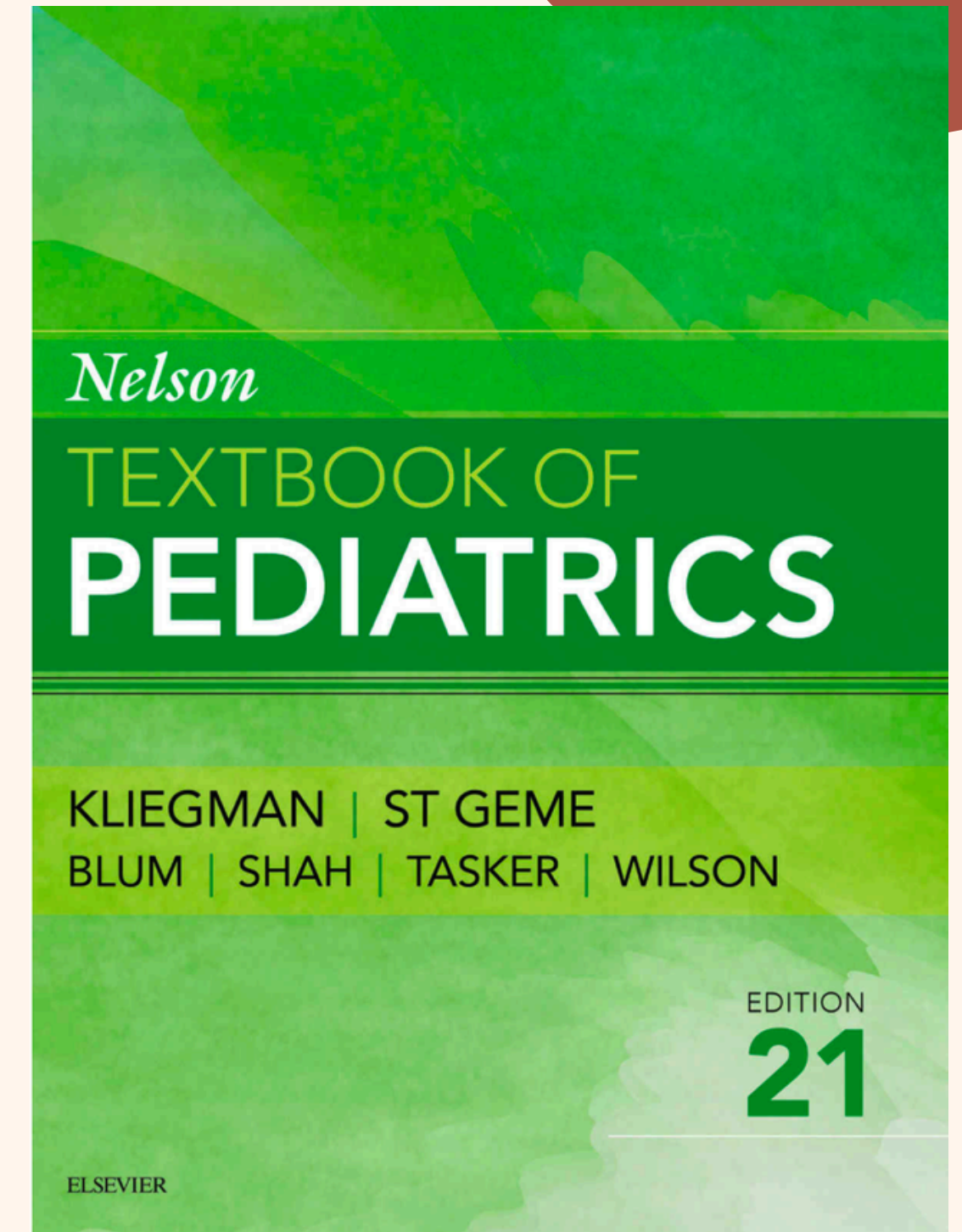
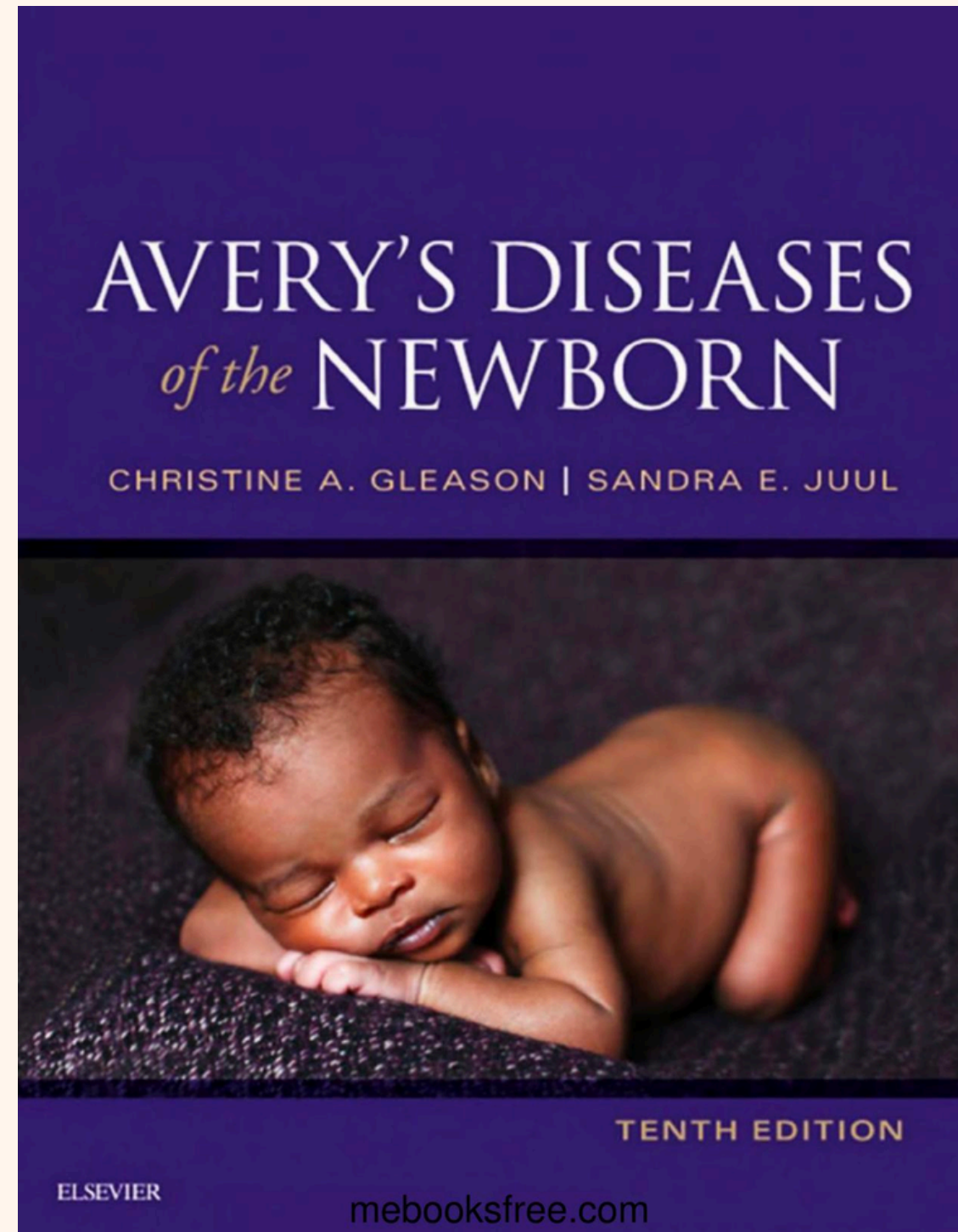
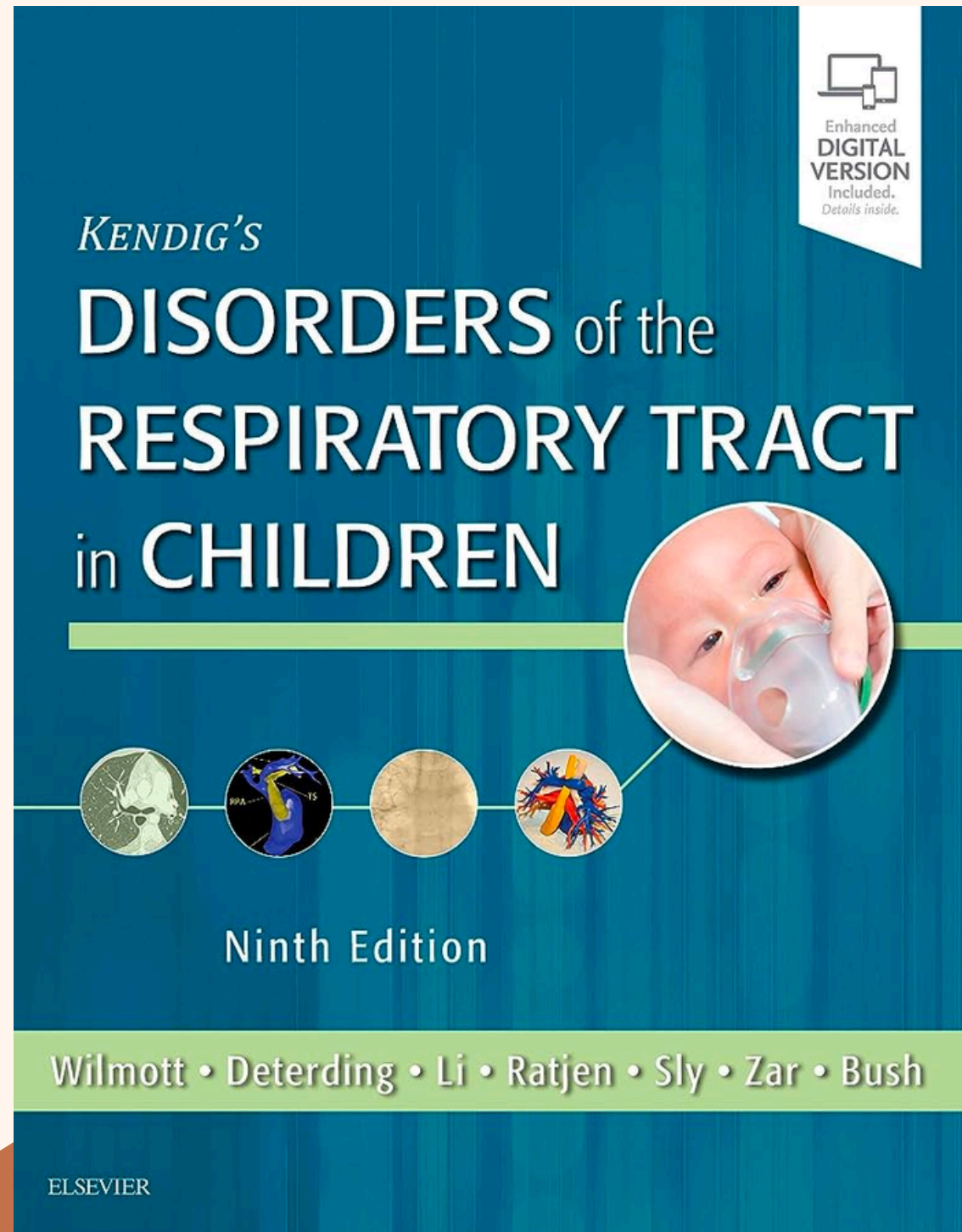
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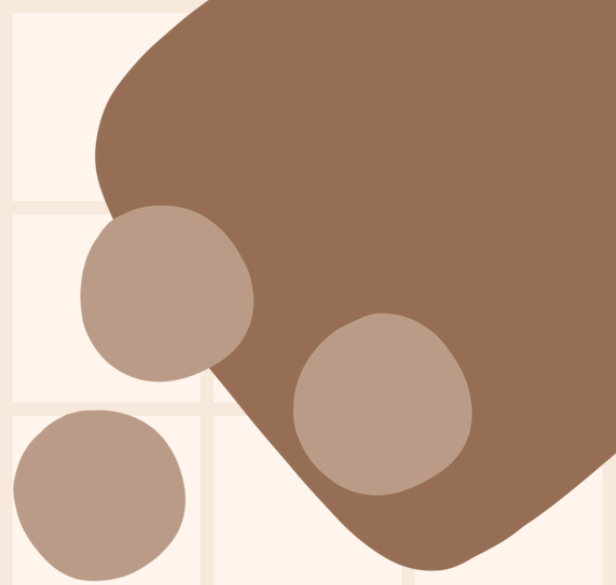
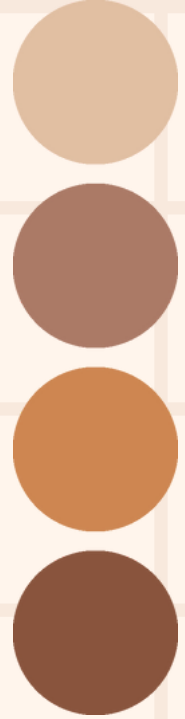


questions ?



Main references





THANK YOU
SO MUCH!

