BASIC CONCEPTS IN LUNG DISEASE

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QUESTIONS

- Why do we need a respiratory system?
- What does it consist of?
- How is it controlled/regulated?
- How is it affected by disease?
- How is disease recognized?
- How can disease be prevented or treated?
- Why do you have to know all of this?

CONTENTS

- Function of the respiratory system
- Embryology
- Anatomic concepts
- Physiologic concepts
- Pathology
- Clinical : symptoms
  physical signs
  disease patterns

FUNCTIONS OF THE LUNG

Respiration: ventilation and gas exchange: O_2, CO_2, pH, warming and humidifying

Non-respiratory functions:

- synthesis, activation and inactivation of vasoactive substances, hormones, neuropeptides, eicosanoids, lipoprotein complexes.
- Hemostatic functions (thromboplastin, heparin)
- Lung defense: complement activation, leucocyte recruitment, cytokines and growth factors
- Speech, vomiting, defecation, childbirth

EMBRYOLOGY

- Embryology : lung development starts from the gut 24 days after conception; diaphragm forms in cervical region at 3-4 weeks and moves progressively downwards carrying the phrenic nerves with; lung lobes are identifiable at 12 weeks; bronchial tree is completed at 16 weeks and alveoli and capillaries appear at 24 – 28 weeks; surfactant appears at 35 weeks.
- Postnatal Alveolarization: intense first 8-10 y (alveolar buds – hyperplastic growth) and enlargement of all structures throughout adolescence and early adulthood (hypertrophic growth)

EMBRYOLOGY AND DISEASE

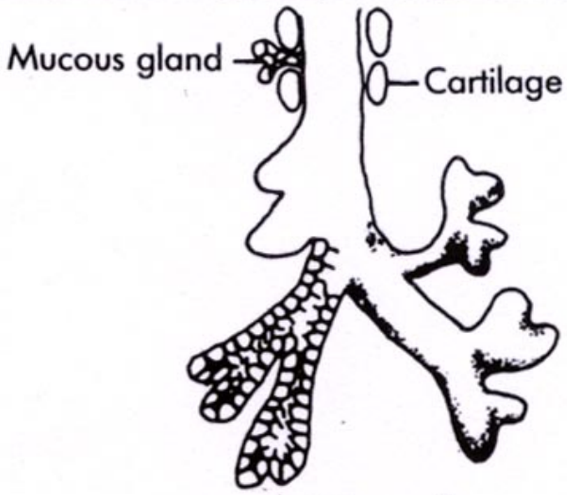
- Developmental abnormalities: tracheo-oesophageal fistula, cleft palate, cysts, agenesis, sequestration, cilia dysfunction and abnormal structure, diaphragmatic hernias.
- Shared nerve supply (Vagus) between respiratory tract and GI tract – Gastro-oesophageal reflux can increase bronchial secretions (reflexively) and cause bronchial constriction (together with oesophageal spasm).
- Diaphragmatic irritation is often experienced as pain in the cervical region (referred pain) from where it evolved.

24 days

Lung bud protrudes from gut

26-28 days

First division branching



1-3 months

Dichotomous branching continues, lung is glandular; ciliated columnar epithelium lines airway.

5 months

Canalized airways lined by cuboidal epithelium. Capillaries arise from vascular structures in mesenchyme.

6½-7 months

Alveoli appear from alveolar ducts; epithelium attenuates; capillaries proliferate around terminal airspaces.

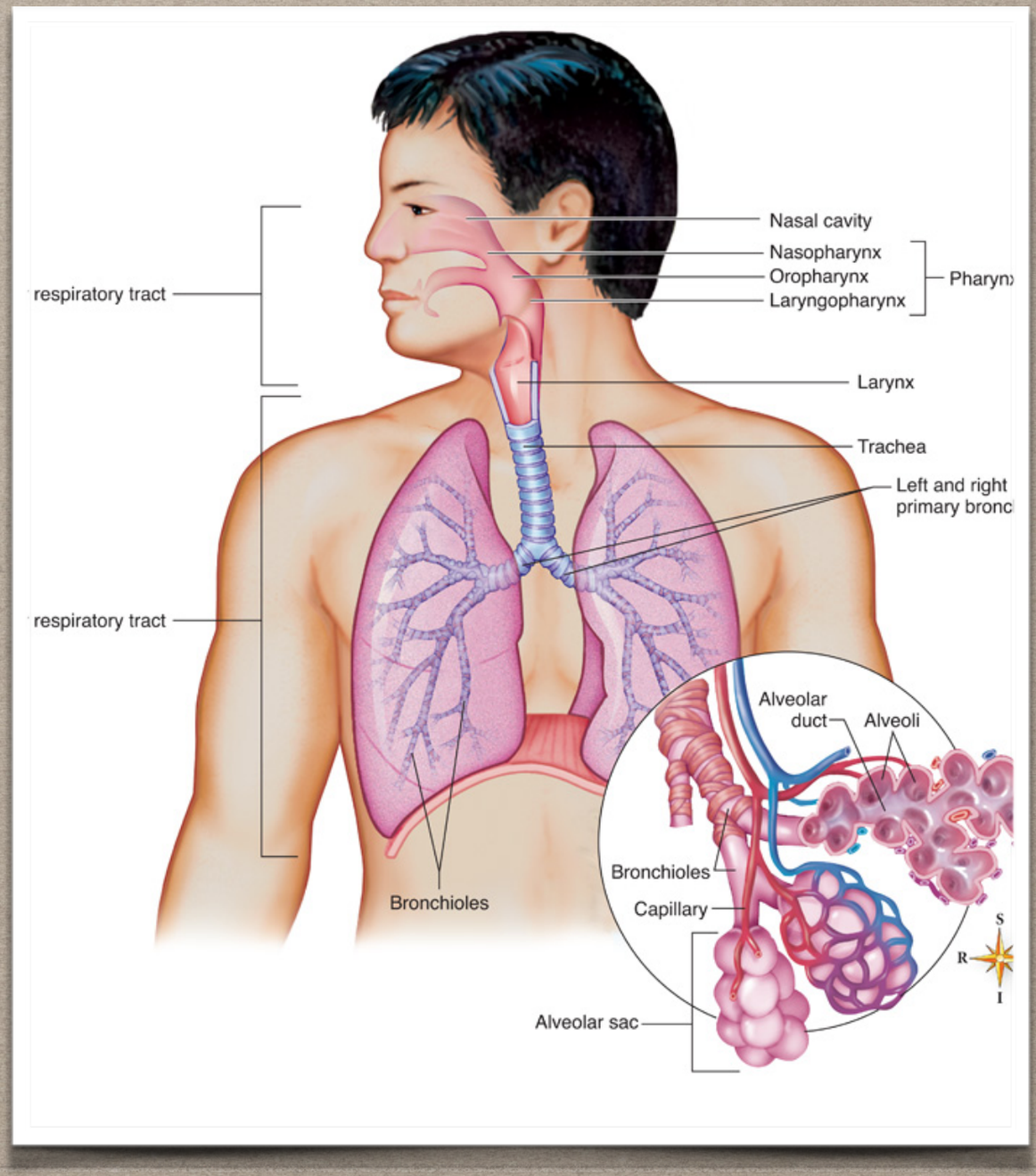
Diagram of the major prenatal stages of lung development. (Redrawn from WB Saunders Co.)

ANATOMY

- Surface Anatomy: borders of the pleura
  borders of the lung
  fissures
  lung lobes
- Bronchial tree, vascular and nerve supply, lymphatics.
- Angle of Louis
- Histology, cilia, secretory and immunologic cells.
- Thoracic cage
- Diaphragm and accessory muscles of breathing

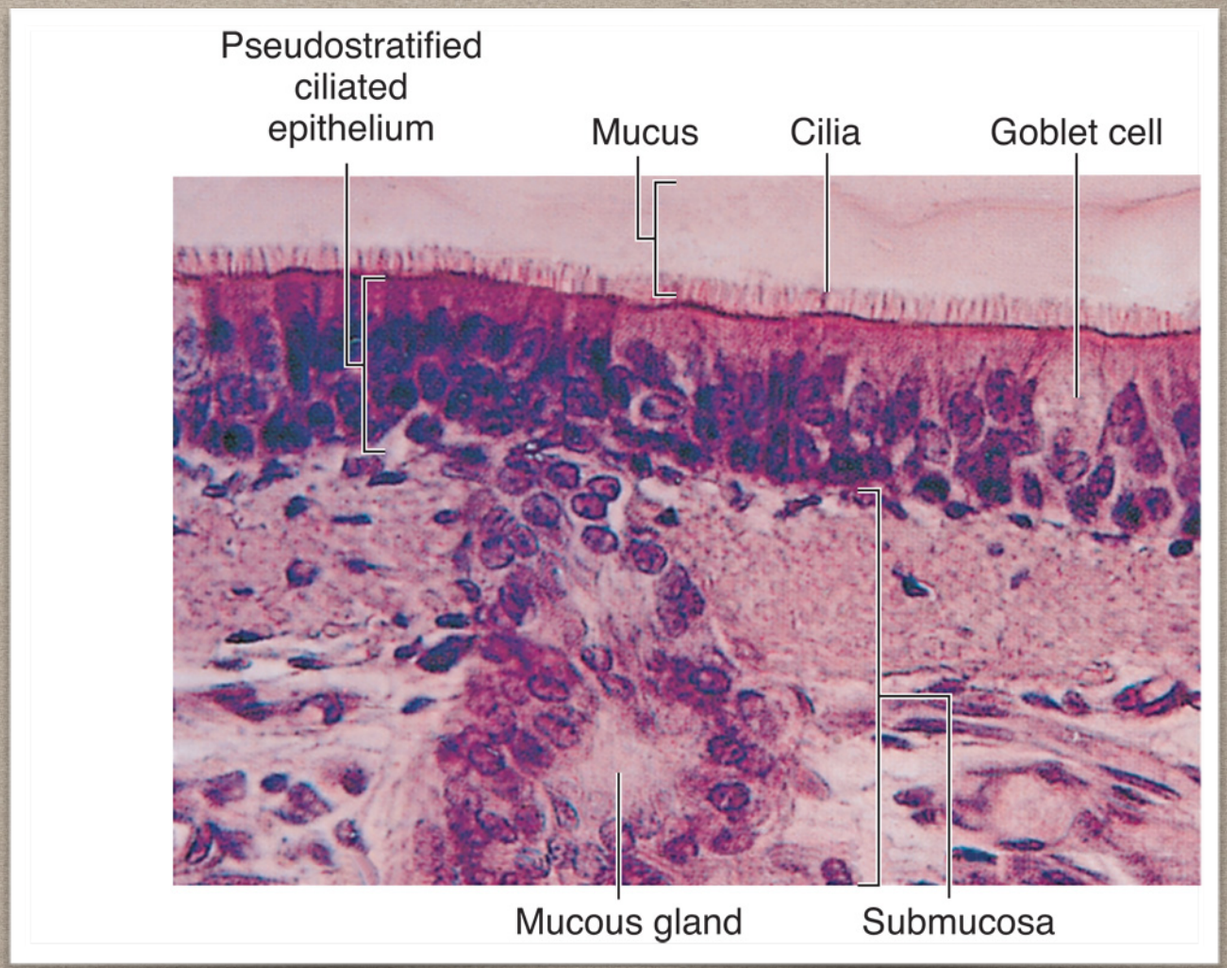
ANATOMY

- Upper respiratory tract–nose, pharynx, and larynx
- Lower respiratory tract–trachea, bronchial tree, and lungs

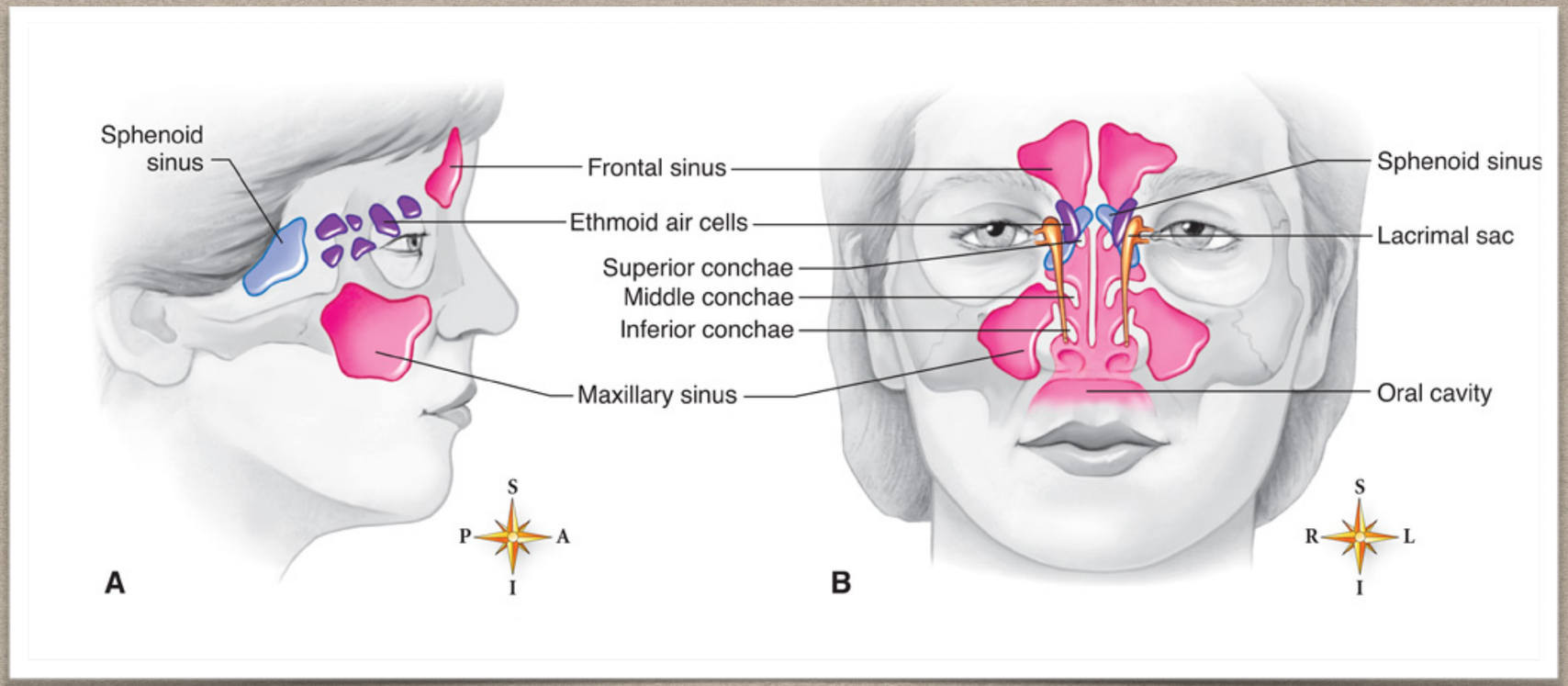


MUCOUS

- Mucous membrane that lines the air distribution tubes in the respiratory tree
- More than 125 mL of mucus produced each day forms a “mucus blanket” over much of the respiratory mucosa
- Mucus serves as an air purification mechanism by trapping inspired irritants such as dust, pollen
- Cilia on mucosal cells beat in only one direction, moving mucus upward to pharynx for removal



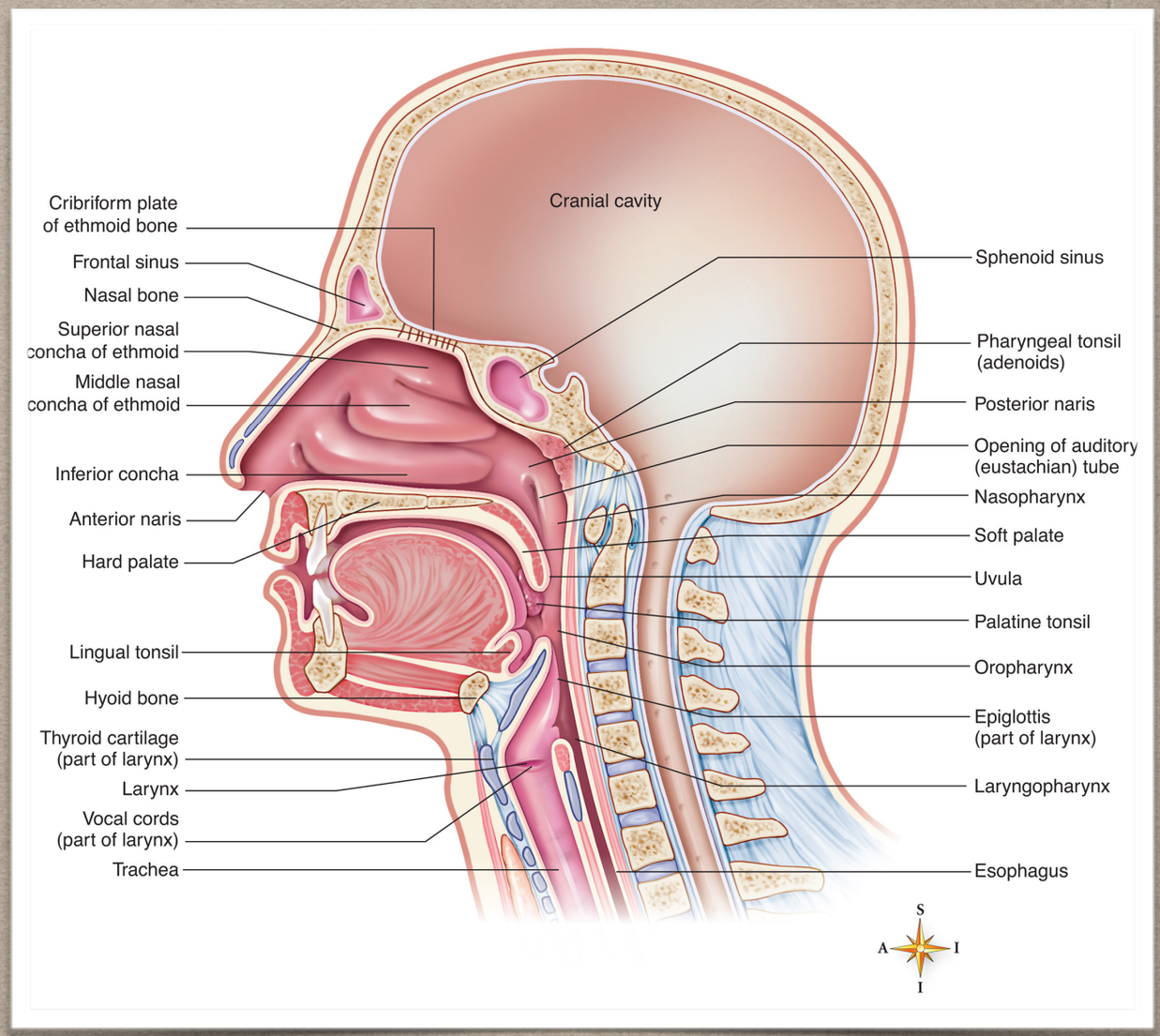
NOSE



- Structure
  - Nasal septum separates interior of nose into two cavities
  - Mucous membrane lines nose
  - Nasal polyp–noncancerous growths that project from nasal mucosa (associated with chronic hay fever)
  - Frontal, maxillary, sphenoidal, and ethmoidal sinuses drain into nose
- Functions
  - Warms and moistens inhaled air
  - Contains sense organs of smell

PHARYNX

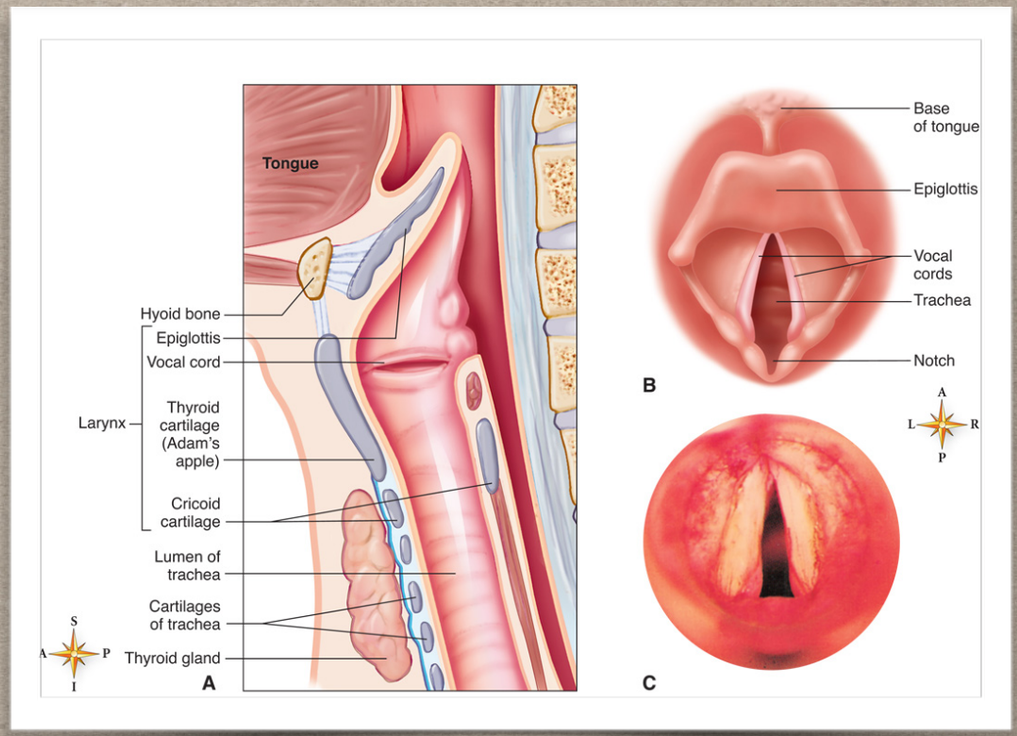
- Structure
  - Pharynx (throat) about 12.5 cm (5 inches) long
  - Divided into nasopharynx, oropharynx, and laryngopharynx
  - Two nasal cavities, mouth, esophagus, larynx, and auditory tubes all have openings into pharynx
- Structure
  - Pharyngeal tonsils and openings of auditory tubes open into nasopharynx; other tonsils found in oropharynx
  - Mucous membrane lines pharynx
- Functions
  - Passageway for food and liquids
  - Air distribution; passageway for air
  - Tonsils—masses of lymphoid tissue embedded in pharynx provide immune protection

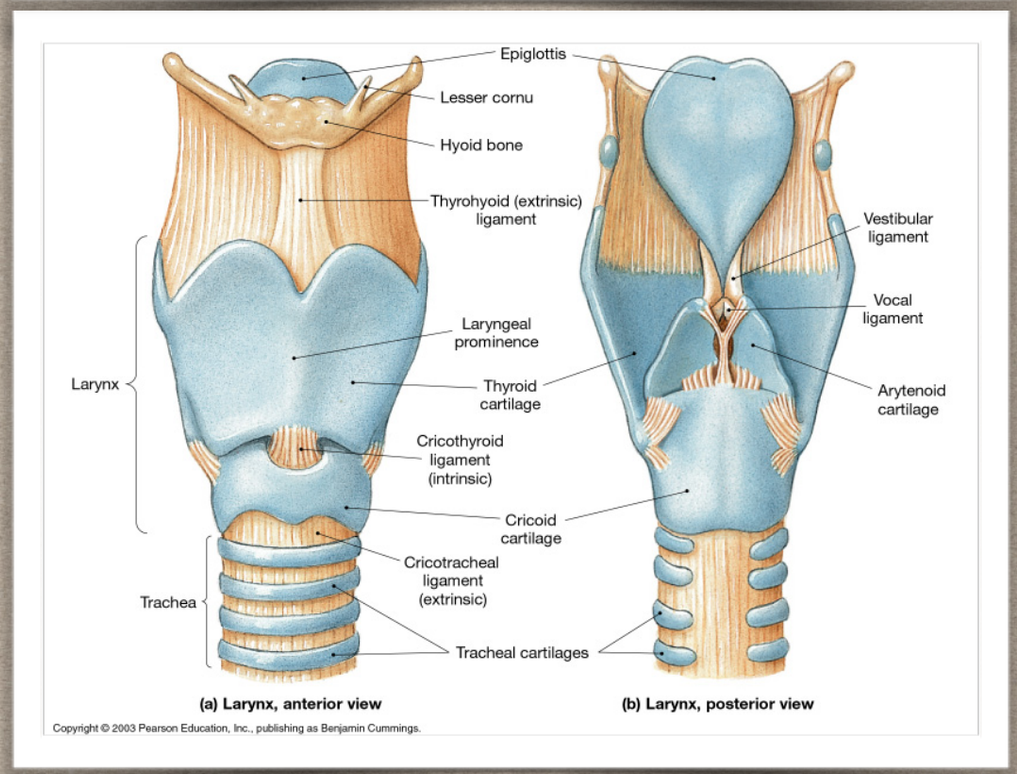


LARYNX

- Structure
  - Located just below pharynx; also referred to as the voice box
  - Several pieces of cartilage form framework
    - Thyroid cartilage (Adam's apple) is largest
    - Epiglottis partially covers opening into larynx
  - Mucous lining
  - Vocal cords stretch across interior of larynx; space between cords is the glottis

  - Functions
  - Air distribution; passageway for air to move to and from lungs
  - Voice production

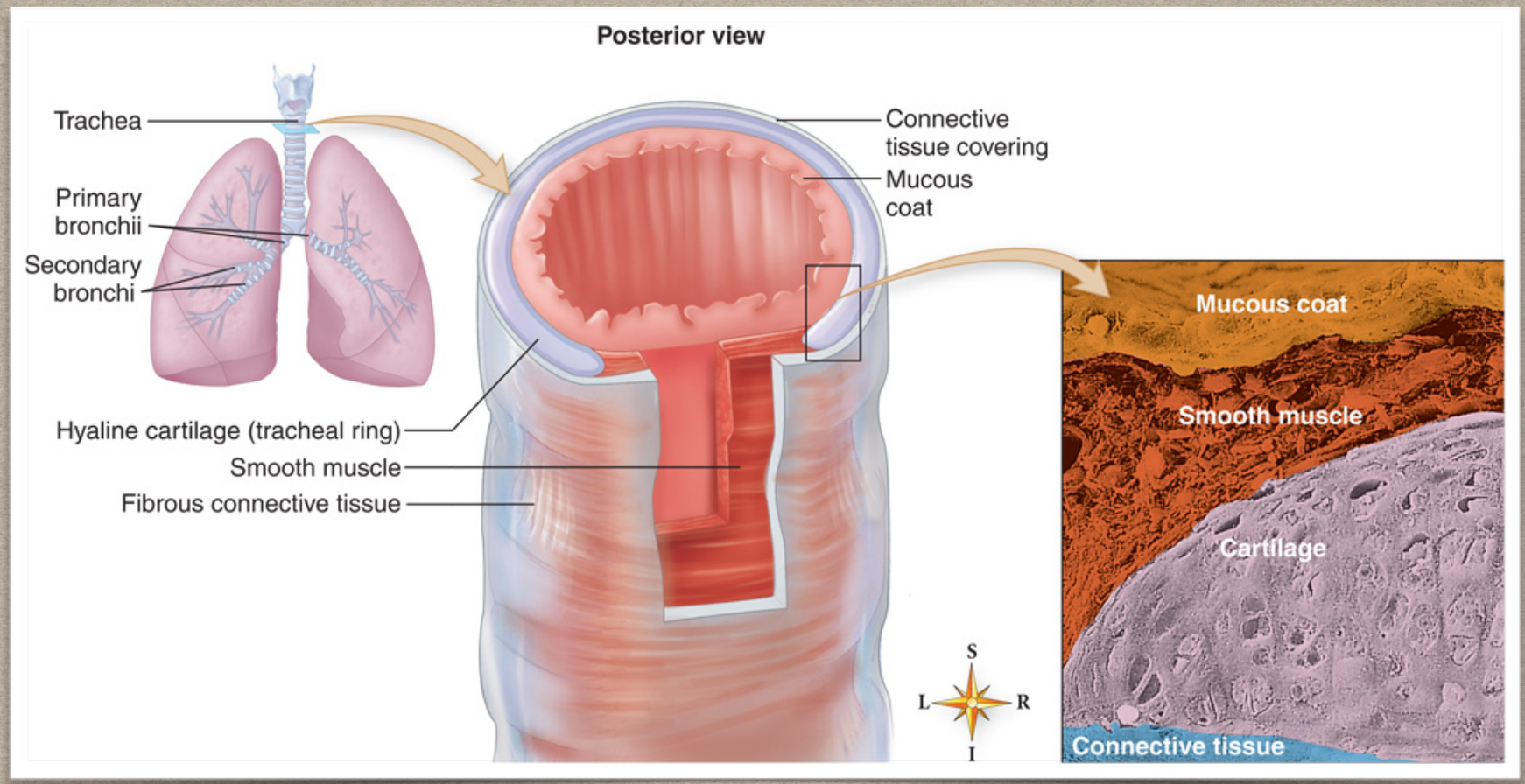




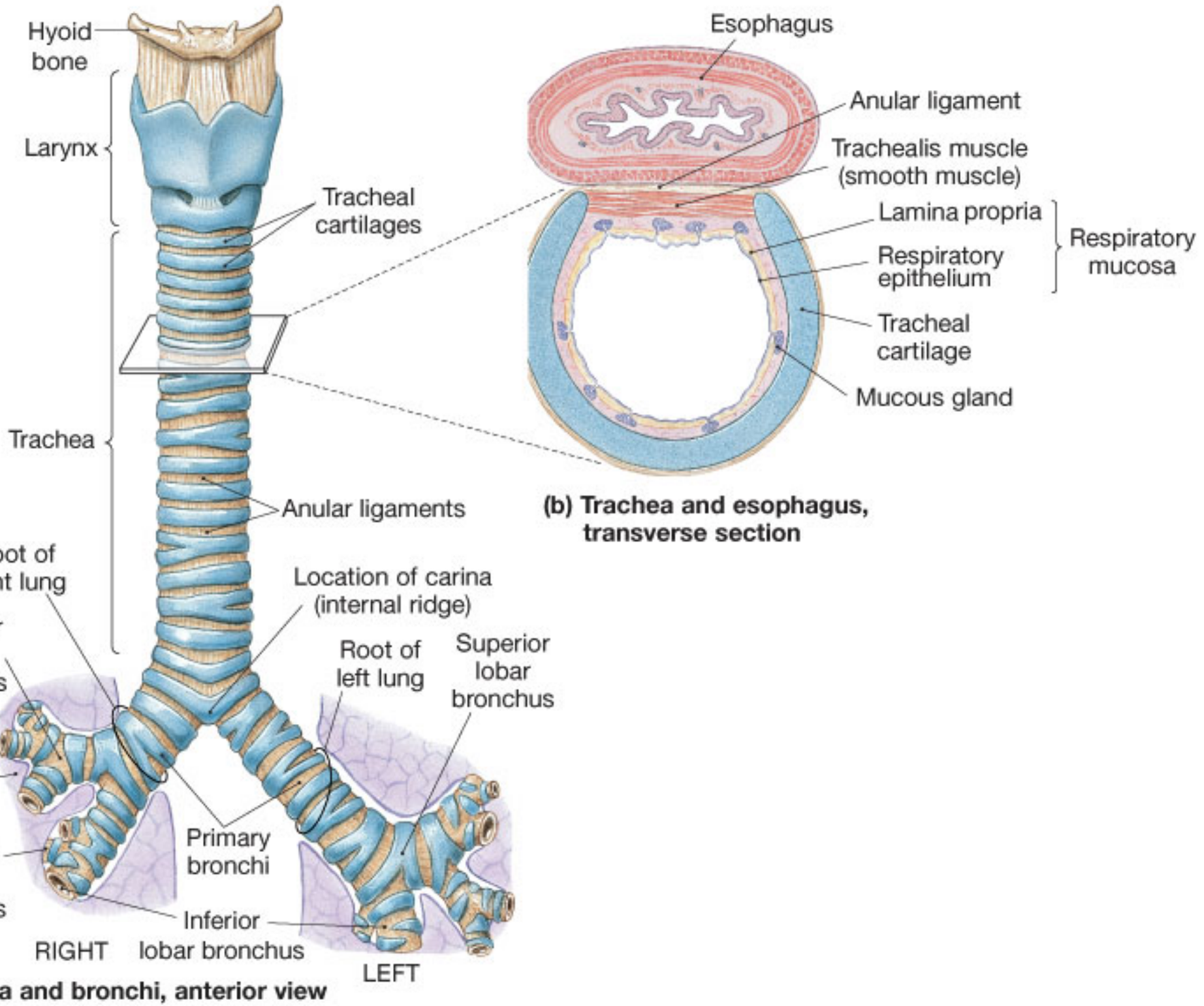
DISORDERS OF THE UPPER RESPIRATORY TRACT

- Upper respiratory infection (URI)
  - Rhinitis—nasal inflammation, as in a cold, influenza, or allergy
    - Infectious rhinitis—common cold
    - Allergic rhinitis—hay fever
  - Pharyngitis (sore throat)—inflammation or infection of the pharynxUpper respiratory infection
  - Laryngitis—inflammation of the larynx resulting from infection or irritation
    - Epiglottis—life threatening
    - Croup—not life threatening

TRACHEA



- Structure
  - Tube (windpipe) about 11 cm (4½ inches) long that extends from larynx into the thoracic cavity
  - Mucous lining
  - C-shaped rings of cartilage hold trachea open
- Function—passageway for air to move to and from lungs

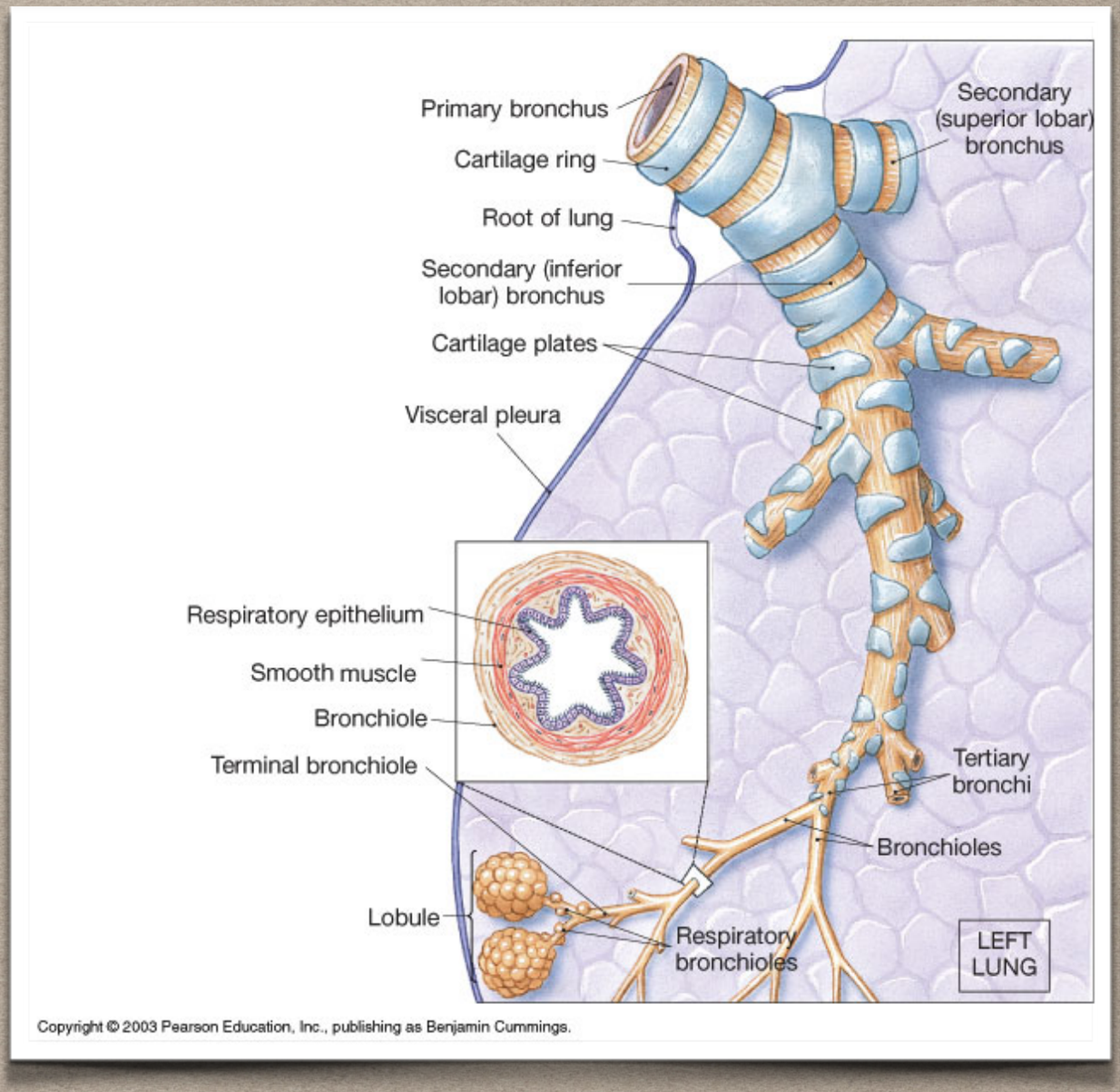


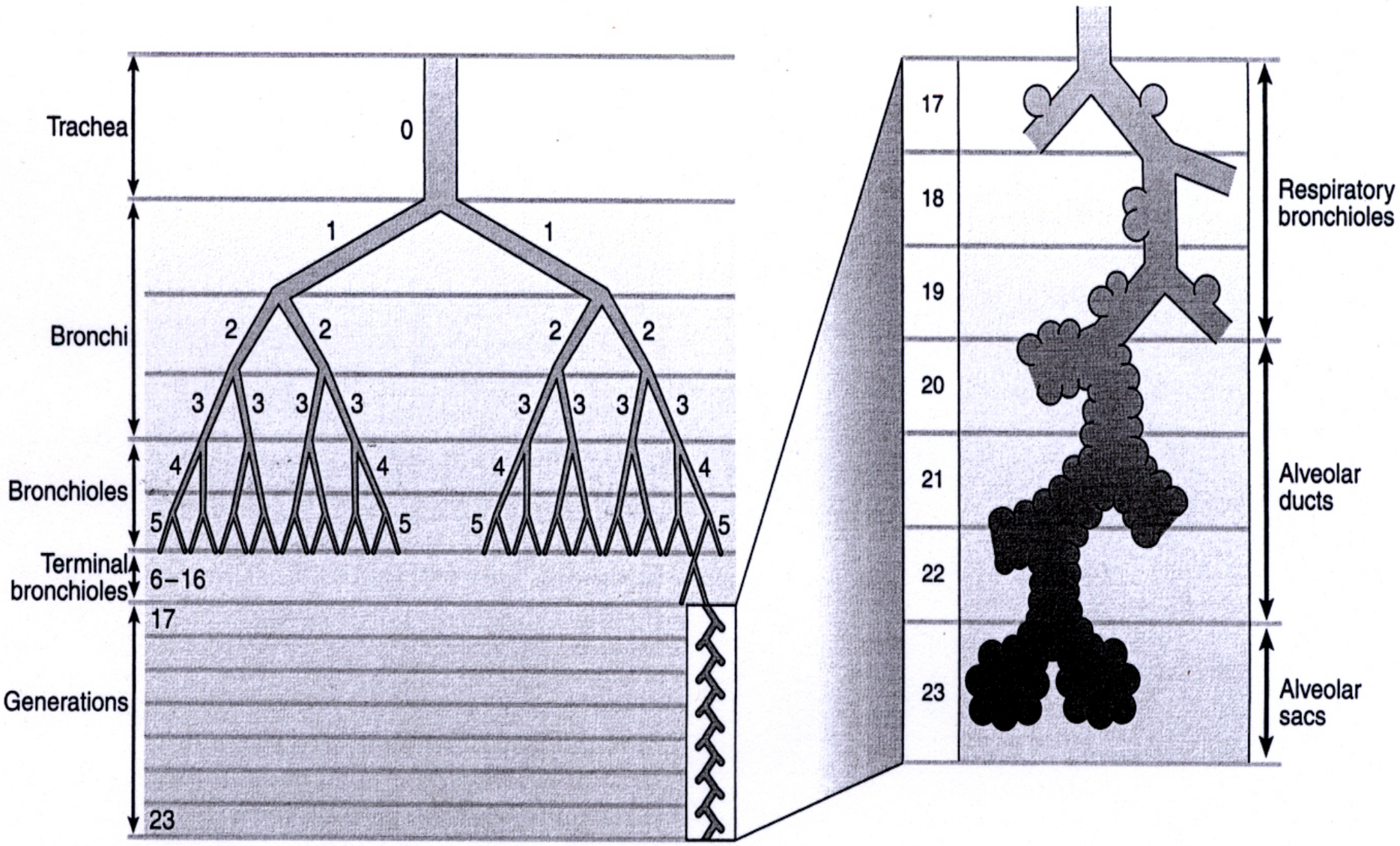
(a) Trachea and bronchi, anterior view

(b) Trachea and esophagus, transverse section

BRONCHI, BRONCHIOLES, AND ALVEOLI

- Structure
  - Trachea branches into right and left bronchi
    - Right primary bronchus more vertical than left
    - Aspirated objects most often lodge in right primary bronchus or right lung
  - Each bronchus branches into smaller and smaller tubes (secondary bronchi), eventually leading to bronchioles
  - Bronchioles end in clusters of microscopic alveolar sacs, whose walls are made of alveoli
- Function
  - Bronchi and bronchioles—air distribution; passageway for air to move to and from alveoli
  - Alveoli—exchange of gases between air and blood

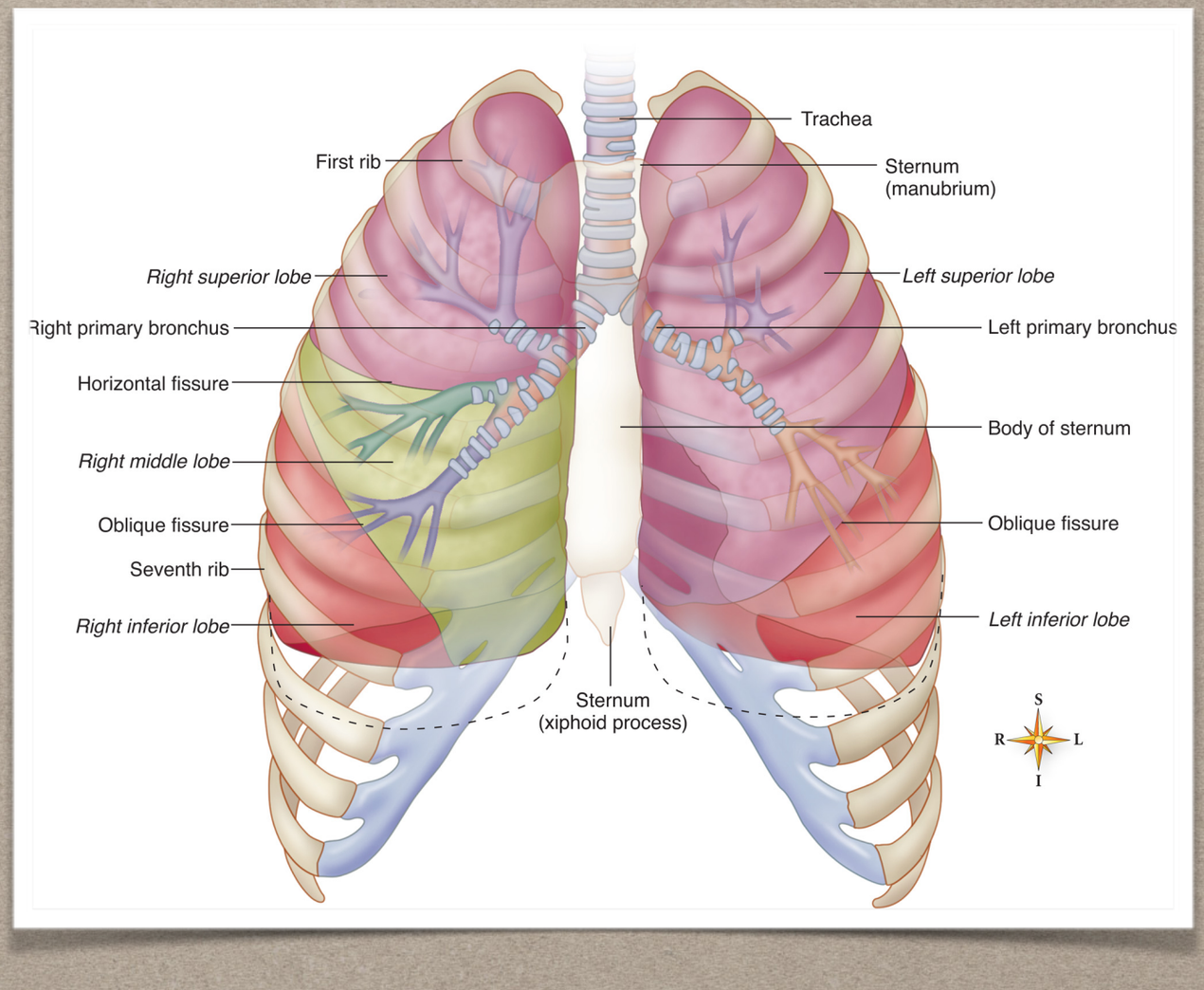




The naming of airways. There is of course a gradual change in structure from one type of airway to another. One particular type of airway can occur at different distances into the lungs. (After Weibel, 1963.)

LUNGS AND PLEURA

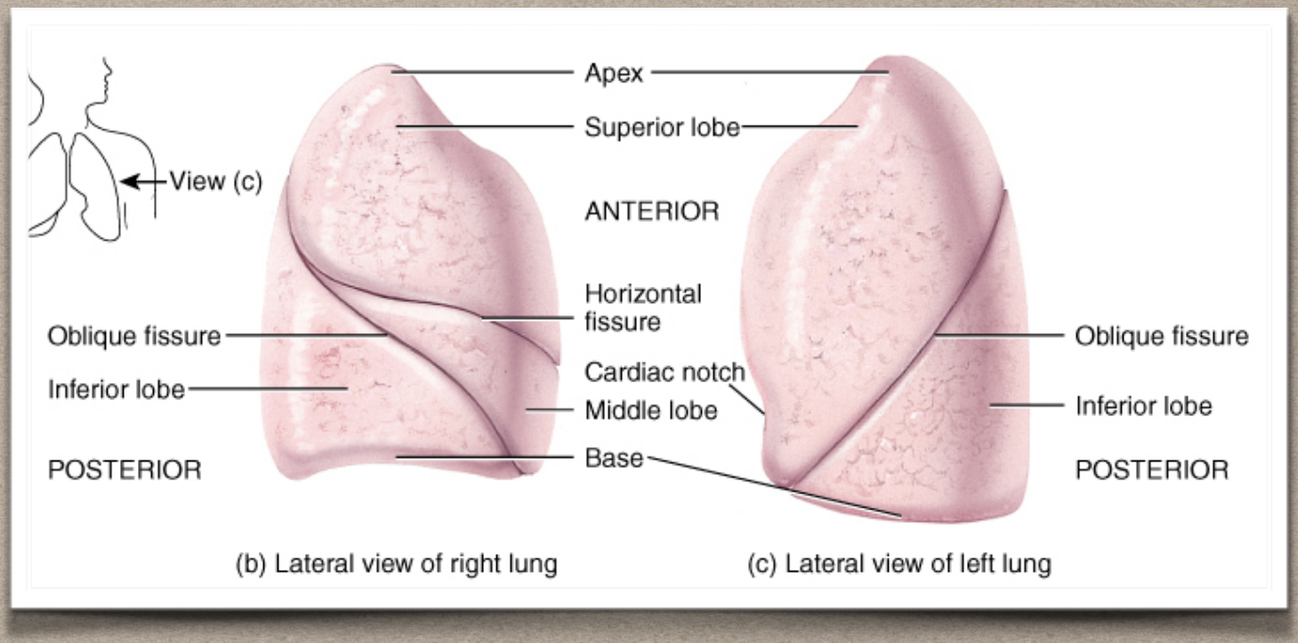
- Structure
  - Size—large enough to fill the chest cavity, except for middle space occupied by heart and large blood vessels
  - Apex—narrow upper part of each lung, under collarbone
  - Base—broad lower part of each lung; rests on diaphragm
- Structure
  - Pleura—moist, smooth, slippery membrane that lines chest cavity and covers outer surface of lungs; reduces friction between the lungs and chest wall during breathing



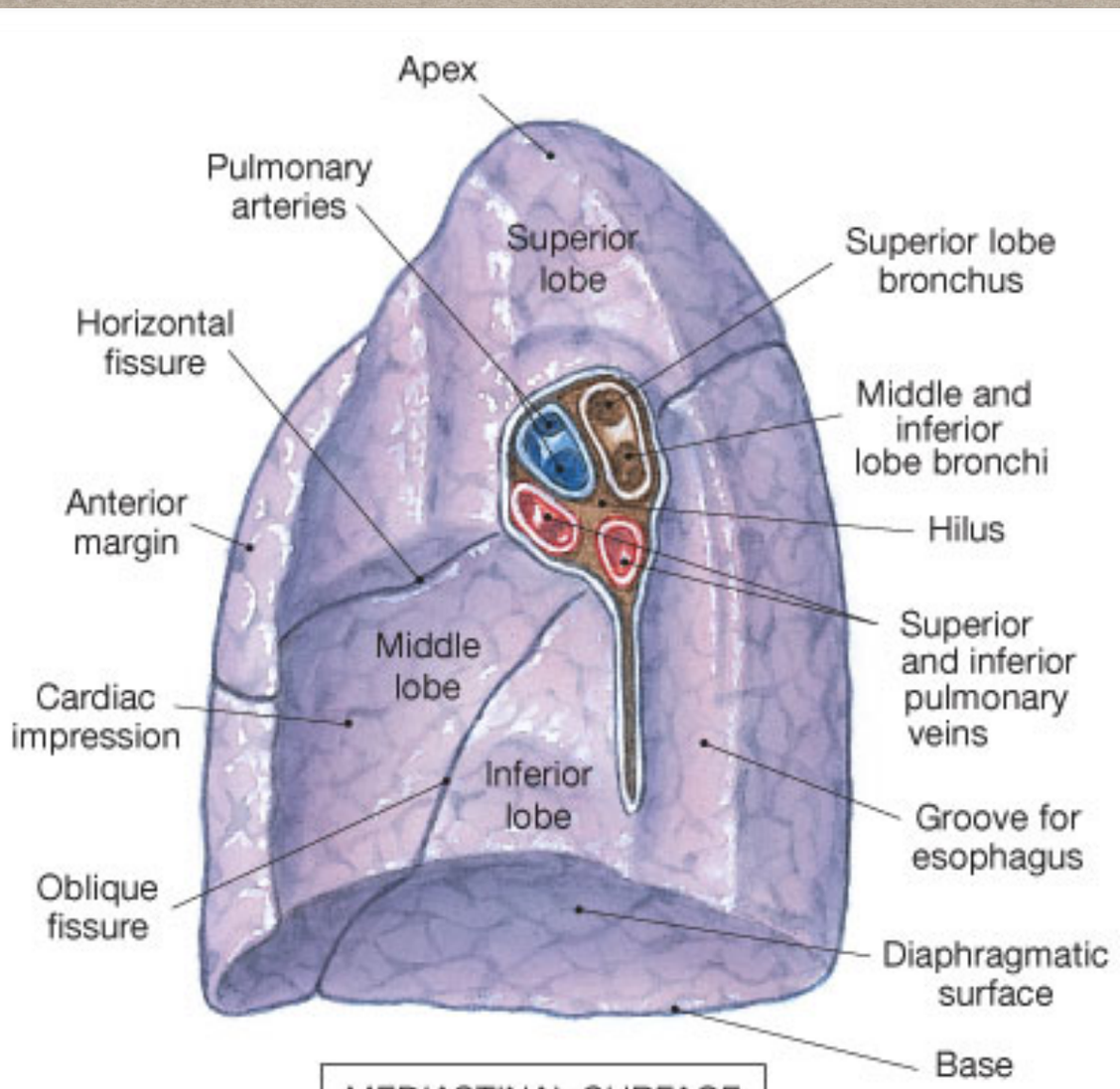
LUNGS

- Lobes
  - Right: 3 Left: 2
  - Right: Superior/middle/inferior
  - Left: superior/middle
- Fissures:
  - Right: horizontal and oblique
  - Left: oblique

- Lobes
  - Right: 3 Left: 2
  - Right: Superior/middle/ inferior
  - Left: superior/middle
- Fissures:
  - Right: horizontal and oblique
  - Left: obliqueSurfaces
  - Costal – anterior – against ribs
  - Mediastinal – medial
    - root of lung and hilus
  - Base
  - apex

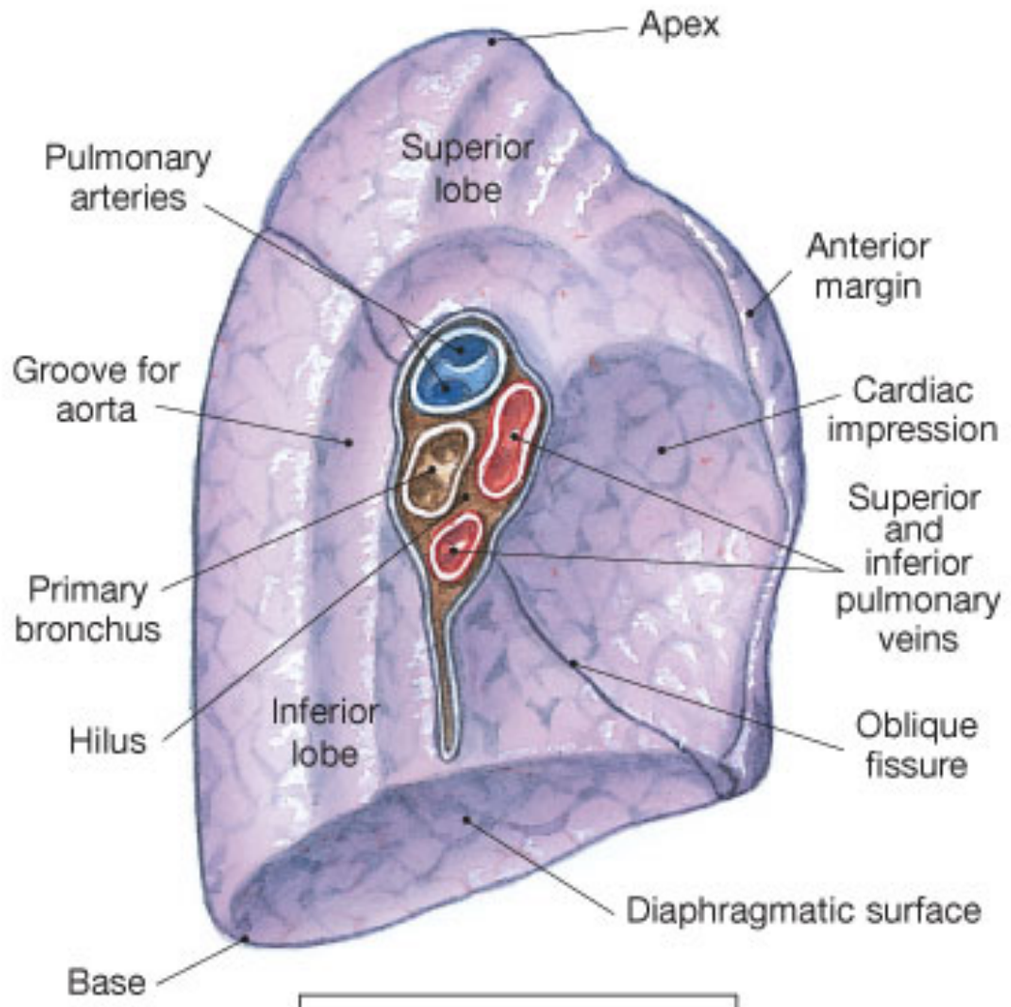


LUNGS- MEDIASTINAL SURFACE



MEDIASTINAL SURFACE

RIGHT LUNG

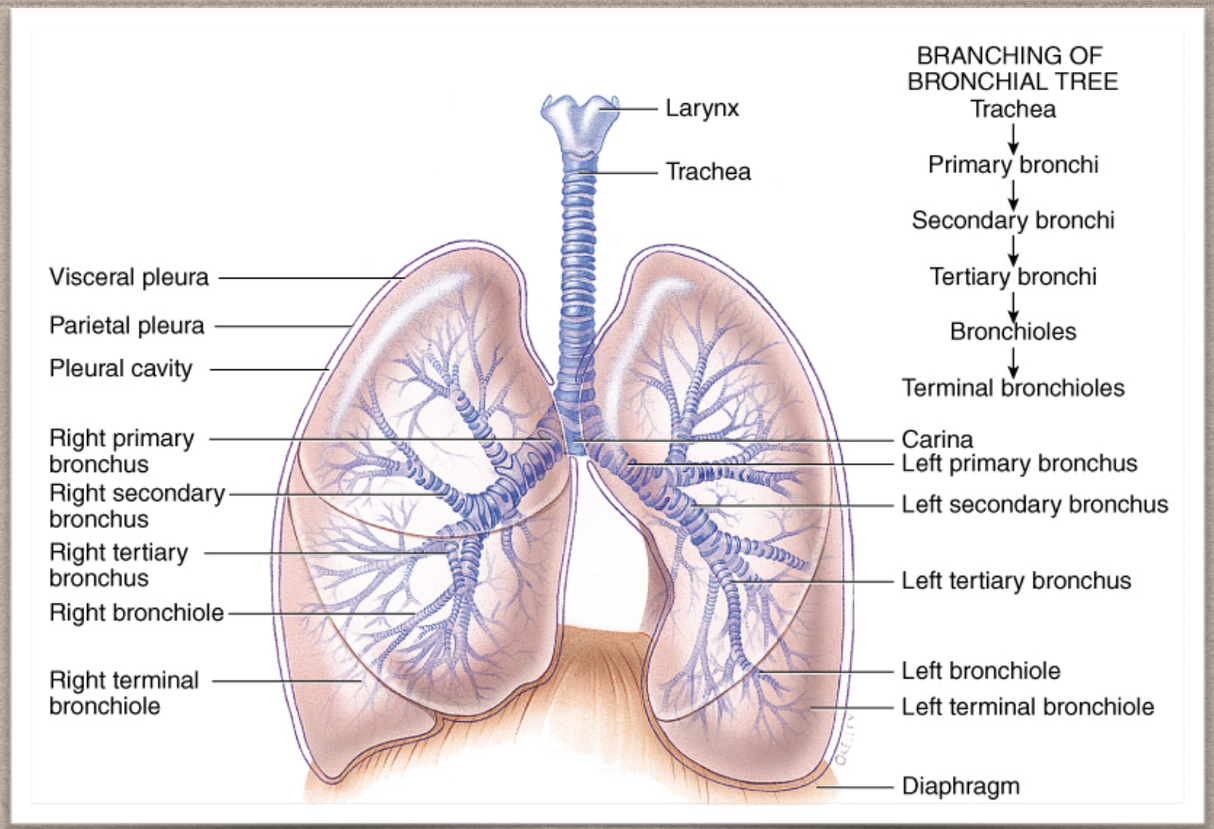


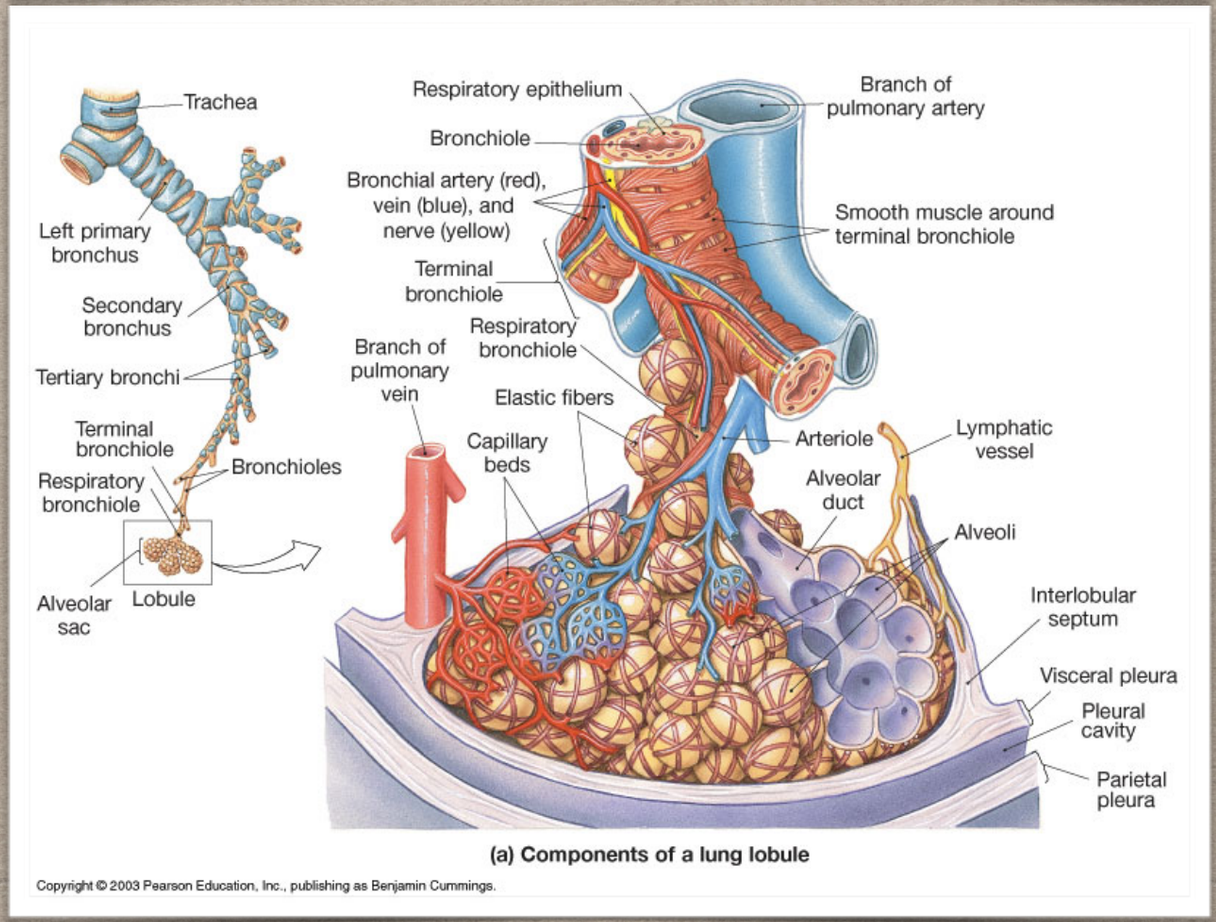
MEDIASTINAL SURFACE

LEFT LUNG

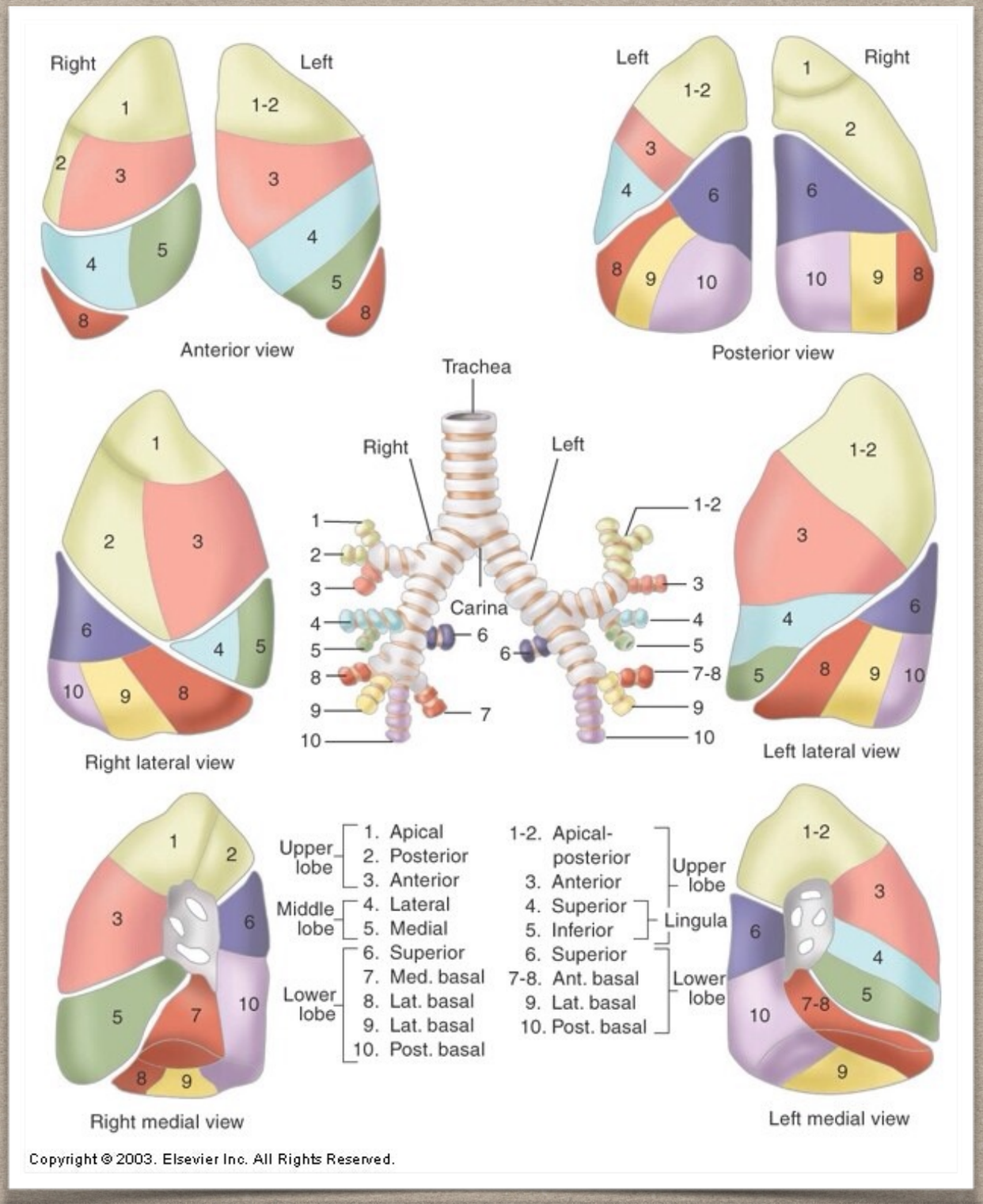
Divisions of Lung Tissue

- Trabeculae divide parenchyma
  - Elastic connective tissue/ smooth muscle
  - Form partitions
- Lobule = smallest self contained bronchio-pulmonary segment of lung
  - Contains own:
    - Arteriole
    - Venule
    - lymphatic vessel
    - Division of tertiary bronchiole
  - 10 right
  - 8-10 left



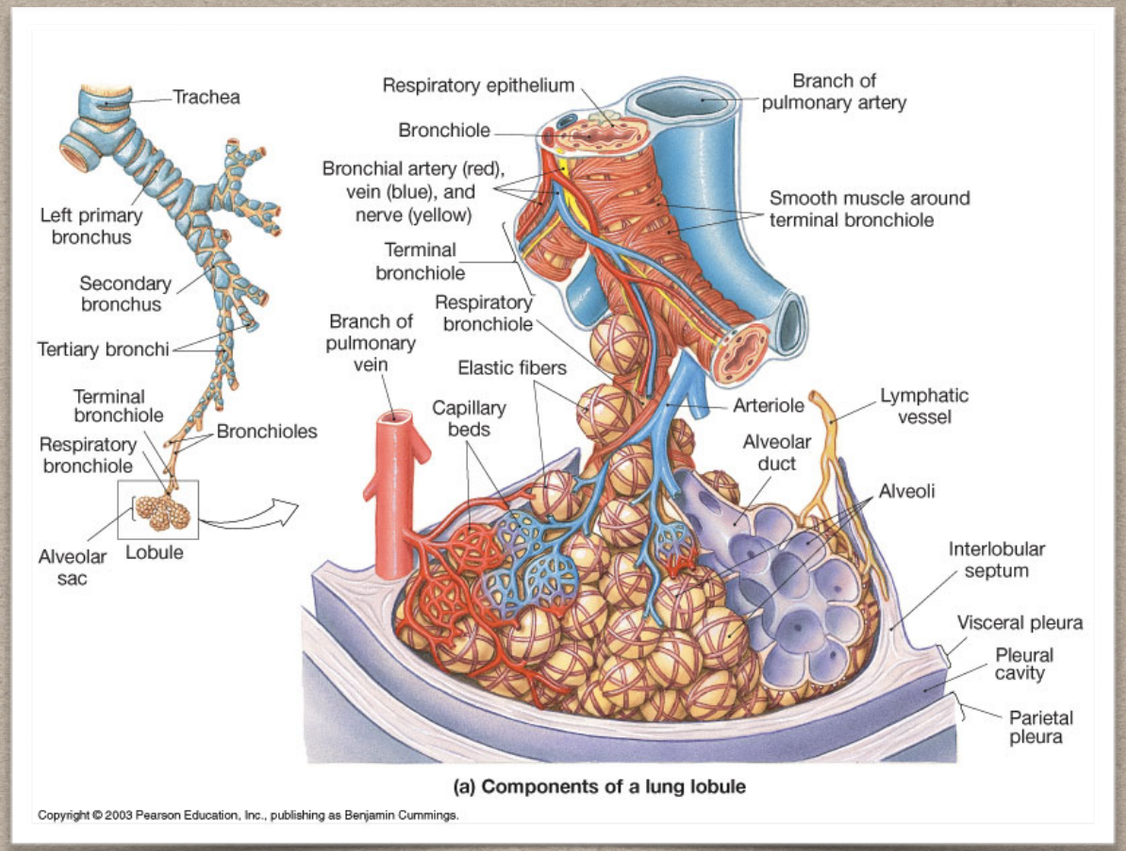


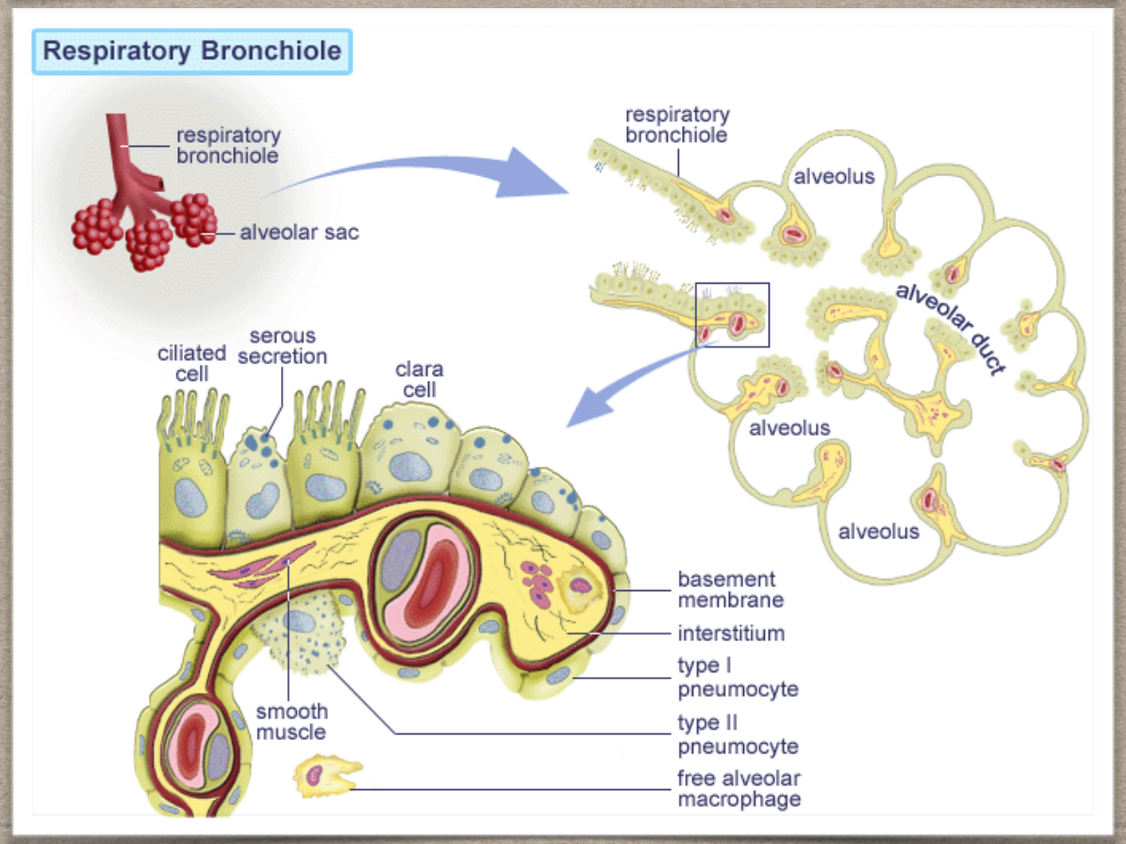
BRONCHOPULMONARY SEGMENTS



- Bronchial Tree – Branching of:
- Intrapulmonary bronchi – within the lungs
  - Primary bronchi divide
    - Secondary bronchi (= lobular bronchi) – to each lobe

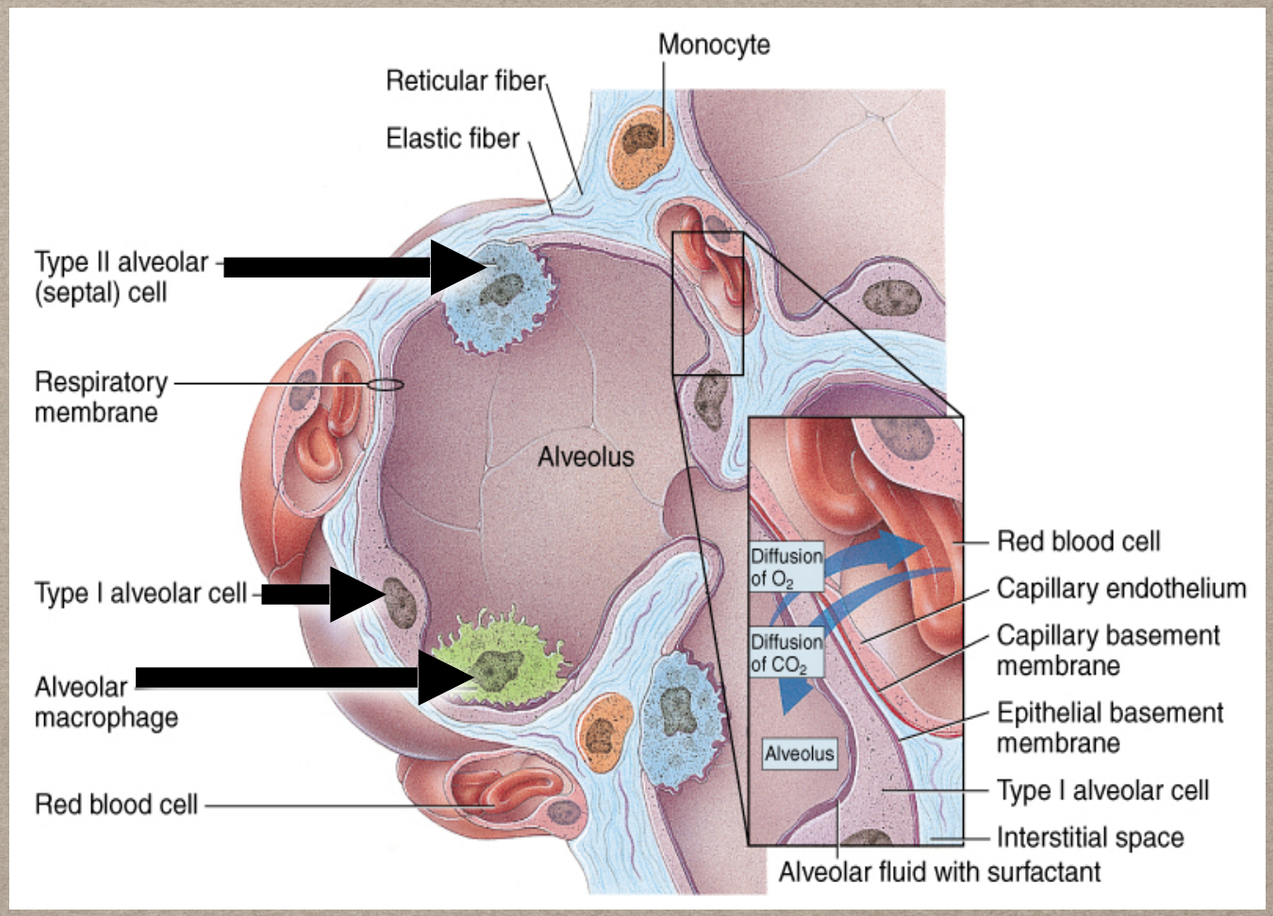
      How many in the right lung? In the left?
    - Tertiary bronchi (= segmental bronchi) – to each bronchiopulmonary segment: ~10/lung
    - Bronchioles
    - terminal bronchioles
    - respiratory bronchioles (microscopic)
    - alveolar ducts
    - alveolar sacs (contain several alveoli)





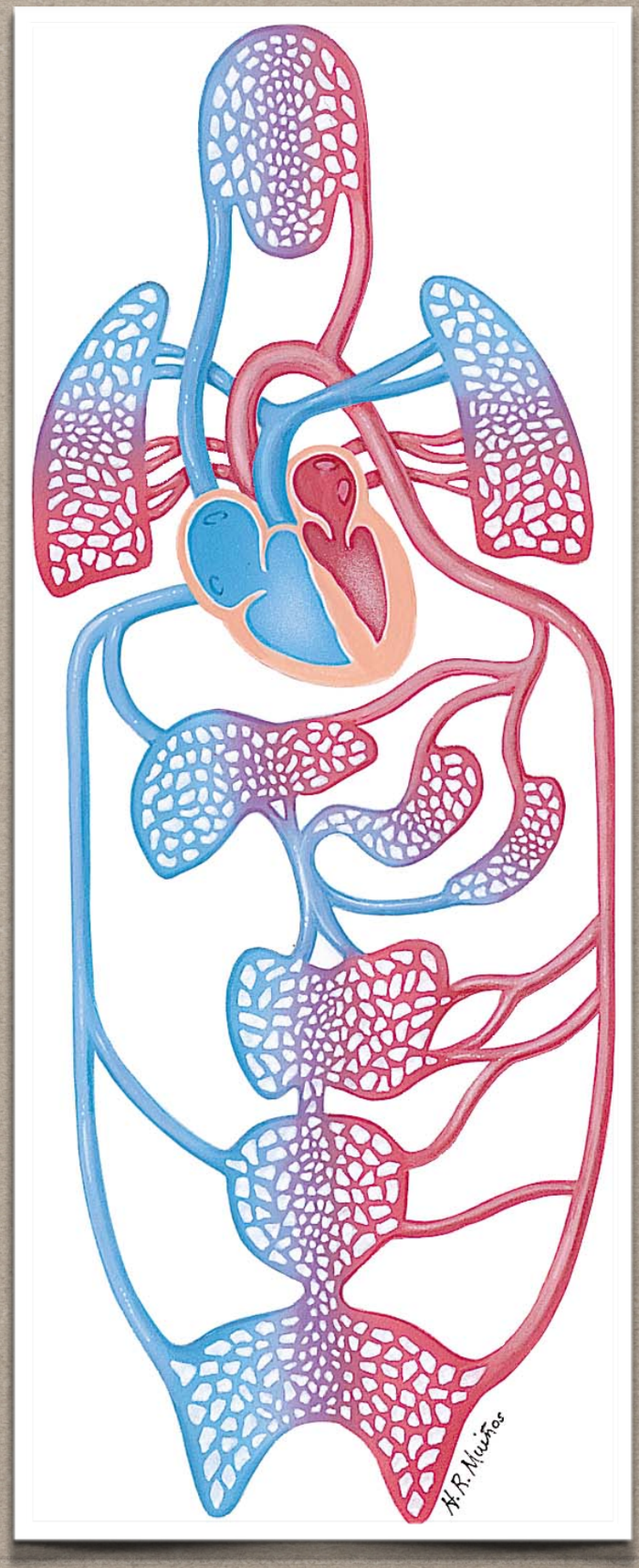
ALVEOLI

- Alveoli – site of gas exchange
- Blind ended (‘cup shaped outpouching) contained in alveolar sac
- Membrane: simple squamous + elastic basement membrane
- Cells:
  - Type I form continuous lining
  - Type II (Spetal cells)
    - Produce alveolar fluid, contains surfactant – prevents collapse of alveoli
  - Alveolar macrophages (dust cells)
- Capillaries surround



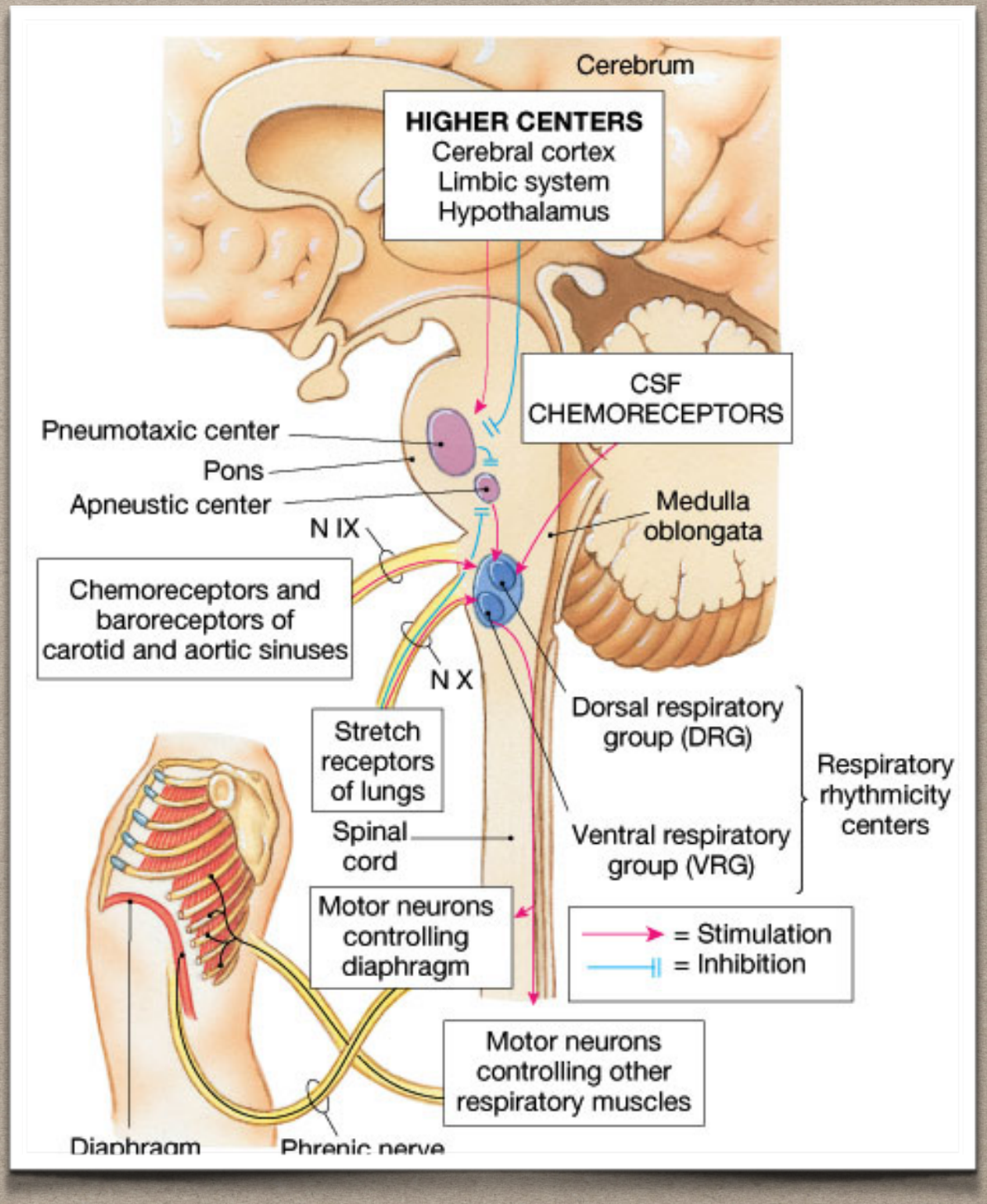
LUNG BLOOD SUPPLY

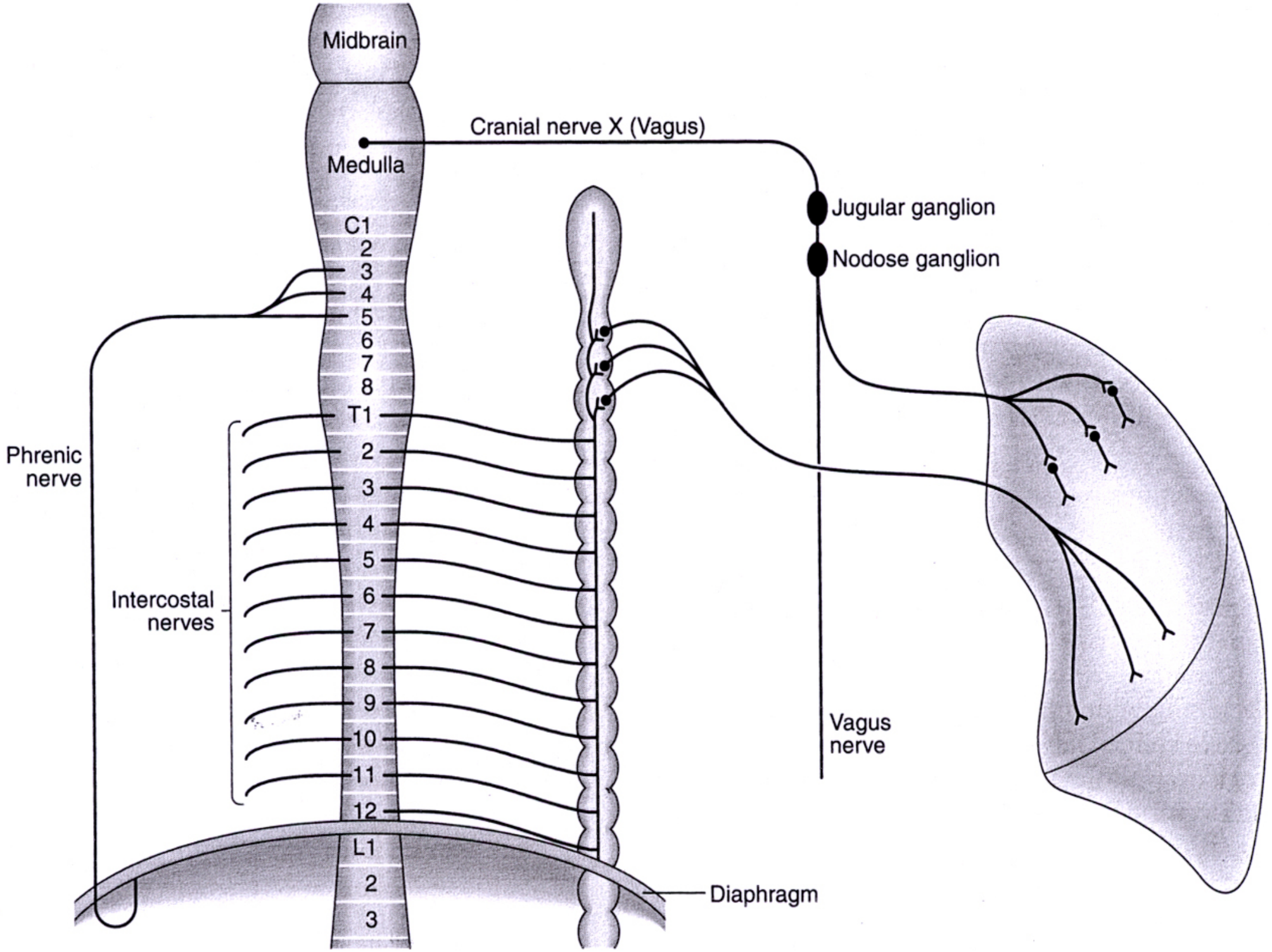
- Two Blood Circulation Patterns in Lungs
- Pulmonary Circuit
  - Oxygen poor/Carbon dioxide rich blood from heart via pulmonary artery to lungs
  - Gas exchange takes place in lungs to supply oxygen to body
  - Blood returns to heart via pulmonary veins
- Bronchial arteries
  - Branch from aorta
  - Supply nutrient and oxygen rich blood to tissues of lungs
  - Drainage via bronchial veins and pulmonary veins



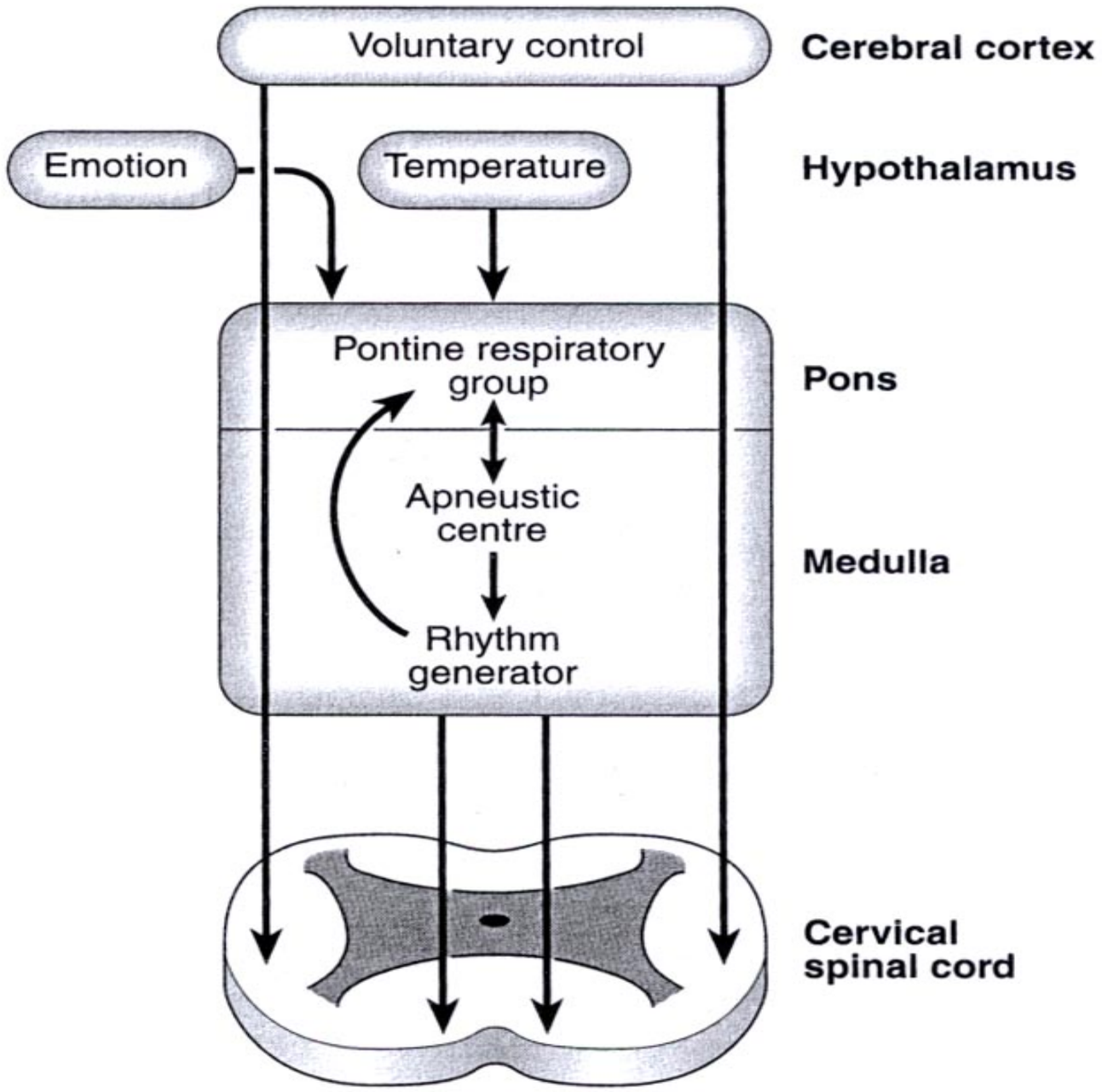
NEURAL CONTROL OF BREATHING

- paired centers in Brain Stem:
  - Medulla:
    - Ventral Respiratory Group (VRG)– sets basic rhythm
    - Dorsal Respiratory Group (DRG)– integrates sensory and input from other regions of brain ⊠ alters activity of VRG
  - Pontine Centers
    - Prev. Pneumotaxic Respiratory , others
    - Adjust frequency & depth – alters activity of ventral group in medulla
    - Responds to sensory input – largely increase in H^+ ion concentration



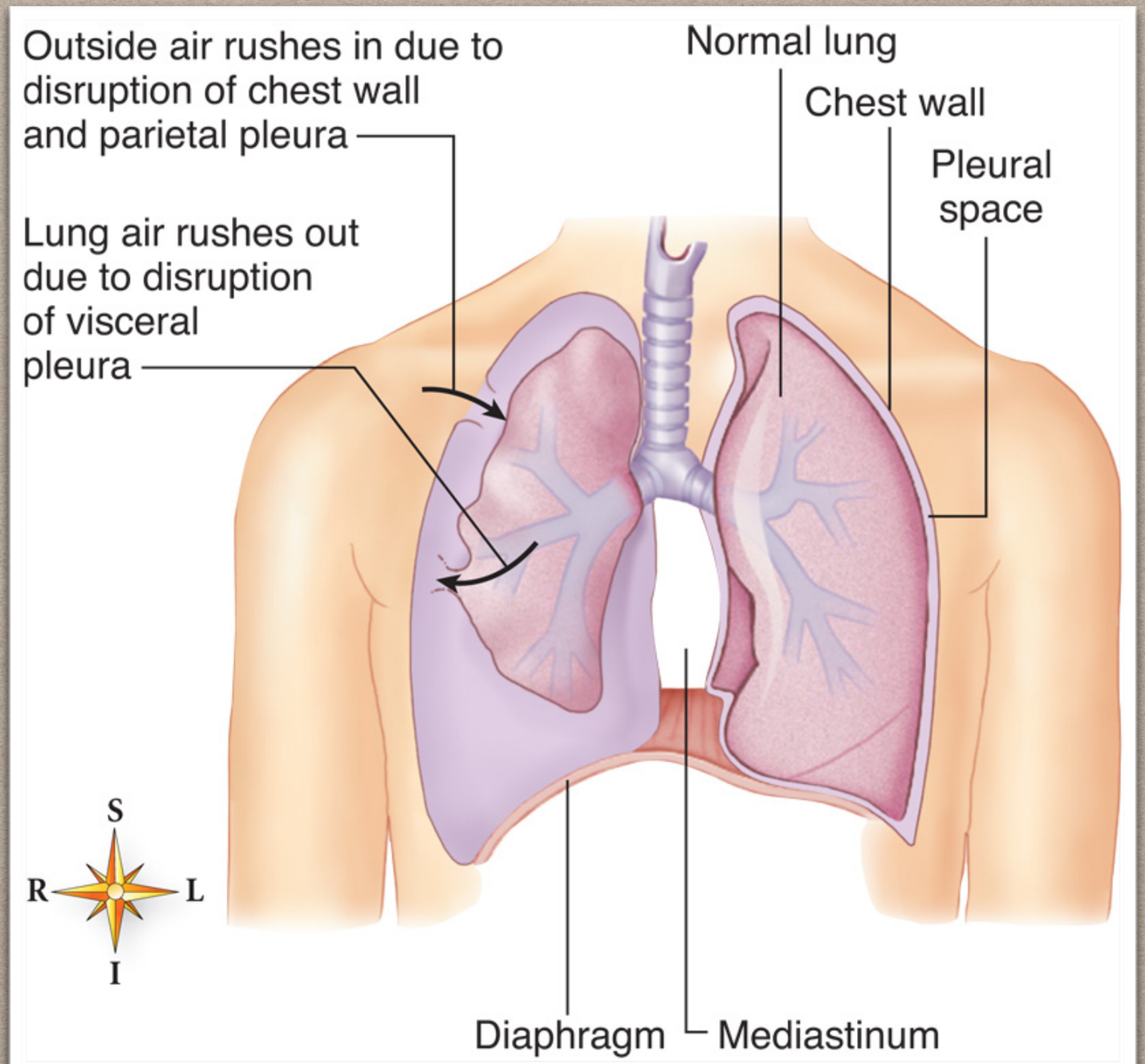


Innervation of the diaphragm, intercostal musles and lungs. The efferent (motor) systems are shown. The affere (sensory) system is mainly in the vagus nerves.



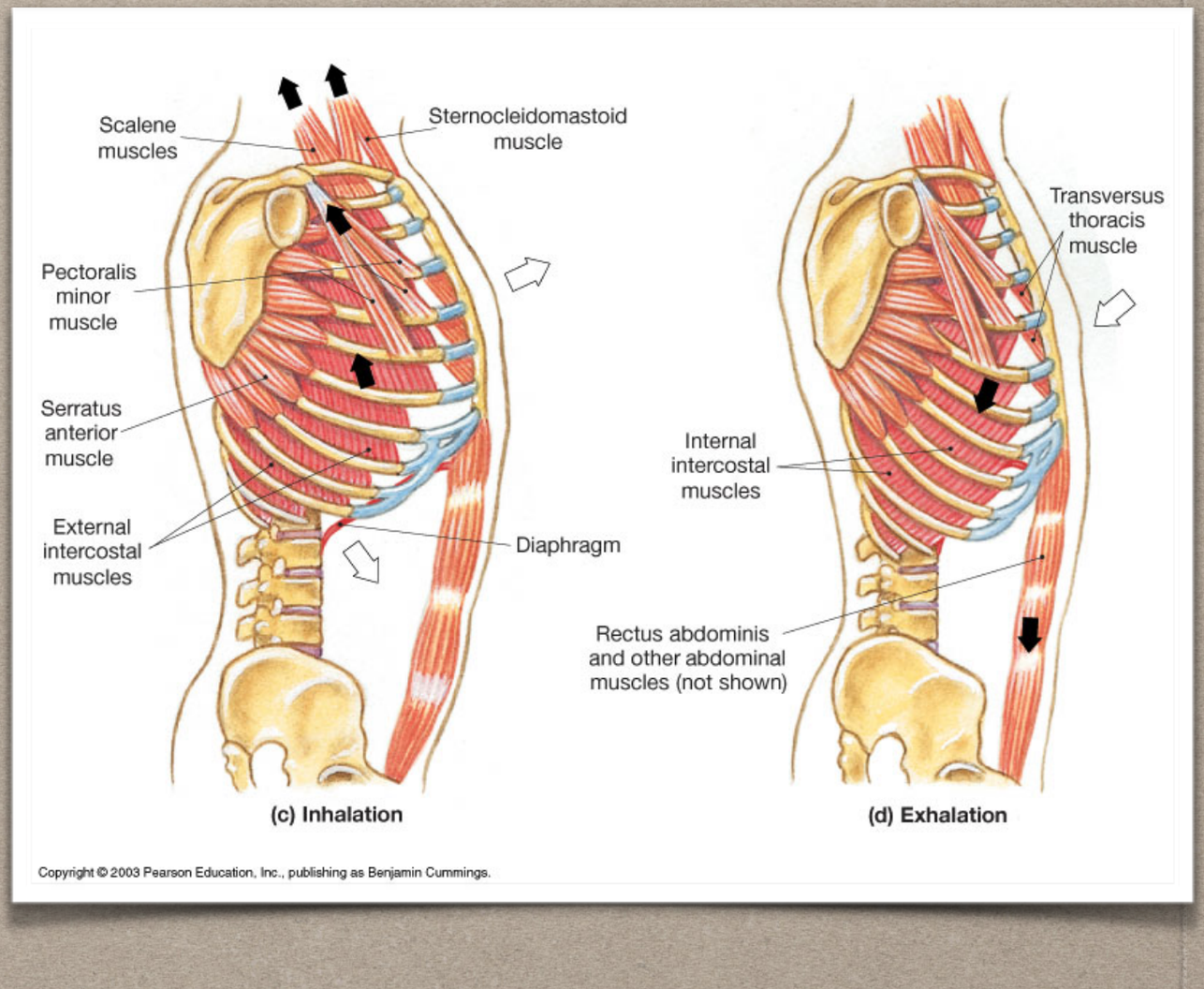
An outline schematic of central neural structures involved in breathing. The centres and generator are collections of neurons that function together rather than specific anatomical structures.

HOW IS THE RESPIRATORY SYSTEM CONTROLLED/REGULATED?



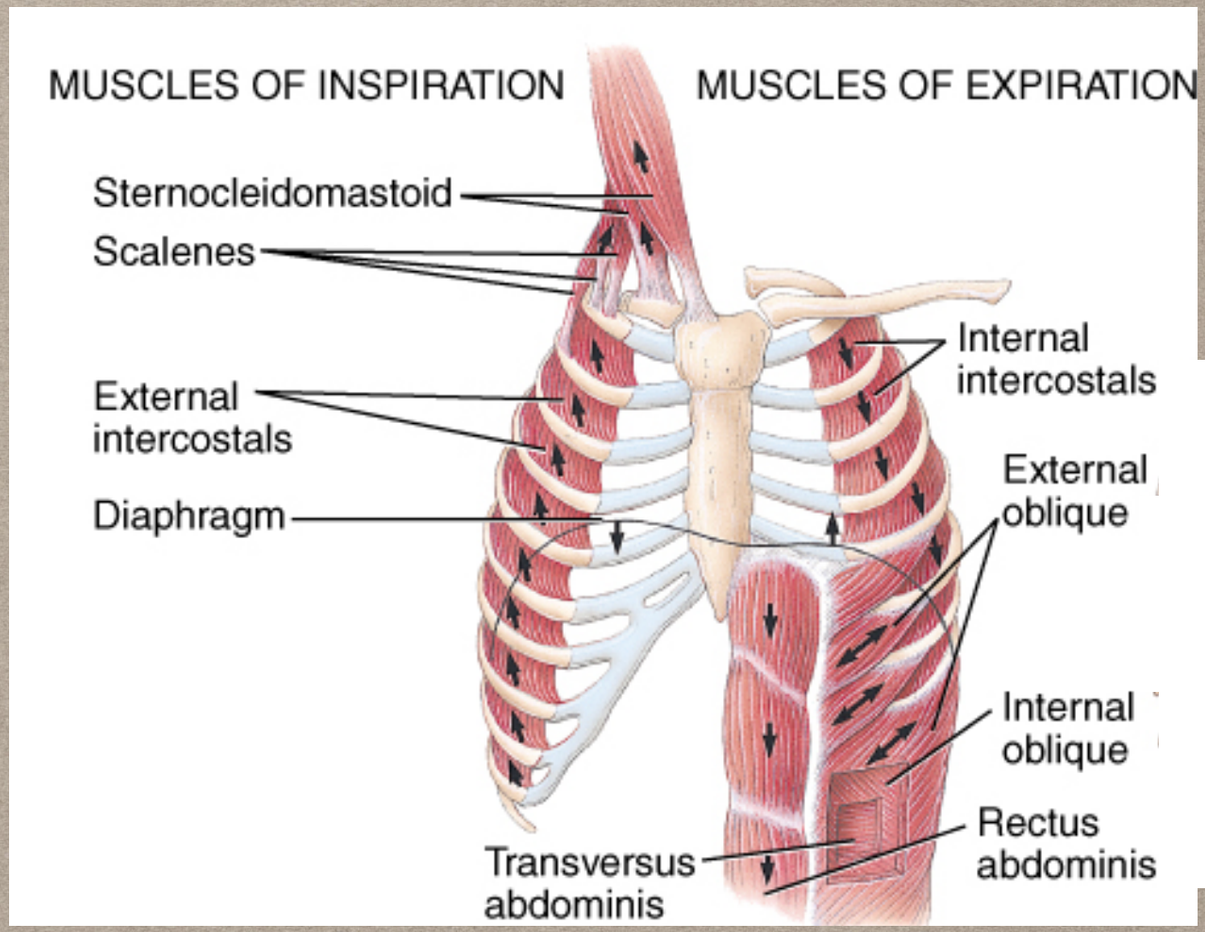
MUSCLES OF RESPIRATION

- Primary Muscles Involved
- Inspiration: (thorax increases in volume and air enters lungs)
  - Diaphragm flattens
  - External intercostals elevate ribs
- Expiration
  - Diaphragm relaxes
  - Internal intercostals depress ribs, reduce width of thoracic cavity
- Shallow Breathing: only intercostals involved
  - At rest
  - During pregnancy (abdominal volume decreases)
- Deep Breathing: (Diaphragmatic) – contraction of diaphragm



ACCESSORY MUSCLES OF RESPIRATION

- Accessory Muscles:
- Assist in elevating ribs during inspiration
  - Sternocleidomastoid
  - Serratus anterior
  - Pectoralis minor
  - Scalenes
- Assist in decreasing thoracic volume during expiration by compressing abdomen:
  - Transversus thoracis
  - Obliques and Rectus abdominis



SURFACTANT

- Reduces surface tension and therefore elastic recoil, making breathing easier
- Reduces the tendency to pulmonary oedema
- Equalises pressure in large and small alveoli

The presence of surfactant is clearly important to normal lung function. It:

- reduces surface tension and therefore elastic recoil, making breathing easier
- reduces the tendency to pulmonary oedema

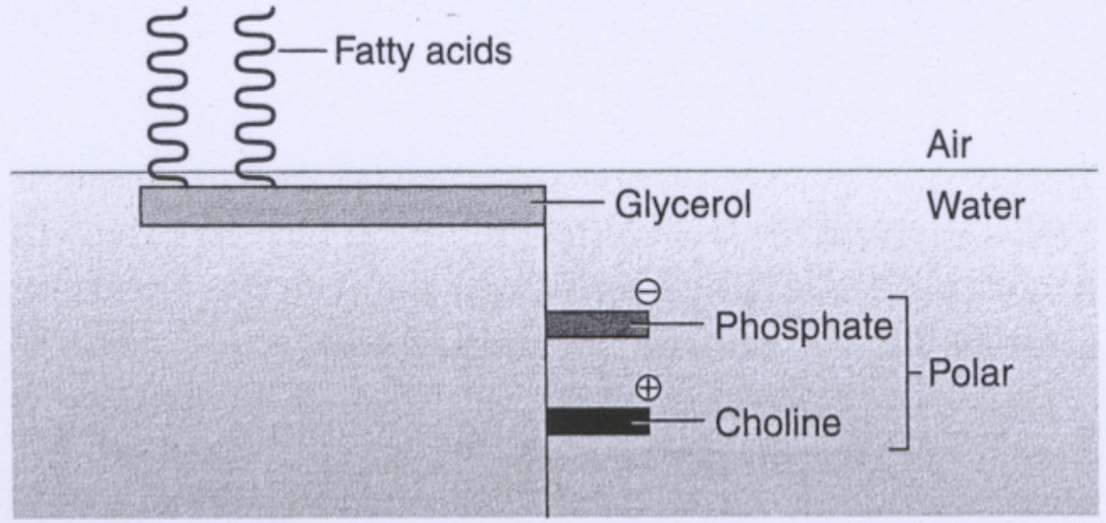
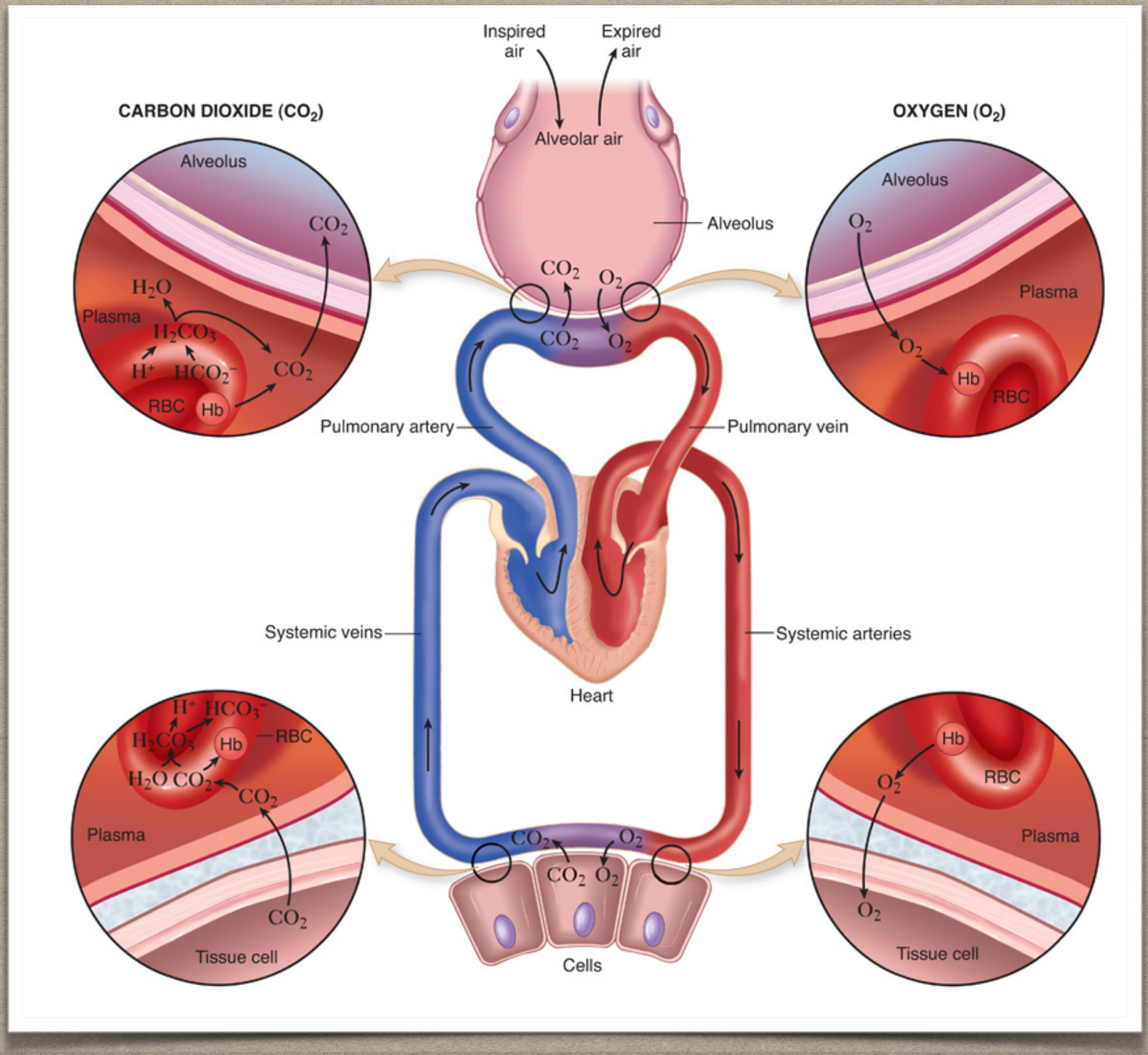
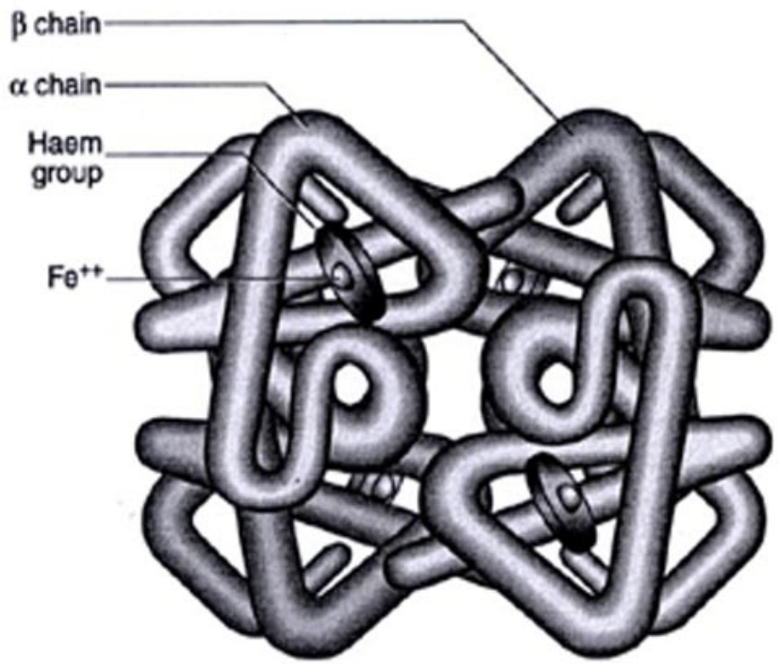


Fig. 3.13
The molecular structure of phosphatidylcholine, and the way it orientates itself at an air–water interface.

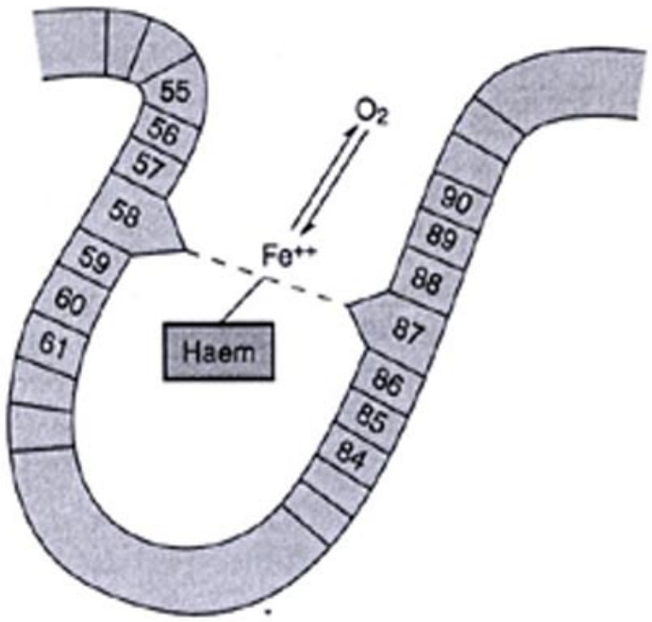
RESPIRATORY PHYSIOLOGY



HEMOGLOBIN



The structure of haemoglobin. Each of the four globin chains (the wormlike structures in the figure) is made up of a spiral of just over 100 amino acids. Each chain is attached at one point to an iron-containing haem group. Each haem group can carry a molecule of O_2, so each haemoglobin molecule has four 'hooks', each of which can carry one O_2.



takes place in four steps, in which case Equation 8.3 should be written:

$$Hb_4 + O_2 \Leftrightarrow Hb_4O_2$$
$$Hb_4O_2 + O_2 \Leftrightarrow Hb_4O_4$$
$$Hb_4O_4 + O_2 \Leftrightarrow Hb_4O_6$$
and finally $$Hb_4O_6 + O_2 \Leftrightarrow Hb_4O_8 \quad \text{(Equation 8.4)}$$

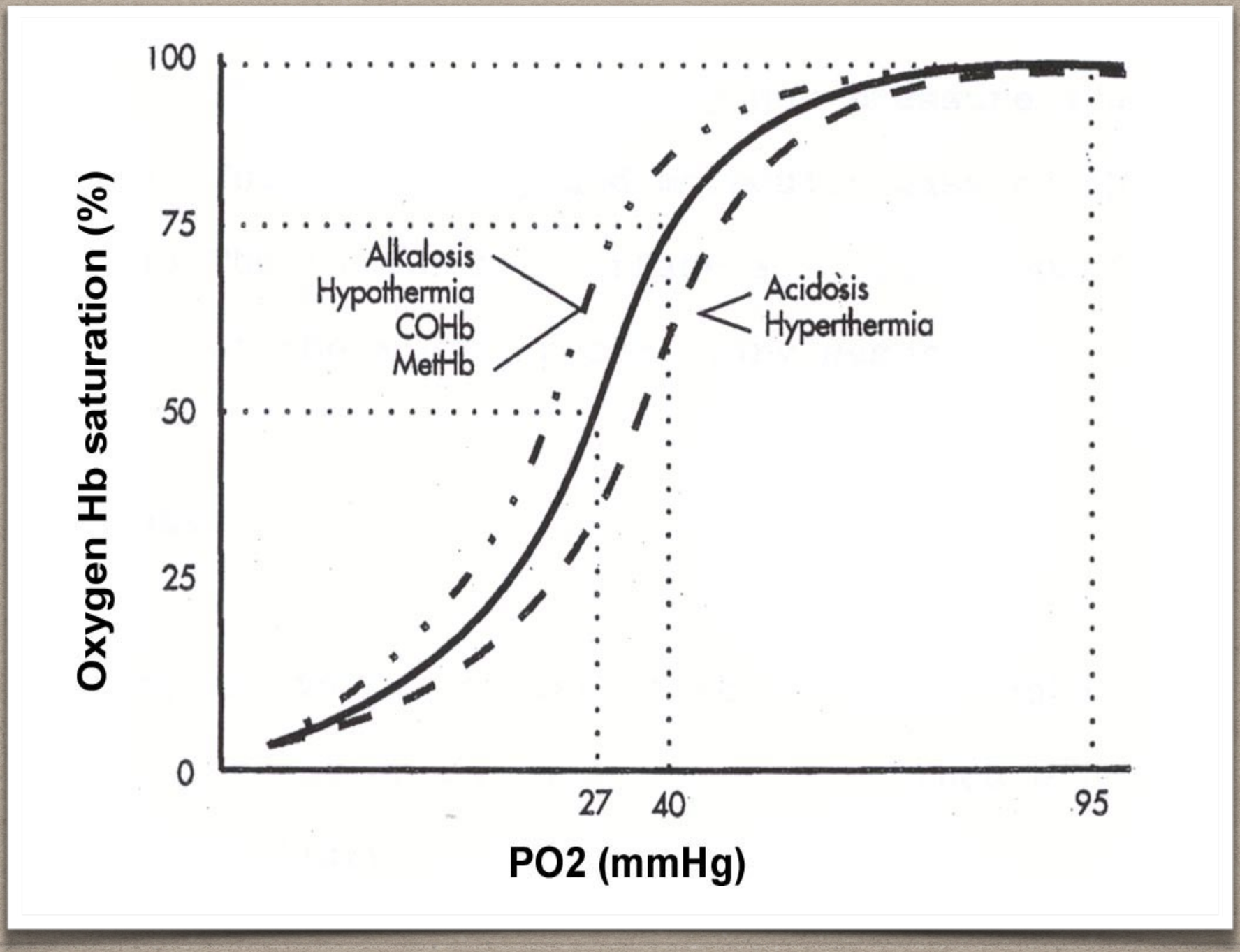
It is conceptually useful to consider each Hb molecule as having only four 'hooks'. On each hook can hang one O_2.

OXYHEMOGLOBIN DISSOCIATION CURVE

- Left shift →increased HB affinty for O_2 (↓ release of O_2 to tissues)
- Alkalosis
- Hypothermia
- ↓2,3 DPG
- COHB
- MetHB

- Right shift→decreased HB affinity for O_2 (↑ release of O_2 to tissues)
- Acidosis
- Hyperthermia
- ↑ 2,3 DPG

OXYHEMOGLOBIN DISSOCIATION CURVE



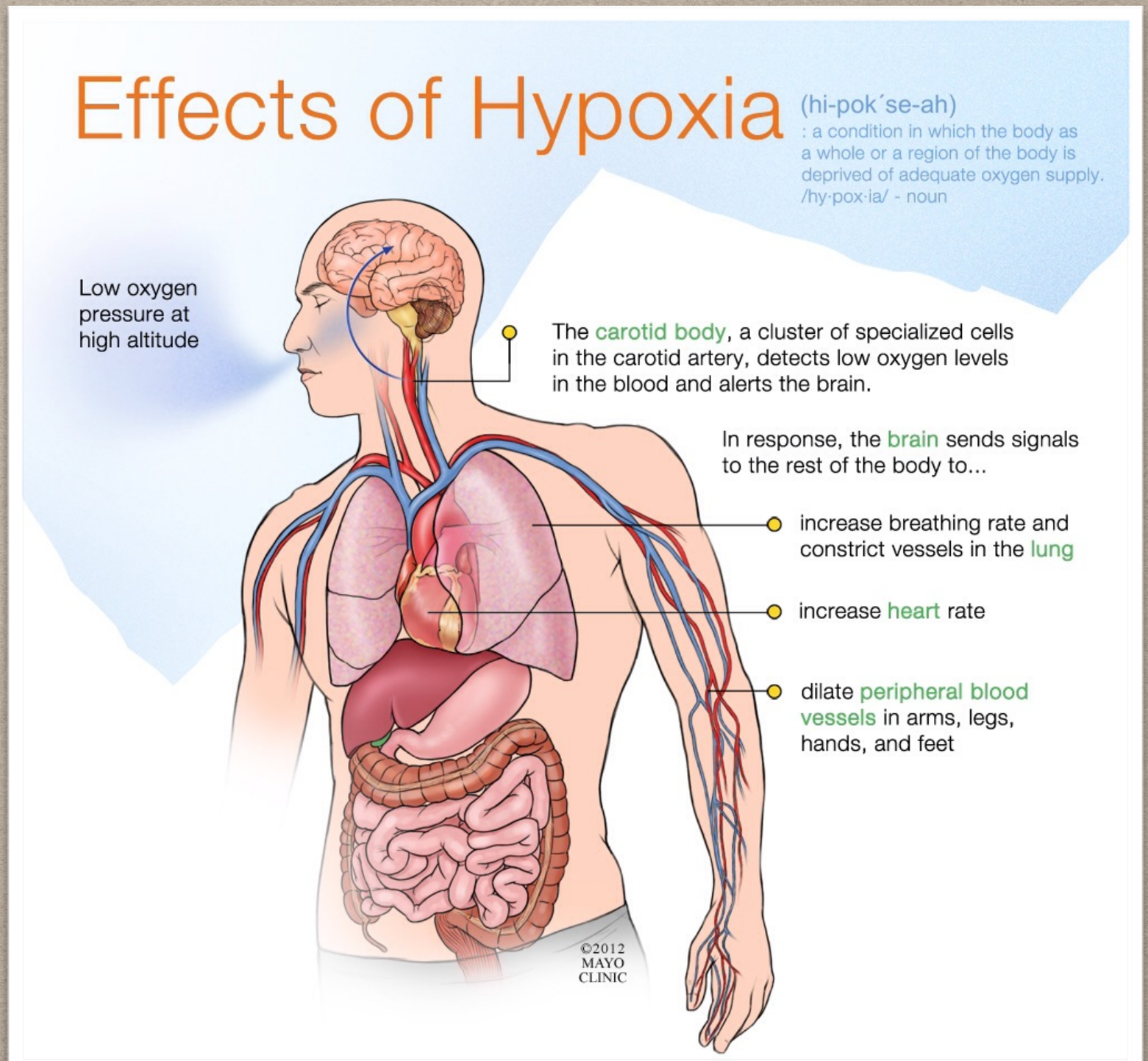
HYPOXIA

4 Causes of Hypoxemia:

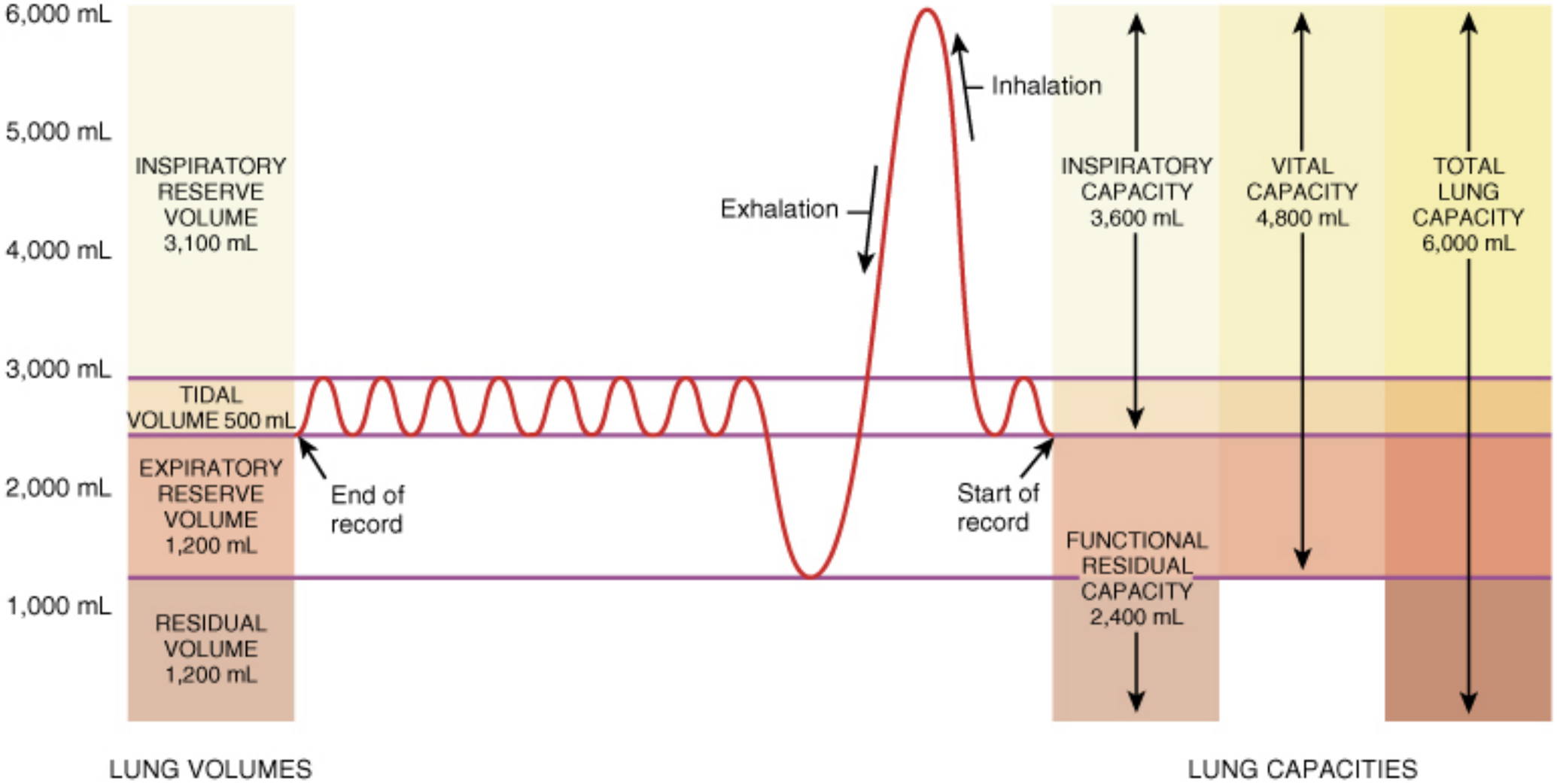
0. Ambient Hypoxemia
1. Hypoventilation
2. Impairment of Diffusion
3. Shunt
4. Ventilation-Perfusion Abnormalities

Classifications	PaO_2 (rule of thumb)
Normal	80-100 mm Hg
Mild hypoxemia	60-80 mm Hg
Moderate hypoxemia	40-60 mm Hg
Severe hypoxemia	<40 mm Hg

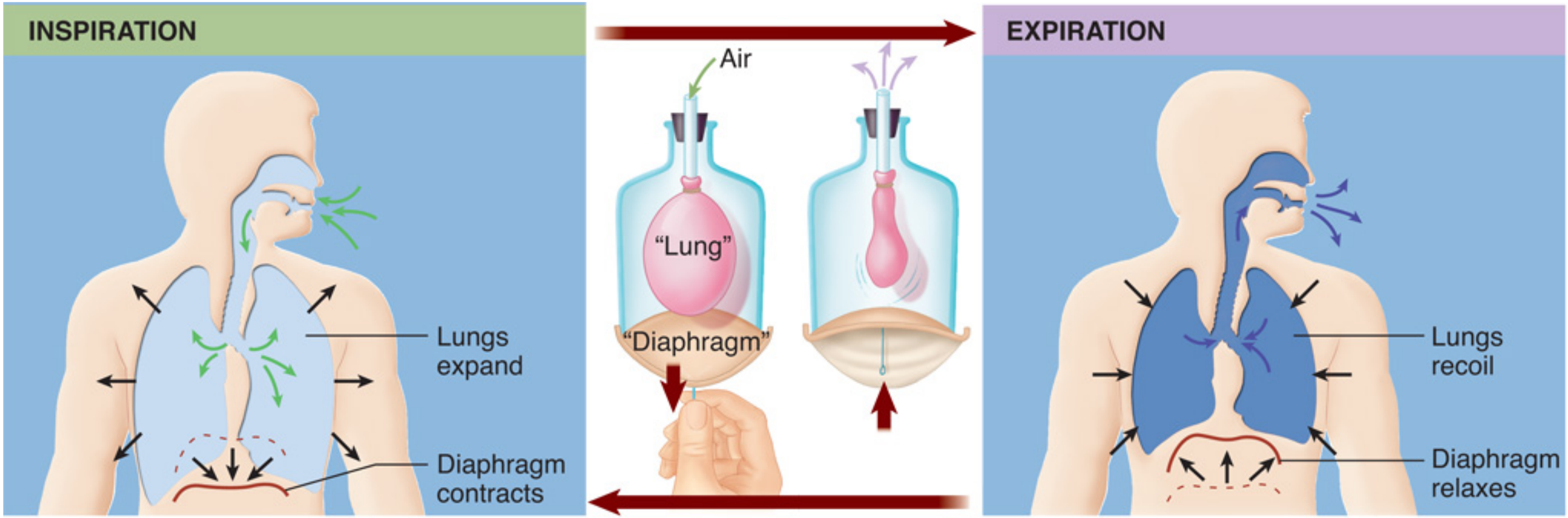
EFFECTS OF HYPOXIA



Lung Volumes and Capacities



- Tidal volume = amount air moved during quiet breathing
- Reserve volumes ---- amount you can breathe either in or out above that amount of tidal volume
- Residual volume = 1200 mL permanently trapped air in system
- Vital capacity & total lung capacity are sums of the other volumes



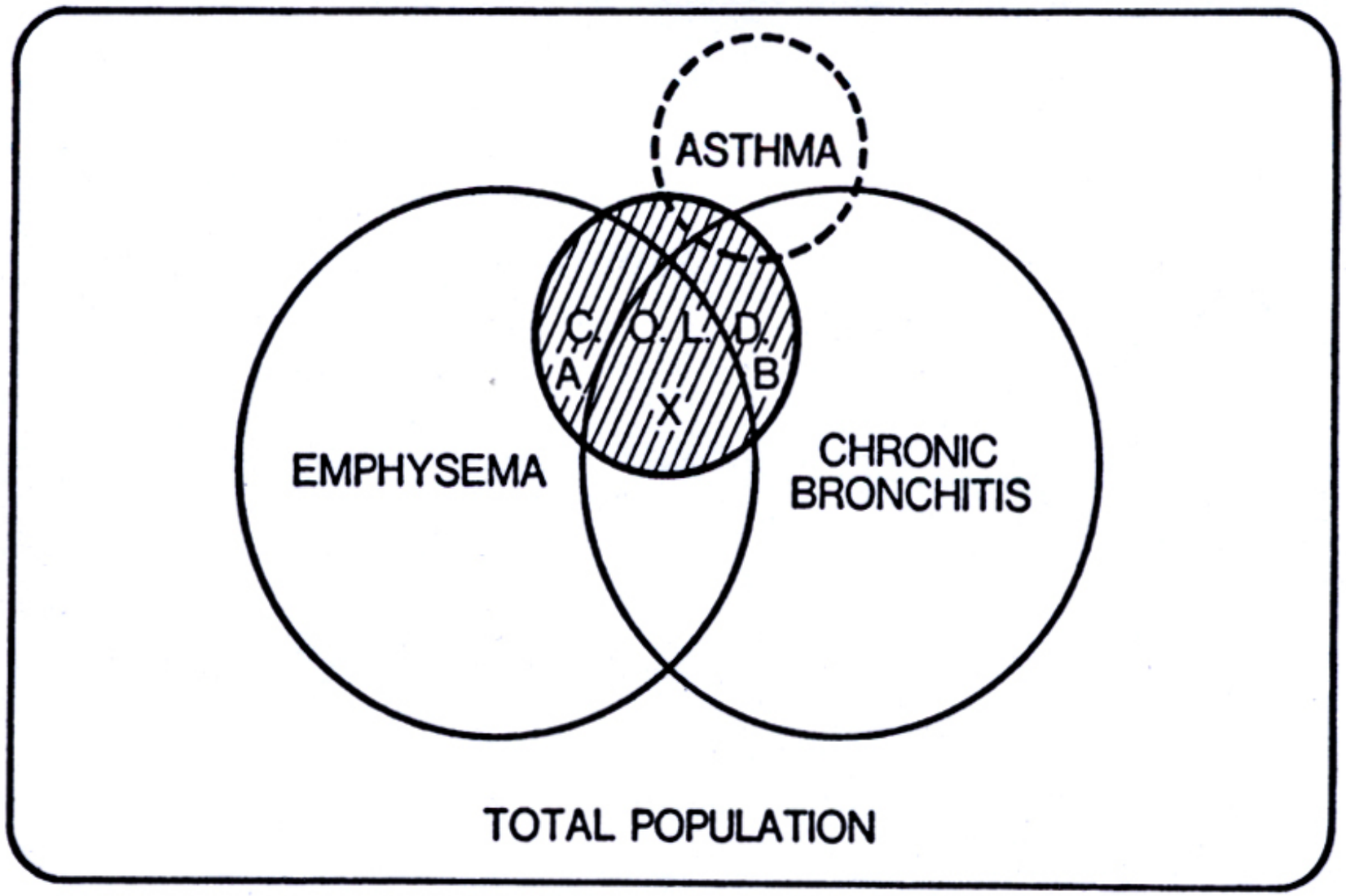
HOW IS THE RESPIRATORY SYSTEM AFFECTED BY DISEASE?

PATHOLOGY

- Airway diseases: COPD, asthma, bronchiectasis, cystic fibrosis, obstructive sleep apnoea
- Parenchymal disease: pneumonia, ARDS, Interstitial lung disease, pneumoconiosis
- Pleural disease: pleural effusion, empyema.
- Vascular disease: thrombo-embolism, primary pulmonar hypertension
- Neoplastic disease: Bronchus Ca, mesothelioma, adenoma, carsinoid

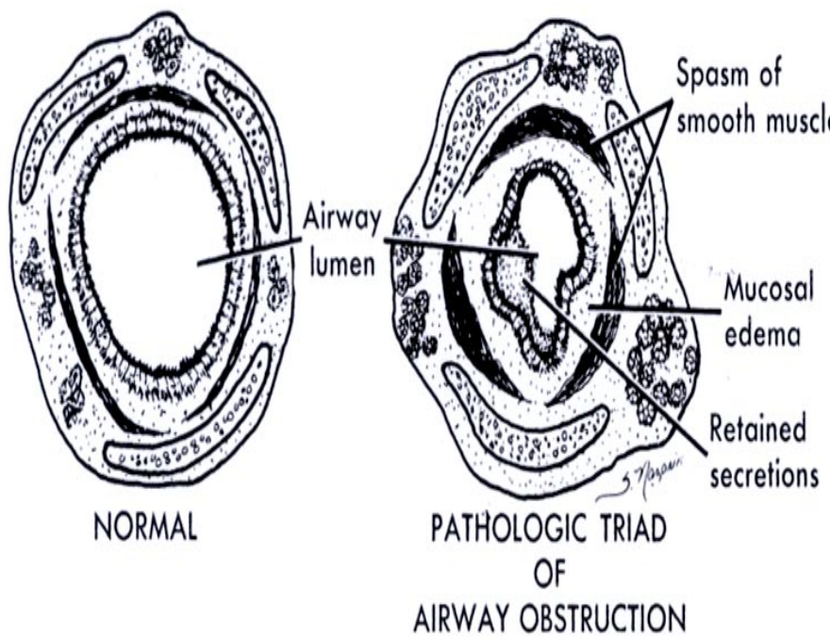
AIRWAY DISEASES

- Causes: atopy, cigarette smoking, infection, abnormal lung defense
- Effect: obstruction to airflow
- Mechanism: bronchospasm, inflammation, airway remodelling, destruction, collapsing airways
- Consequences: ↓ air flow (↓ FEV1, PEF);↑ work of breathing →resp muscle fatigue → respiratory failure; ↓PaO_2, ↑$PaCO_2$ →PHT →cor pulmonale

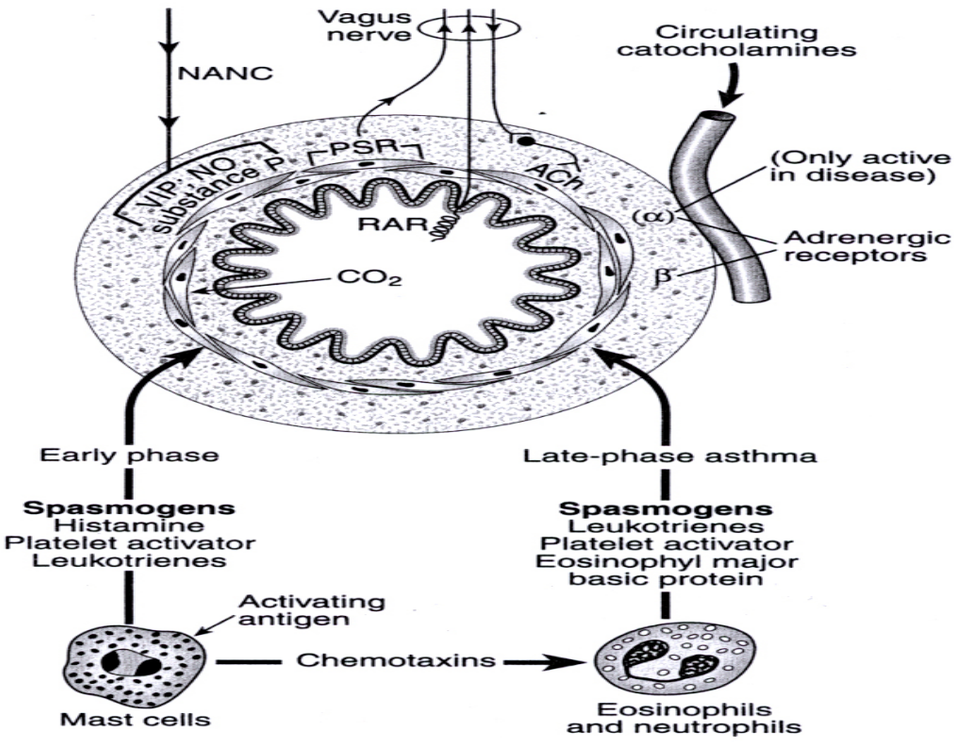


Interrelationships among chronic bronchitis, emphysema, asthma, and chronic obstructive lung disease (COLD). The shaded area roughly indicates the proportions of symptomatic individuals with COLD. Patients with severe anatomic emphysema with little bronchitis are designated type A emphysema. Those with severe bronchial abnormalities with emphysema are designated type B bronchitis. The many patients with a mixed syndrome are depicted in the X zone. (From Burrows B, Knudson RJ, and Kettrl LG: Respiratory insufficiency, Chicago, 1975, Year Book Medical Publishers.)

PATHOLOGY: ASTHMA

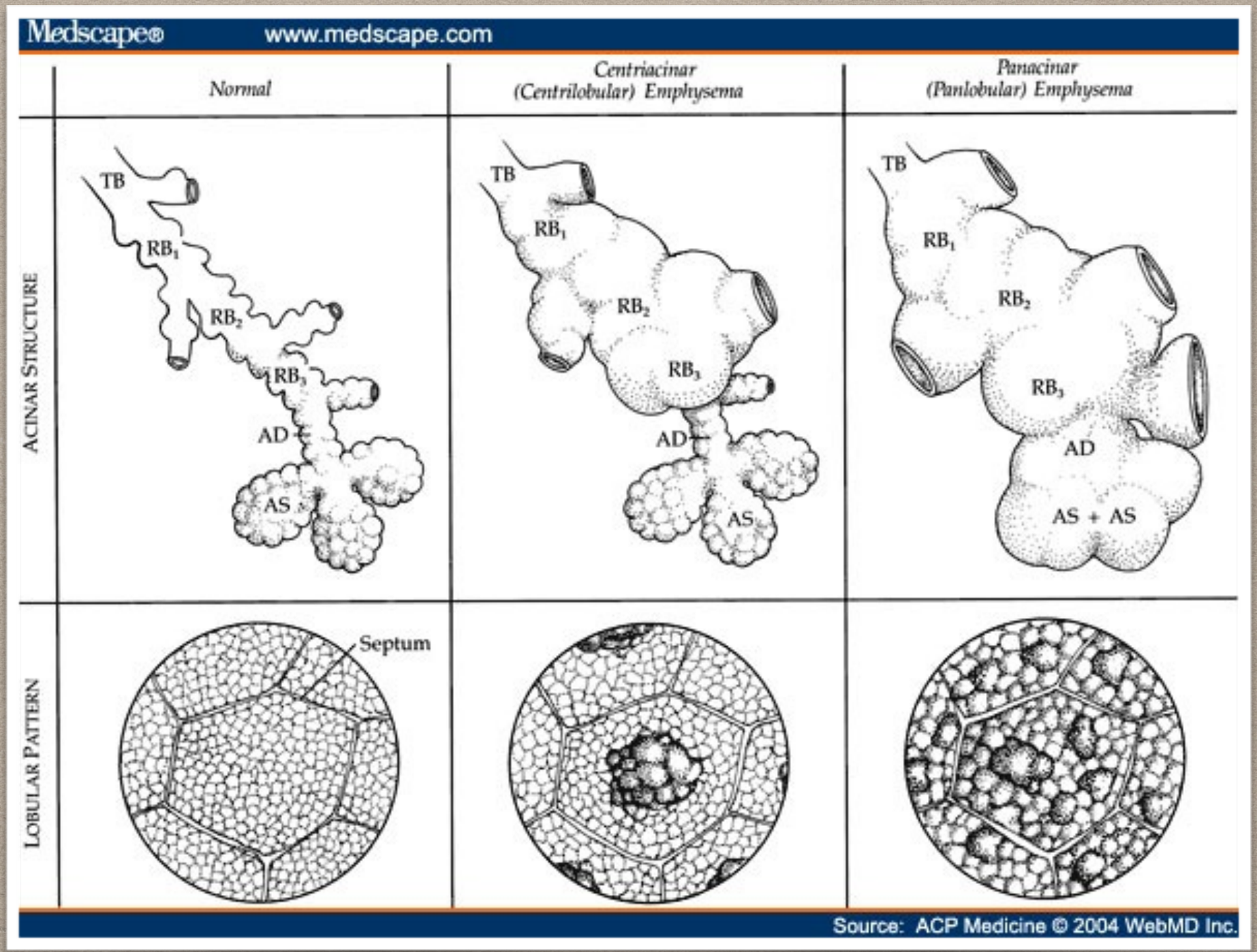


Cross-sections of airways comparing normal with obstruction caused by pathologic triad. Note narrowed airway lumen (opening) in obstructed airway.

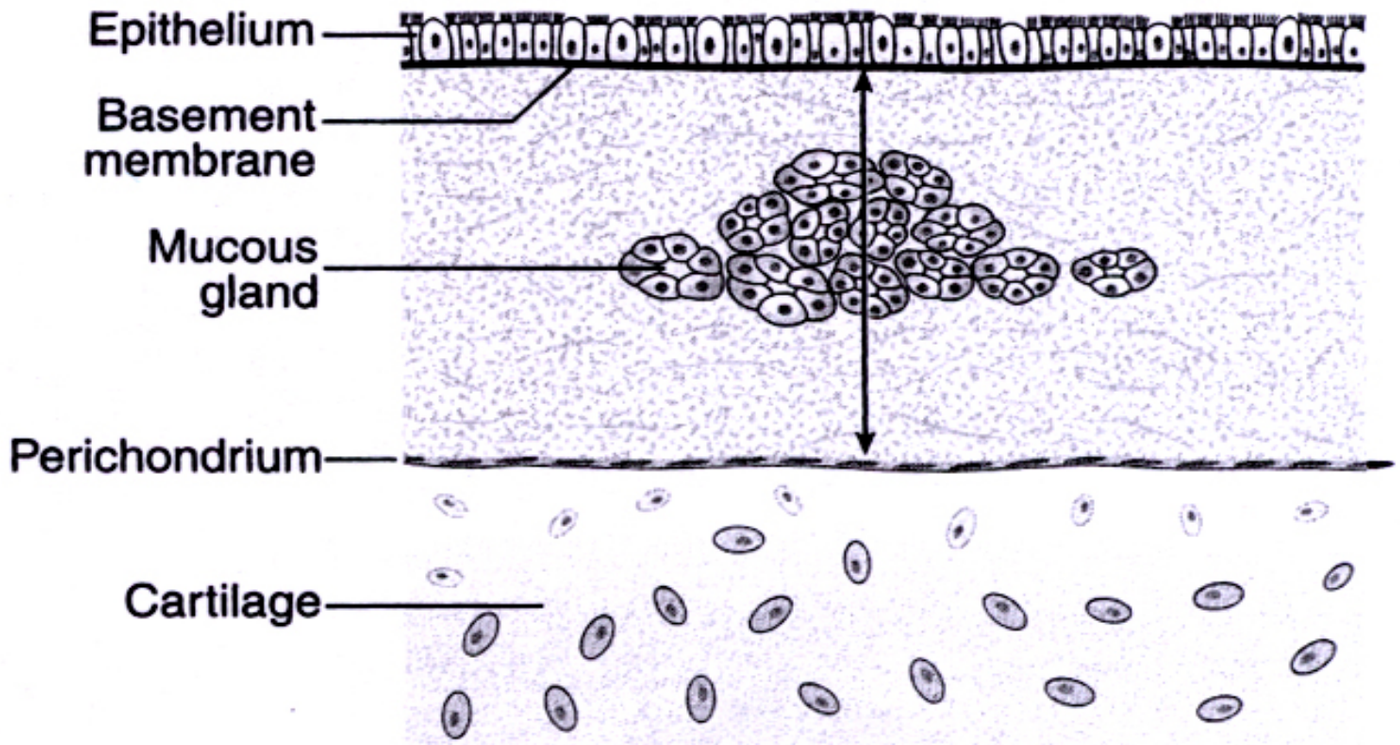


Factors that affect bronchomotor tone. These are implicated in early- and late-phase asthma. (NANC, non-adrenergic non-cholinergic nerve; VIP, vasoactive intestinal peptide; NO, nitric oxide; RAR, rapidly adapting pulmonary sensory receptor; PSR, slowly adapting pulmonary sensory receptor.)

PATHOLOGY
EMPHYSEMA

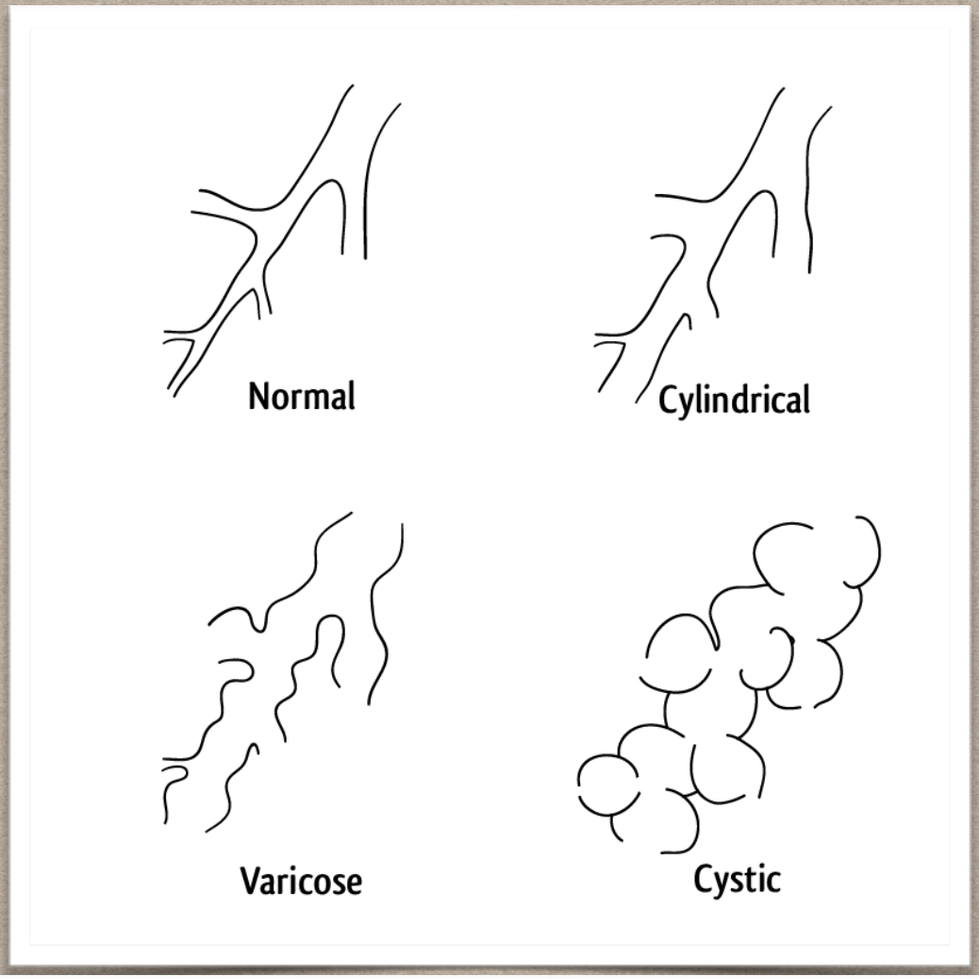


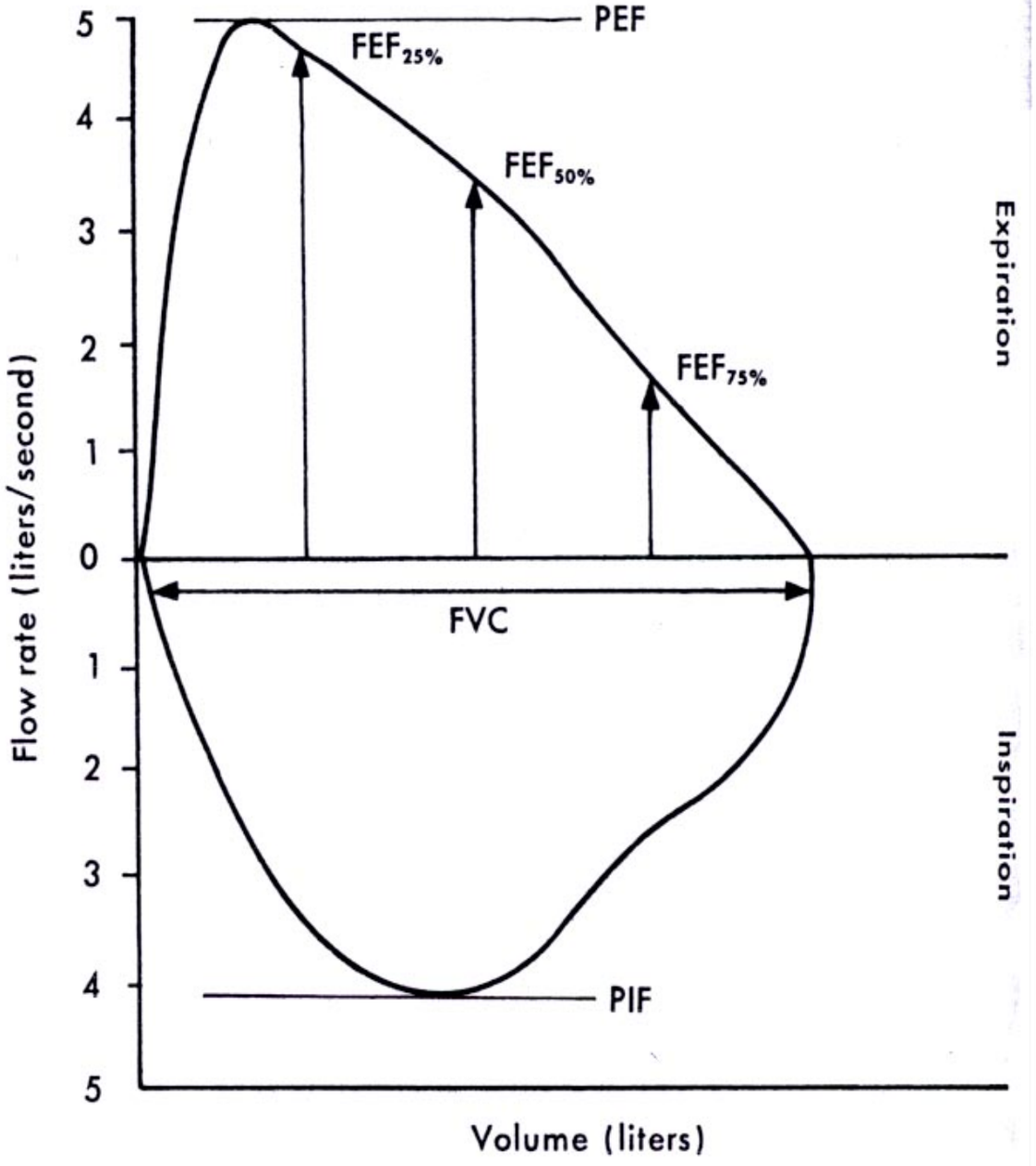
PATHOLOGY: CHRONIC BRONCHITIS



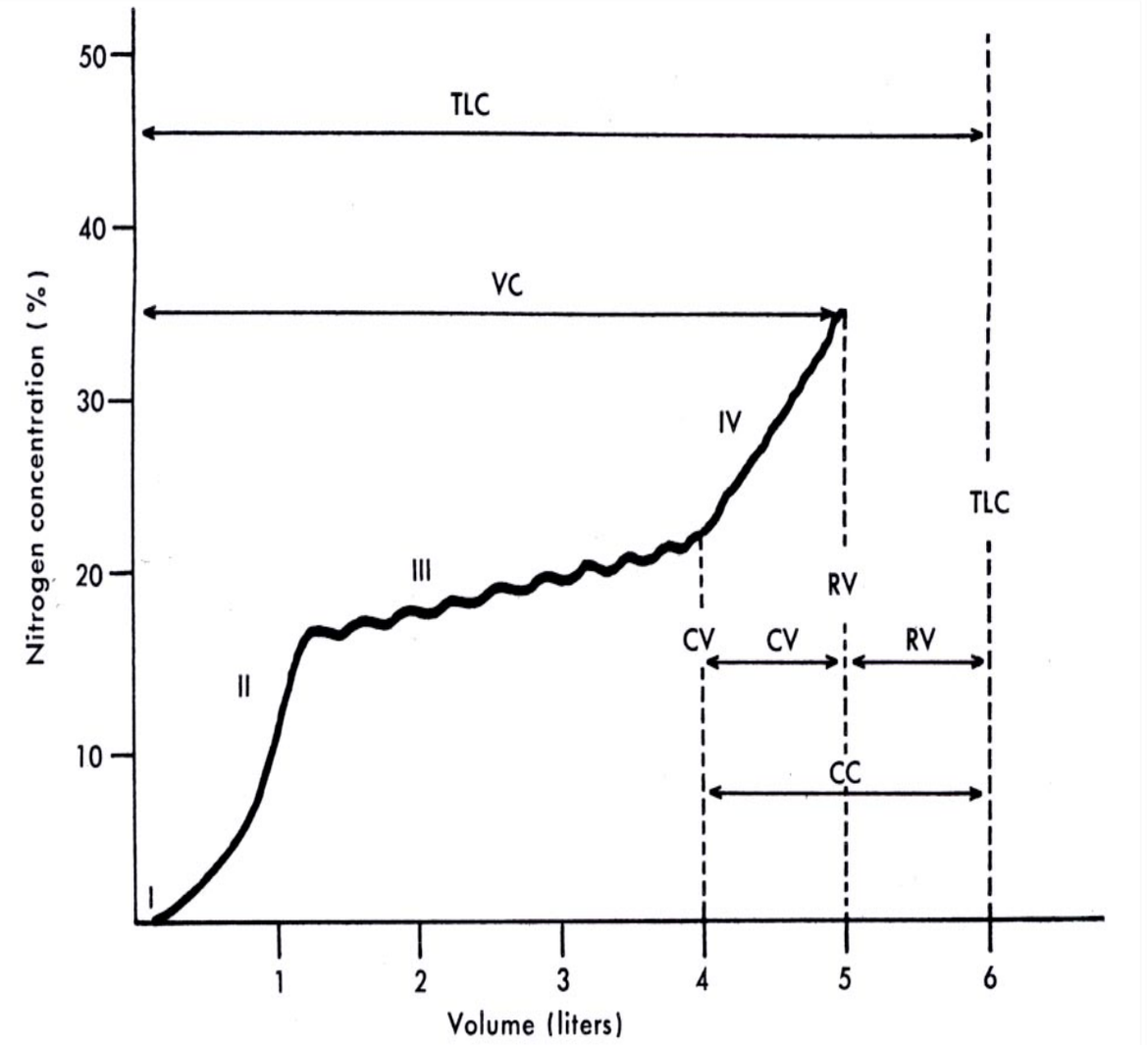
The Reid Index. The percentage of bronchial wall thickness occupied by gland tissue is known as the Reid Index, and is used as a measure of chronic bronchitis.

BRONCHIECTASIS





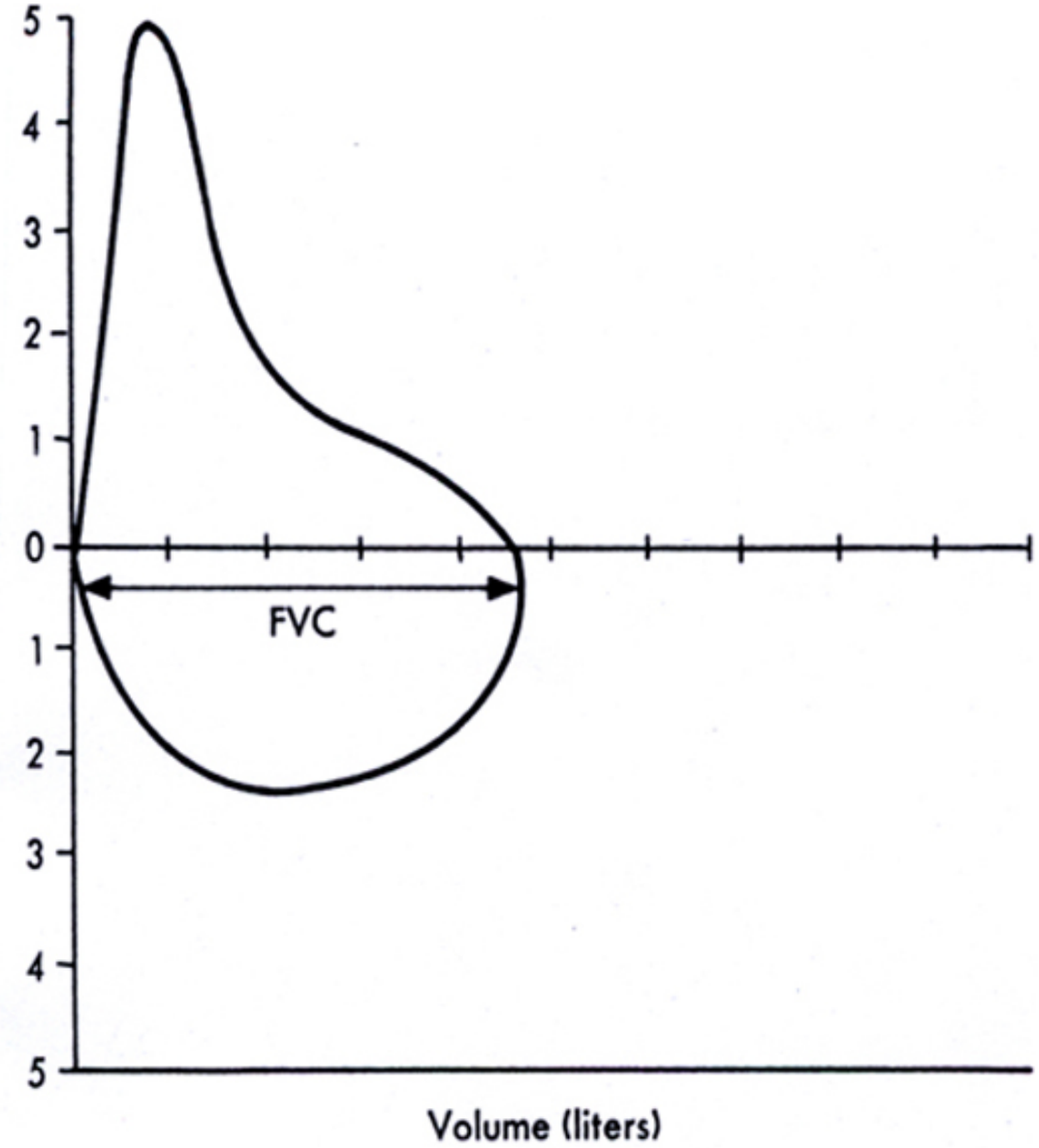
Flow volume loop. *PEF*, Peak expiratory flow; *PIF*, peak inspiratory flow; *FEF%*, forced expiratory flow at x% of FVC; *FVC*, forced vital capacity.

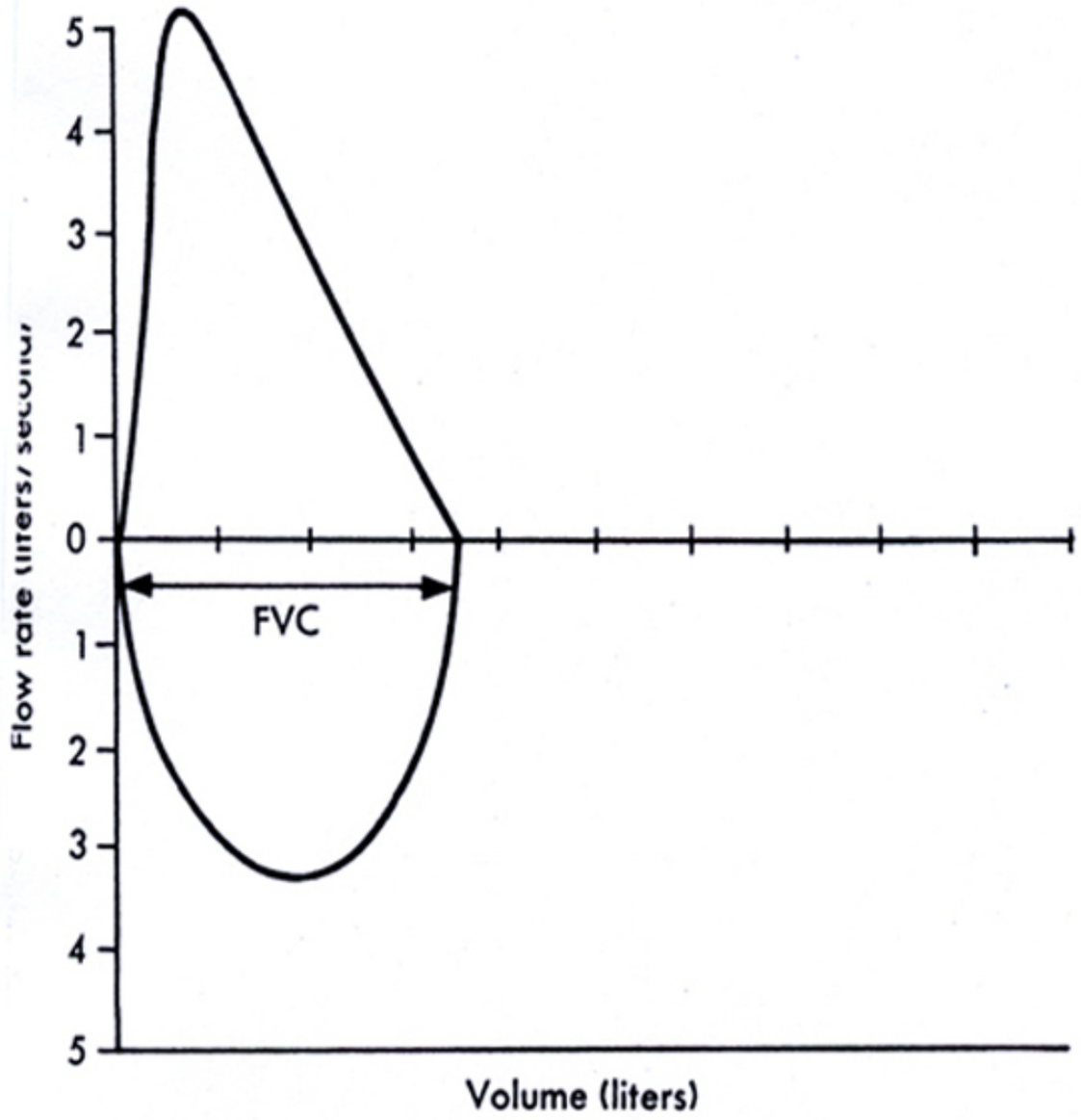


Single-breath nitrogen test curve for measuring closing volume and capacity. *Phase I*, expired dead space gas; *phase II*, mixed dead space and alveolar gas; *phase III*, alveolar plateau; *phase IV*, airway closure.

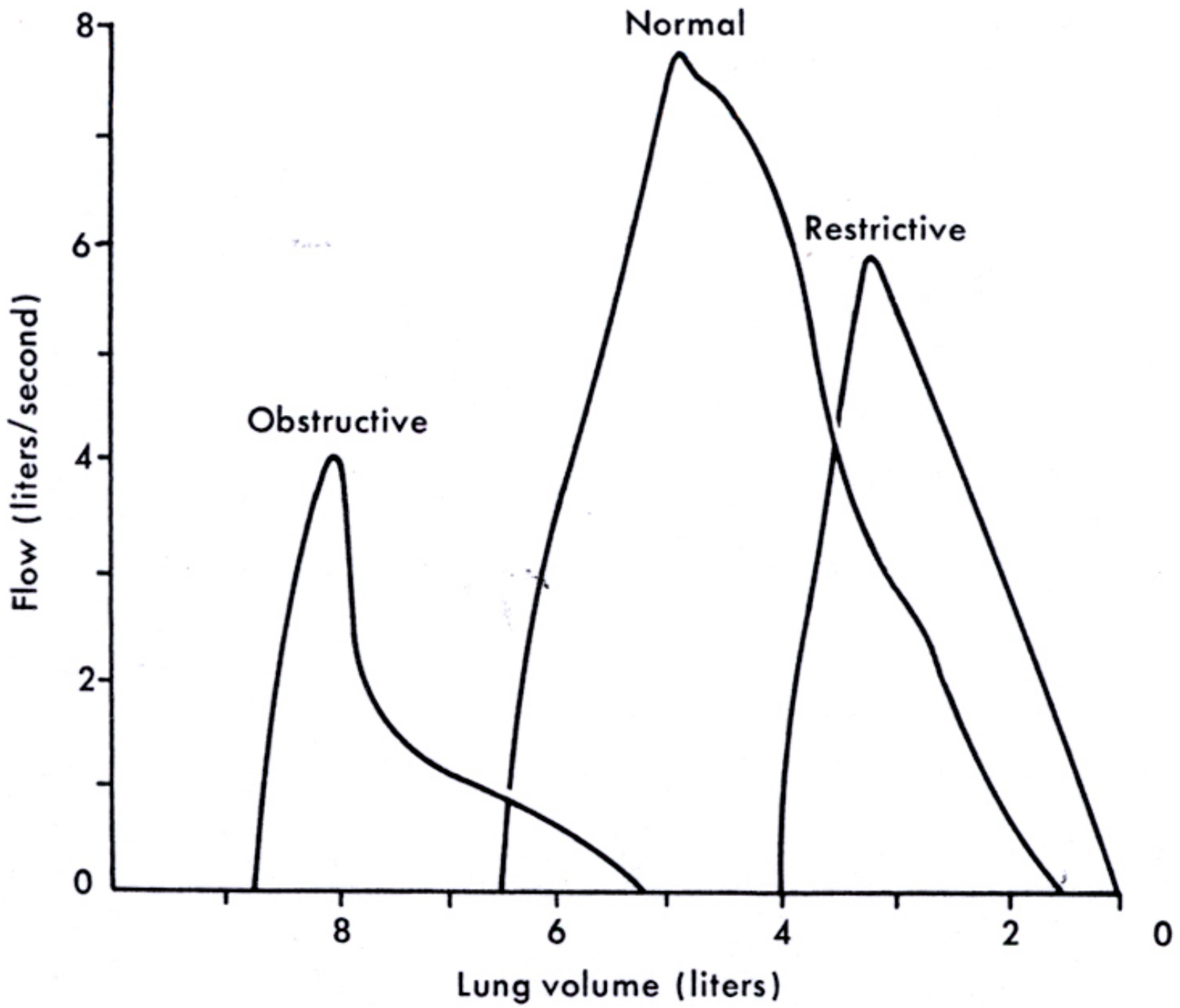
PARENCHYMAL DISEASE

- consolidation - infection - typical/atypical
- Oedema - cardiac vs non-cardiac (ARDS)
- interstitial lung disease - idiopathic fibrosis, sarcoidosis, hypersensitivity pneumonitis, pneumoconiosis
- Vascular – secondary/primary PHT, cor pulmonale, pulmonary thrombo-embolism (unexplained dyspnea); Virchow triade: stasis, ↑ coagulability, blood vessel abnormality, varicose veins, endothelial dysfunction → ↑DVT risk





Flow volume loops comparing, A, obstructive and, B, restrictive disorders.



Maximum expiratory flow volume curve example comparing normal with obstructive and restrictive disorders. Displayed as flows at actual lung volumes.

PARENCHYMAL DISEASE

- consolidation - infection - typical/atypical
- Oedema - cardiac vs non-cardiac (ARDS)
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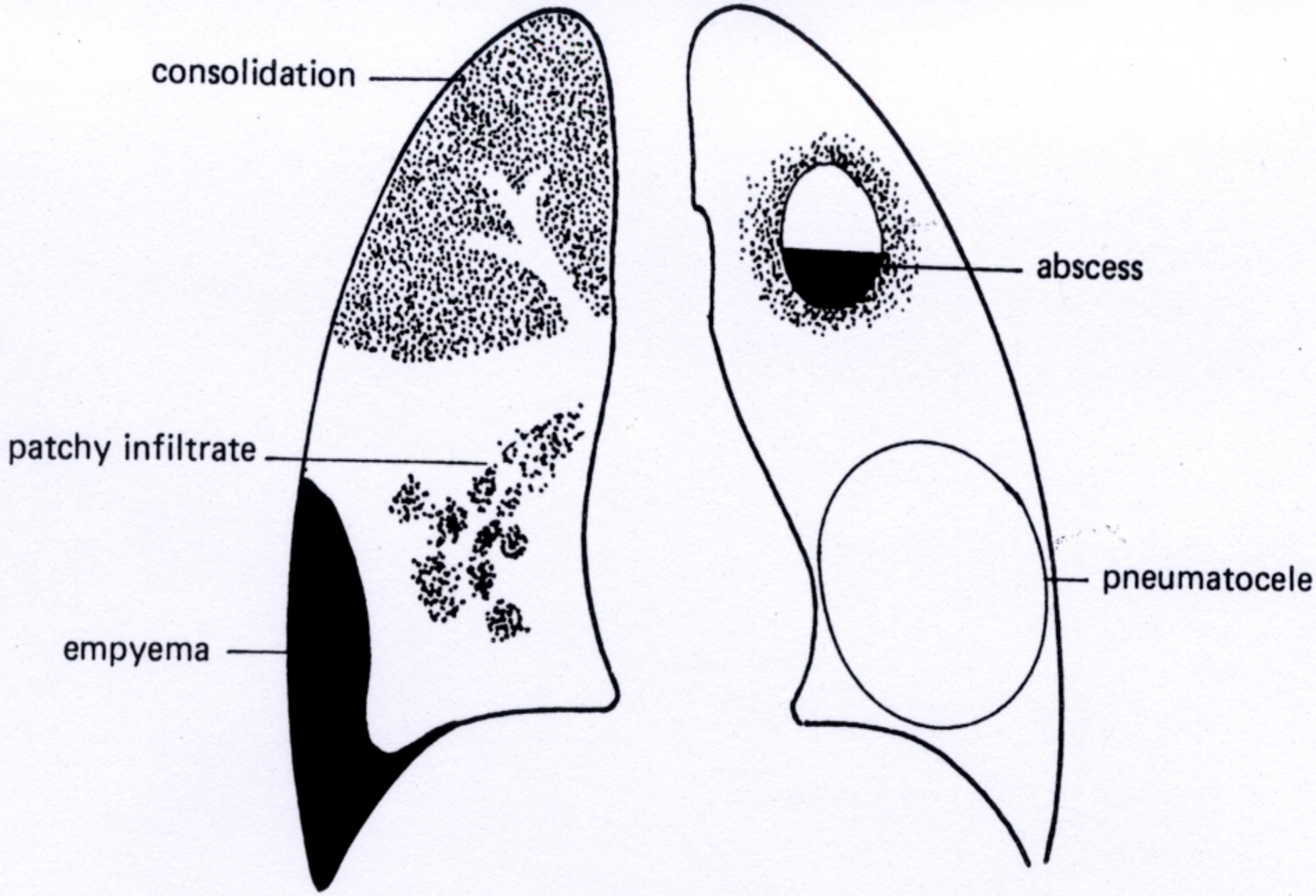


Schema of various radiographic manifestations of staphylococcal pneumonia. (From Farzan S: A concise handbook of respiratory diseases, ed 2, East Norwalk, Conn, 1985, Appleton & Lange.)

PLEURAL DISEASE

- Pleural effusion: alb, LDH, pleural/serum, cholesterol, glucose, ADA, pH.
- exudate: infection, inflammation, neoplastic, blood (↑ permeability)
- transudate: hypoproteinemia (renal, liver - ↓ oncotic pressure), systemic venous hypertension (↑ hydrostatic pressure - Heart failure)
- Empyema
- Chylothorax, pseudo-chylothorax

NEOPLASTIC DISEASE

- Bronchus Ca: squamous, small cell ca, adeno ca, large cell ca, broncho-alveolar ca
- Mesothelioma
- Metastatic ca
- Rare tumours: lymphoma, malt-lymphoma
- Benign tumours

HOW IS DISEASE OF THE RESPIRATORY SYSTEM RECOGNIZED?

CLINICAL MANIFESTATIONS

- Dyspnea, PND, orthopnea, trepopnea, platypnea and orthodeoxia.
- Cough: productive vs non-productive, volume, character, blood, post-nasal discharge
- Chest pain: ischaemic, pleuritic, chest wall, GE reflux, tearing of tissue
- Constitutional: fever, night sweats, weight loss
- RHF: swelling, pain R hypochondrium, abdominal distention, palpitations

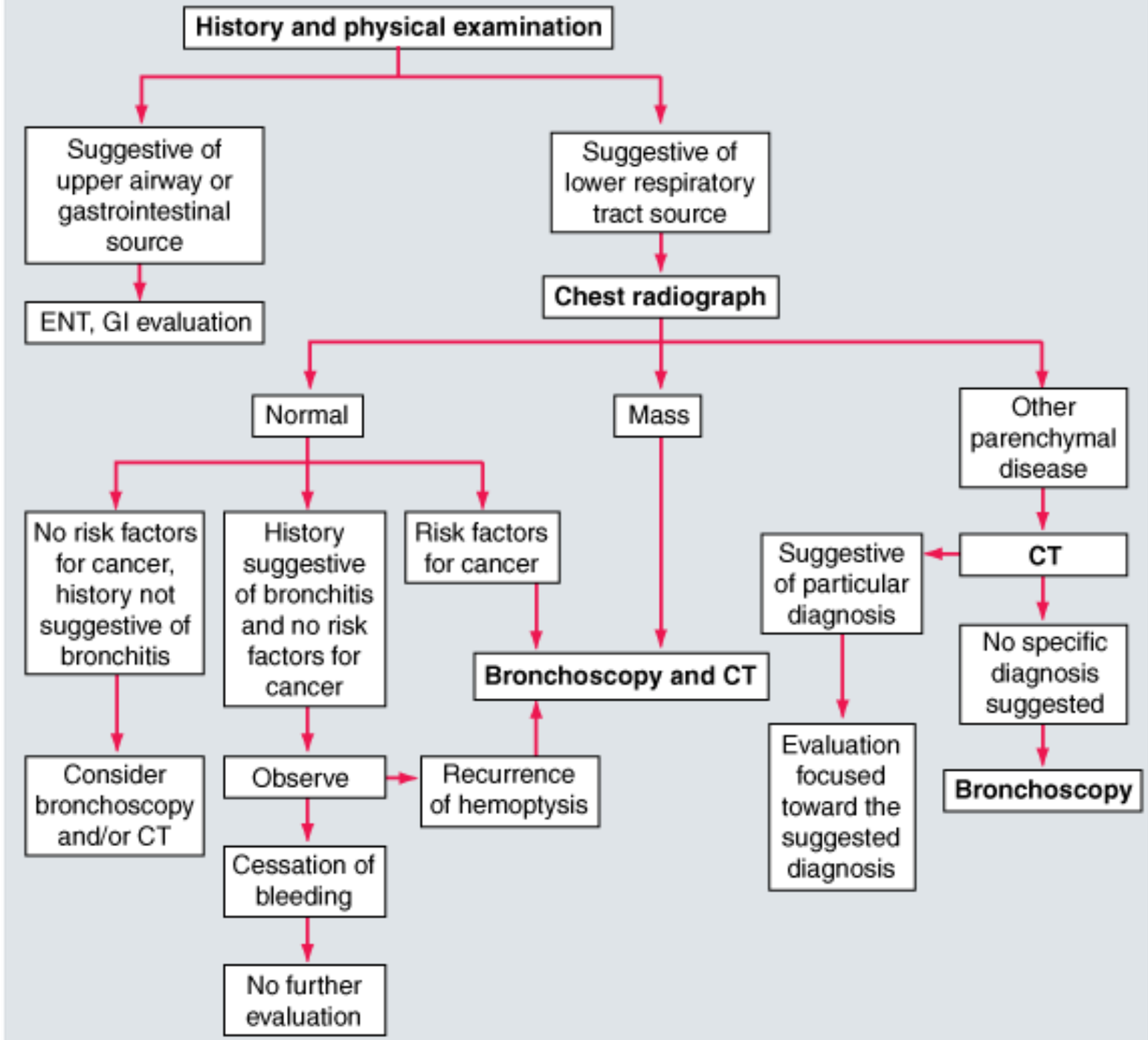
HEMOPTYSIS

- Upper airway: nasopharyngeal, GIT
- Tracheobronchial: neoplasm, bronchitis, bronchiectasis, trauma, foreign body
- Parenchyma: pneumonia, lung abscess, TB, mycetoma, SLE, Wegeners, Goodpasture, lung contusion
- Primary vascular disease: AV malformations, pulmonary embolism, ↑pulmonary venous pressure
- Others: Systemic coagulopathy, anticoagulants, pulmonary endometriosis

MASSIVE HEMOPTYSIS

- 100 – 250 ml blood per day
- Causes: most frequently PTB and bronchiectasis
- Rx: maintain oxygenation and prevent blood spilling into unaffected regions, avoid asphyxiation
- Suppress cough
- Invasive management: double lumen endotracheal tube or balloon catheter to seal off site of bleeding, mechanical ventilation, laser phototherapy, embolotherapy, resection

Evaluation of Nonmassive Hemoptysis



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

RESPIRATORY SYSTEM

- signs of respiratory distress,
- hyperinflation,
- consolidation,
- pleural effusion,
- pneumothorax,
- sup vena cava obstruction

PHYSICAL SIGNS

- General: Cyanosis, anaemia, *jaundice,* oedema, lymphadenopathy, clubbing
- Respiratory examination:
- Observation
- Palpation
- Percussion
- Auscultation

APPLICATION OF ADVENTITIOUS LUNG SOUNDS

Lung sounds	Possible mechanism	Characteristics	Causes
Wheezes	Rapid airflow through obstructed airways caused by bronchospasm, mucosal edema	High-pitched; most often occur during exhalation	Asthma, congestive heart failure, bronchitis
Stridor	Rapid airflow through obstructed airway caused by inflammation	High-pitched; often occurs during inhalation	Croup, epiglottitis, postextubation
Crackles			
Insp & exp	Excess airway secretions moving with airflow	Coarse and often clear with cough	Bronchitis, respiratory infections
Early insp	Sudden opening of proximal bronchi	Scanty, transmitted to mouth; not affected by cough	Bronchitis, emphysema, asthma
Late insp	Sudden opening of peripheral airways	Diffuse, fine; occur initially in dependent regions	Atelectasis, pneumonia, pulmonary edema, fibrosis

Abnormality	Initial impression	Inspection	Palpitation	Percussion	Ausculation	Possible causes
Acute airways obstruction	Appears acutely ill	Use of accessory muscles	Reduced expansion	Increased resonance	Expiratory wheezing	Asthma, bronchitis
Chronic airways obstruction	Appears chronically ill	Increased antero-posterior diameter, use of accessory muscles	Reduced expansion	Increased resonance	Diffuse reduction in breath sounds; early inspiratory crackles	Chronic bronchitis, emphysema
Consolidation	May appear acutely ill	Inspiratory lag	Increased fremitus	Dull note	Bronchial breath sounds; crackles	Pneumonia, tumor
Pneumothorax	May appear acutely ill	Unilateral expansion	Decreased fremitus	Increased resonance	Absent breath sounds	Rib fracture, open wound
Pleural effusion	May appear acutely ill	Unilateral expansion	Absent fremitus	Dull note	Absent breath sounds	Congestive heart failure
Local bronchial obstruction	Appears acutely ill	Unilateral expansion	Absent fremitus	Dull note	Absent breath sounds	Mucous plug
Diffuse intersitial fibrosis	Often normal	Rapid shallow breathing	Often normal; increased fremitus	Slight decrease in resonance	Late inspiratory crackles	Chronic exposure to inorganic dust
Acute upper airway obstruction	Appears acutely ill	Laboured breathing	Often normal	Often normal	Inspiratory or expiratory stridor or both	Epiglottitis, croup, foreign body aspiration

DIAGNOSTIC PROCEDURES

- CXR, CT scan, MRI scan
- Lung functions
- Blood
- Blood gases
- Sputum, cilia function
- Bronchoscopy, biopsy
- Nuclear medicine

HOW CAN DISEASE OF THE RESPIRATORY SYSTEM BE TREATED OR PREVENTED?

TREATMENT/PREVENTION

- Patient education
- Immunization
- Medication: antibiotics, bronchodilators, anti-inflammatory drugs,diuretics, anti-coagulants
- Ventolators
- Physiotherapy
- Surgery

WHY DO YOU HAVE TO KNOW ALL THIS?

BECAUSE SO THAT YOU CAN ONE DAY SAY:
" TRUST ME, I AM YOUR DOCTOR!"