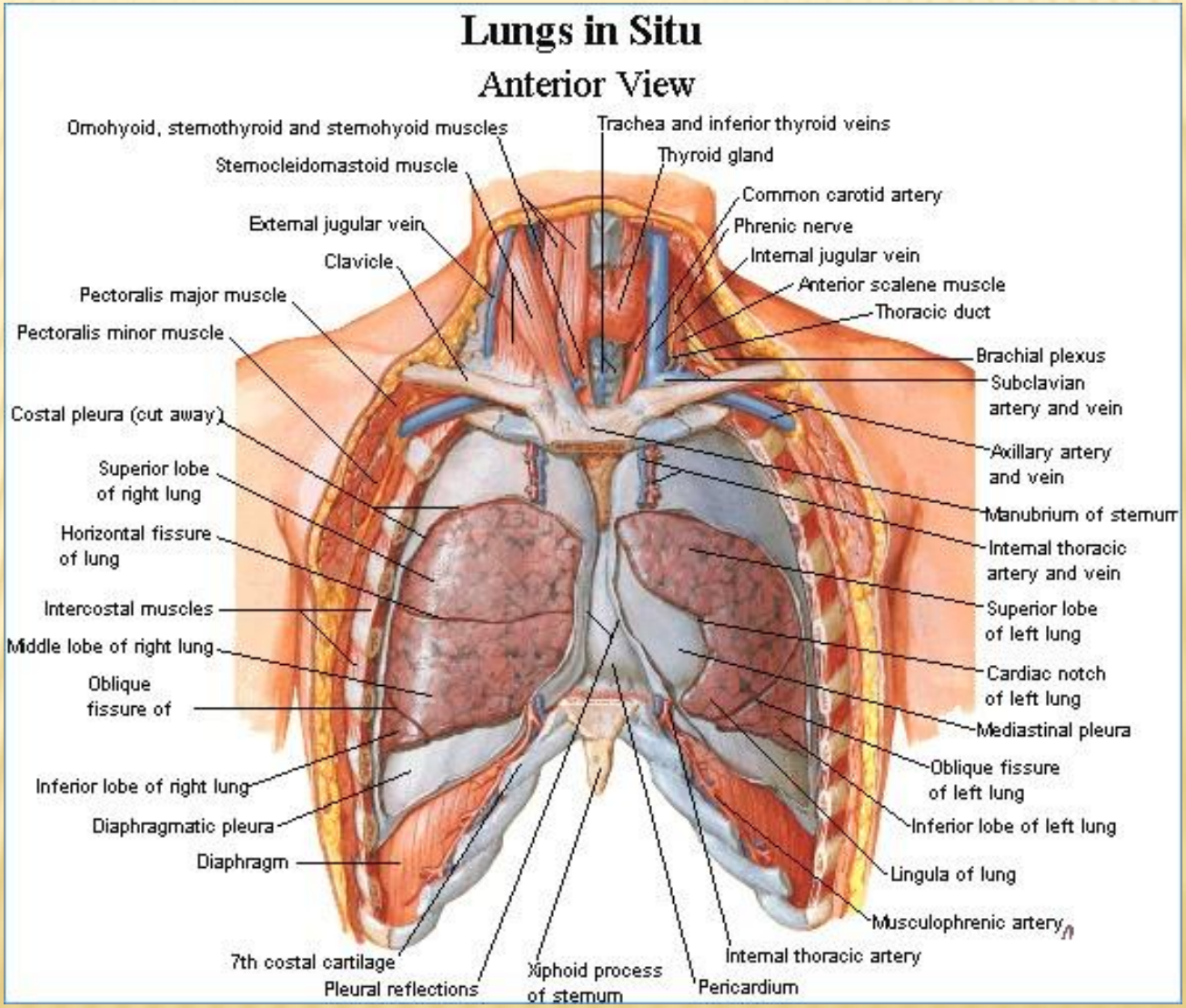
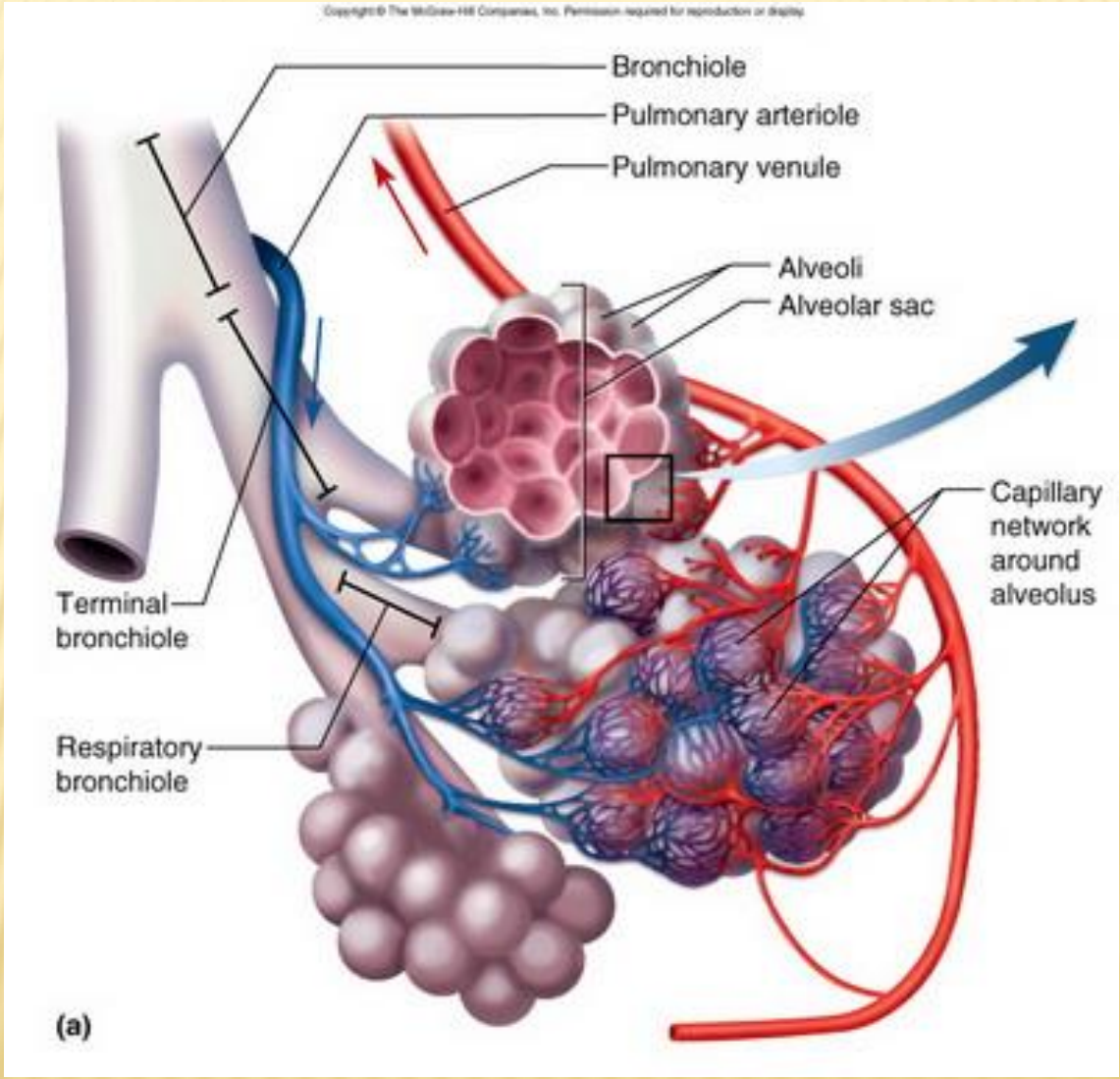
Pulmonary Anatomy and application to current therapies.

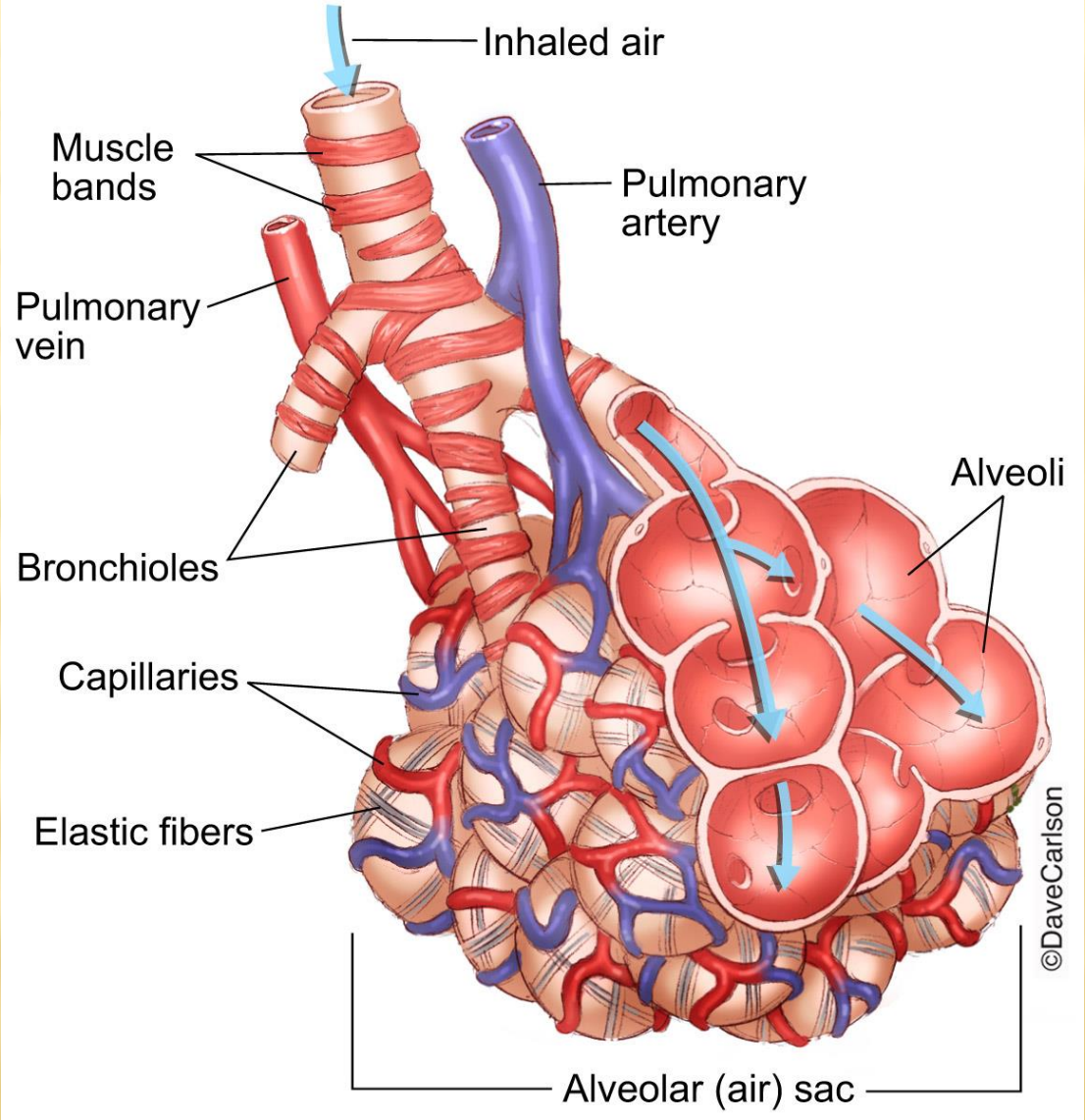
PULMONARY ANATOMY:



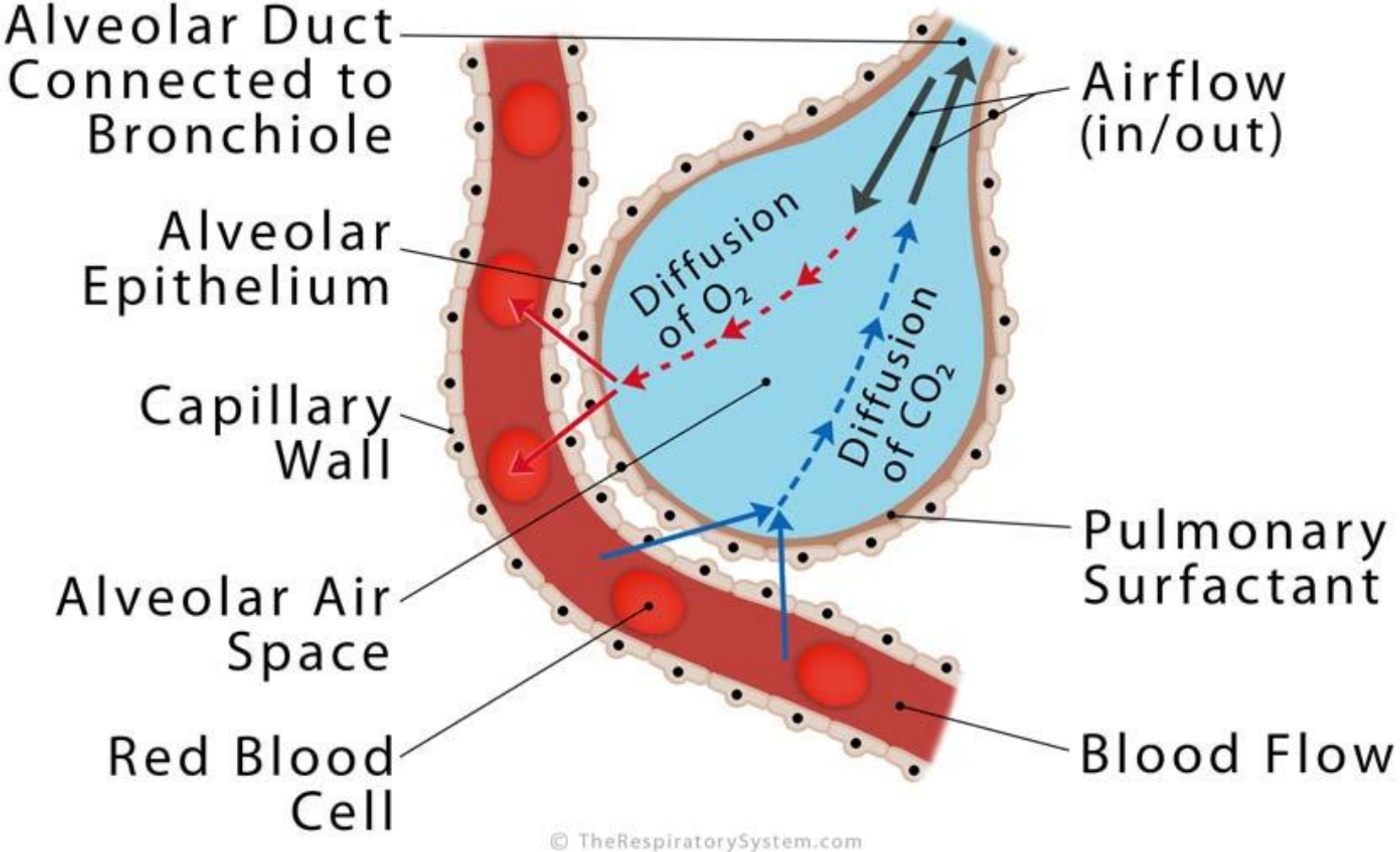
ANATOMY:


Bronchiole
Pulmonary arteriole
Pulmonary venule
Alveoli
Alveolar sac
Capillary network around alveolus
Terminal bronchiole
Respiratory bronchiole
(a)

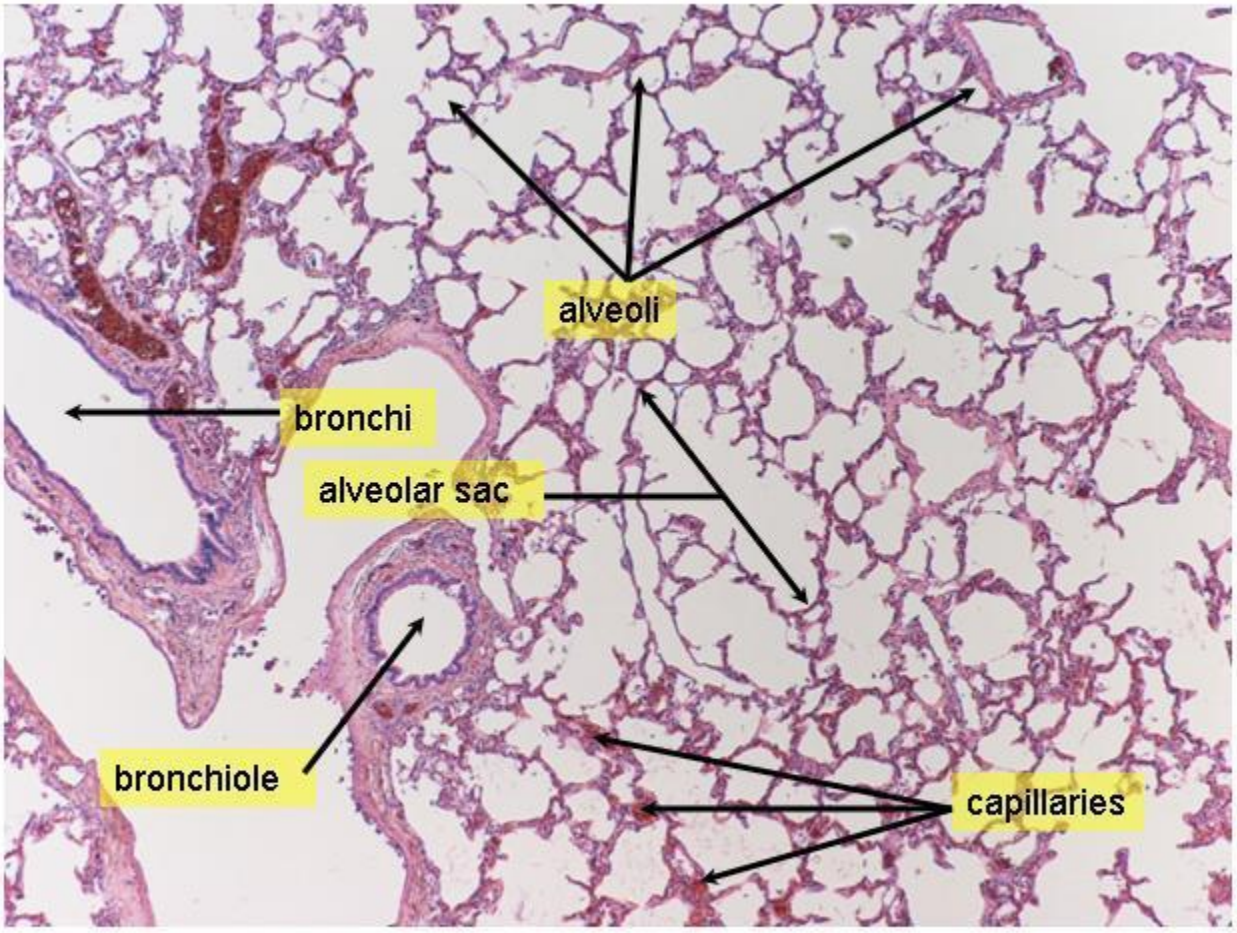
ANATOMY:


Inhaled air
Muscle bands
Pulmonary artery
Pulmonary vein
Alveoli
Bronchioles
Capillaries
Elastic fibers
Alveolar (air) sac
©DaveCarlson

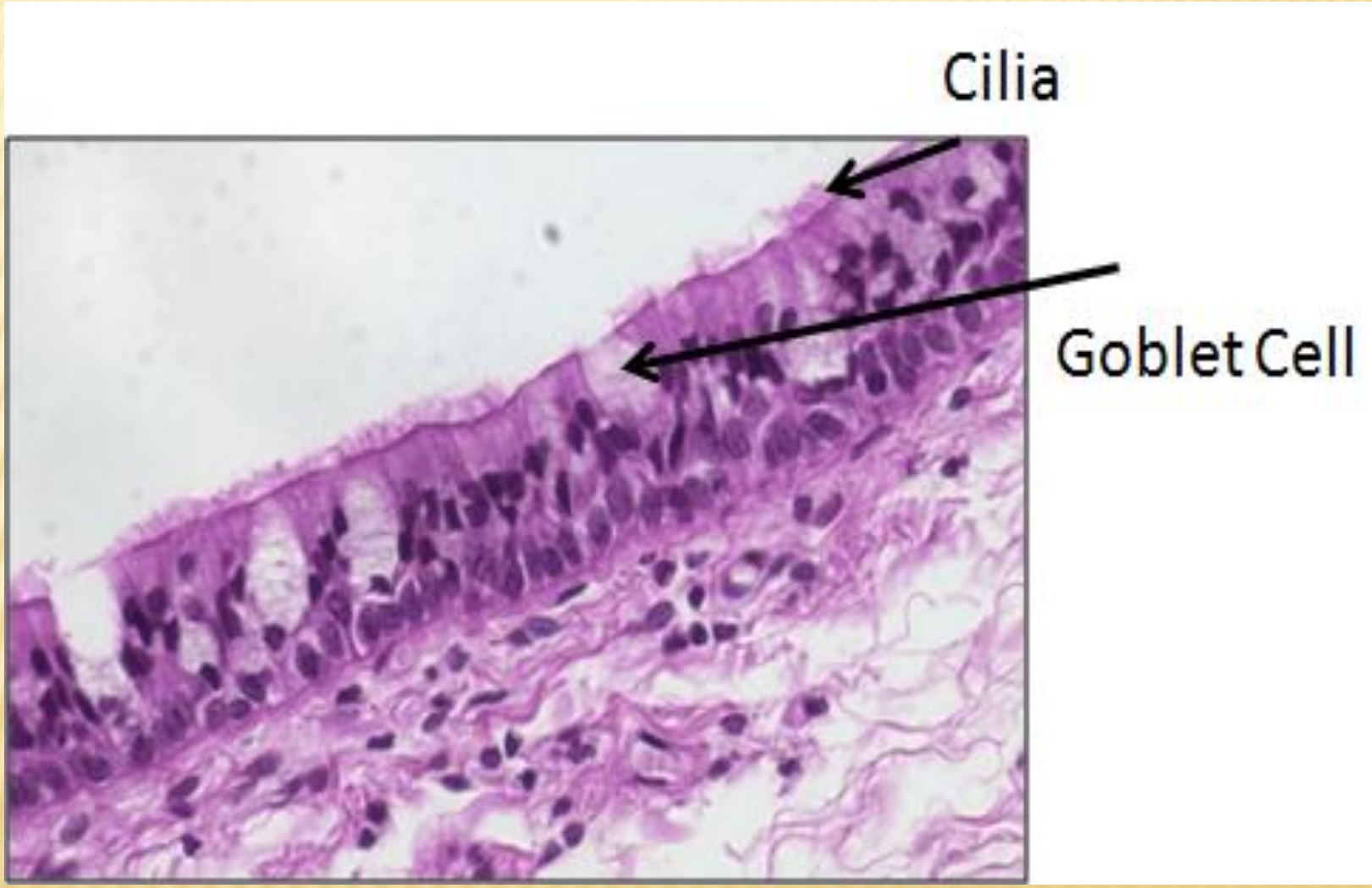
Gas Exchange within Alveoli



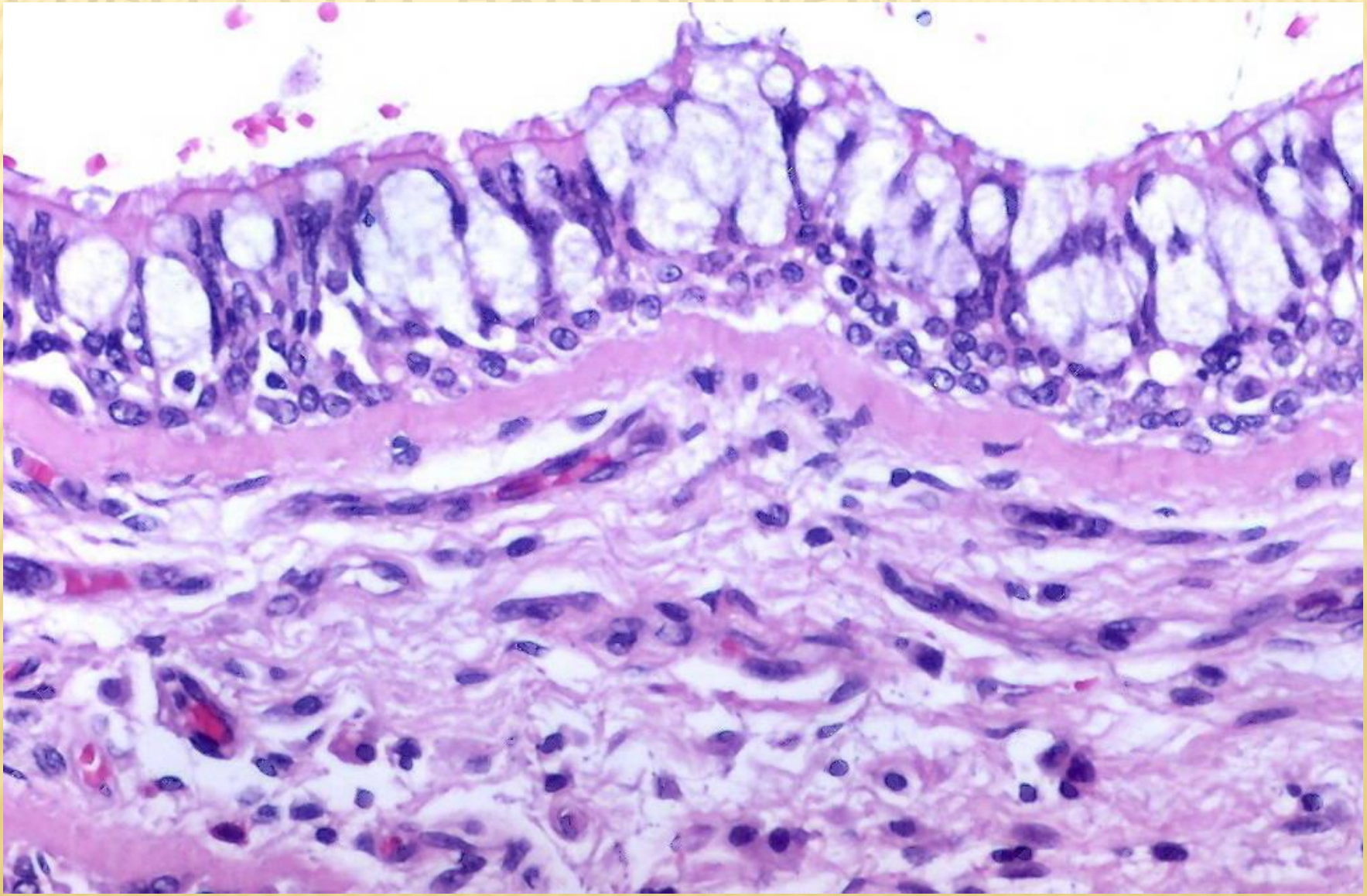
MICROSCOPIC VIEW:



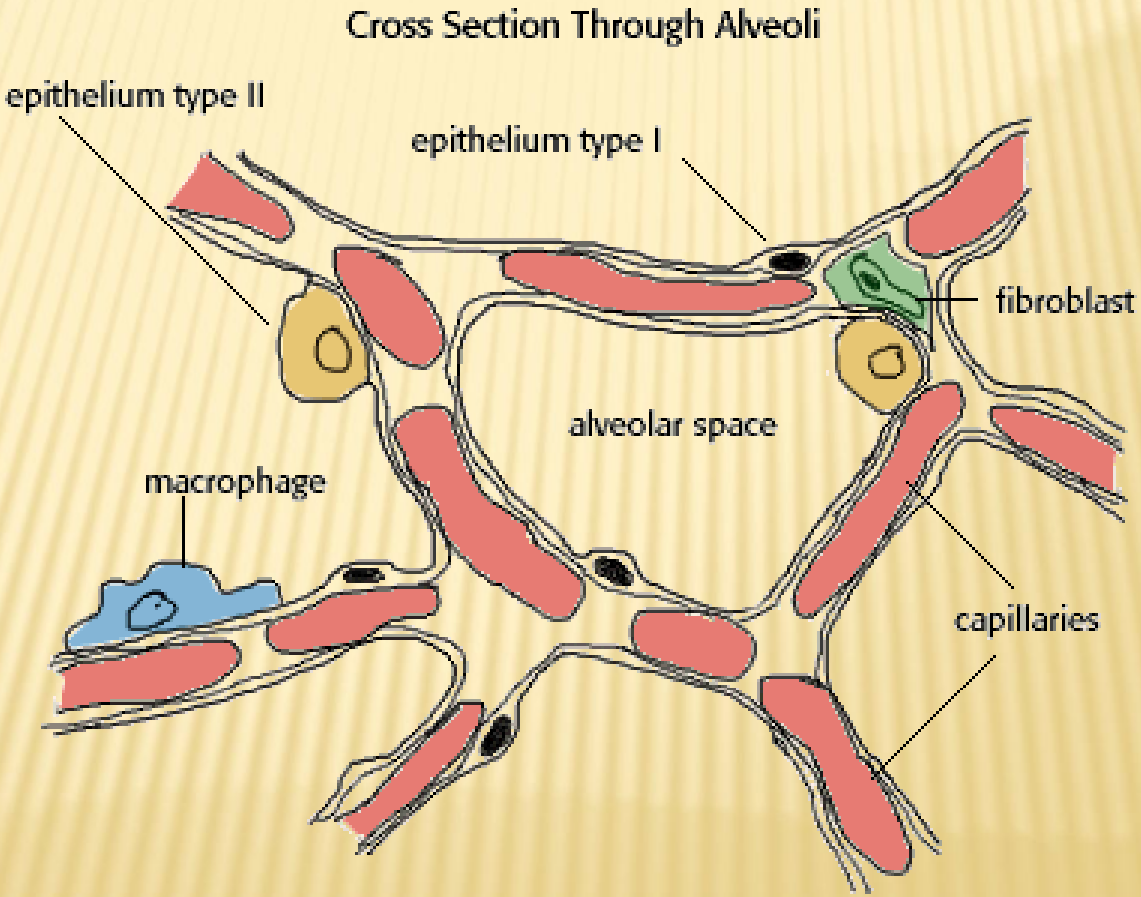
BRONCHUS:



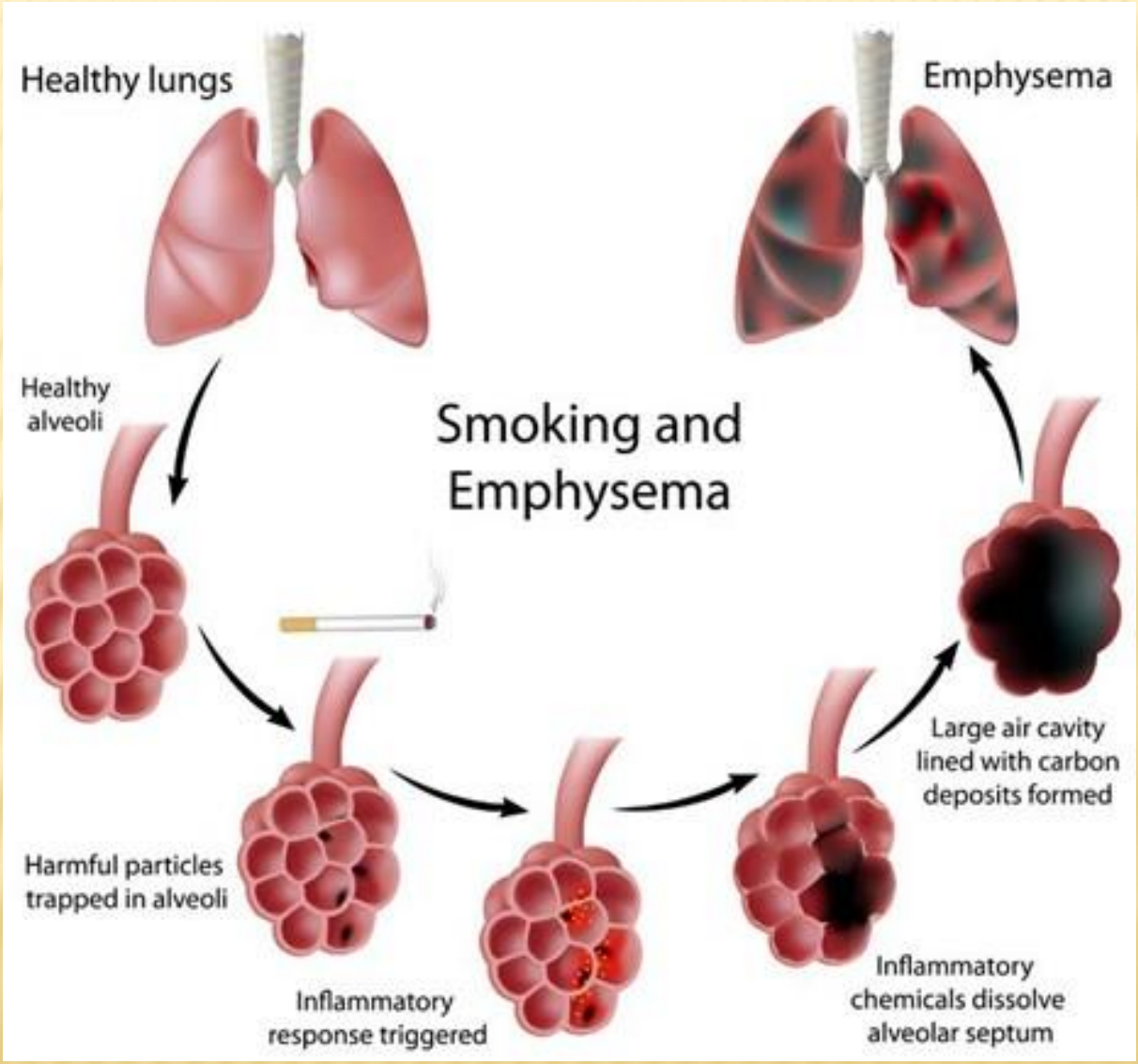
GOBLET CELL HYPERPLASIA:



NORMAL AIRWAY CELLS:

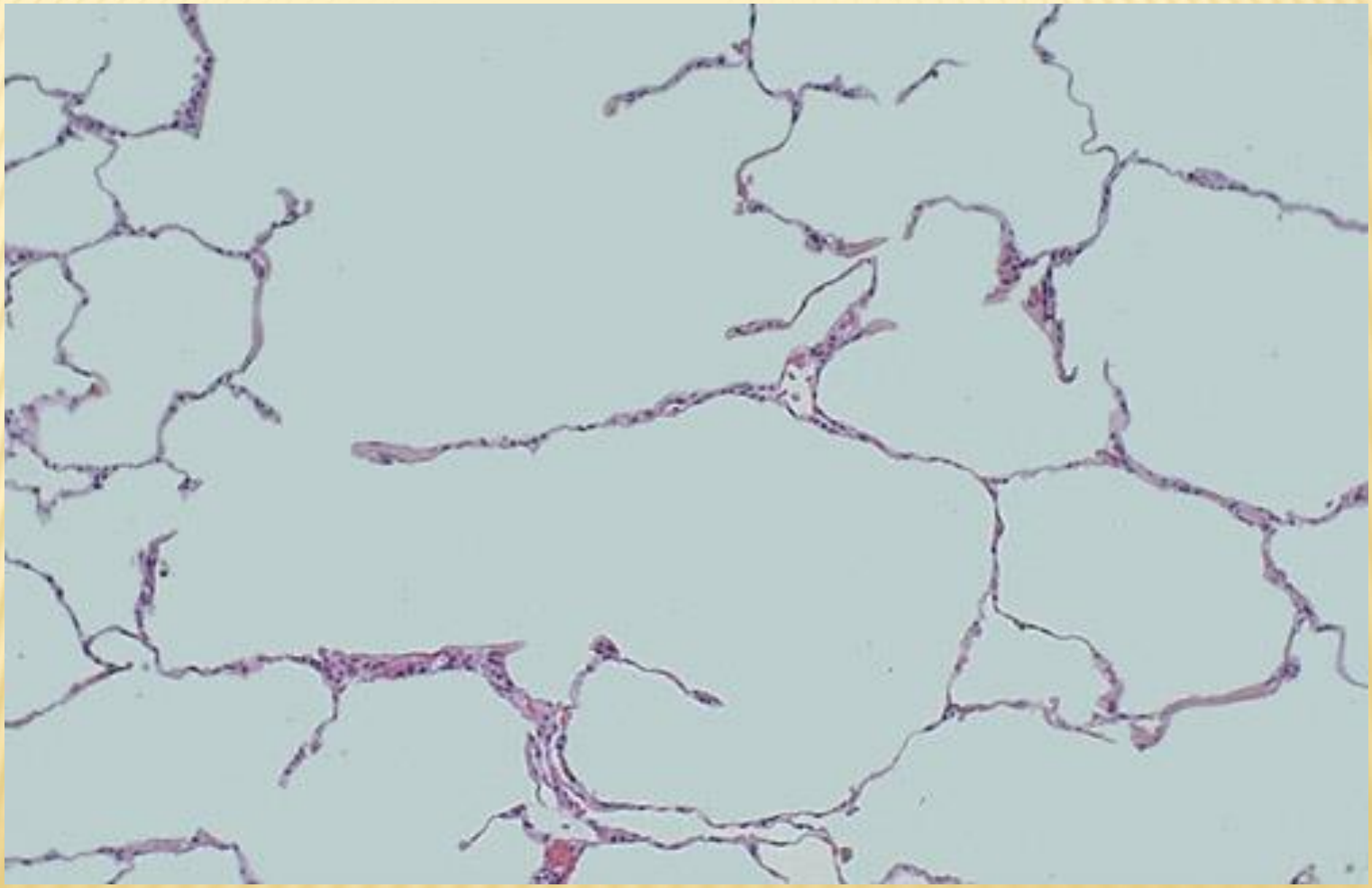


EMPHYSEMA:

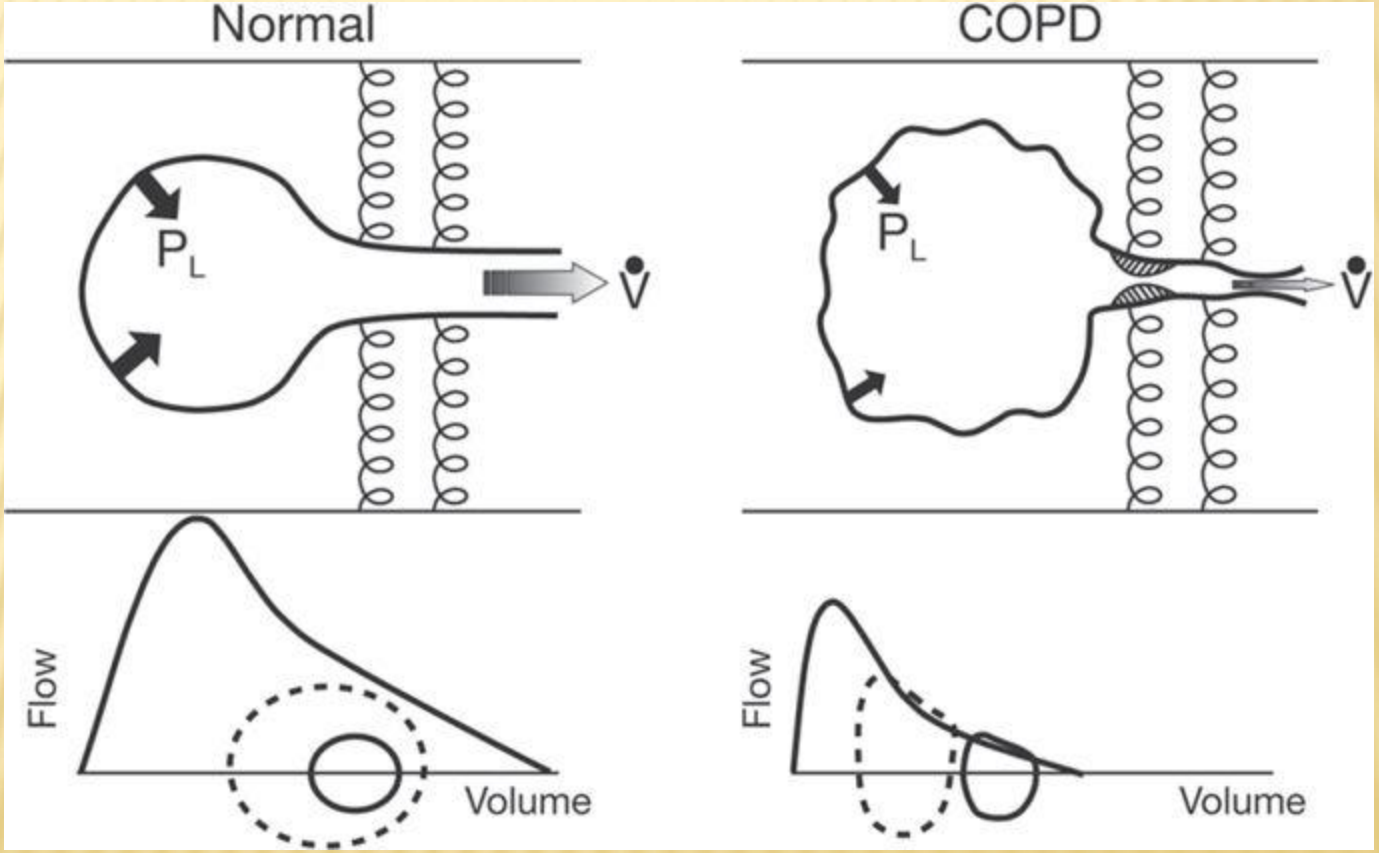

Healthy lungs
Emphysema
Healthy alveoli
Smoking and Emphysema
Large air cavity lined with carbon deposits formed
Harmful particles trapped in alveoli
Inflammatory response triggered
Inflammatory chemicals dissolve alveolar septum

EMPHYSEMA:

EMPHYSEMA, MICROSCOPIC:

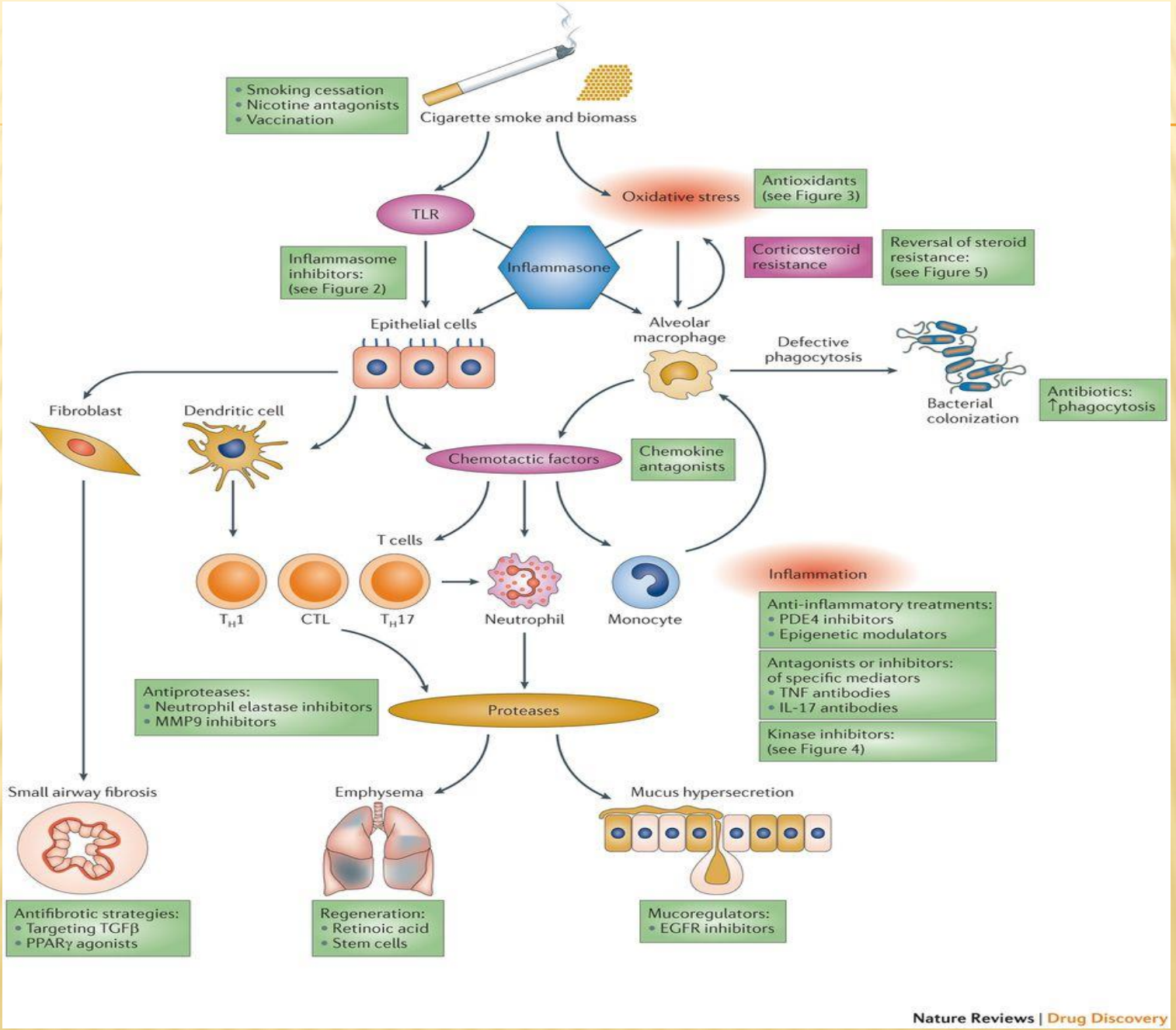


DYNAMIC HYPERINFLATION:

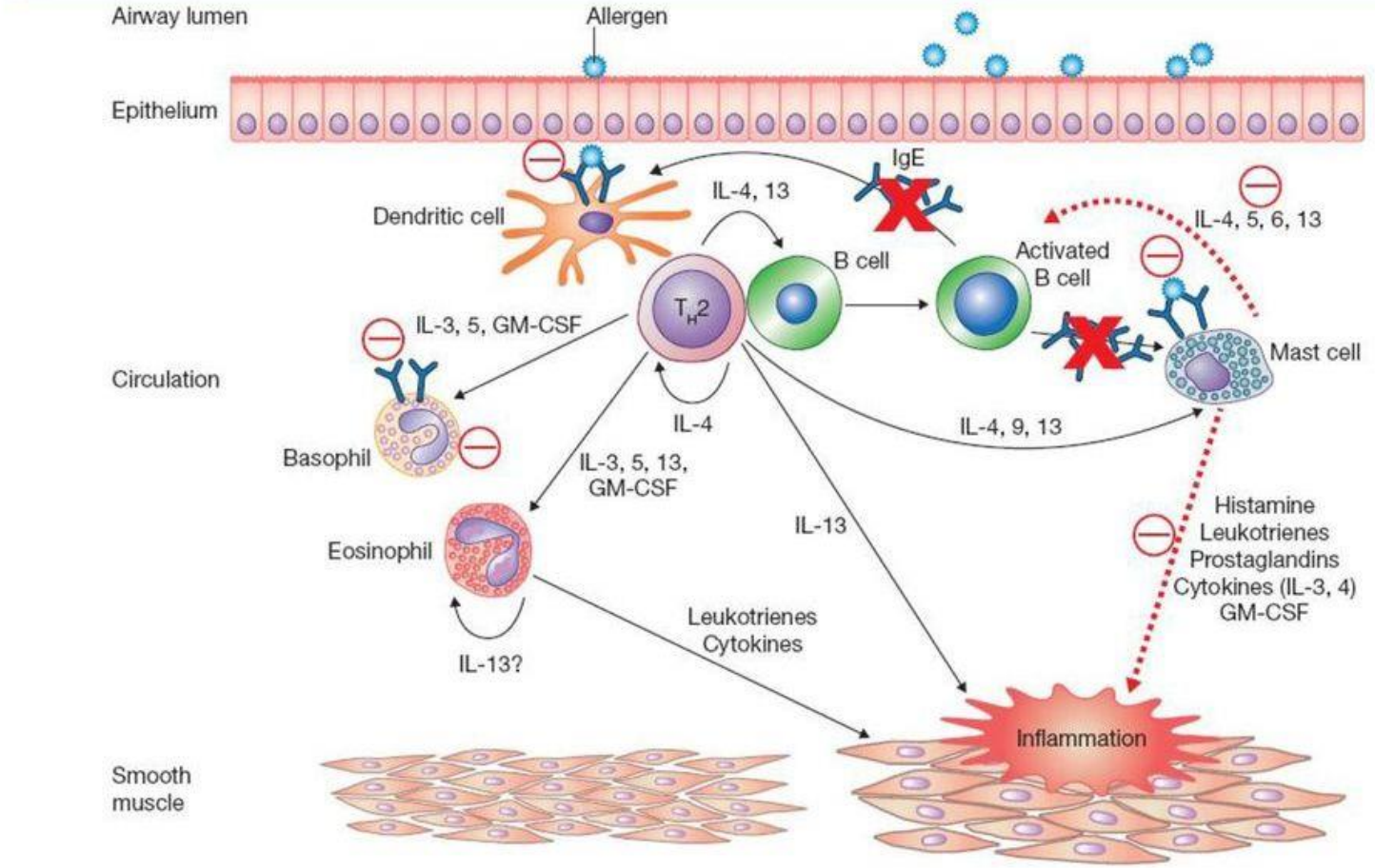


TREATMENT OF COPD:

- ICS/LABA
- LABA/LAMA
- SABA
- PDE4 Inhibitors
- Oral steroids
- Pulmonary rehab/exercise
- Theophylline
- Oxygen
- Stem cell therapy?

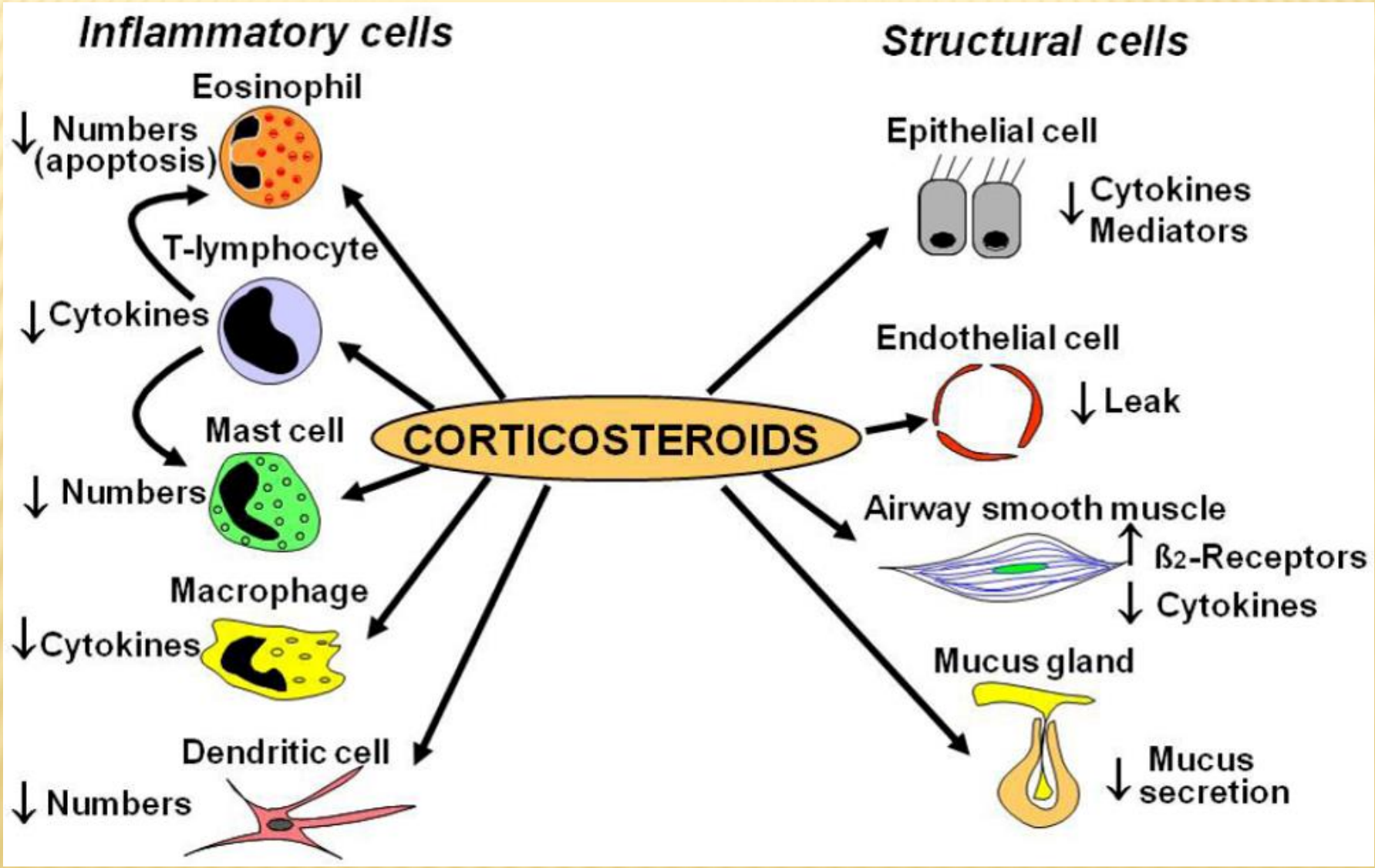

• Smoking cessation
• Nicotine antagonists
• Vaccination
Cigarette smoke and biomass
Oxidative stress
Antioxidants (see Figure 3)
TLR
Inflammasome
Inflammasome inhibitors: (see Figure 2)
Corticosteroid resistance
Reversal of steroid resistance: (see Figure 5)
Epithelial cells
Alveolar macrophage
Defective phagocytosis
Bacterial colonization
Antibiotics: ↑phagocytosis
Fibroblast
Dendritic cell
Chemotactic factors
Chemokine antagonists
T cells
T_H1
CTL
T_H17
Neutrophil
Monocyte
Inflammation
Anti-inflammatory treatments:
• PDE4 inhibitors
• Epigenetic modulators
Antagonists or inhibitors: of specific mediators
• TNF antibodies
• IL-17 antibodies
Kinase inhibitors: (see Figure 4)
Antiproteases:
• Neutrophil elastase inhibitors
• MMP9 inhibitors
Proteases
Small airway fibrosis
Emphysema
Mucus hypersecretion
Antifibrotic strategies:
• Targeting TGFβ
• PPARγ agonists
Regeneration:
• Retinoic acid
• Stem cells
Mucoregulators:
• EGFR inhibitors
Nature Reviews | Drug Discovery

AIRWAY INFLAMMATION: XOLAIR

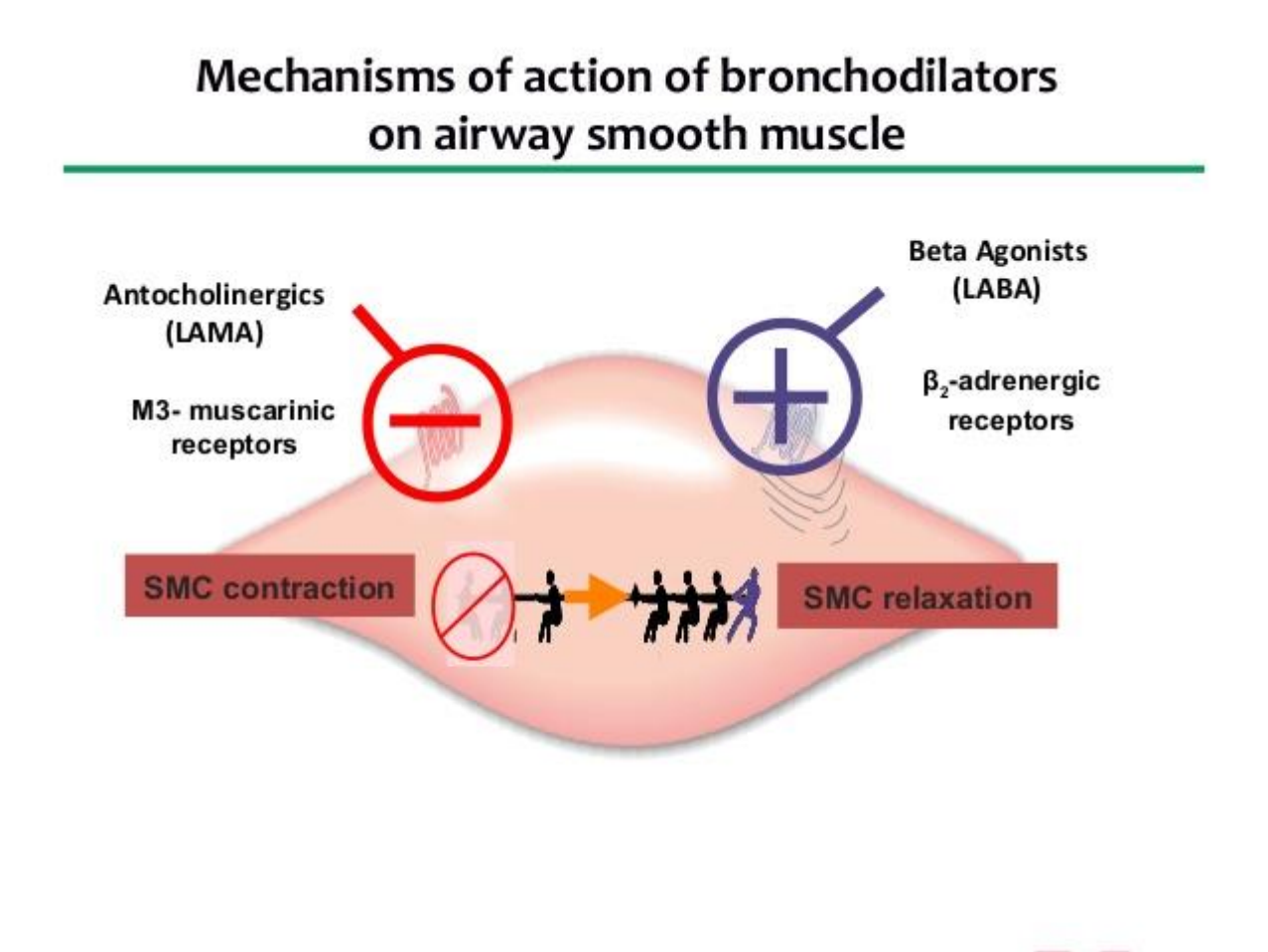


Rabe KF, et al. Allergy 2011;66:1142–51;
Galli SJ, Tsai M. Nat Med 2012;18:693–704.

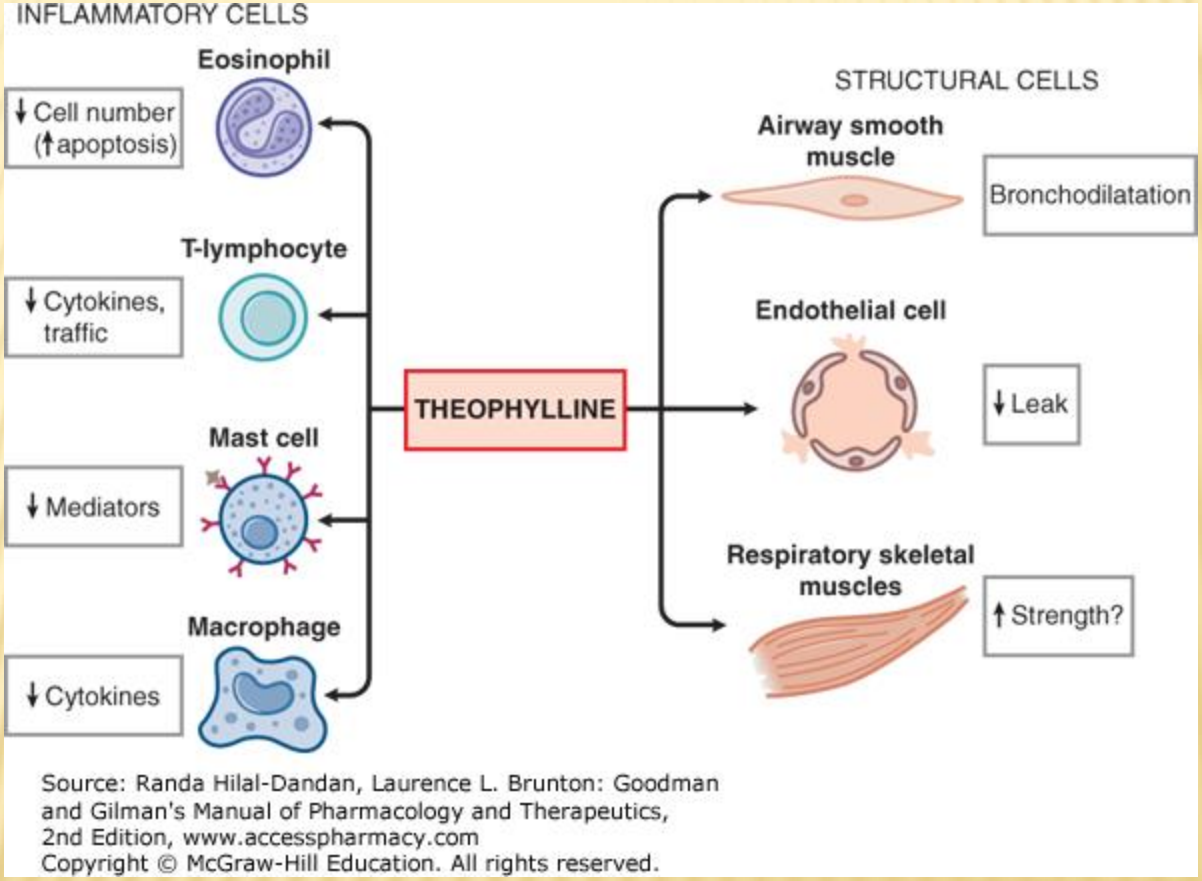
STEROID EFFECTS ON THE AIRWAYS:



SMOOTH MUSCLE HYPERTROPHY:



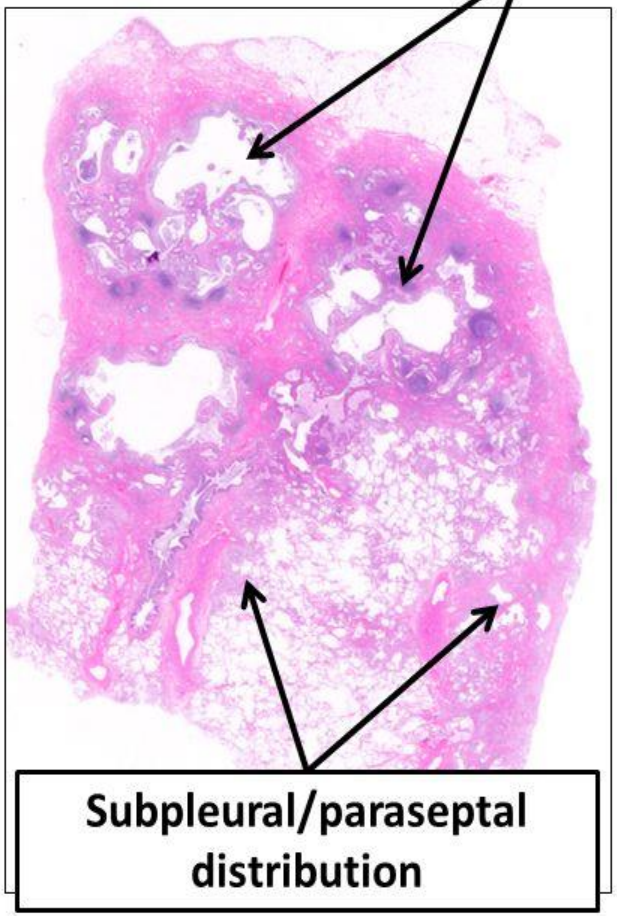
THEOPHYLLINE:



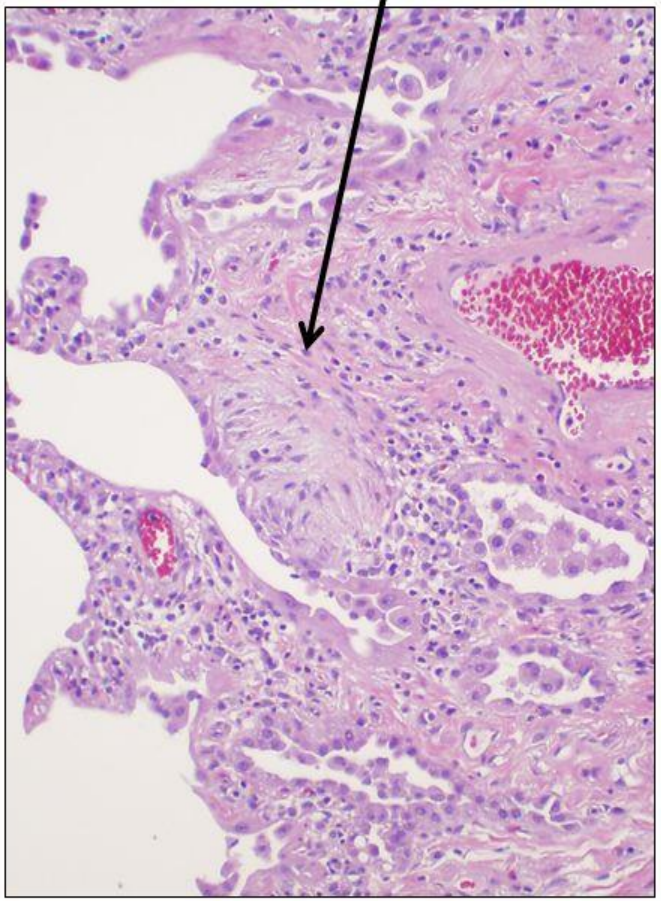
Source: Randa Hilal-Dandan, Laurence L. Brunton: Goodman and Gilman's Manual of Pharmacology and Therapeutics, 2nd Edition, www.accesspharmacy.com

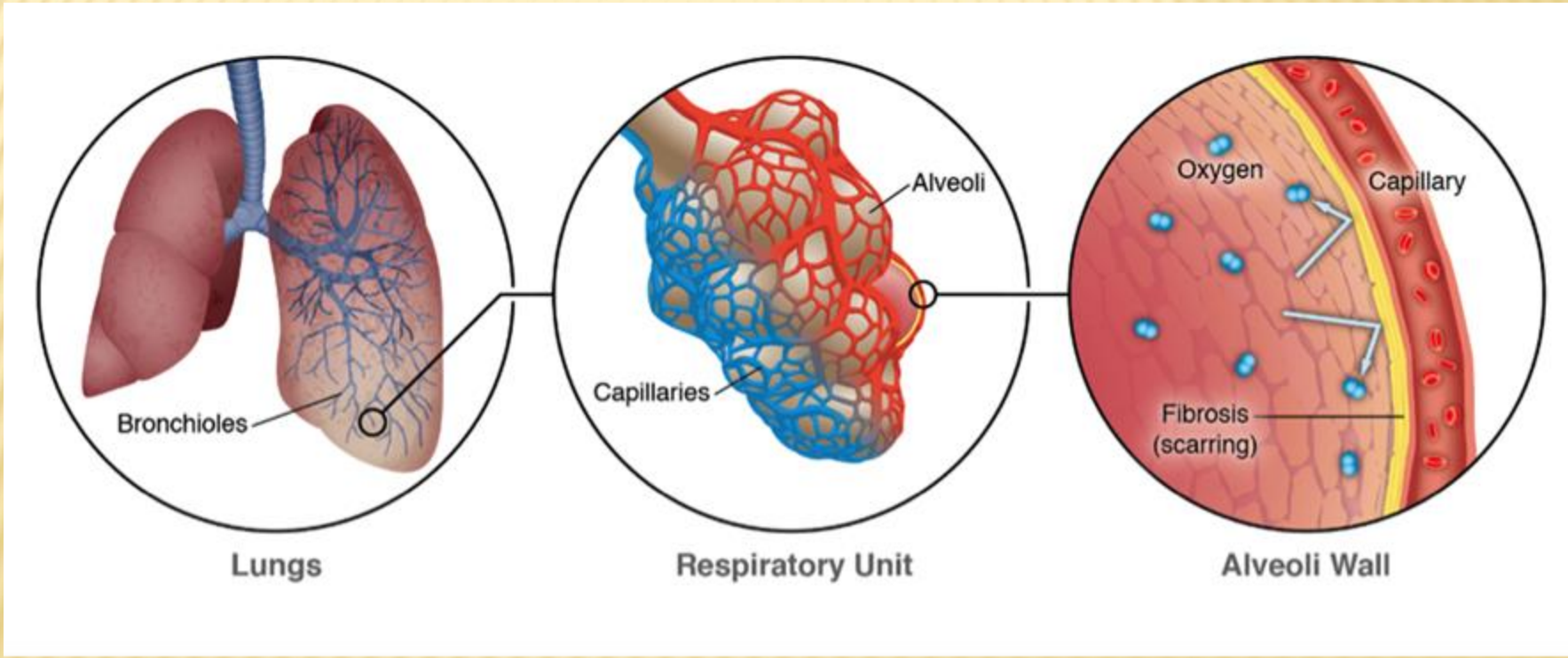
PULMONARY FIBROSIS:

Usual interstitial pneumonia (UIP) Histopathology:
Patchy scarring/honeycombing with active fibroblast foci

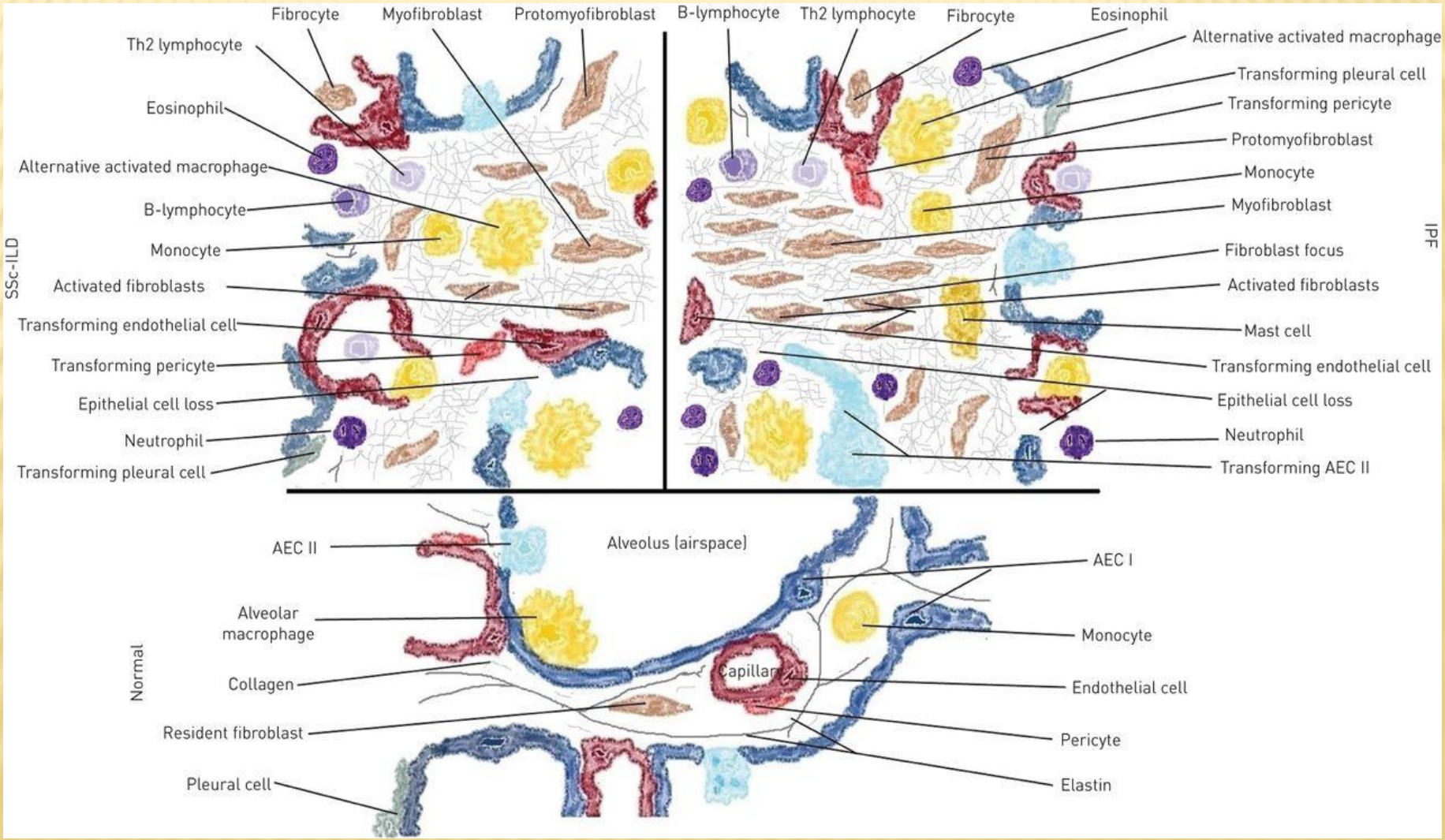


Subpleural/paraseptal distribution

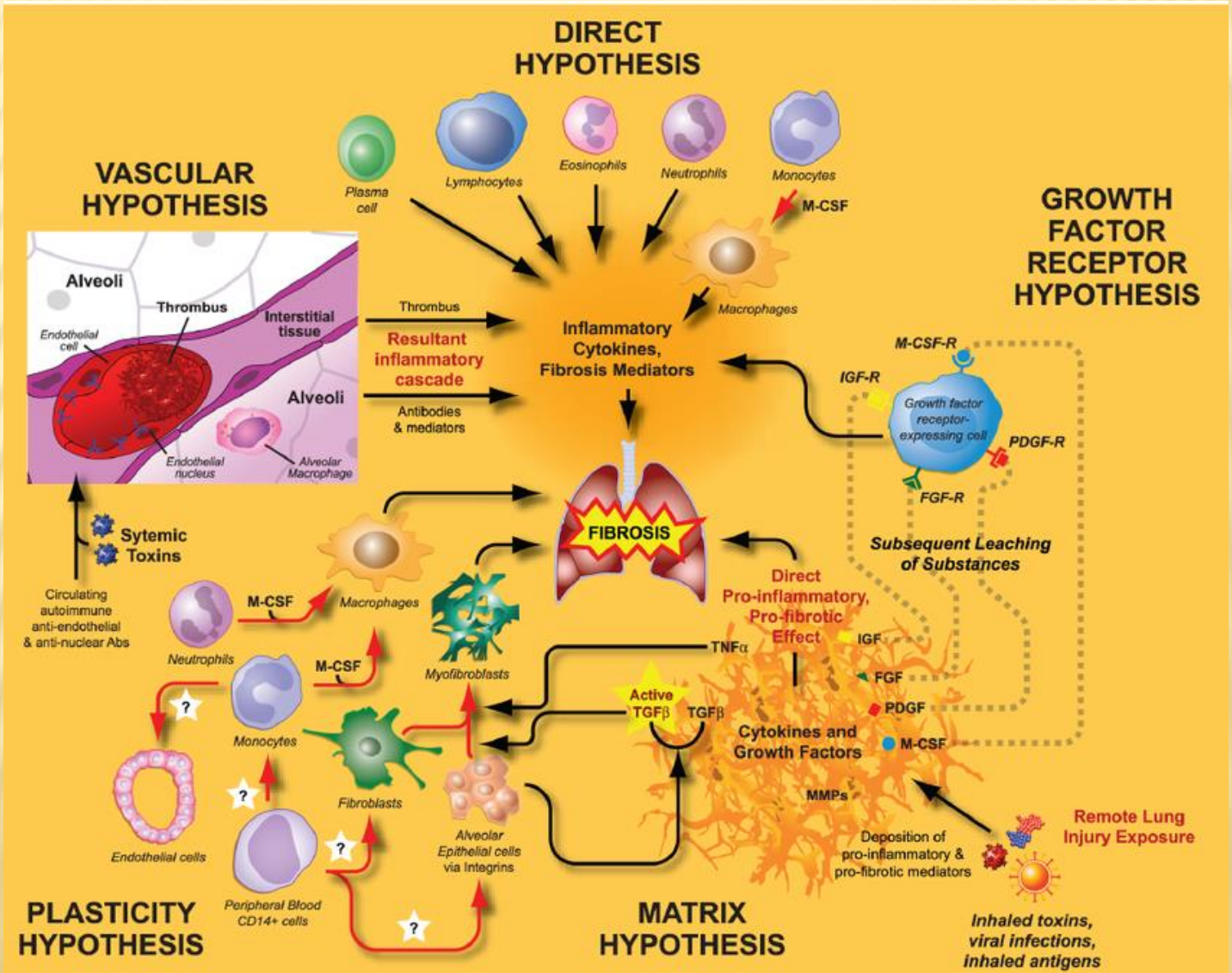



Bronchioles
Lungs
Alveoli
Capillaries
Respiratory Unit
Oxygen
Capillary
Fibrosis
(scarring)
Alveoli Wall

CELLS INVOLVED IN IPF:



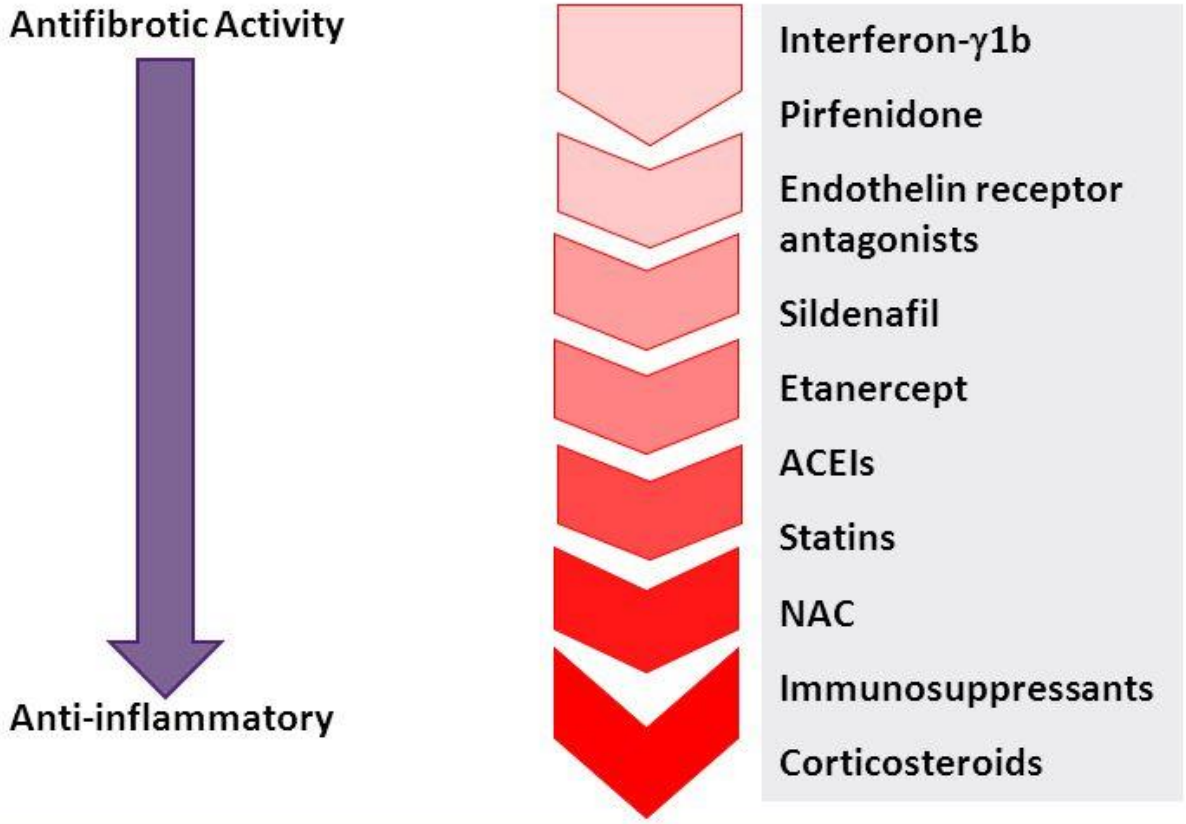
INFLAMMATION IN IPF:



TREATMENT OF PULMONARY FIBROSIS:

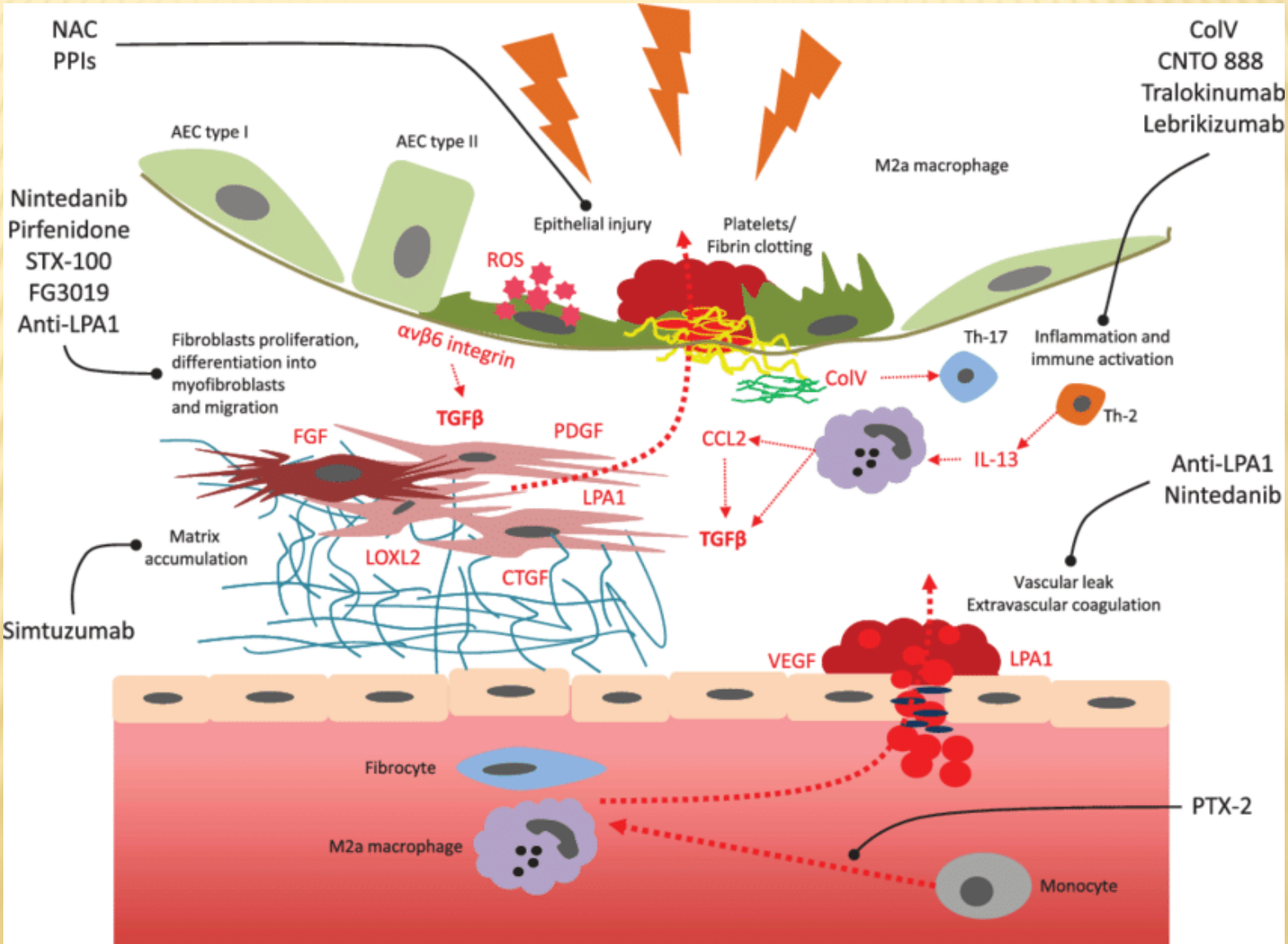
- UIP
- NSIP
- DIP
- HSP
- LIP
- Sarcoidosis
- RA
- Scleroderma
- Ofev
- Pirfenidone
- N-acetyl-cysteine
- Oxygen
- Pulmonary rehab

Treatments tried in IPF

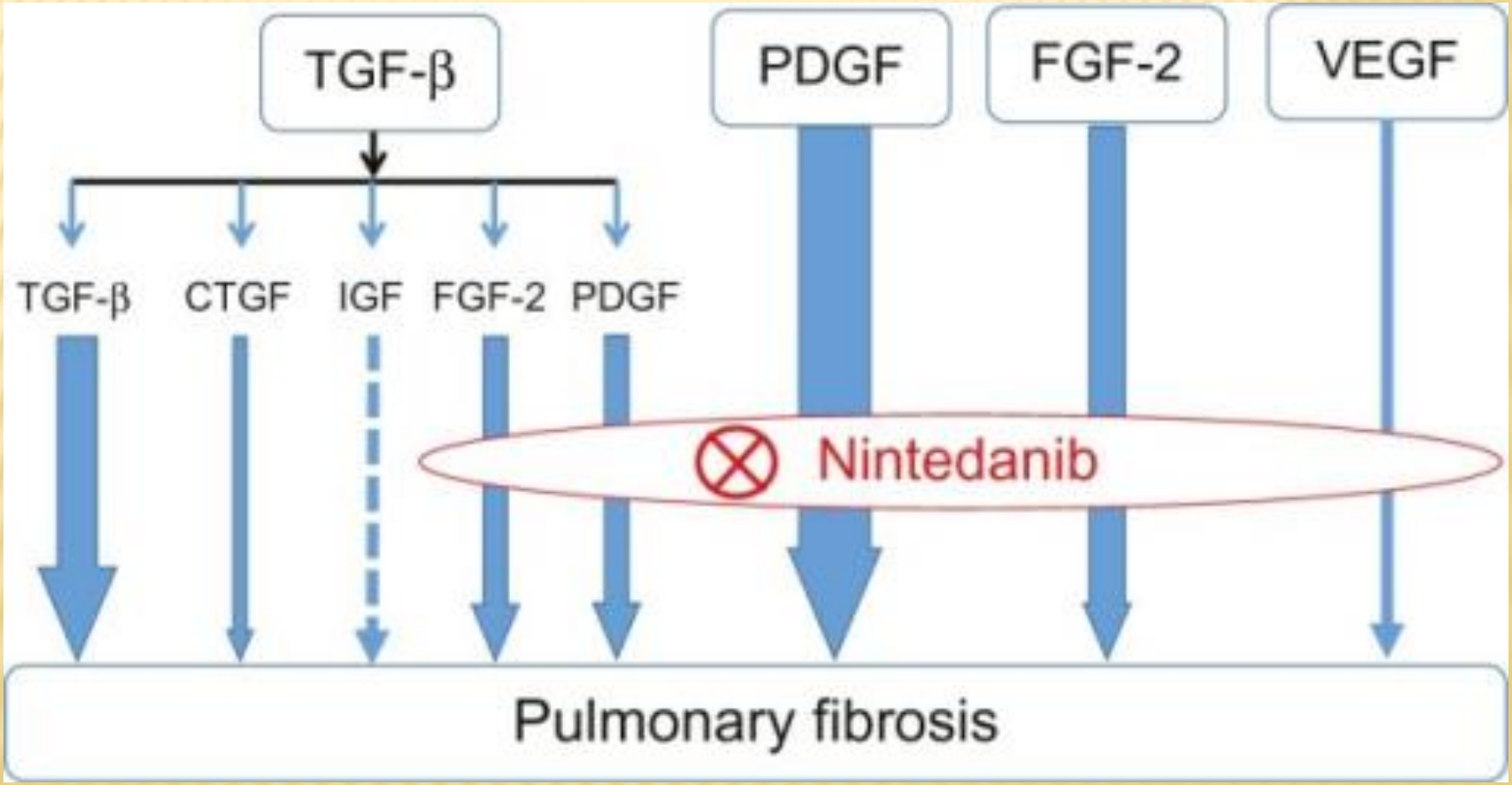


Treatment options include **corticosteroids, immunosuppressive/cytotoxic agents** (e.g., azathioprine, cyclophosphamide) , **and antifibrotic agents** alone or in

MECHANISM OF ACTION:

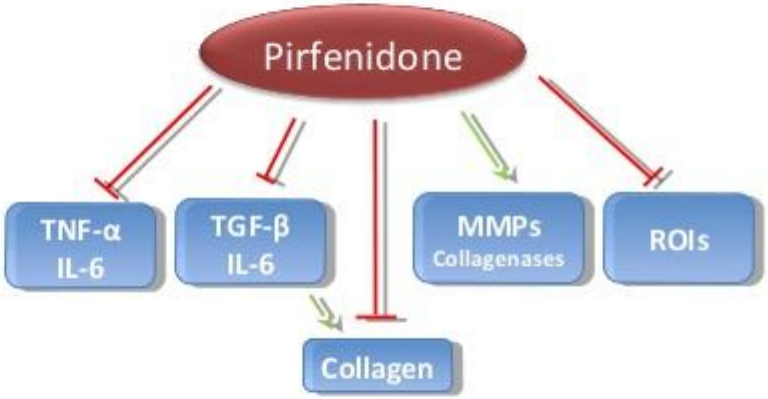


OFEV:


TGF-β
PDGF
FGF-2
VEGF
TGF-β
CTGF
IGF
FGF-2
PDGF
Nintedanib
Pulmonary fibrosis

Possible Mechanisms of Pirfenidone Action

- Antifibrotic
- Molecular target unclear
- Active in several animal models of fibrosis (lung, liver, kidney)




BOSTON
RED SOX

- Questions?