Pulmonary circulation

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Lecture objectives

1. Contrast the systemic and pulmonary circulations with respect to pressures, resistance to blood flow, and response to hypoxia.
2. Describe how pulmonary vascular resistance changes with alterations in cardiac output or pulmonary arterial pressure. Explain in terms of distention and recruitment of pulmonary vessels.
3. Identify the neural and humoral factors that influence pulmonary vascular resistance and pulmonary blood flow.
4. Describe how pulmonary vascular resistance changes with lung volume. Explain in terms of alterations in alveolar and extra-alveolar blood vessels.
5. Describe the consequence of hypoxic pulmonary vasoconstriction on the distribution of pulmonary blood flow.
6. Explain development of pulmonary edema by a) increased hydrostatic pressure, b) increased permeability, c) impaired lymphatic outflow or increased central venous pressure,
7. Describe the major functions of the bronchial circulation.

Pulmonary circulation versus systemic circulation:

1. The pulmonary artery is thin, with a wall thickness about one-third that of the aorta.
2. The pulmonary arterial branches are very short.
3. The pulmonary arteries, and even the smaller arteries and arterioles, have larger diameters and thinner wall thickness than their counterpart systemic arteries → greater compliance.
4. The greater pulmonary compliance allows the lung to accommodate any increase in cardiac output as what happens during exercise and prevent the development of pulmonary edema.

Pulmonary circulation versus systemic circulation (cont.):

5. The distensibility of pulmonary veins is similar to that of systemic circulation.
6. Supporting tissues of the lungs (connective tissue, septa, and large and small bronchi) receive oxygenated blood through small bronchial arteries (1-2% of the total cardiac output).
7. Pulmonary lymphatics drain into the right lymphatic duct. As they can remove leaking plasma proteins, so they help to prevent pulmonary edema.

Secondary functions of the pulmonary circulation:

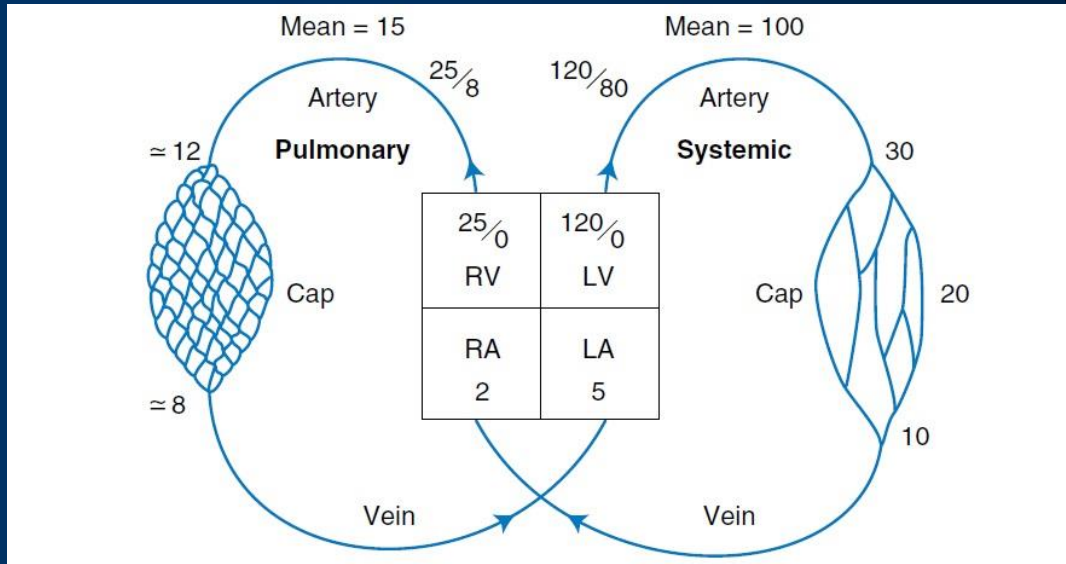
1. Filters the blood from thrombi and emboli (fat or air)
   - Endothelial cells lining the pulmonary vessels release fibrinolytic substances that dissolve thrombi
2. Metabolizes vasoactive hormones (converts angiotensin I to angiotensin II; inactivates NE, bradykinin, serotonin, and prostaglandins E_1, E_2, and $E_{2\alpha}$)
   - In acute lung injury (e.g. O_2 toxicity, fat embolism) lung tissue releases histamine, prostaglandins, and leukotrienes → vasoconstriction of pulmonary arteries and pulmonary endothelial damage
3. Blood reservoir, as 10% of total circulating blood volume is in the pulmonary circulation
4. Many white blood cells are trapped by the lung and later released. In addition, the lung is able to secrete immunoglobulins, particularly IgA, in the bronchial mucus that contribute to its defenses against infection.

Table **Fate of Substances in the Pulmonary Circulation**

Substance	Fate
Peptides	
Angiotensin I	Converted to angiotensin II by ACE
Angiotensin II	Unaffected
Vasopressin	Unaffected
Bradykinin	Up to 80% inactivated
Amines	
Serotonin	Almost completely removed
Norepinephrine	Up to 30% removed
Histamine	Not affected
Dopamine	Not affected
Arachidonic acid metabolites	
Prostaglandins E_2 and $F_{2\alpha}$	Almost completely removed
Prostaglandin A_2	Not affected
Prostacyclin (PGI_2)	Not affected
Leukotrienes	Almost completely removed

Pressure in the pulmonary system:

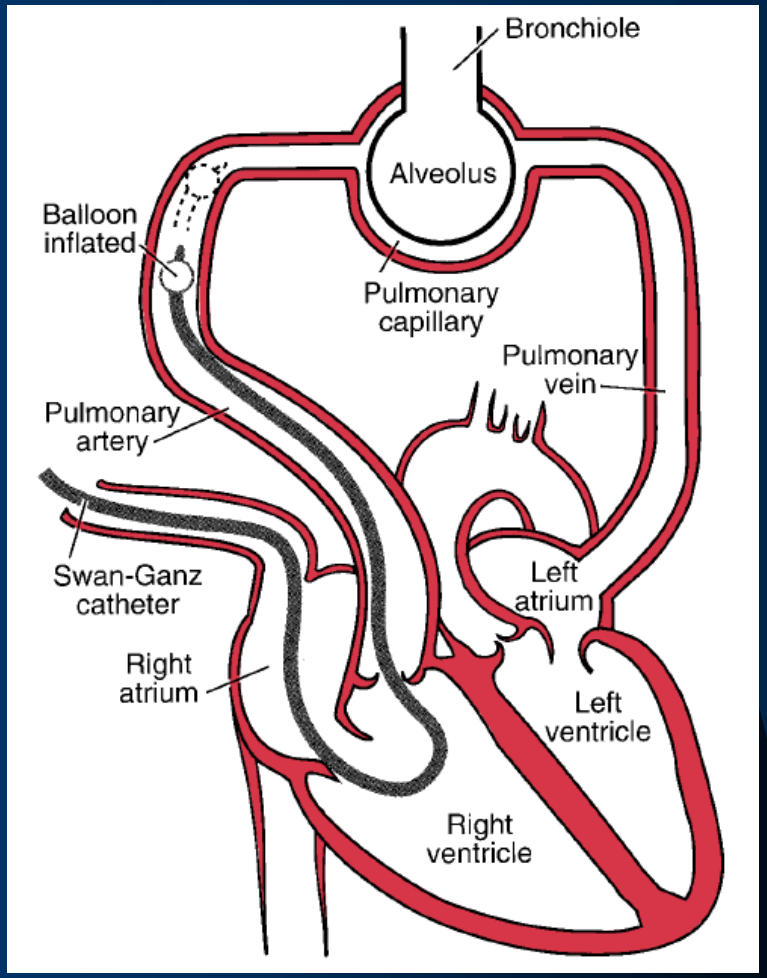
- In contrast to the systemic circulation, the pulmonary circulation is a *low pressure circulation* (one-tenth the resistance of the systemic circulation), with a systolic pressure of about 20-25 mmHg and a diastolic pressure of;
  - 0-1 mmHg in the right ventricle
  - 8 mmHg in the pulmonary artery
- The mean arterial pulmonary pressure is about 15 mmHg.
- The pulmonary capillary pressure is about 7 mmHg. The blood volume in the pulmonary capillaries is approximately equal to the stroke volume of the right ventricle.



Comparison of pressures (mm Hg) in the pulmonary and systemic circulations

Pressure in the pulmonary system (Cont):

- The mean pressure in the left atrium is 2 mmHg (1-5 mmHg). *Pulmonary wedge pressure* is a good estimate of left atrial pressure (just 2-3 mmHg higher).



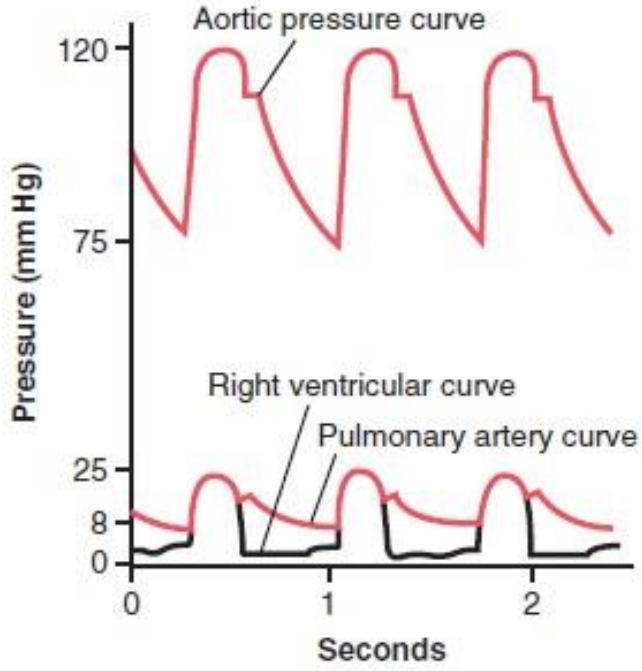


Figure Pressure pulse contours in the right ventricle, pulmonary artery, and aorta.

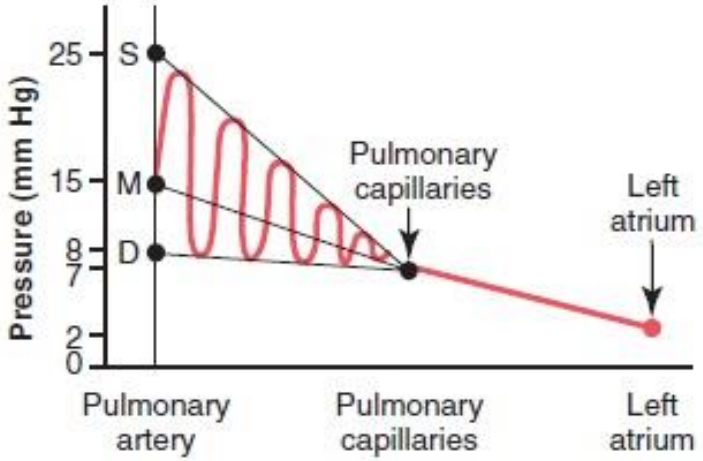
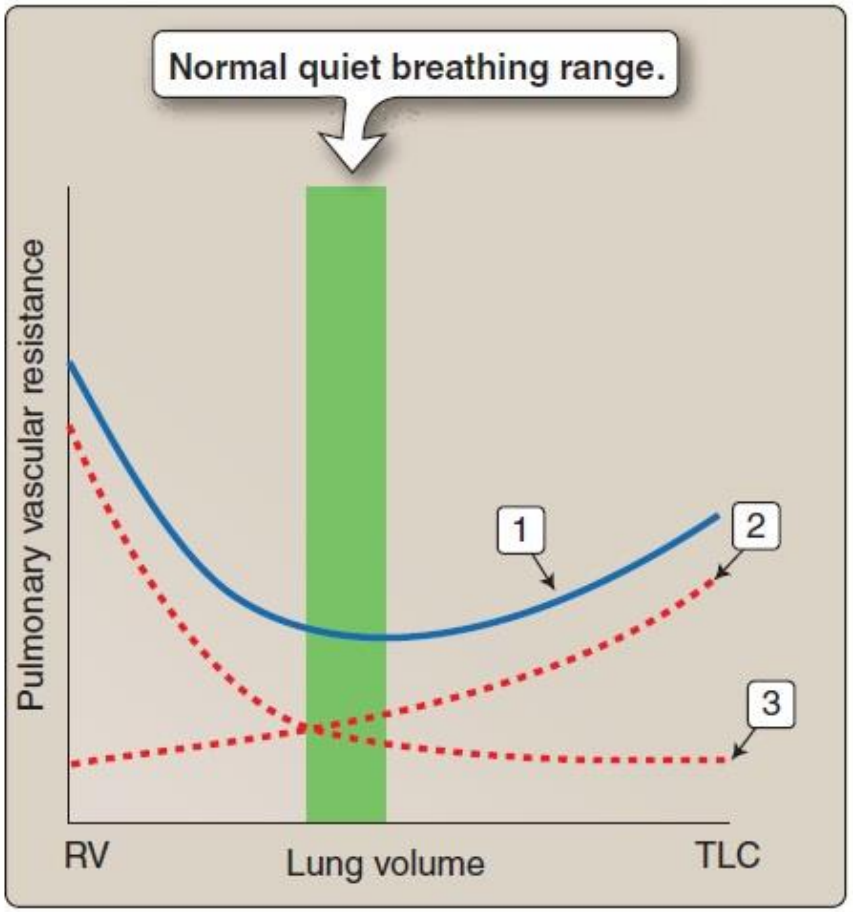


Figure Pressures in the different vessels of the lungs. The red curve denotes arterial pulsations. D, diastolic; M, mean; S, systolic.

The Pulmonary Vascular Resistance



1. Pulmonary vascular resistance (PVR) dependence on lung volume
2. Capillary contribution to PVR (alveolar inflation stretches and compresses capillaries, increasing flow resistance)
3. Supply vessel effects on PVR (vessels dilate by radial traction when lungs inflate, reducing flow resistance)

Pulmonary vascular resistance:

The capillary resistance of pulmonary circulation

- The pulmonary capillary bed is a network of tubular vessels with interconnections, so that blood flows as a thin sheet.
- The pulmonary capillary bed is collapsible if local alveolar pressure exceeds capillary pressure

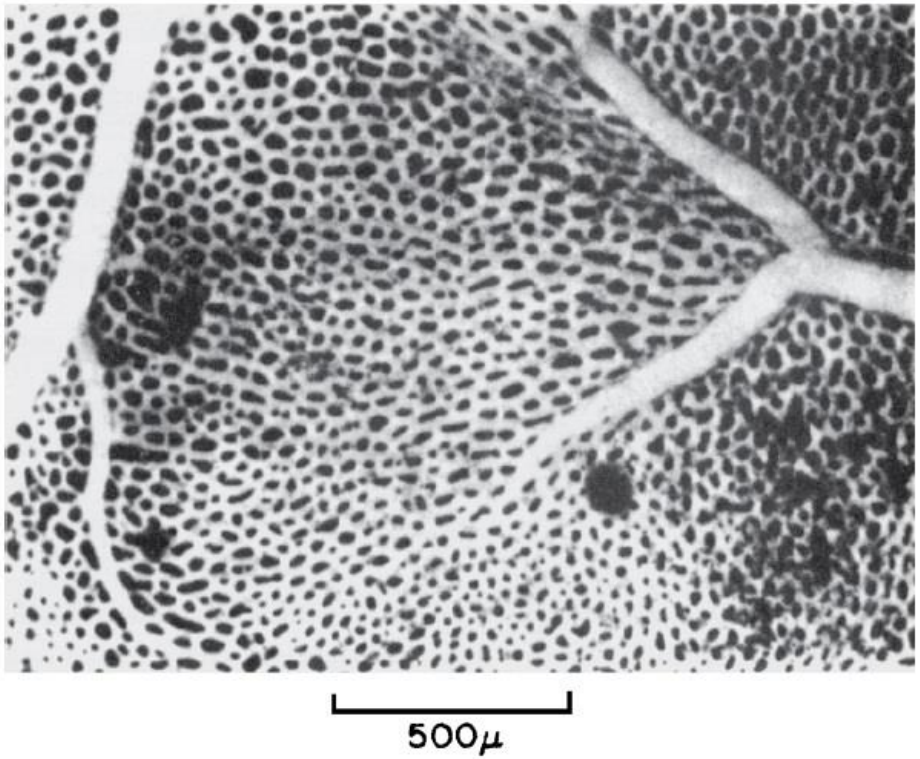
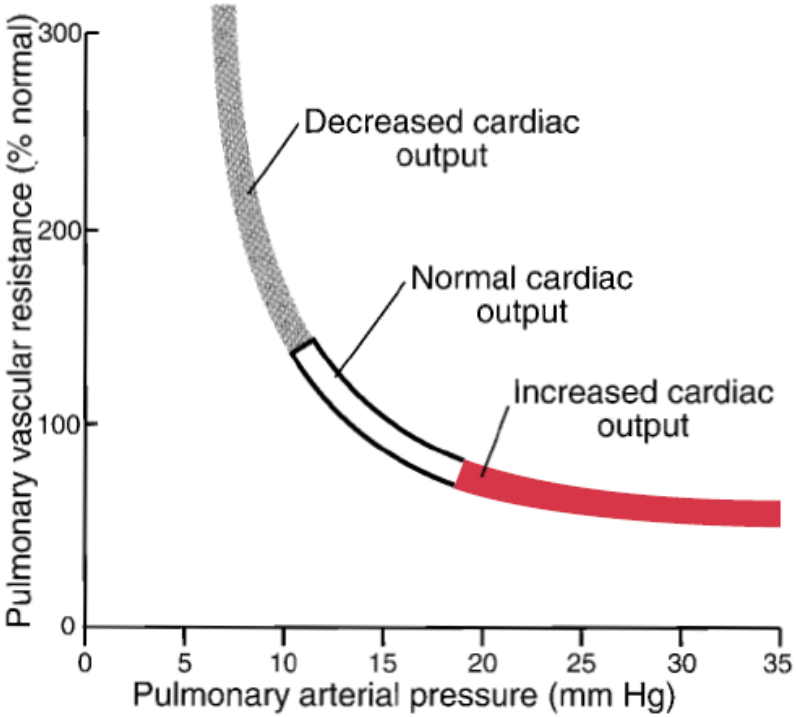


Figure View of an alveolar wall (in the frog) showing the dense network of capillaries. A small artery (**left**) and vein (**right**) can also be seen. The individual capillary segments are so short that the blood forms an almost continuous sheet.

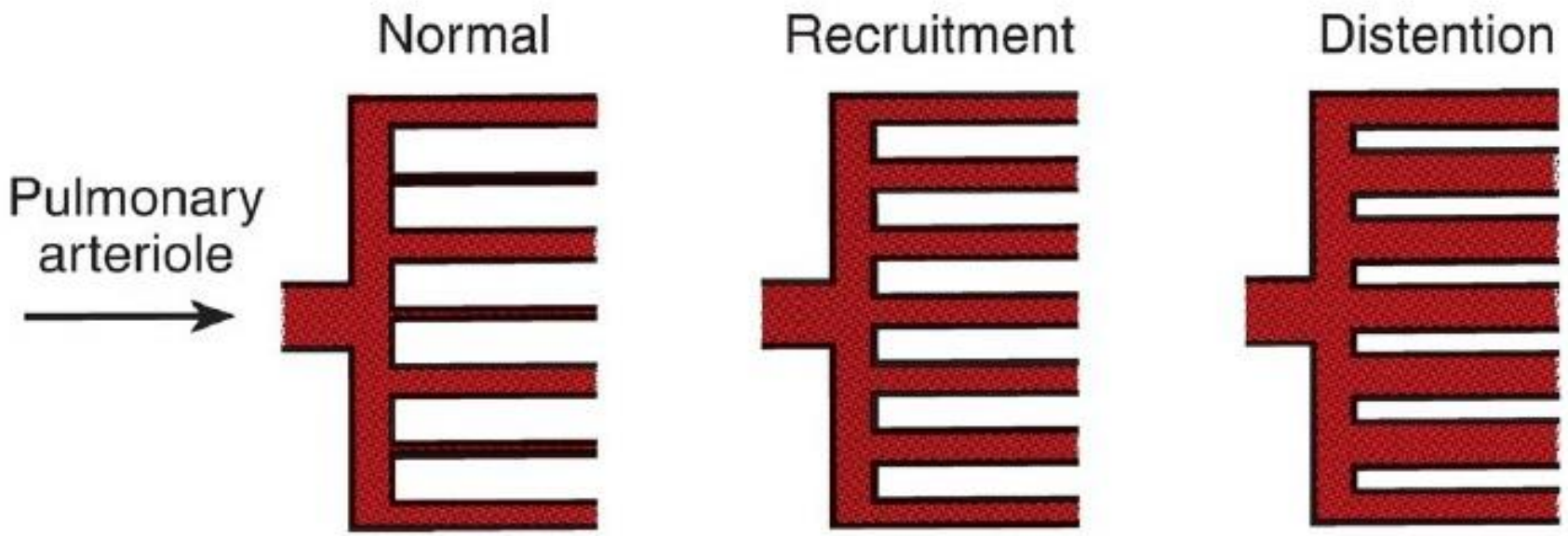
Pulmonary vascular resistance:

The capillary resistance of pulmonary circulation

- The capillary resistance of pulmonary circulation is passively reduced with increased cardiac output (advantage; minimal rise in capillary pressure and blood velocity)
- The mechanisms for decreasing pulmonary resistance are the;
  1. Capillary recruitment
  2. Capillary distention



Effect of cardiac output on pulmonary vascular resistance. Pulmonary vascular resistance falls as cardiac output increases. Note that if pulmonary arterial pressure rises, pulmonary vascular resistance decreases.

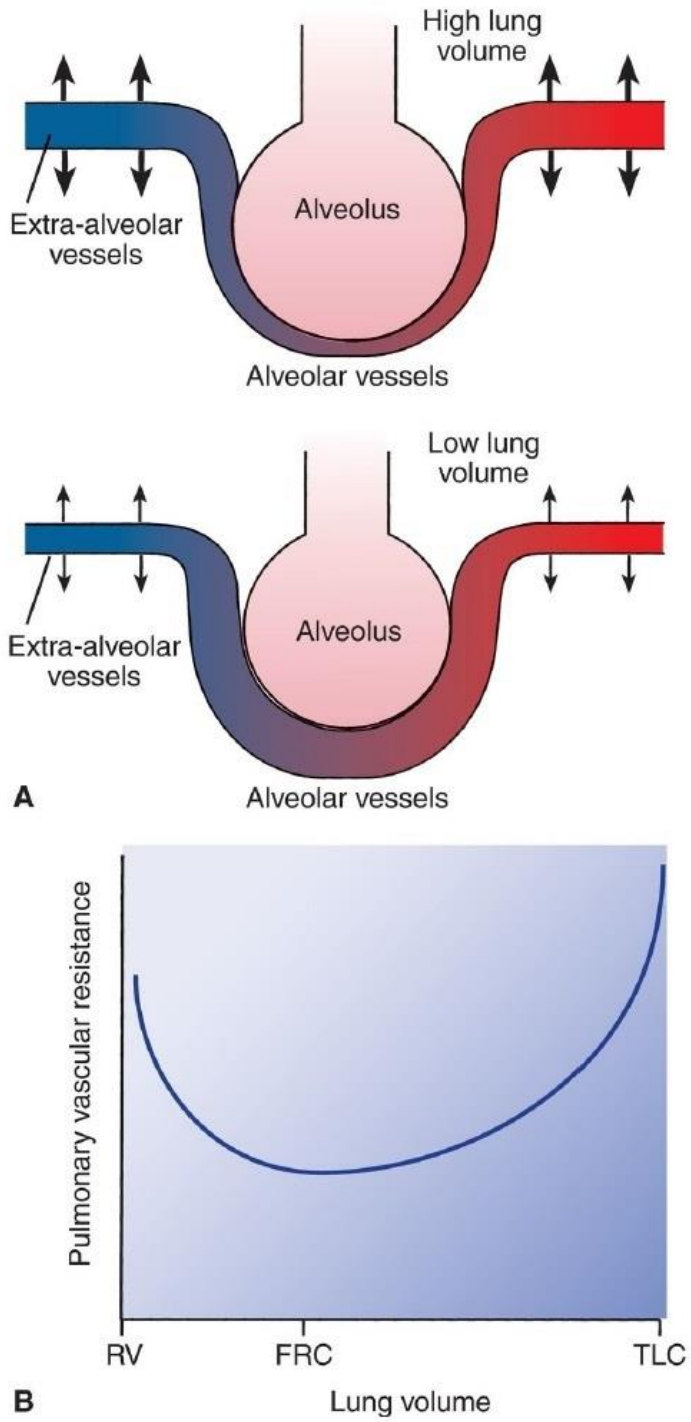


Capillary recruitment and capillary distention decrease pulmonary vascular resistance. In the normal condition, not all capillaries are perfused. Capillary recruitment (the opening up of previously closed vessels) results in the perfusion of an increased number of vessels with a concomitant decrease in resistance. Capillary distention (an increase in the caliber of vessels) resulting from high vessel compliance also results in a lower resistance and higher blood flow.

Pulmonary vascular resistance (cont.):

The resistance of extra-alveolar vessels (pulmonary arteries and veins)

- The pulmonary vascular resistance can be affected if extravascular vessels dilate or constrict in response to changes in pleural pressure.
- The pulmonary vascular resistance increases at high and low lung volumes. It is lowest at functional residual capacity (FRC).
- The vasoconstrictors of the extra-alveolar vessels are; hypoxia, serotonin, NE, histamine, thromboxane A_2, and leukotrienes.
- The vasodilators of the extra-alveolar vessels are; NO, Calcium channel blockers, adenosine, Ach, prostacyclin (PG I_2), and isoproterenol.
- Although the pulmonary circulation is richly supplied with sympathetic nerve terminals, however, pulmonary vascular resistance is unaffected by autonomic nerves under normal conditions.



Changes in lung volumes affect pulmonary vascular resistance

(A) At high lung volumes, extra-alveolar vessels are actually distended because of the lower pleural pressure. However, alveolar vessels are compressed, causing a rise in pulmonary vascular resistance. At low lung volumes, alveolar vessels are distended, but the extra-alveolar vessels are compressed from the rise in pleural pressure, which results in a rise in pulmonary vascular resistance.

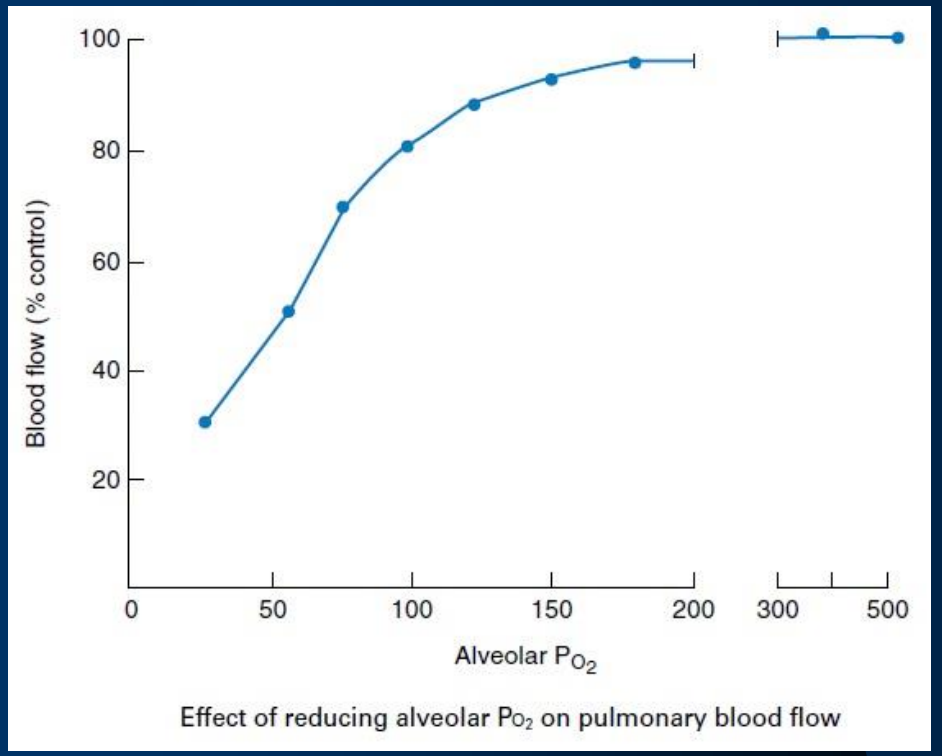
(B) Total pulmonary vascular resistance as a function of lung volumes follows a U-shaped curve, with resistance lowest at functional residual capacity (FRC). RV, residual volume; TLC, total lung capacity.

Effect of alveolar hypoxia and hypoxemia:

Note: Alveolar hypoxia induces hypoxic pulmonary vasoconstriction. The precise mechanism of this response is not known. The PO_2 of the alveolar gas, not the pulmonary arterial blood, chiefly determines the response.

An increase in cytoplasmic calcium ion concentration is the major trigger for smooth muscle contraction and occurs as a result of a variety of factors.

Vascular tone is regulated by endothelial nitric oxide (NO) which increases the synthesis of cyclic GMP that subsequently inhibits calcium channels and promotes vasodilation.



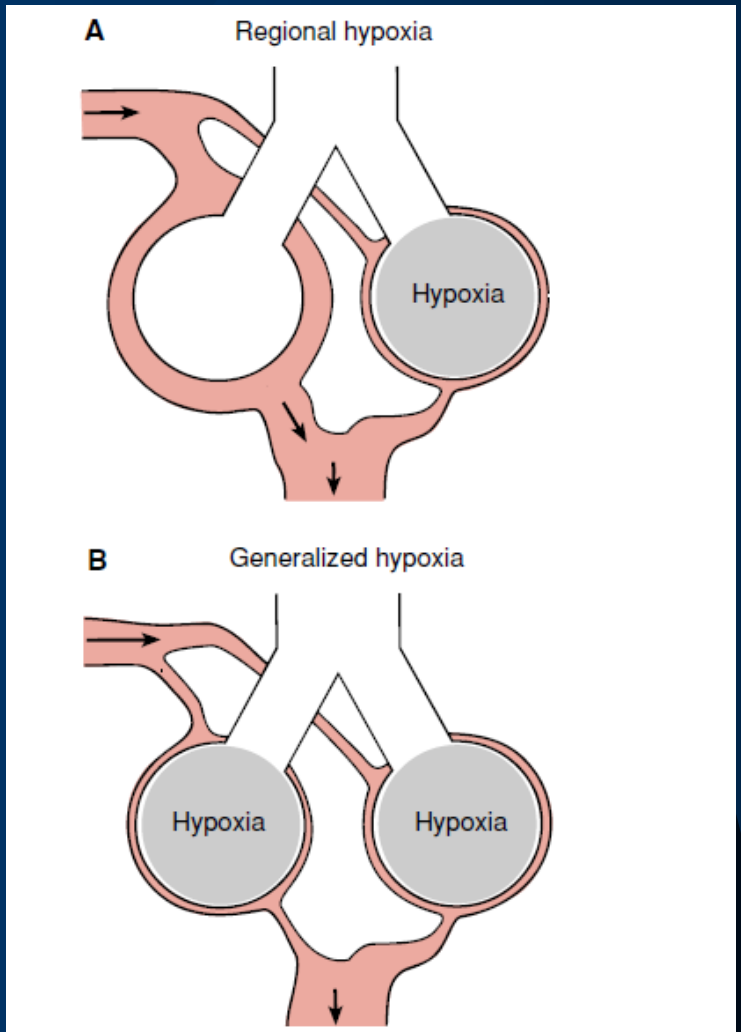
Effect of reducing alveolar P_{O_2} on pulmonary blood flow

Effect of alveolar hypoxia and hypoxemia:

1. Regional hypoxia (e.g. bronchial obstruction) → divert blood away from a poorly ventilated region

2. Generalized hypoxia (e.g. in high altitude or chronic hypoxia as in asthma) → vasoconstriction in both lungs → increased pulmonary artery pressure (pulmonary hypertension) → Rt. Ventricular hypertrophy

Note: generalized hypoxia plays an important non-pathophysiological role before birth



Effect of alveolar hypoxia on pulmonary arteries.

Note:

Any rise in left atrial pressure above 7 mmHg; such as in left heart failure, mitral stenosis, or mitral regurgitation causes blood to dam up in the pulmonary circulation. Above 30 mmHg → pulmonary edema.

Blood flow through the lungs:

Pulmonary blood flow equals the cardiac output. It is affected by ***two*** factors;

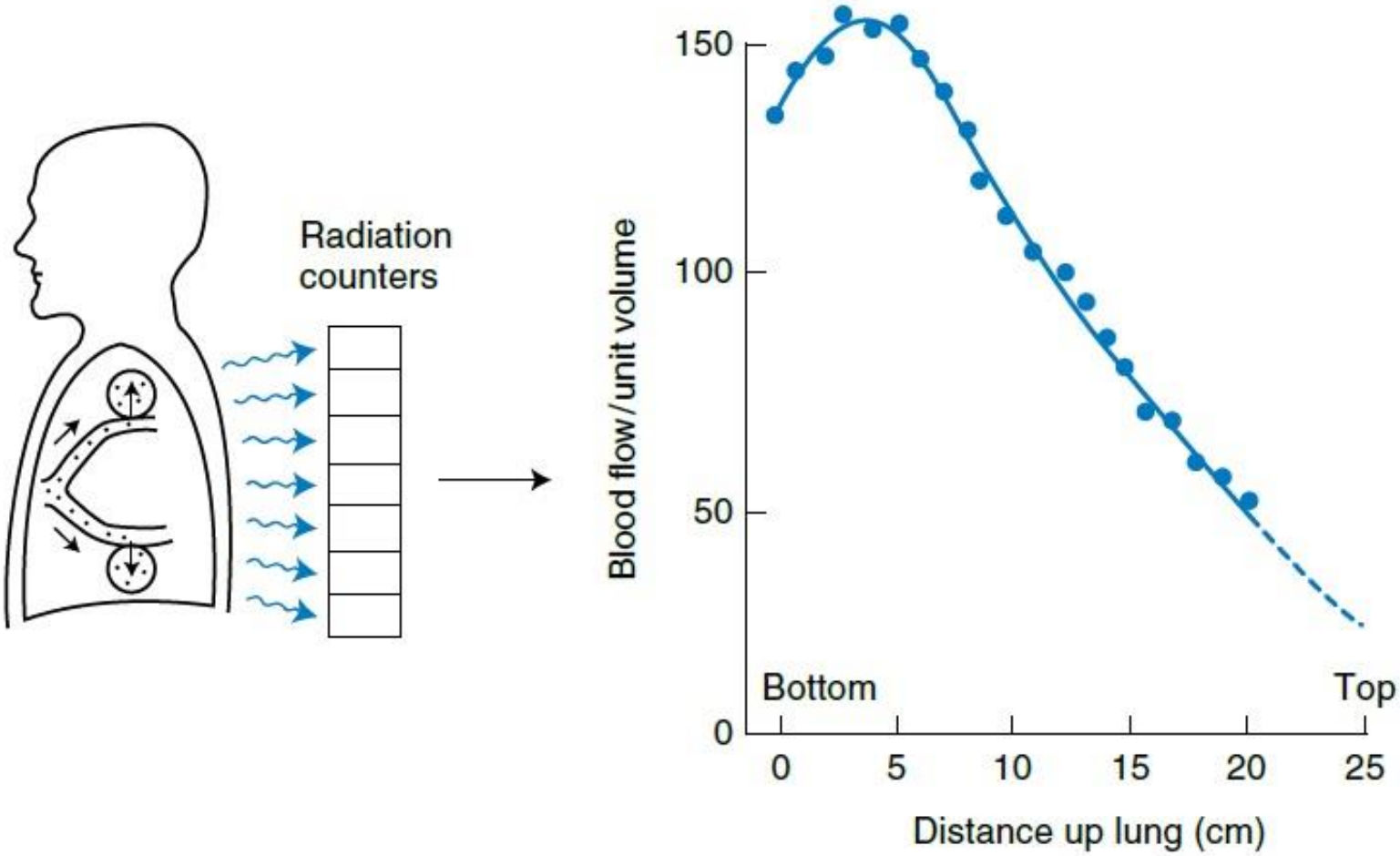
1. Alveolar oxygenation
2. Hydrostatic pressure gradients

* Alveolar oxygenation:

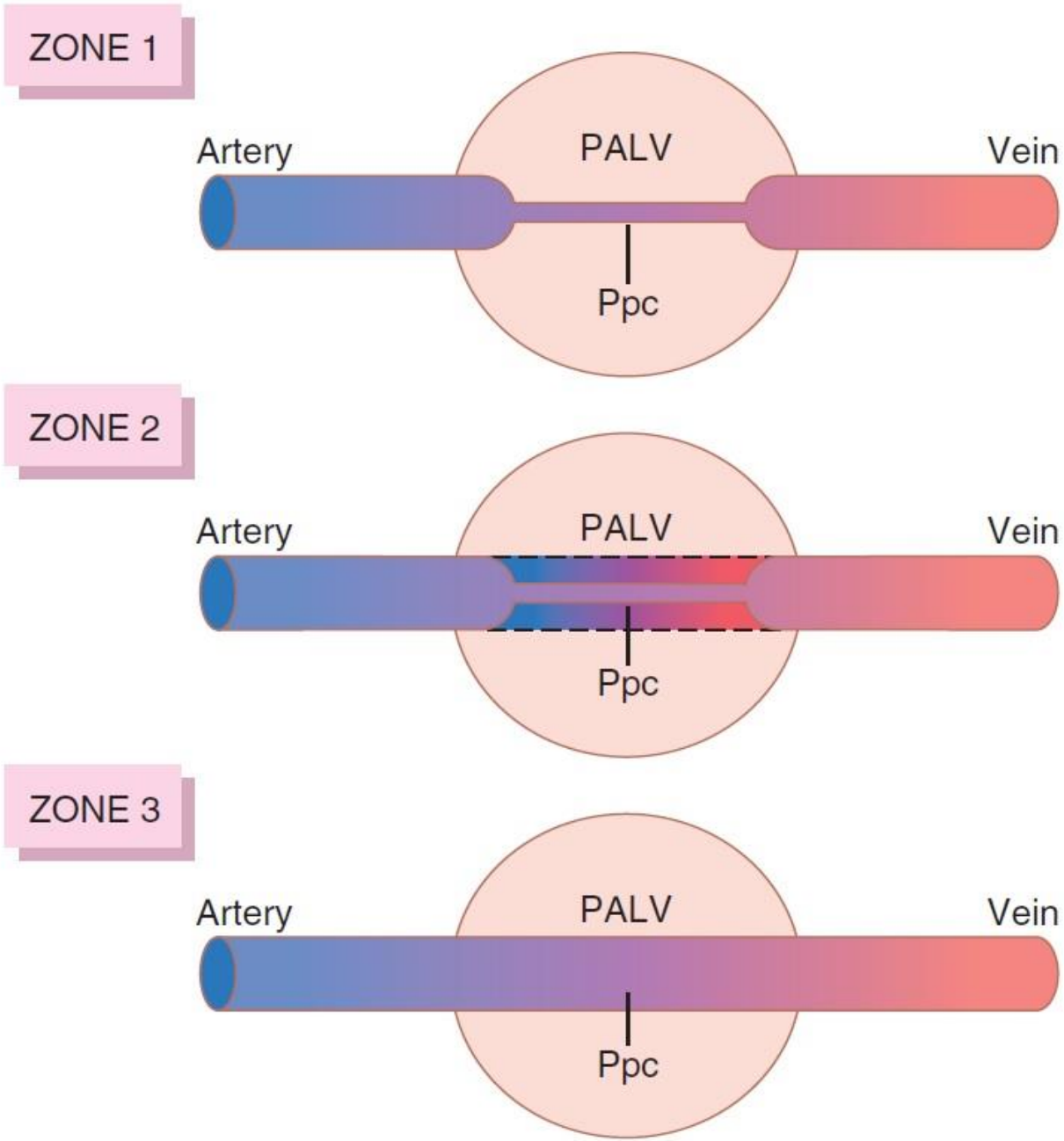
  ↓ **Oxygenation** (PO_2 less than 73 mmHg) → **Vasoconstriction** (reduced nitric oxide, reason ??) → **Automatic redistribution** of blood flow to well oxygenated areas.

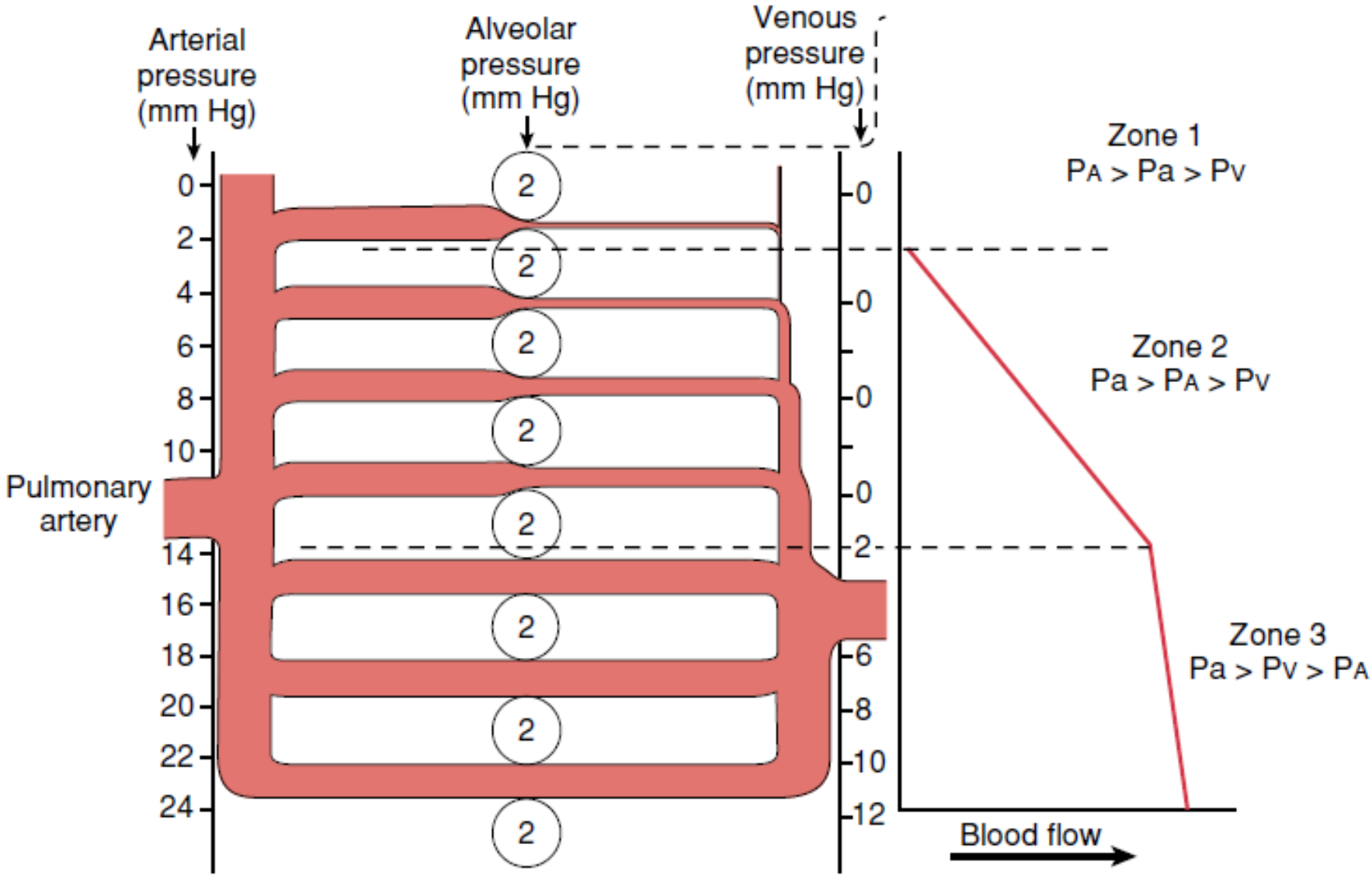
* Hydrostatic pressure gradients:

- In upright adult, pressure at the highest point of the lungs is 15 mmHg less than the pressure at the level of the heart.
- In upright adult, pressure at the lowest portion of the lungs is 8 mmHg greater than the pressure at the level of the heart.
- In upright adult, the flow in the lower portion of the lungs is 5 times that in the top of the lung.
- Theoretically it is possible to have 3 types of blood flow zones in the lung;
  - Zone 1 = No blood flow during any part of the cardiac cycle ($P_a < P_A$)
  - Zone 2 = Intermittent blood flow ($P_a > P_A > P_V$)
  - Zone 3 = Continuous blood flow ($P_a > P_V > P_A$)



Measurement of the distribution of blood flow in the upright human lung, using radioactive xenon. The dissolved xenon is evolved into alveolar gas from the pulmonary capillaries. The units of blood flow are such that if flow were uniform, all values would be 100. Note the small flow at the apex.


ZONE 1
Artery
PALV
Vein
Ppc
ZONE 2
Artery
PALV
Vein
Ppc
ZONE 3
Artery
PALV
Vein
Ppc



Zones of the lungs and the uneven distribution of pulmonary blood flow.

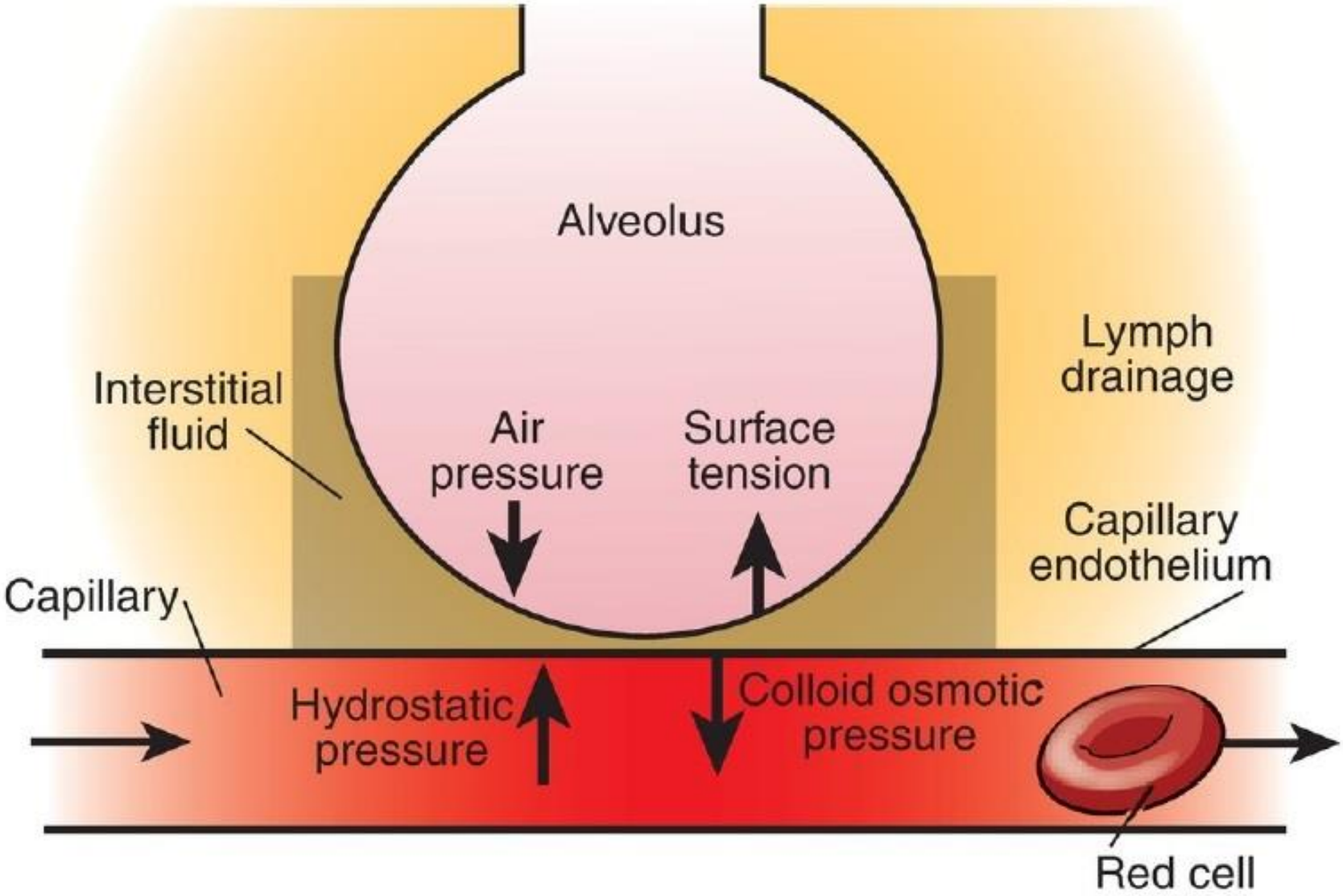
* Hydrostatic pressure gradients:

- Normally the lungs have only zone 2 (in the apices) and zone 3 (in all the lower areas).
- Zone 2 blood flow begins in the normal lungs about 10 cm above the level of the heart and extends to the top of the lungs. Venous pressure in this zone has no effect on flow.
- In lying position and during heavy exercise, the entire lung is converted into zone 3 blood flow.
- Physiologically, zone 1 blood flow occurs only when an upright person is breathing against a positive air pressure. Pathologically, zone 1 blood flow can occur when pulmonary pressure is low as in **hypovolemic shock**, or when occlusion of pulmonary vessels takes place (e.g. **pulmonary embolism**). Alveolar dead space is increased in the lung in such conditions.

Dynamics of capillary fluid exchange:

The quantitative differences between systemic and pulmonary capillary dynamics are;

1. The pulmonary capillary hydrostatic pressure is low → less chance of capillary filtration
2. The interstitial fluid hydrostatic pressure in the lung is more negative (-8 mmHg) than that in the peripheral subcutaneous tissue (-5 mmHg) → absorb fluid from the alveoli.
3. The pulmonary capillaries are relatively **leaky to protein** molecules → greater extravascular colloid osmotic pressure.
4. Fluid can pass easily from interstitium into alveoli if interstitial pressure turns positive.
5. In the pulmonary circulation, two additional forces play a role in fluid transfer-surface tension (pulls inwardly) and alveolar pressure (tends to raise interstitial pr.).



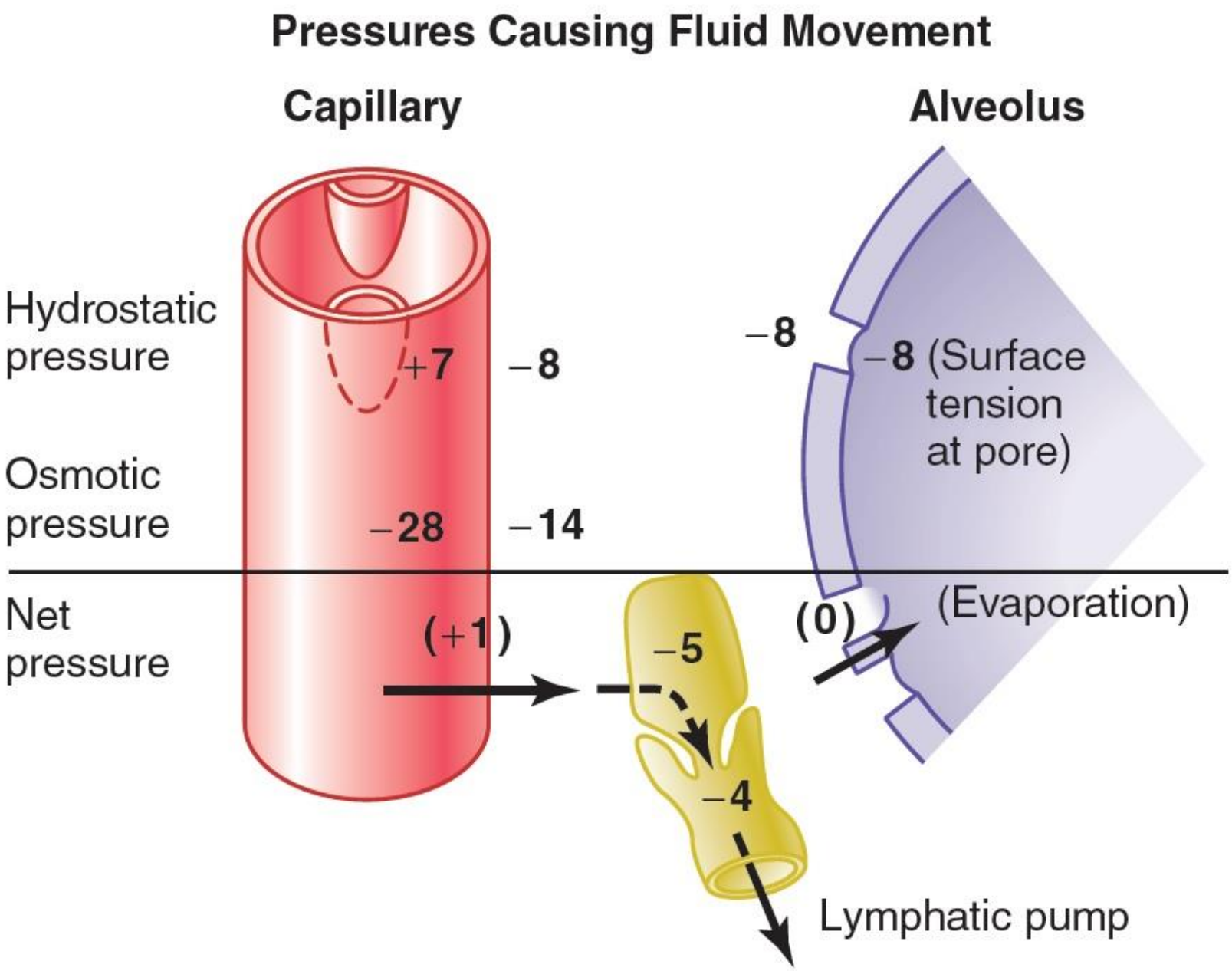
Alveolar surface tension and alveolar pressure affect fluid exchange in pulmonary capillaries

Interrelations between interstitial fluid pressure and other pressures in the lung:

1. Relationship between pulmonary interstitium and pulmonary capillaries;
   - Factors responsible for capillary filtration (to pulmonary interstitium).
     - Capillary hydrostatic pressure 7 mmHg
     - Interstitial colloid osmotic pr. 14 mmHg
     - Interstitial hydrostatic pressure 8 mmHg

     29 mmHg (Total)
   - Factors responsible for capillary absorption.
     - Plasma colloid osmotic pressure 28 mmHg

     28 mmHg (Total)
   - Thus the mean filtration pressure is +1 mmHg → slight continuous filtration that will be taken by pulmonary lymphatic system.


Pressures Causing Fluid Movement
Capillary
Alveolus
Hydrostatic pressure
Osmotic pressure
Net pressure
+7
−8
−28
−14
(+1)
−5
−4
−8
−8 (Surface tension at pore)
(0)
(Evaporation)
Lymphatic pump

Interrelations between interstitial fluid pressure and other pressures in the lung:

2. Relationship between pulmonary interstitium and alveoli;

- The negative hydrostatic pressure in the pulmonary interstitium → suction of any fluid in the alveoli (keeps alveoli almost **dry**).
- The sucked fluid is carried away through pulmonary lymphatic system (to the hilar lymph nodes), or the pulmonary capillaries.
- The lungs have a more extensive lymphatic system than most organs. The lymphatic vessels are not found in the alveolar-capillary area but are strategically located near the terminal bronchioles to drain off excess fluid.

Pathophysiology of pulmonary edema:

Pulmonary edema occurs when pulmonary interstitial pressure turns positive. This can be due to;

1. Cardiogenic pulmonary edema (more common)

   Left sided heart failure or mitral valvular disease → ↑ left atrial pressure → ↑ pulmonary hydrostatic pressure.

2. Noncardiogenic pulmonary edema

   Damage of pulmonary capillaries (such as by pneumonia or breathing noxious substances), increased surface tension as in acute respiratory distress syndrome (ARDS), or living at high elevations (part of mountain sickness or high-altitude pulmonary edema) especially when exercising in the first few days.

   Damage of capillaries → leak of plasma proteins into interstitium and alveoli → ↑ extravascular colloid osmotic pressure.

Note:

The main defensive mechanism against the development of pulmonary edema is the activity of pulmonary lymphatic system.

Pulmonary lymphatics proliferate in cases of chronic rise in left atrial pressure, and thus increasing their capability of carrying fluid away from the interstitial spaces perhaps as much as 10-fold.

Test Question 1

Concerning the extra-alveolar vessels of the lung:

A. Tension in the surrounding alveolar walls tends to narrow them.

B. Their walls contain smooth muscle and elastic tissue.

C. They are exposed to alveolar pressure.

D. Their constriction in response to alveolar hypoxia mainly takes place in the veins.

E. Their caliber is reduced by lung inflation.

Test Question 2

Which is a feature of high altitude pulmonary edema?

A. Associated with low cardiac output.
B. Associated with pulmonary hypertension.
C. Occurs only in unacclimatized persons.
D. Exercise has no effect.
E. Associated with increased left atrial pressure.