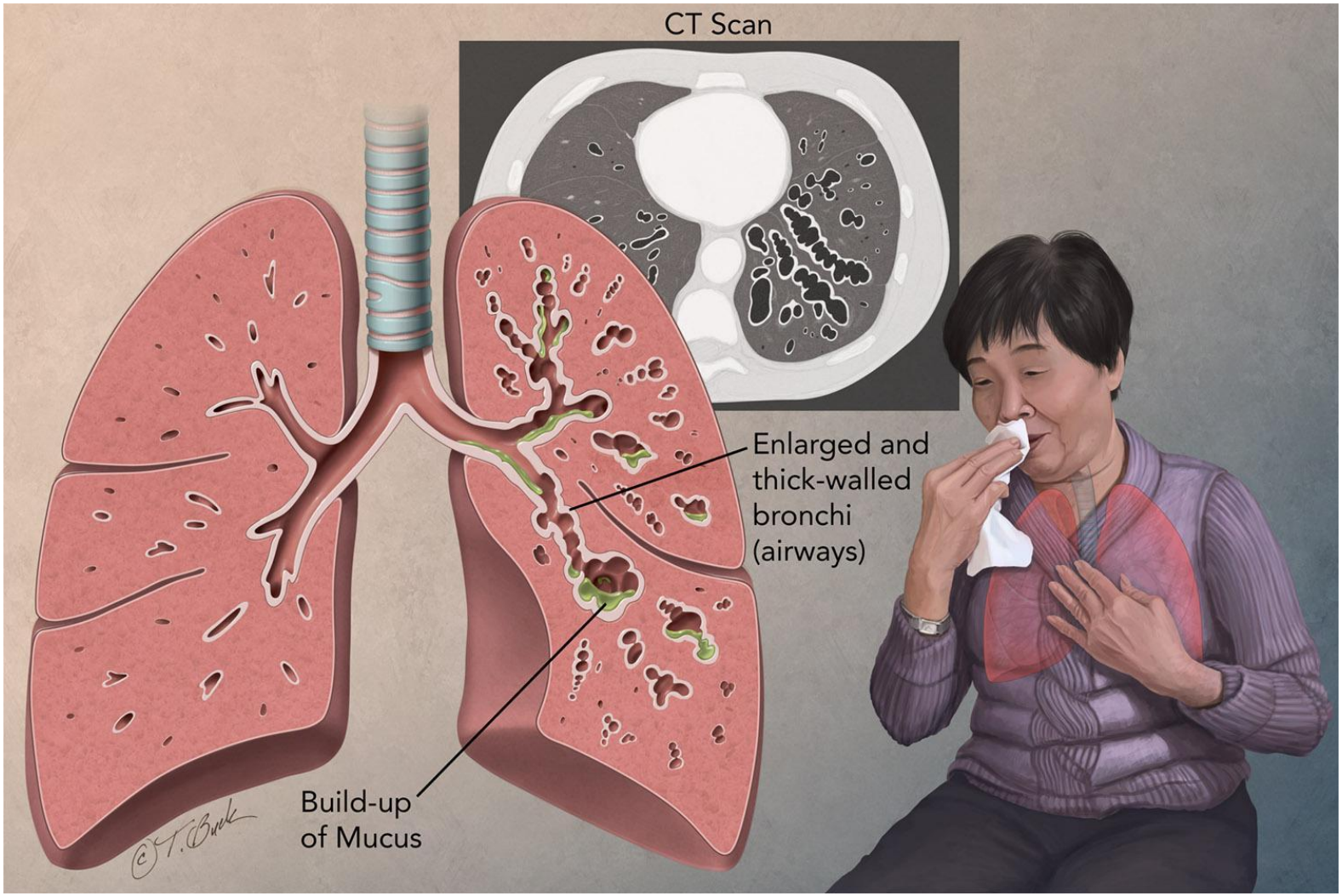
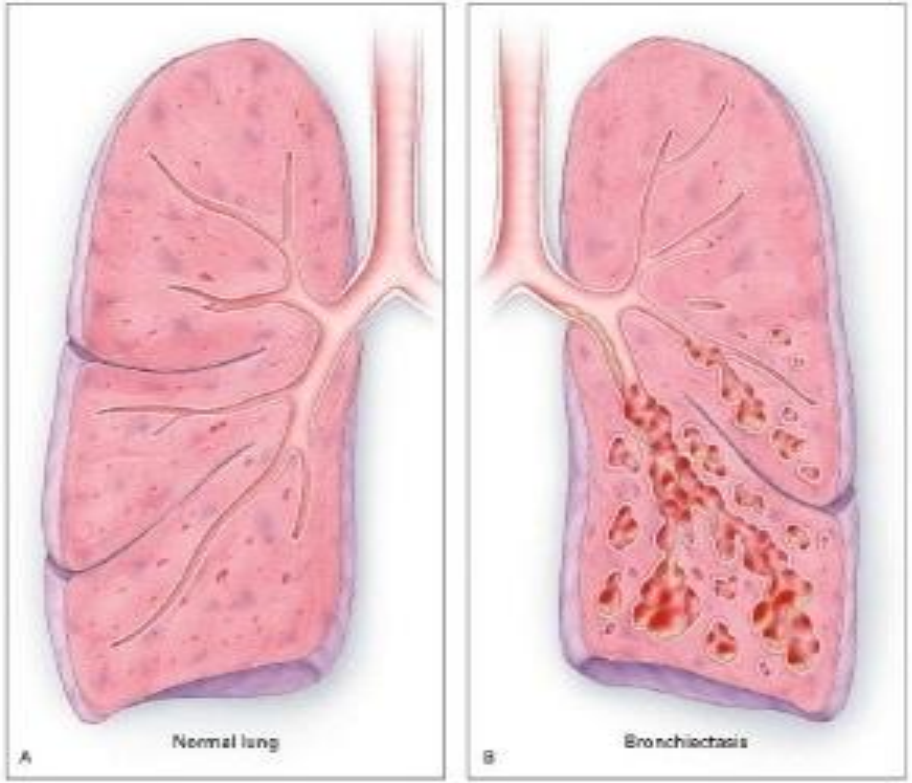
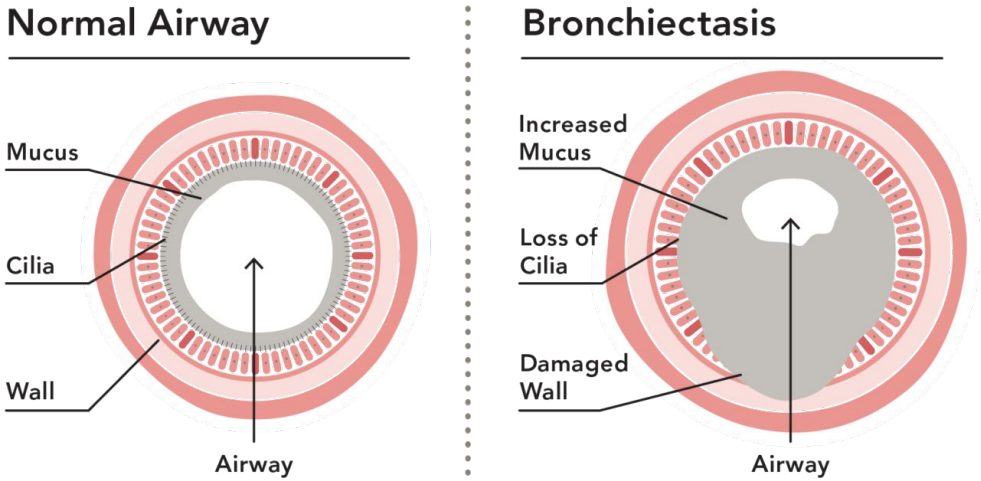
Bronchiectasis



- Bronchiectasis is defined as the irreversible dilatatio of the cartilage-containing airways bronchi or bronchioles.



- Bronchiectasis - involve the lung in a focal or a diffuse manner .
- (1) Cylindrical or tubular (the most common form)
- (2) Varicose, or cystic.



Bronchiectasis with predominant involvement of the :

- Upper lung fields:

1. Cystic fibrosis (CF)
2. Postradiation fibrosis corresponding to the lung region encompassed by the radiation port.
3. Tuberculosis

- Midlung fields:

1. Infection by nontuberculous mycobacteria (NTM), most commonly the Mycobacterium avium-intracellulare complex (MAC),
2. Congenital causes of bronchiectasis - the dyskinetic/ immotile cilia syndrome.

- Lower lung fields:

1. Chronic recurrent aspiration (e.g. due to esophageal motility disorders like those in scleroderma),
2. End stage fibrotic lung disease (e.g. traction bronchiectasis from idiopathic pulmonary fibrosis),
3. Recurrent immunodeficiency-associated infections (e.g. hypogammaglobulinemia).

- Central airways:

1. Allergic bronchopulmonary aspergillosis (ABPA), in which an immune-mediated reaction to Aspergillus damages the bronchial wall.
2. Congenital causes of central airway-predominant bronchiectasis resulting from cartilage deficiency include tracheobronchomegaly (Mounier-Kuhn syndrome) and Williams-Campbell syndrome.

EPIDEMIOLOGY

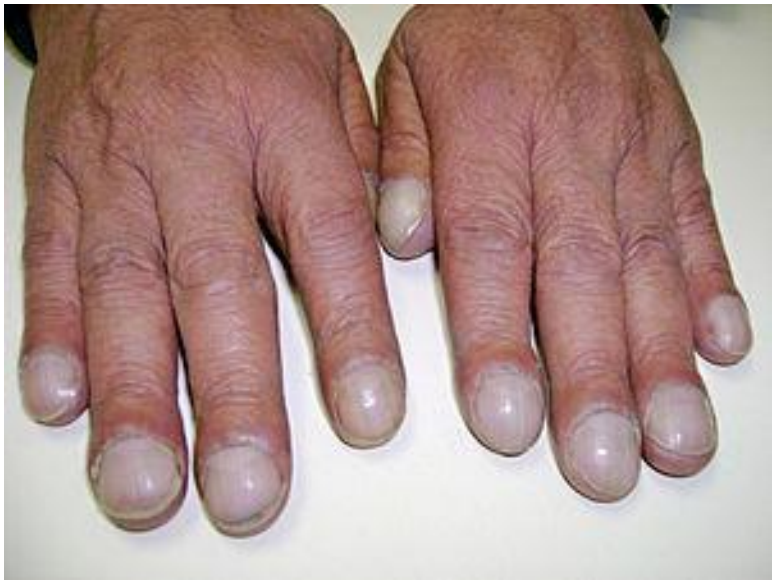
- The incidence of bronchiectasis increases with age.
- Bronchiectasis is more common among women than among men.
- Bronchiectasis resulting from MAC infection classically affects nonsmoking women >50 years of age.

CLINICAL MANIFESTATIONS

- The most common clinical presentation is a persistent productive cough with ongoing production of thick, tenacious sputum.
- Acute exacerbations of bronchiectasis are usually characterized by changes in the nature of sputum production, with increased volume and purulence.

Physical findings:

- 1. crackles
- 2. wheezing
- 3.clubbing of the digits(some patients).

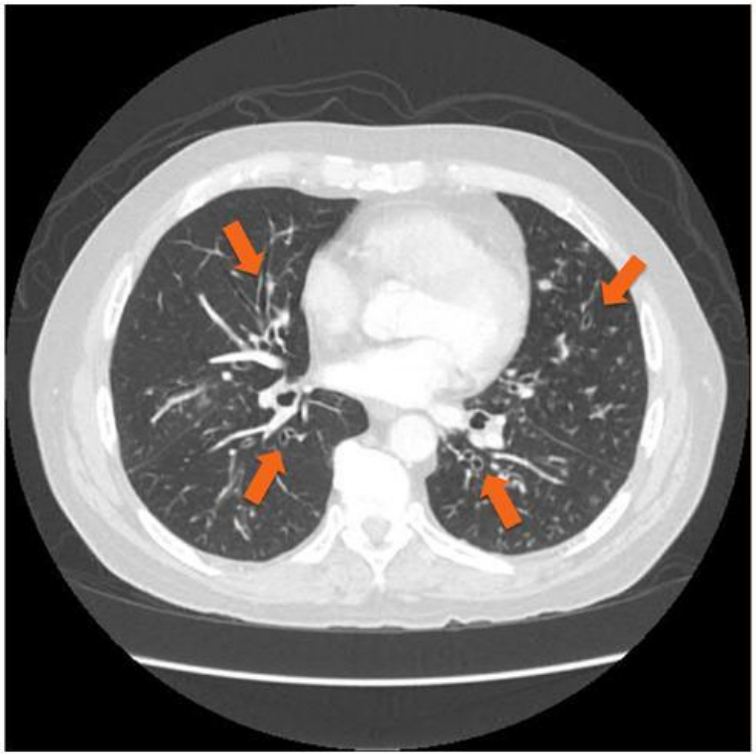


- Pulmonary function tests: mild to moderate airflow obstruction, overlapping with that seen at presentation with other conditions, such as chronic obstructive pulmonary disease (COPD).

CT findings

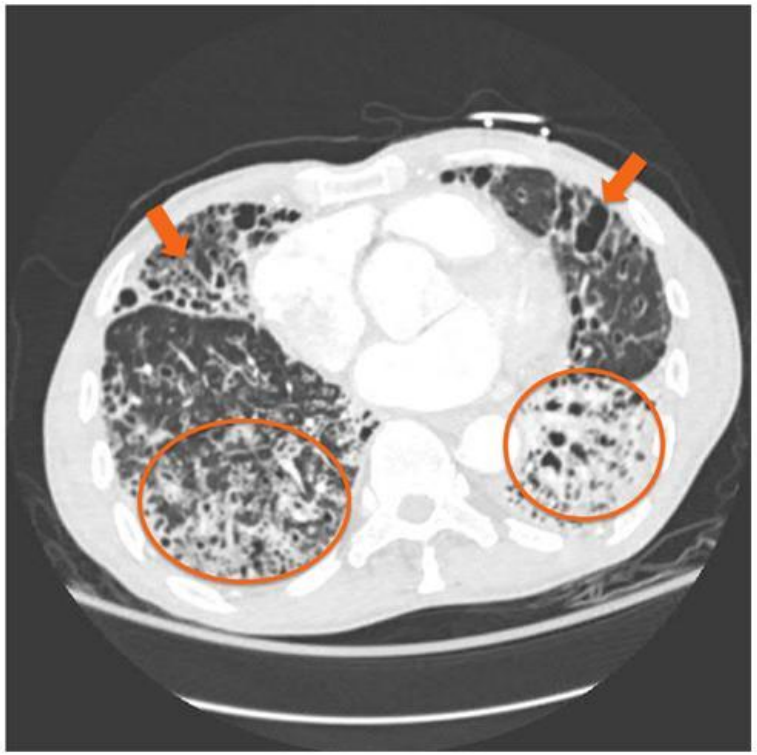
- Airway dilation (detected as parallel "tram tracks" or as the "signet-ring sign" -a cross-sectional area of the airway with a diameter at least 1.5 times that of the adjacent vessel).
- Bronchial wall thickening in dilated airways.
- Lack of bronchial tapering (including the presence of tubular structures within 1 cm from the pleural surface).
- Inspissated secretions (e.g. the "tree-in-bud" pattern.

Bronchiectasis

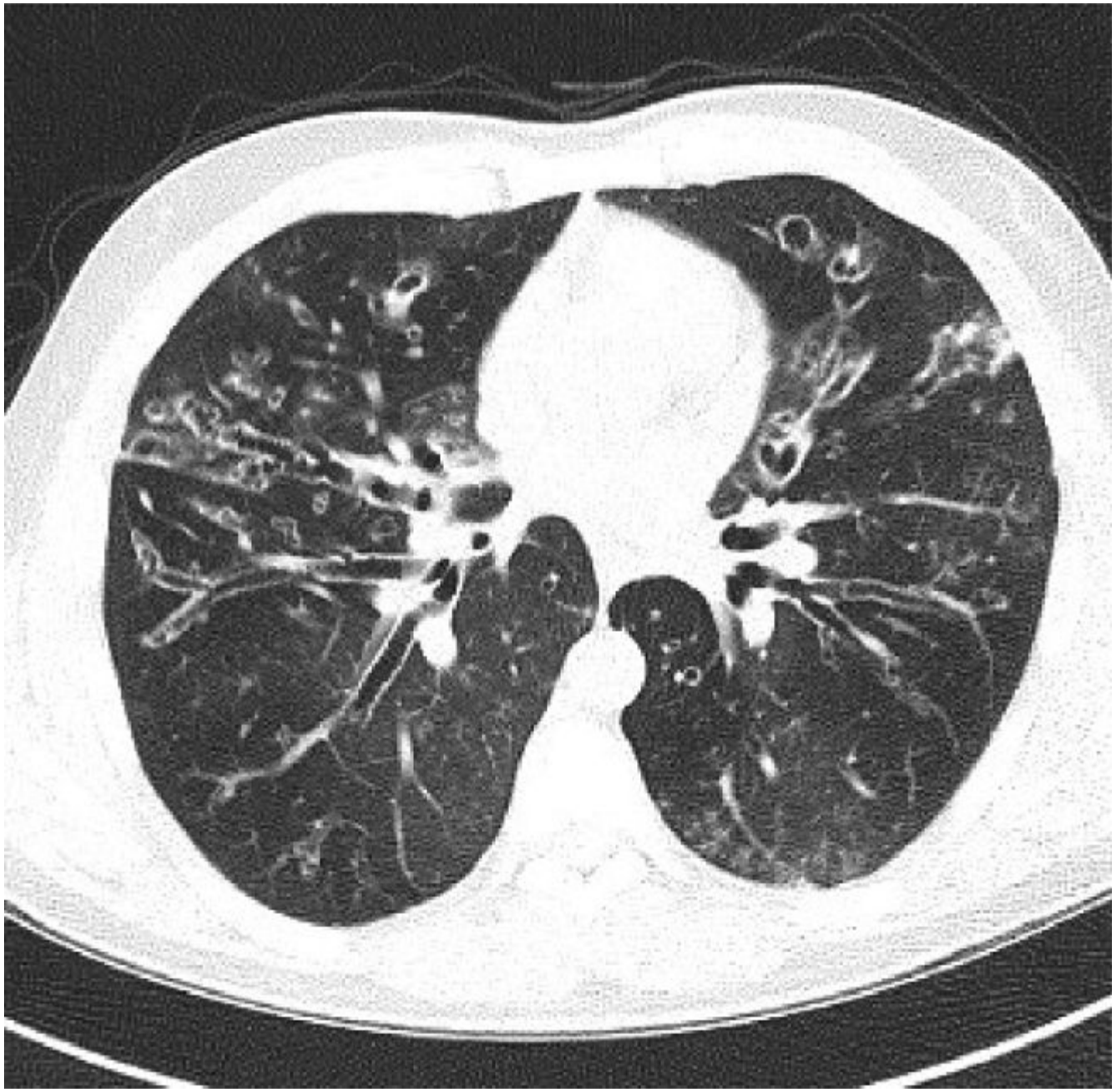


Enlargement of the small airways with thickened bronchial walls (bronchiectasis) are seen in both lungs (depicted by arrows).

Advanced Bronchiectasis



Many enlarged airways with thickened walls (depicted by arrows) are seen, some of which are also filled with mucous (depicted by circles).



TREATMENT

- 1. Control of active infection
- 2. Minimlize the risk of repeated infections by improvements in secretion clearance and bronchial hygiene so as to decrease the microbial load with in the airways.
- Treatment of acute exacerbations: Antibiotics targeting the causative or presumptive pathogen (with Haemophilus influenzae and P. aeruginosa isolated commonly) should be administered in acute exacerbations, for a minimum of 7-14 days.
- In many cases, the etiology of bronchiectasis is not determined. In case series, as many as 25-50% of patients referred for bronchiectasis have idiopathic disease.
- MAC strains are the most common NTM pathogens, and the recommended regimen for HIV-negative patients includes a macrolide combined with rifampin and ethambutol.

BRONCHIAL HYGIENE

Numerous approaches used to enhance secretion clearance include:

- hydration
- mucolytic administration,
- aerosolization of bronchodilators and hyperosmolar agents (e.g. hypertonic saline)
- chest physiotherapy (e.g. postural drainage…)

REFRACTORY CASES

- In select cases, surgery can be considered, with resection of a focal area of suppuration.
- In advanced cases, lung transplantation can be considered .

PROGNOSIS

Outcomes of bronchiectasis can vary widely with:

- the underlying etiology
- the frequency of exacerbations
- the specific pathogens involved (in infectious cases). With worse outcomes associated with P. aeroginosa colonization.

PREVENTION

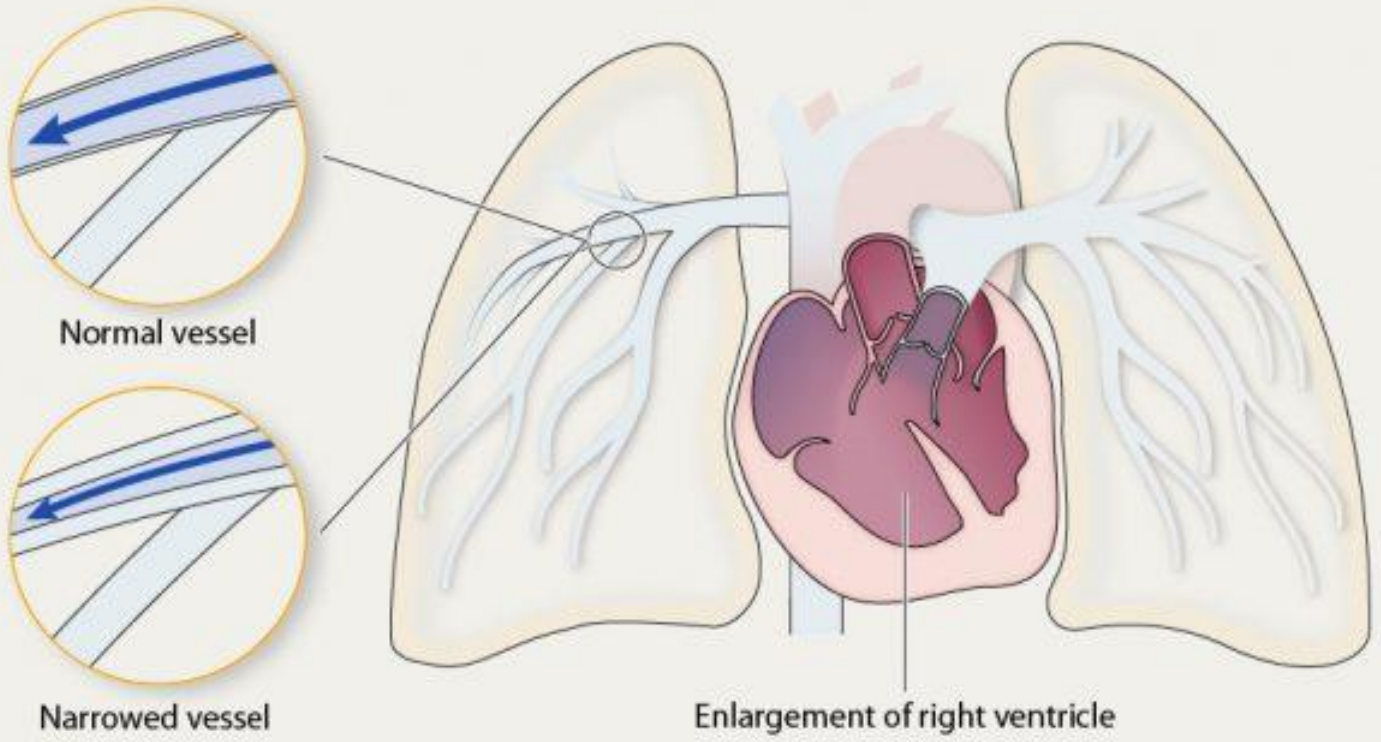
Trying to decrease the risk of recurrent infections by:

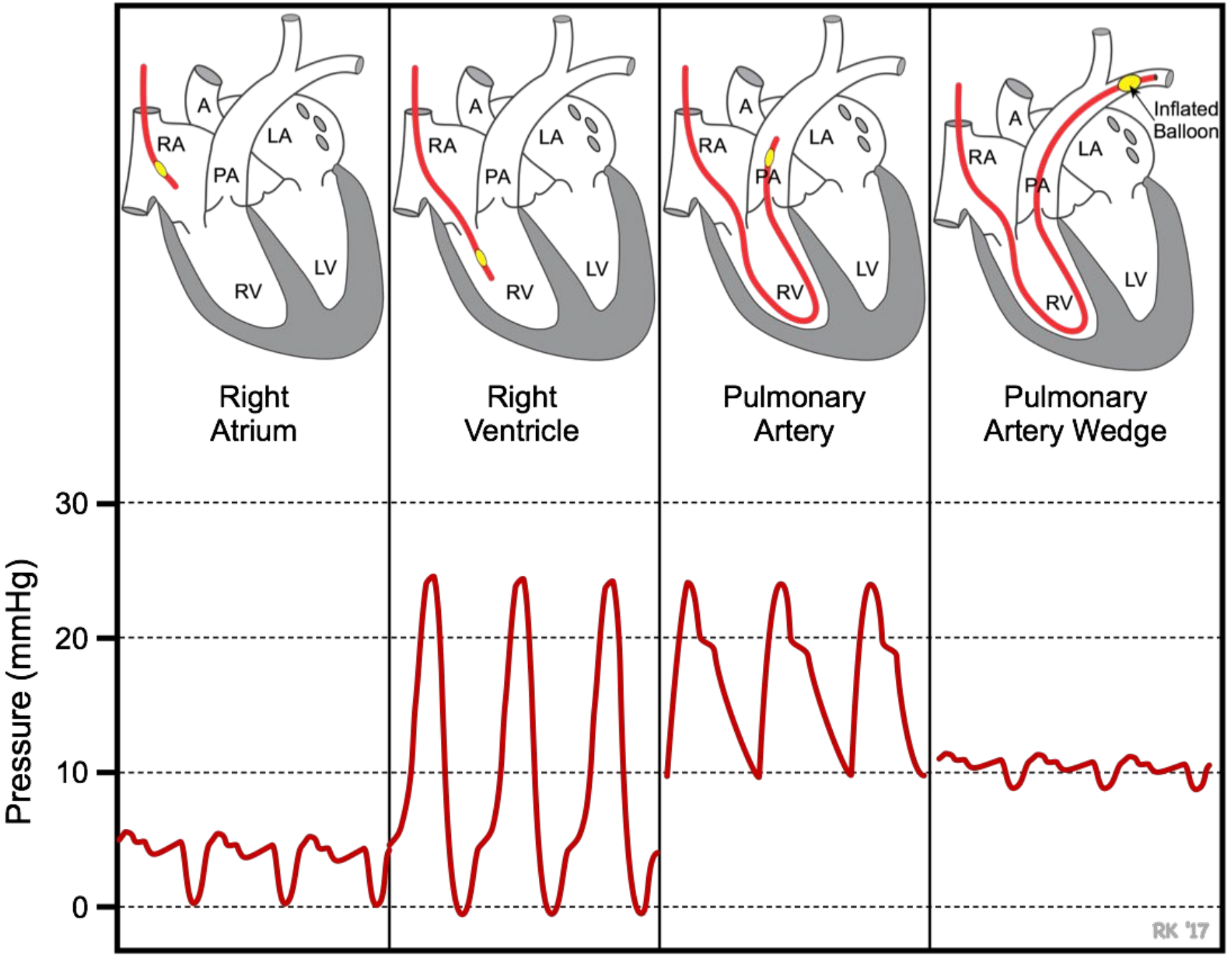
- Reversal of an underlying immunodeficient state (e.g. by administration of gamma globulin for immunoglobulin-deficient patients).
- Vaccination of patients with chronic respiratory conditions (e.g. influenza and pneumococcal).
- Smoking cessation.
- After resolution of an acute infection in patients with recurrences (e.g.> 3 episodes per year), the use of suppressive antibiotics to minimize the microbial load and reduce the frequency of exacerbations has been proposed.

Possible suppressive treatments

- Administration of an oral antibiotic (e.g. ciprofloxacin) daily for 1-2 weeks per month.
- Use of a rotating schedule of oral antibiotics (to minimize the risk of development of drug resistance).
- Administration of a macrolide antibiotic daily or three times per week
- Inhalation of aerosolized antibiotics (e.g.tobramycin inhalation solution) by select patients on a rotating schedule (e.g. 30 days on, 30 days off), with the goal of decreasing the microbial load without eliciting the side effects of systemic drug administration.
- Intermittent administration of IV antibiotics (e.g. "clean-outs") for patients with more severe bronchiectasis and/or resistant pathogens.

Pulmonary Hypertension




A
RA
LA
PA
RV
LV
Inflated Balloon
Right Atrium
Right Ventricle
Pulmonary Artery
Pulmonary Artery Wedge
Pressure (mmHg)
30
20
10
0
RK '17

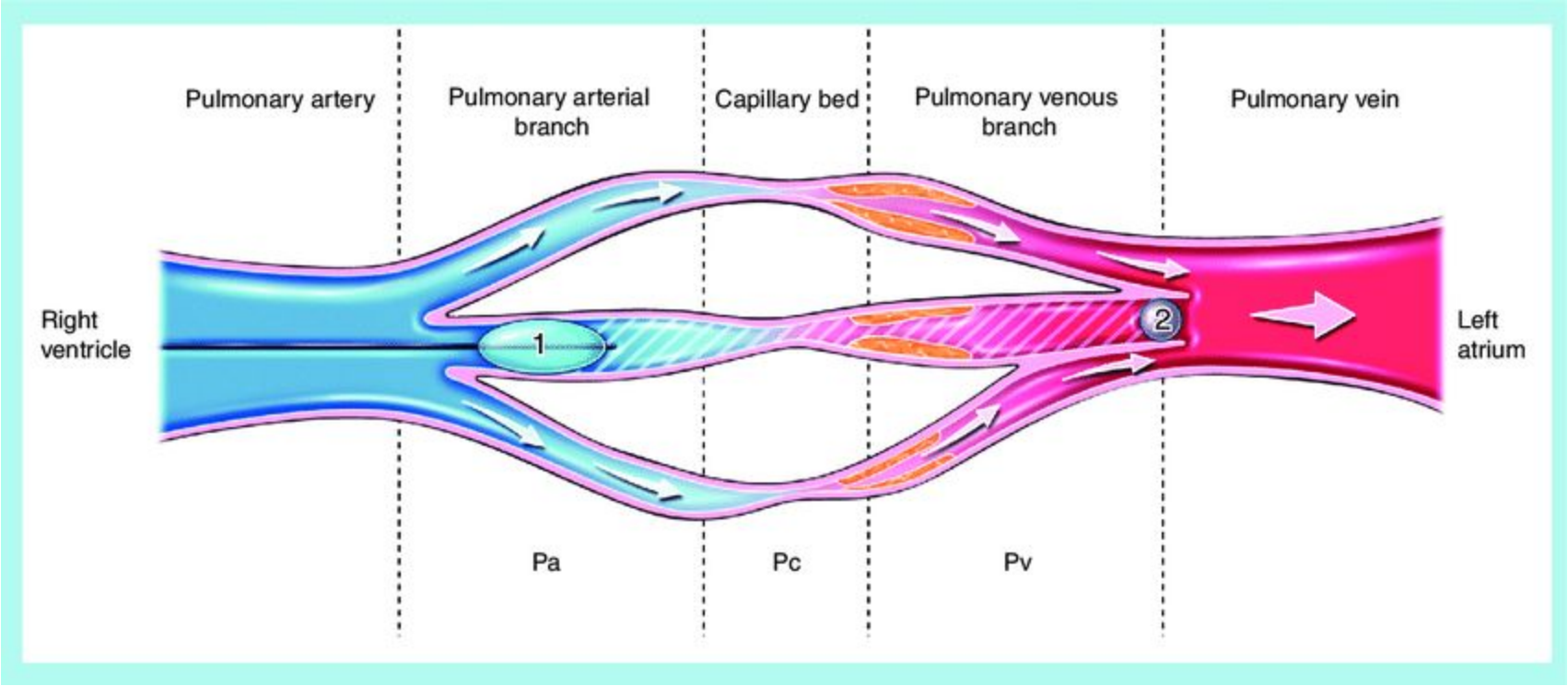
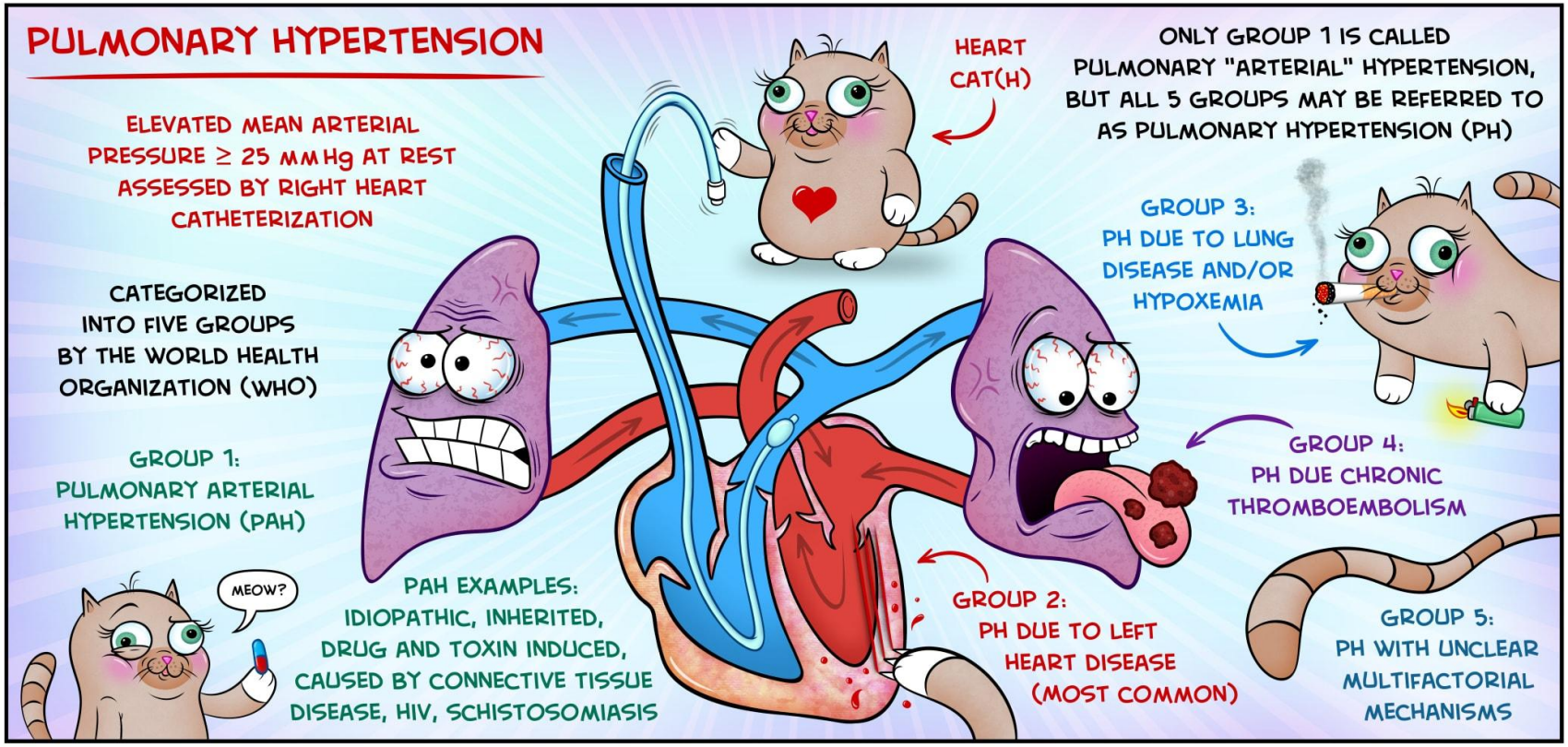

Pulmonary artery
Pulmonary arterial branch
Capillary bed
Pulmonary venous branch
Pulmonary vein
Right ventricle
1
2
Left atrium
Pa
Pc
Pv

Table 1: Classification Pulmonary Hypertension

Group 1	Pulmonary Arterial Hypertension
Group 2	PH from left-sided heart disease
Group 3	PH from chronic hypoxic lung disease
Group 4	PH from chronic blood clots
Group 5	Unclear multifactorial mechanisms (sarcoidosis, hematological disorders, etc)



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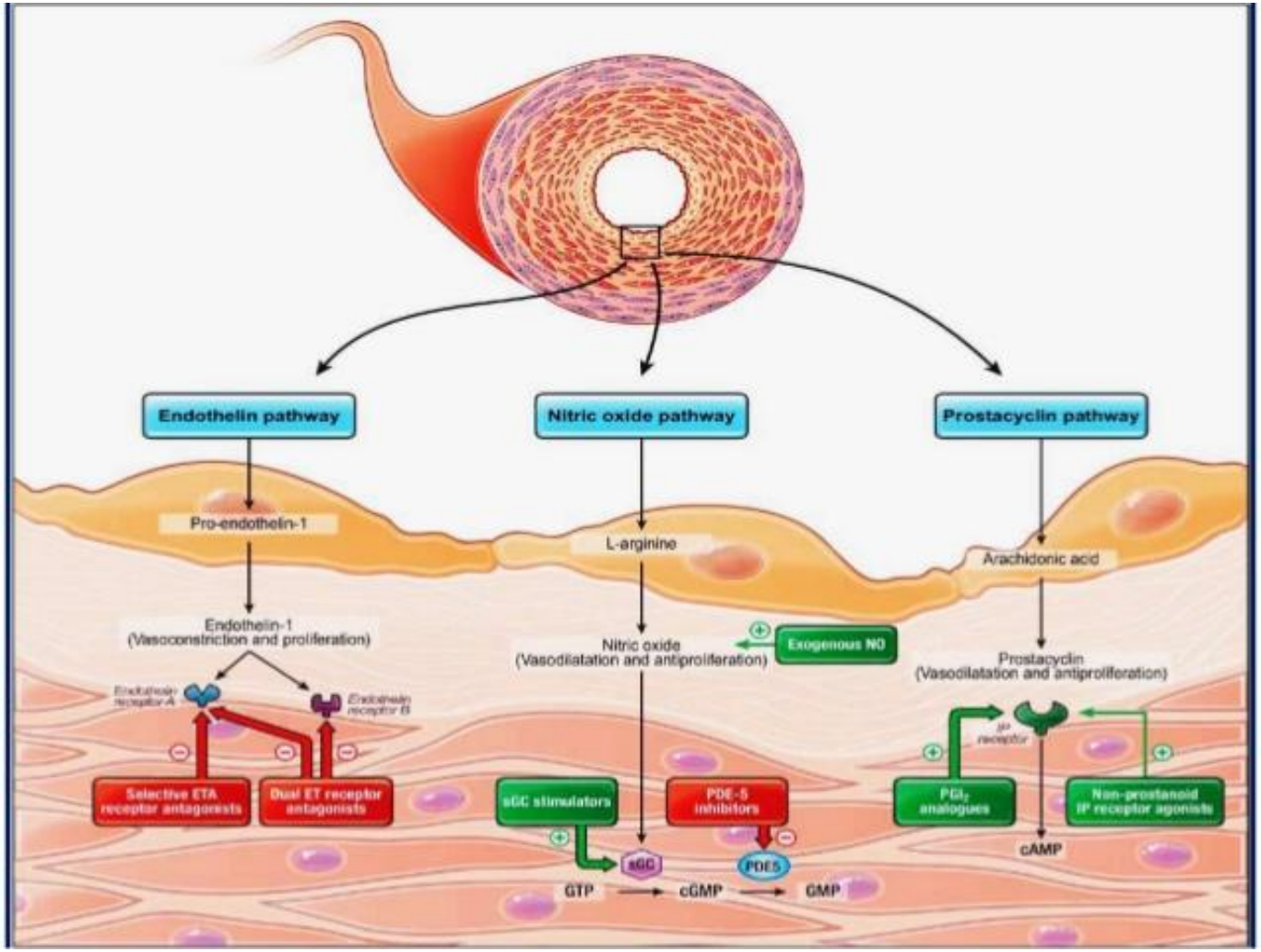
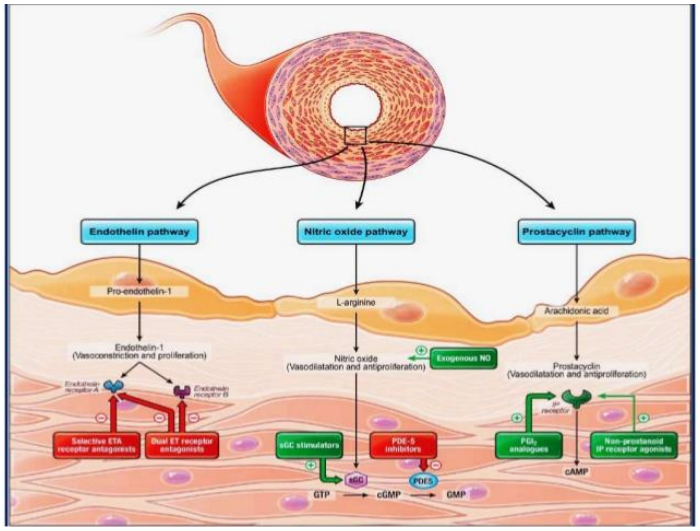
Haemodynamic definitions of pulmonary hypertension

Definition	Characteristics	Clinical group(s)
Pulmonary hypertension (PH)	Mean PAP ≥ 25 mmHg	All
Pre-capillary PH	Mean PAP ≥ 25 mmHg PWP ≤15 mmHg CO normal or reduced	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	Mean PAP ≥ 25 mmHg PWP ≥ 15 mmHg CO normal or reduced	2. PH due to left heart disease
Passive	TPG ≤ 12 mmHg	
Reactive (out of proportion)	TPG > 12 mmHg	

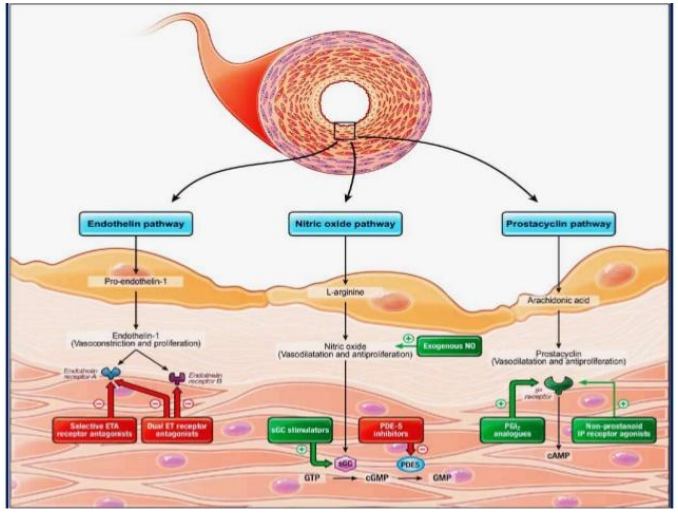

Endothelin pathway
Nitric oxide pathway
Prostacyclin pathway
Pro-endothelin-1
L-arginine
Arachidonic acid
Endothelin-1
(Vasoconstriction and proliferation)
Nitric oxide
(Vasodilatation and antiproliferation)
Exogenous NO
Prostacyclin
(Vasodilatation and antiproliferation)
Endothelin receptor A
Endothelin receptor B
Selective ETA receptor antagonists
Dual ET receptor antagonists
sGC stimulators
PDE-5 inhibitors
PGI2 analogues
Non-prostanoid IP receptor agonists
sGC
PDE5
GTP
cGMP
GMP
cAMP

Characteristics of medications used in the treatment of pulmonary hypertension

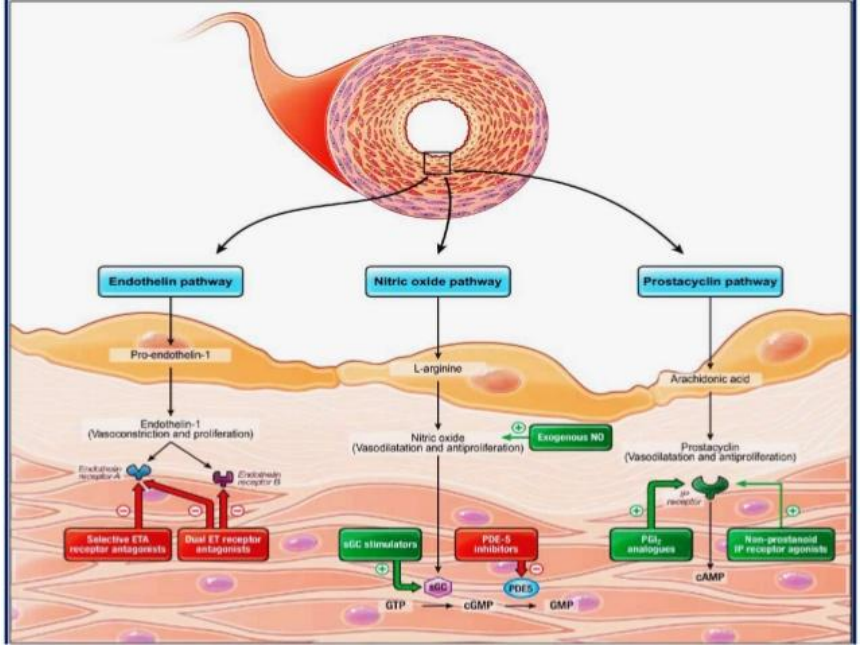
Drug	Route of administration	Dose range (adult)	Half-life
Prostacyclin pathway agonists			
Epoprostenol	Continuous IV infusion via central venous catheter	1 to 12 nanograms/kg/minute initially Dose titrated up every one to two weeks until therapeutic response or dose limiting toxicity occurs	3 to 5 minutes (single dose) 15 minutes (continuous infusion)
Treprostinil	Continuous IV infusion via central venous catheter or continuous subcutaneous infusion	0.625 to 1.25 nanograms/kg/minute initially Dose titrated up every one to two weeks until therapeutic response or dose limiting toxicity occurs	4 hours
	Inhaled	One to three inhalations (ie, 6 to 18 micrograms), four times daily initially Maintenance dose may be gradually titrated up to nine inhalations (ie, 54 micrograms), four times daily	4 hours
Iloprost	Inhaled	2.5 to 5 micrograms, six to nine times daily	20 to 30 minutes (half-life of pulmonary vasodilating effect)
Selexipag	Oral	200 to 1600 micrograms twice daily Dose titrated up every one to two weeks until therapeutic response or dose limiting toxicity occurs	0.8 to 2.5 hours (selexipag) 6.2 to 13.5 hours (active metabolite)



Endothelin receptor antagonists			
Bosentan	Oral	62.5 to 125 mg, two times daily Dose is adjusted for low body weight or drug interactions*	5 hours
Ambrisentan	Oral	5 to 10 mg daily	9 hours
Macitentan	Oral	10 mg per day	14 to 18 hours (parent drug)



Nitric oxide-cyclic guanosine monophosphate enhancers			
Soluble guanylate cyclase stimulant			
Riociguat	Oral	Initial dose 0.5 to 1 mg three times daily, titrated up by 0.5 mg three times per day every two weeks until therapeutic response or dose limiting toxicity occurs (maximum dose 2.5 mg three times daily)	12 hours
Phosphodiesterase type 5 inhibitors			
Sildenafil	Oral	20 mg, three times daily	4 hours
	IV	10 mg, three times daily Dose is adjusted for drug interactions*	4 hours
Tadalafil	Oral	40 mg daily Dose is adjusted for drug interactions*	35 hours



Calcium channel blockers[1]			
Nifedipine	Oral	Start 30 mg per day. Increase to the maximum tolerated dose over days to weeks.	7 hours
Diltiazem extended-release	Oral	Start 120 mg per day. Increase to the maximum tolerated dose over days to weeks.	6 to 9 hours
Amlodipine	Oral	Start 2.5 mg per day. Increase to the maximum tolerated dose over days to weeks.	30 to 50 hours

ARDS

ARDS

- ARDS is an acute, diffuse, inflammatory form of lung injury that is associated with a variety of etiologies. Recognizing and promptly treating ARDS is critical to reduce the associated high mortality.
- ARDS should be suspected in patients with progressive symptoms of dyspnea, an increasing requirement for oxygen, and alveolar infiltrates on chest imaging within 6 to 72 hours of an inciting event.

Etiology of acute respiratory distress syndrome*

Etiology	Clinical features	Diagnostic tests
Sepsis	Fever hypotension, leukocytosis, lactic acidosis, infectious source	Appropriate clinical context and positive cultures
Aspiration pneumonitis	Witnessed or risk for aspiration, food, lipid laden macrophages, airway erythema on bronchoscopy	Presumptive diagnosis with negative cultures
Infectious pneumonia (including mycobacterial, viral, fungal, parasitic)	Productive cough, pleuritic pain, fever, leukocytosis, lobar consolidation or bilateral infiltrates in an immunosuppressed patient	Appropriate clinical context and positive respiratory cultures
Severe trauma and/or multiple fractures	History of trauma or fractures within the last week	Diagnosis is apparent
Pulmonary contusion	History of chest trauma (blunt or penetrating), chest pain	Presumptive diagnosis in the correct clinical context, negative cultures
Burns and smoke inhalation	Exposure to fire or smoke, cough, dyspnea, DIC, particulate matter on bronchoscopy, surface burns	Presumptive diagnosis in the correct clinical context, negative cultures
Transfusion related acute lung injury and massive transfusions	History of transfusion, dyspnea during or shortly after transfusion	Diagnosis of exclusion
HSCT¶	History of HSCT	Diagnosis of exclusion
Pancreatitis	Abdominal pain, vomiting, risk actors (eg, gallstones, alcohol, viral infection)	Elevated amylase and lipase, with or without abnormal imaging
Inhalation injures other than smoke (eg, near drowning, gases)	History of inhalation exposure (eg, chlorine gas)	Diagnosis of exclusion
Thoracic surgery (eg, post-cardiopulmonary bypass) or other major surgery	History of surgery, intraoperative ventilation, intraoperative transfusion	Diagnosis of exclusion
Drugs (chemotherapeutic agents, amiodarone, radiation)	New drugs or radiation exposure on history, lymphocytosis on lavage, lavage may have suggestive features of amiodarone toxicity ("foamy macrophages") but is nonspecific	Diagnosis of exclusion, lung biopsy occasionally helpful

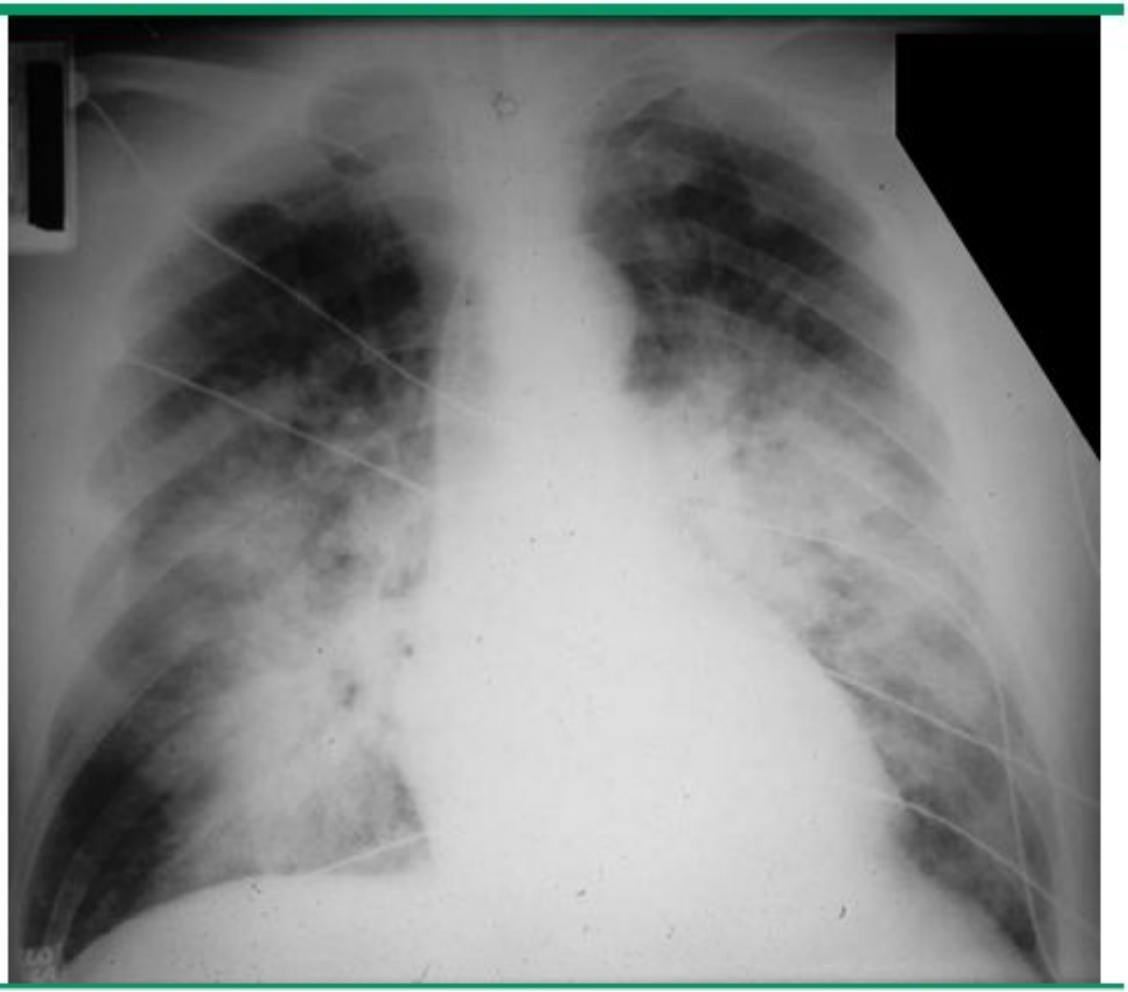
ARDS has over 60 etiologies. This is an abbreviated list of the common causes of ARDS.

ARDS: acute respiratory distress syndrome; DIC: disseminated intravascular coagulation; HSCT: hematopoietic stem cell transplant; AEP: acute eosinophilic pneumonia; COP: cryptogenic organizing pneumonia; DAD: diffuse alveolar damage.

* Use of the term ARDS to describe conditions such as AEP or COP is somewhat controversial. However, some experts consider these a "subtype" of ARDS since they present in a similar fashion to ARDS, although the pathology of such entities is different from DAD, which is the classic pathology associated with ARDS. Similarly, while neurogenic pulmonary edema meets the definition of ARDS, since it causes hypoxemia and bilateral infiltrates in the absence of pulmonary edema due to heart failure, the pathology and clinical course is likely different. Similarly, embolism of fat, air, and amniotic fluid may mimic ARDS but it is uncertain as to whether they cause ARDS.

¶ Many patients with HSCT may develop a form of lung injury after transplant but the distinction between this and ARDS due to complications of HSCT (eg, pneumonia) is often unclear.

Acute respiratory distress syndrome



Chest radiograph showing diffuse, bilateral, alveolar infiltrates without cardiomegaly in a patient with ARDS.

ARDS: acute respiratory distress syndrome.

Courtesy of Steven E Weinberger, MD.

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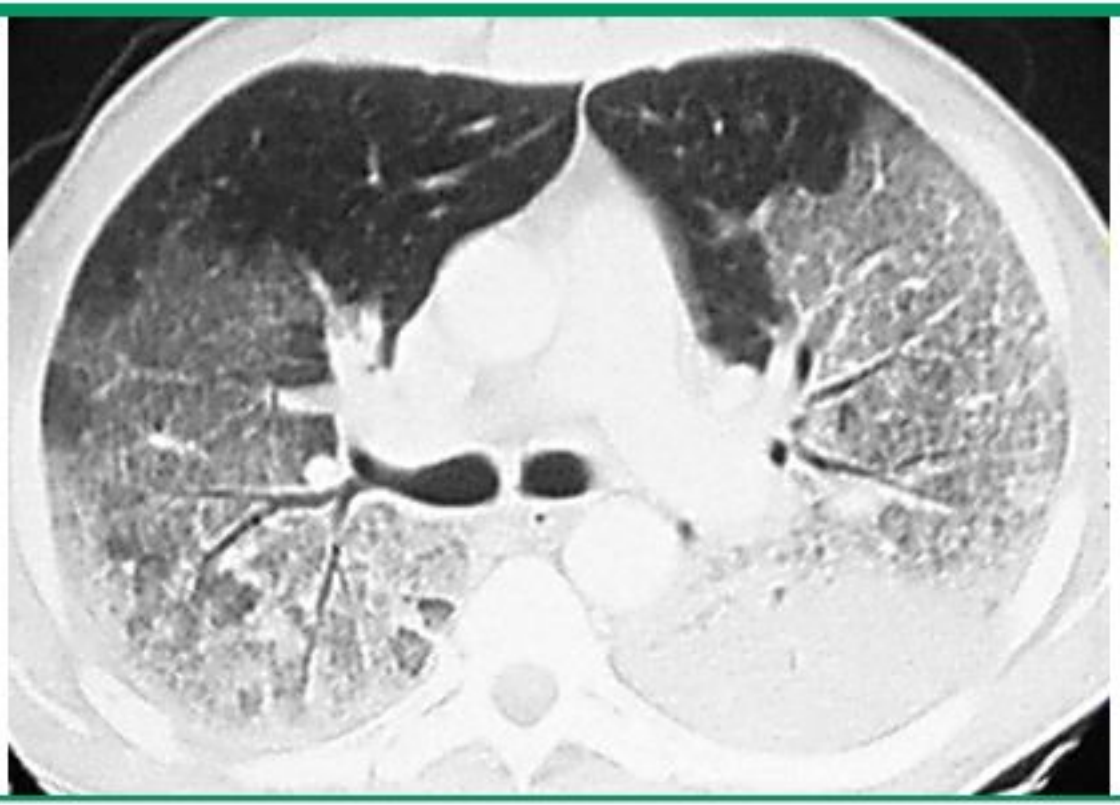
ARDS CT



ARDS due to sepsis after pneumococcal pneumonia.

ARDS: acute respiratory distress syndrome; CT: computed tomography.

Courtesy of Paul Stark, MD.

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Differential Diagnosis

- A variety of conditions may present as acute hypoxemic respiratory failure with bilateral alveolar opacities.
- **Acute cardiogenic pulmonary edema**
- **Bilateral pneumonia**
- **Diffuse alveolar hemorrhage**
- **Inflammatory or autoimmune conditions**
- **Acute eosinophilic pneumonia** — AEP occurs in previously healthy individuals and is characterized by cough, fever, dyspnea, and sometimes chest pain. It can be distinguished from ARDS on BAL specimens by the identification of a large number of eosinophils, typically 35 to 55 percent of all recovered cells. Peripheral eosinophilia may or may not be present [
- **Pulmonary vasculitis**
- **Cryptogenic organizing pneumonia (COP)** — COP may be suspected in patients who present with the symptoms of nonresolving
- **Acute interstitial pneumonitis (AIP; Hamman-Rich syndrome)**
- **Acute exacerbation of idiopathic pulmonary fibrosis (AEIPF)**
- **Disseminated malignancy** — Cancer can disseminate through the lungs (invasive cancer) or lymphatics (lymphangitic spread) so rapidly that the ensuing respiratory failure may be mistaken for ARDS

Clinical diagnosis (Berlin definition)

- ARDS can be diagnosed once cardiogenic pulmonary edema and alternative causes of acute hypoxemic respiratory failure and bilateral infiltrates have been excluded.
- Respiratory symptoms must have begun within one week of a known clinical insult, or the patient must have new or worsening symptoms during the past week.
- Bilateral opacities must be present on a chest radiograph or computed tomographic (CT) scan. These opacities must not be fully explained by pleural effusions, lobar collapse, lung collapse, or pulmonary nodules.
- The patient's respiratory failure must not be fully explained by cardiac failure or fluid overload.
- A moderate to severe impairment of oxygenation must be present, as defined by the ratio of arterial oxygen tension to fraction of inspired oxygen (PaO_2/FiO_2). The severity of the hypoxemia defines the severity of the ARDS:
- Mild ARDS – The PaO_2/FiO_2 is >200 mmHg, but ≤300 mmHg, on ventilator settings that include positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) ≥5 cm H_2O.
- Moderate ARDS – The PaO_2/FiO_2 is >100 mmHg, but ≤200 mmHg, on ventilator settings that include PEEP ≥5 cm H_2O.
- Severe ARDS – The PaO_2/FiO_2 is ≤100 mmHg on ventilator settings that include PEEP ≥5 cm H_2O.