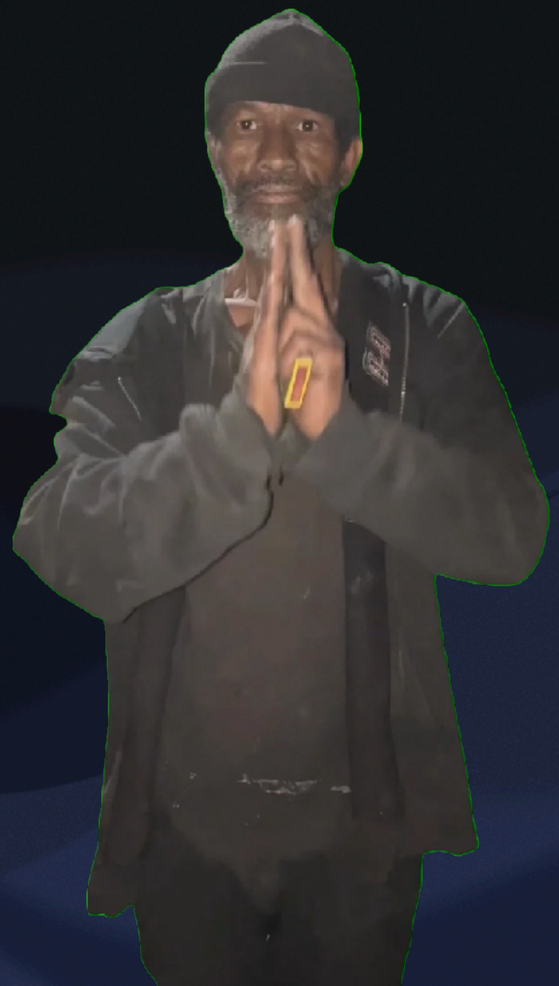
Lung Embryology and Defence



Embryology

Lung Formation

- Respiratory system is derived from the FOREGUT

- 4th week of development :

Endodermal lining of Laryngotracheal groove gives rise to the:

TRACHEA

BRONCHI

TRACHEOBRONCHIAL TREE

GLANDS OF LARYNX

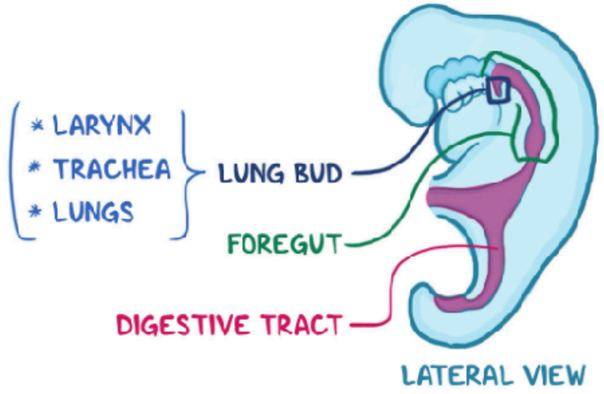


Figure 29.30 Week 4: lung bud sprouts from foregut.

Visceral Pleura derived from Splanchnic Mesoderm

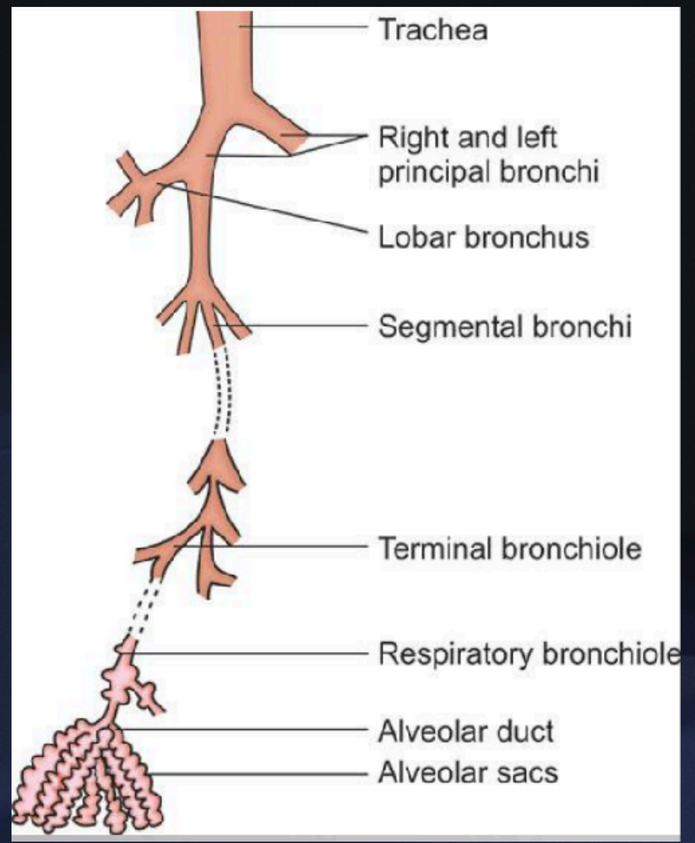
Parietal Pleura derived from Somatic Mesoderm

Tracheobronchial Tree

First part of the Respiratory zone is the ***RESPIRATORY BRONCHIOLES***

The role of the respiratory zone is to produce ***SURFACTANT***

Learn the order of this tree guys trust me



The 4 stages of Lung Maturation

PRE-TERM CHILDREN SUCK AIR

1 - PSEUDOGLANDULAR STAGE (6-16 weeks)

Creation on bronchial tree

If a foetus is born at this stage, it will not survive because respiration is not possible yet.
All parts of the lung have formed EXCEPT the parts involved in gas exchange.

2 - CANALICULAR STAGE (16-26 weeks)

Bronchi and Terminal Bronchiole lumen becomes LARGER.

At 24 weeks at least 2 respiratory bronchioles arise from the terminal bronchioles

If a foetus is born at this stage it is UNLIKELY to survive due to lack of surfactant.

3. TERMINAL SAC / SACCULAR STAGE (26 weeks - birth)

Type 2 alveolar cells now produce surfactant which prevents alveoli from collapsing. Gas exchange can now occur.

If a foetus is born at this stage, it is likely to survive.

4. ALVEOLAR STAGE (32 weeks - 8 years)

This is where the majority (95%) of alveoli develop. Remember the lungs increase in SIZE postnatally because of an increase in the NUMBER OF ALVEOLI...not the size of the existing alveoli

Surfactant reduces SURFACE TENSION and stops alveolar collapse

Embryonic period (weeks 4–7)	• Lung bud at the distal end of the respiratory diverticulum develops into:
	  ◦ Trachea
	  ◦ Bronchial buds → mainstem bronchi, secondary (lobar) bronchi, tertiary (segmental) bronchi
		• Errors lead to tracheoesophageal fistula or pulmonary sequestration.

Pseudoglandular period (weeks 5–17)	• Development of:
	  ◦ Bronchioles and terminal bronchioles from the endodermal tubules
	  ◦ Fine lung capillaries (surrounding terminal bronchioles)
	  ◦ Development of type II pneumocytes
		• Bronchopulmonary epithelium begins to produce amniotic fluid.
		• Errors lead to bronchogenic cyst.
		• Nonviable state: immature lung tissue incapable of gas exchange

Canalicular period (weeks 16–25)	• Development of:
	  ◦ Respiratory bronchioles, alveolar ducts and primitive alveoli
	  ◦ Blood-air barrier
	  ◦ Prominent lung capillaries (surrounding alveolar ducts)
	• Airway diameter increases
		• Errors lead to pulmonary hypoplasia or respiratory distress syndrome [6]
		• Pneumocyte development and surfactant production begin at 20–22 weeks' gestation; mature surfactant levels are reached at 35 weeks' gestation.
		• Respiration first possible at 25 weeks
		• Corticosteroids are crucial for lung development and surfactant production

Saccular period (weeks 26–birth)	• Development of terminal sacs (thin-walled alveoli separated by primary septa) from alveolar ducts	• Fetus can breathe outside the uterus from about 24–25 weeks of gestation with intensive care.

Alveolar period (week 36–8 years)	• Development of:
	  ◦ Mature type II pneumocytes
	  ◦ Definitive alveoli (separated by secondary septa) from terminal sacs
		• Following birth, alveoli increase in number but not in size
		  ◦ At birth: approx. 20–70 million alveoli
		  ◦ In adults: approx 300 million alveoli
		• In utero: increased vascular resistance due to aspiration of amniotic fluid
		• Postpartum: inspiration of air leads to a drop in pulmonary vascular resistance

Changes at birth

Amniotic fluid is cleared in 3 ways at birth

1) Through nose and mouth by vaginal wall pressure during labour

2) Into Pulmonary circulation

3) Into Pulmonary lymphatics

Respiratory distress syndrome is caused by insufficient surfactant production or immature lung with low numbers of alveoli

Which of the following cells produce SURFACTANT?

A. Alveolar Type I

B. Alveolar Type II

C. Alveolar Type III

D. Macrophages

E. Epithelial Cells

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In which stage of lung development do Type II alveolar cells produce SURFACTANT?

A. Embryonic

B. Pseudoglandular

C. Canalicular

D. Saccular / Terminal Sac

E. Alveolar

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When do most Alveoli develop?

A. Post Natally

B. Pseudoglangular stage

C. Alveolar stage

D. Terminal Sac stage

E. Embryonic stage

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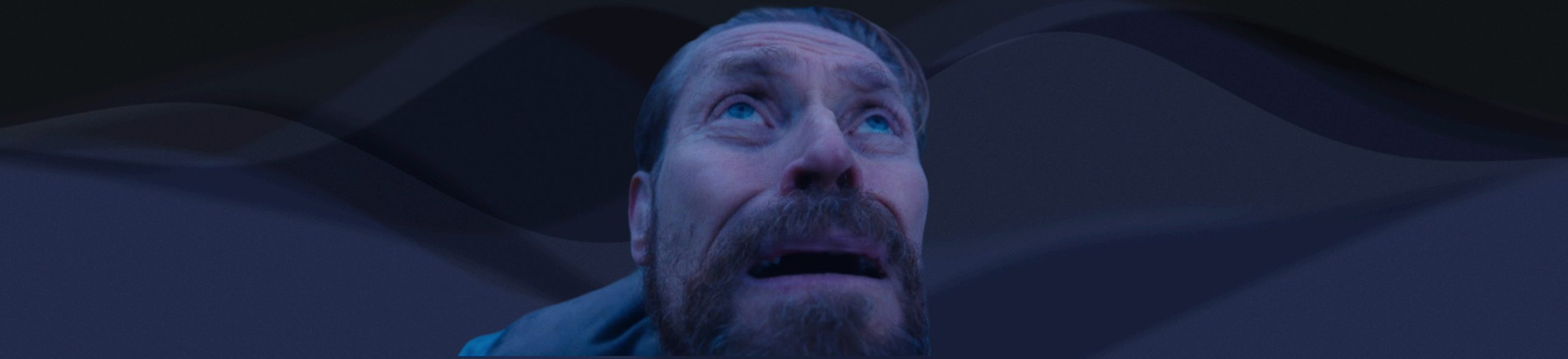
Lung defence

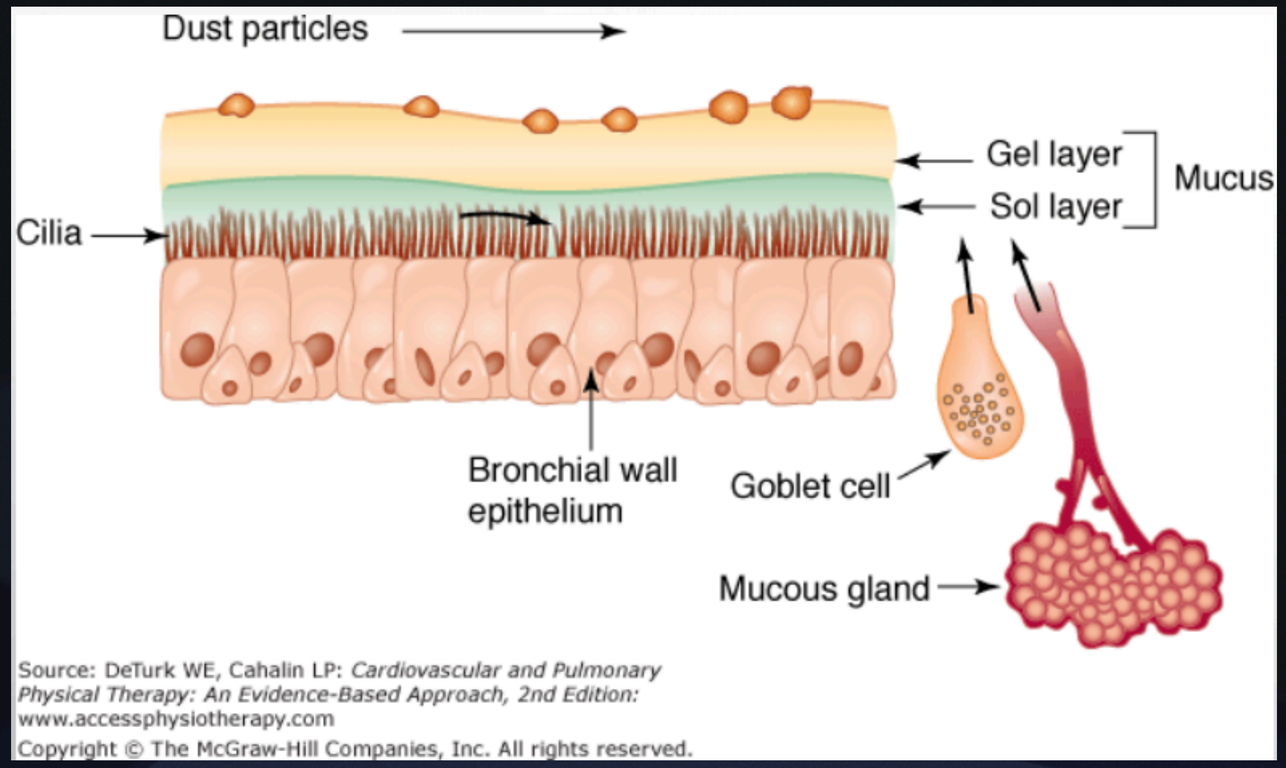


Mucociliary Clearance

The Mucociliary Escalator helps clear out pathogens from inside our AIRWAYS

Sol layer is where the cilia wave around and help push pathogens around.

Gel layer contains mucins which make up MUCUS (no way). This traps pathogens so we can cough it out or let the stomach's acidity kill them.



There are 2 important facts to remember here...

I. PSEUDO-STRATIFIED CILIATED COLUMNAR EPITHELIUM line the Respiratory airways

2. Sol Layer needs to be maintained at 7μm so cilia move efficiently. This is achieved by Na^+ transport.

Regulation of Water

TOO MUCH WATER

ENaC transports Na+ OUT OF the ASL (Airway Surface Liquid) and into the epithelial cell.

The Na+ is removed on the basolateral side by Na+/K+ pumps into the blood stream.

This makes water follow it = Less water in ASL.

TOO LITTLE WATER

CFTR channels down regulate ENaC channels. Now not as much Na+ movement out.

ADDITIONALLY, CFTR pumps Cl- ions into ASL.

This attracts water into ASL.

Cystic Fibrosis

Autosomal Recessive condition

Common pathogen which is seen in CF patients is **PSEUDOMONAS AERUGINOSA**
(Gram neg)

What happens in CF?

CFTR channel is mutated -> No down regulation of ENaC + no Cl- ions being pumped out -> water moves out of ASL uninhibited -> ASL becomes a thick, stagnant mucous that houses pathogens

To make matters worse, cilia cannot move in the thick mucous or reach the top of the sol layer. So thick mucous does not move easily and pathogens can live there.

Cystic Fibrosis (continued)

When infected you get an intense NEUTROPHIL MEDIATED IMMUNE RESPONSE

Cytokines released as well as Leukocytes -> Scarring

Long term CF can cause bronchiectasis (airway becomes wide and has big mucous build up)

Immune system in Lung defence

IGA:

PRESENT ON MUCOSAL MEMBRANES, IN GUT,

RESPIRATORY TRACT AND SKIN.

PRIMARILY FUNCTIONS THROUGH BLOCKING ADHESION + AIRWAY SECRETIONS

IGG:

INVOLVED WITH SECONDARY IMMUNE RESPONSE

IGE:

FOUND IN MUCOSAL MEMBRANES

IMPORTANT FOR DEFENCE AGAINST ALLERGY

IGE BINDS TO FC RECEPTORS ON MAST CELLS ? CAUSES DEGRANULATION OF MAST CELLS

IGM:

INVOLVED WITH PRIMARY IMMUNE RESPONSE

Alveolar Macrophages:	Airway Epithelial Cells:
✿ **primary phagocytes of innate immune system** ✿ are phagocytes that remove fine dust particles and other debris from alveolar spaces → clean inhaled particles and lung surfactant Precursors to macrophages = monocytes	✿ **main function = Removal + neutralisation of harmful substances from inhaled air** ✿ also secretes cytokines, chemokines and antimicrobial peptides ✿ play active role in innate immunity → primary defence = mucociliary escalator

What are the precursors of macrophages called?

A. Neutrophils

B. Pre-Macrophagic Cells

C. Monocytes

D. Basophils

E. Lymphocytes

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The optimum height of ASL for efficient clearance is...?

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B. 7mm

C. 7 grams

D. 7 micrometers

E. 0.7 micrometers

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What is the primary embryological origin of the epithelium lining the respiratory tract?
a) Endoderm
b) Mesoderm
c) Ectoderm
d) Neural crest cells
e) Paraxial mesoderm

Which germ layer gives rise to the connective tissue and smooth muscle of the lungs?
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b) Endoderm
c) Mesoderm
d) Neural crest cells
e) Lateral plate mesoderm

What stimulates the production of surfactant by type II pneumocytes?
a) Hypoxia
b) High levels of oxygen
c) Glucocorticoids
d) Low levels of carbon dioxide
e) Reduced lung compliance

What effect does smoking have on the function of the mucociliary escalator?
a) Increases mucus production
b) Enhances ciliary movement
c) Impairs ciliary function and reduces mucus clearance
d) Stimulates surfactant secretion
e) Promotes macrophage activation

What propels the mucus along the respiratory tract in the mucociliary escalator?
a) Peristaltic contractions of smooth muscle
b) Ciliary movement
c) Action of surfactant
d) Phagocytosis by macrophages
e) Secretion of lysozyme

Which cell type secretes the mucus that traps inhaled particles in the respiratory tract?
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