MUNI
MED

Respiratory system
&
Lung diseases

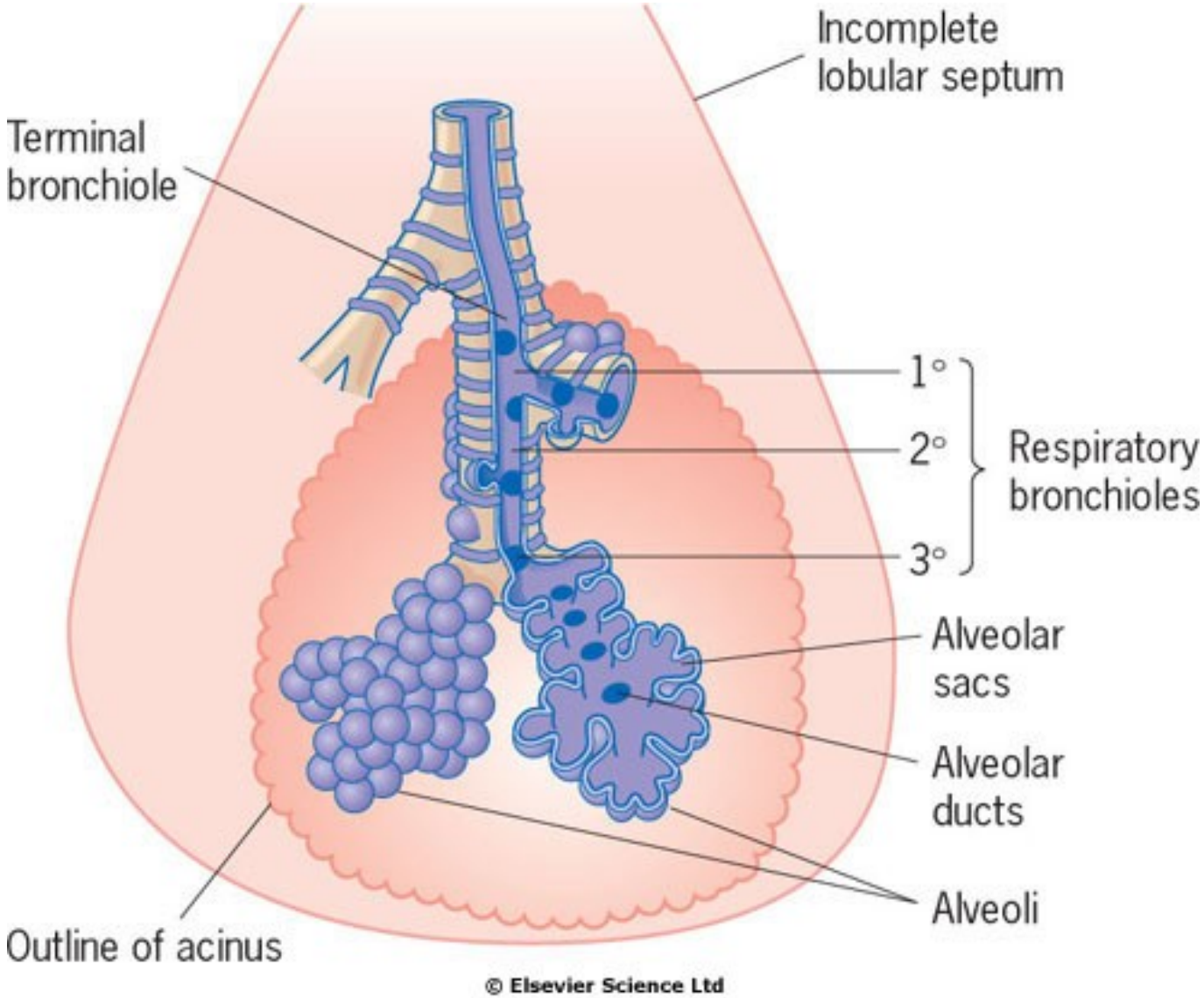
Points

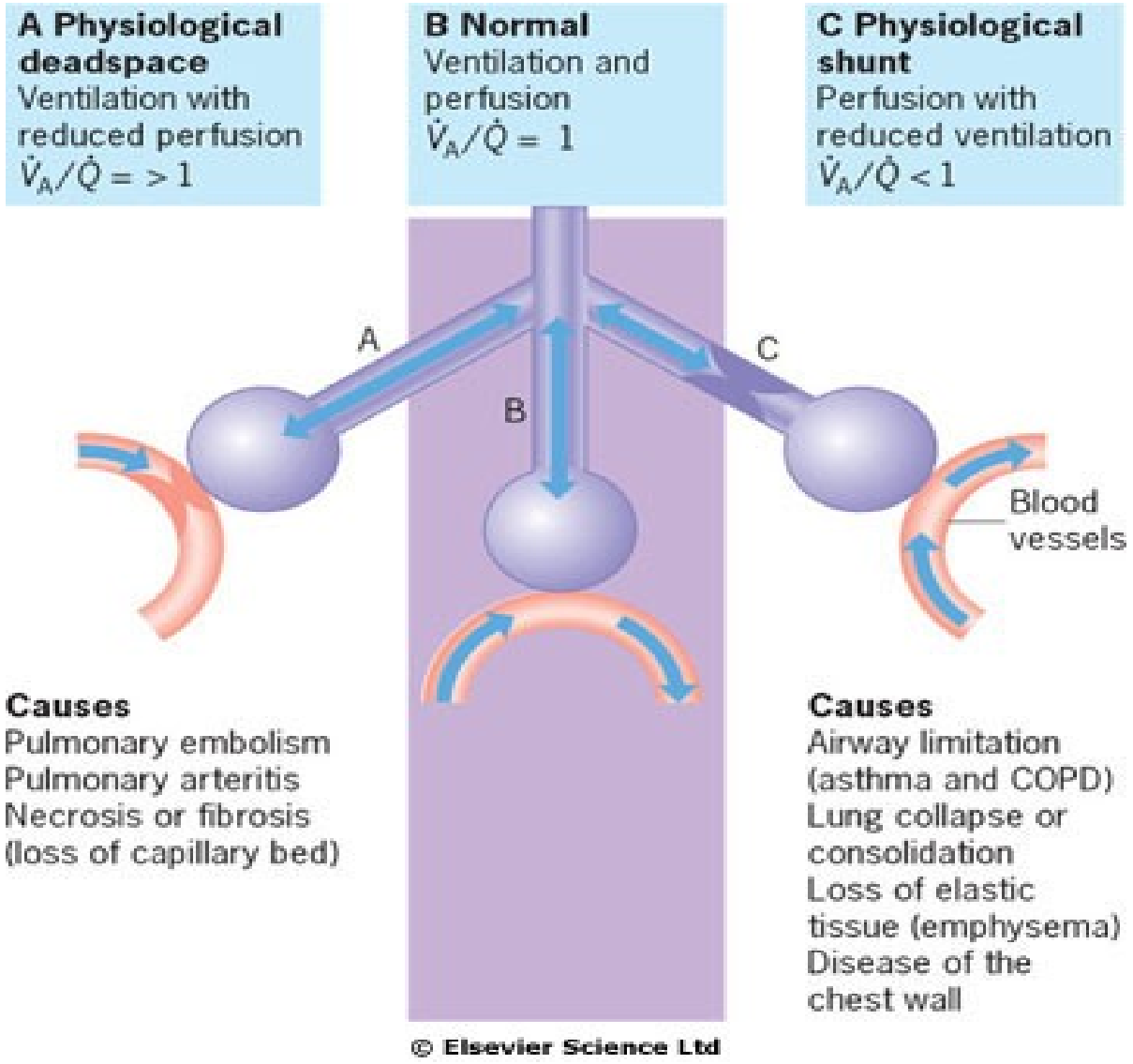
- Ventilation
- Diffusion
- Perfusion

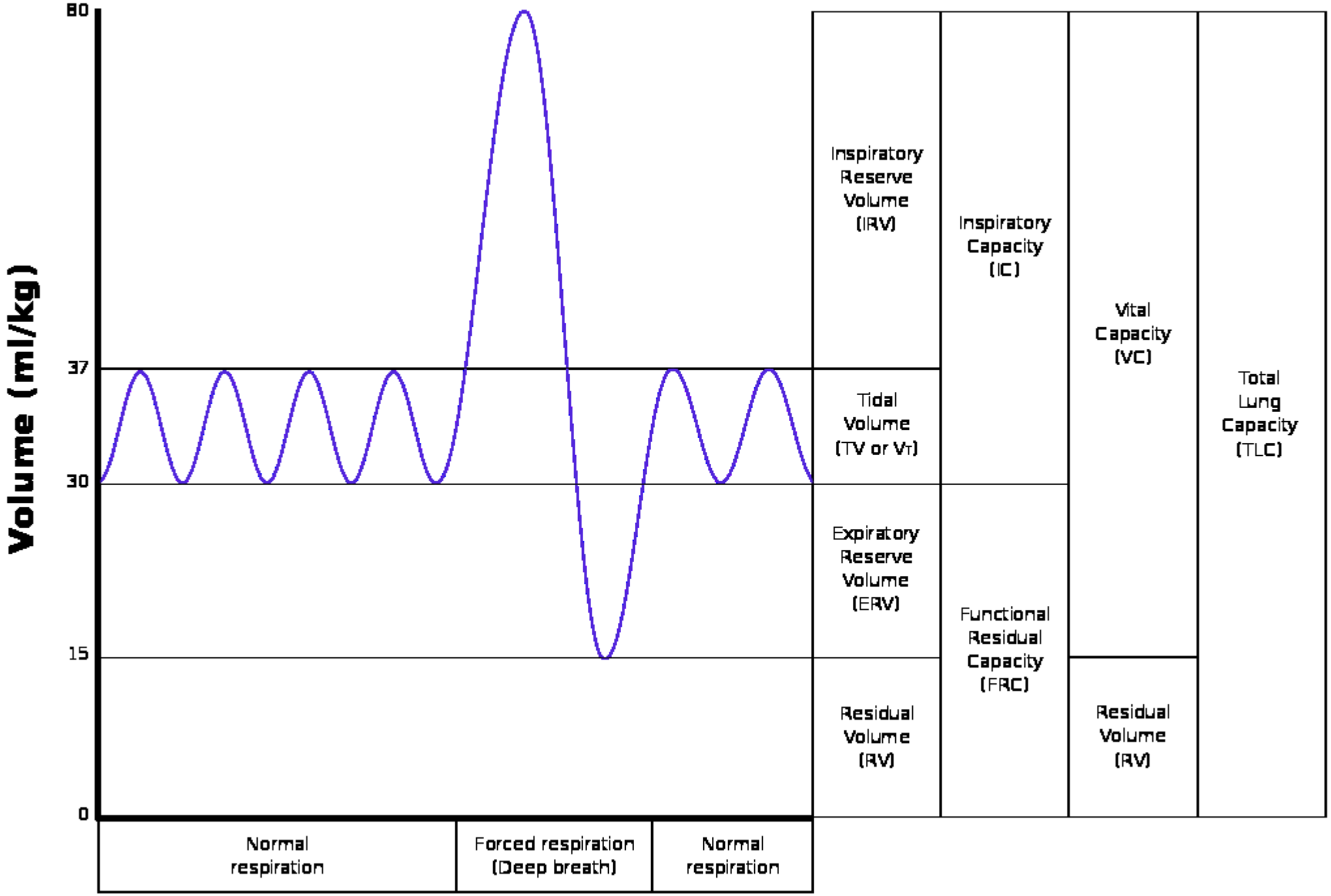
MUNI MED

Breathing

- Lung ventilation can be considered in two parts:
- the mechanical process of inspiration and expiration
- the control of respiration to a level appropriate for the metabolic needs.


Incomplete
lobular septum
Terminal
bronchiole
1°
2°
3°
Respiratory
bronchioles
Alveolar
sacs
Alveolar
ducts
Alveoli
Outline of acinus
© Elsevier Science Ltd


A Physiological deadspace
Ventilation with reduced perfusion
$\dot{V}_A/\dot{Q} = > 1$
B Normal
Ventilation and perfusion
$\dot{V}_A/\dot{Q} = 1$
C Physiological shunt
Perfusion with reduced ventilation
$\dot{V}_A/\dot{Q} < 1$
A
B
C
Blood vessels
Causes
Pulmonary embolism
Pulmonary arteritis
Necrosis or fibrosis (loss of capillary bed)
Causes
Airway limitation (asthma and COPD)
Lung collapse or consolidation
Loss of elastic tissue (emphysema)
Disease of the chest wall
© Elsevier Science Ltd


Volume (ml/kg)
80
37
30
15
0
Inspiratory Reserve Volume (IRV)
Tidal Volume (TV or VT)
Expiratory Reserve Volume (ERV)
Residual Volume (RV)
Inspiratory Capacity (IC)
Functional Residual Capacity (FRC)
Vital Capacity (VC)
Residual Volume (RV)
Total Lung Capacity (TLC)
Normal respiration
Forced respiration (Deep breath)
Normal respiration

Lung Volume Patterns

- **Obstructive Disease**: Characterized by hyperinflation and gas trapping (increased TLC and RV/TLC)
  - asthma, chronic COPD (bronchitis, emphysema)

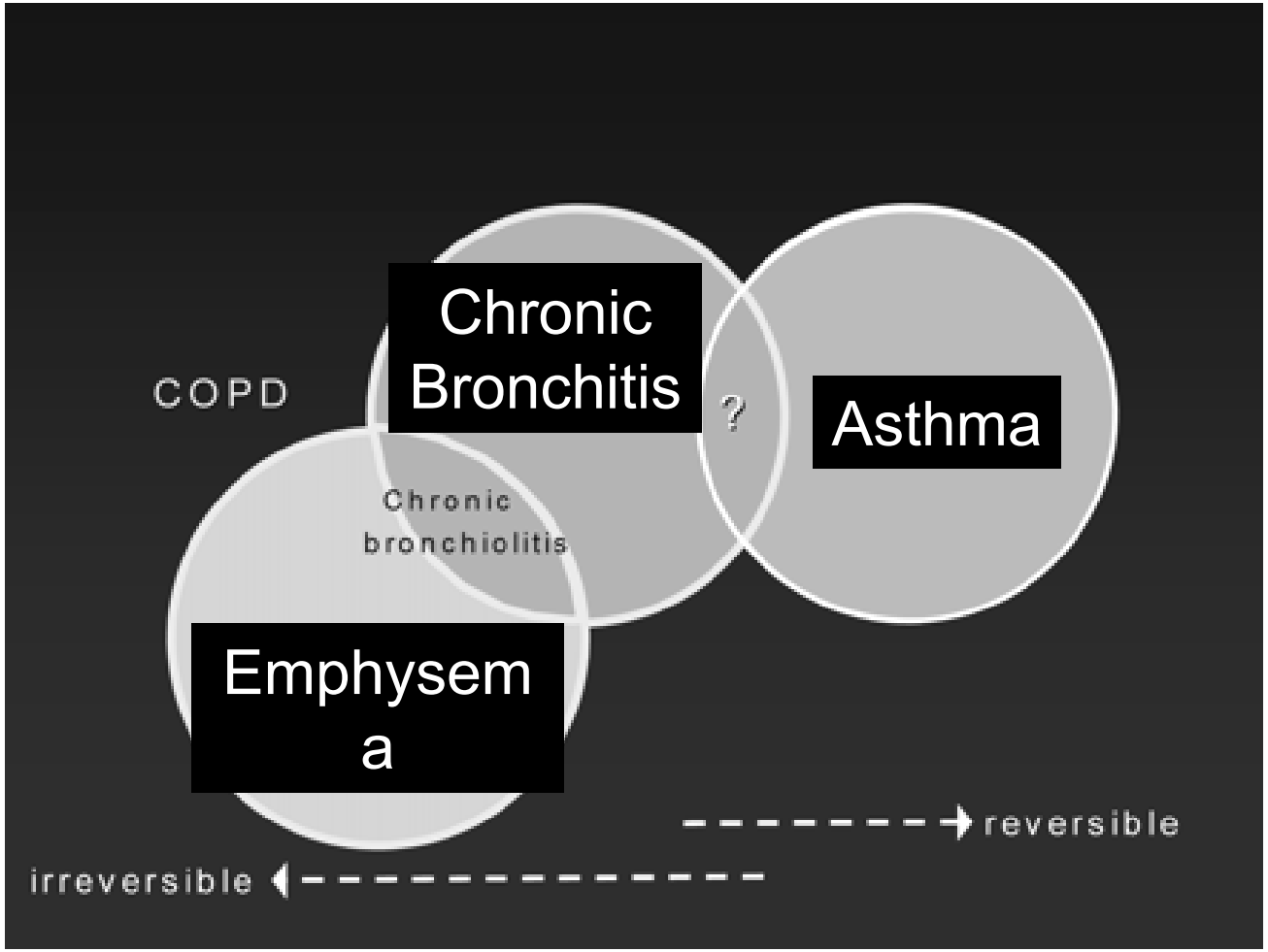
- **Restrictive Disease**: Characterized by generalized reduction in lung volume (decreased TLC, RV and FRC)
  - interstitial lung diseases (pulmonary fibrosis, sarcoidosis), pneumothorax, lung resection

Obstructive pulmonary diseases

- They are characterized by airway obstruction that is worse with expiration.
- Either more force (i.e., use of accessory muscles of expiration) is required to expire a given volume of air or emptying of the lungs is slowed or both.
- The unifying symptom of obstructive disease is dyspnea, the unifying sign is wheezing.

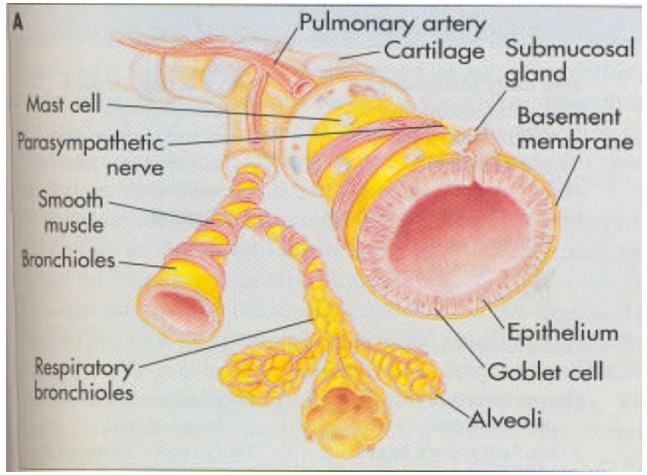
- The most common obstructive diseases are asthma, chronic bronchitis and emphysema.
- Because many individuals have both bronchitis and emphysema, they are often called COPD

Spectrum of Obstructive Lung Disease Syndromes

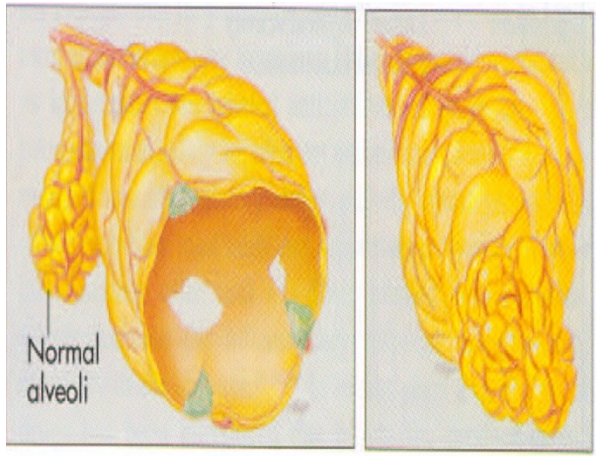


Airway obstruction caused by emphysema, chronic bronchitis, and asthma

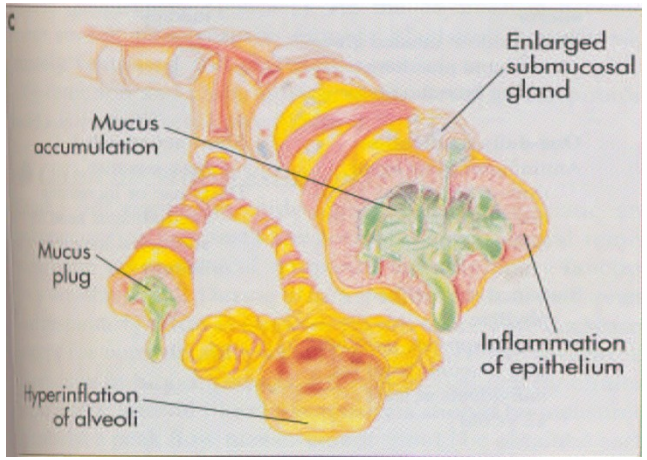
Normal lung



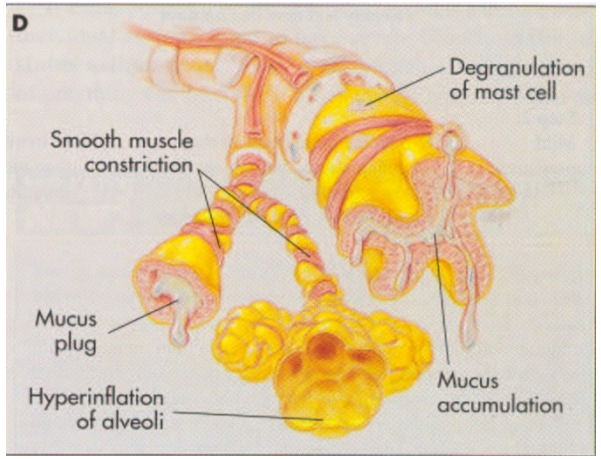
Emphysema



Bronchitis



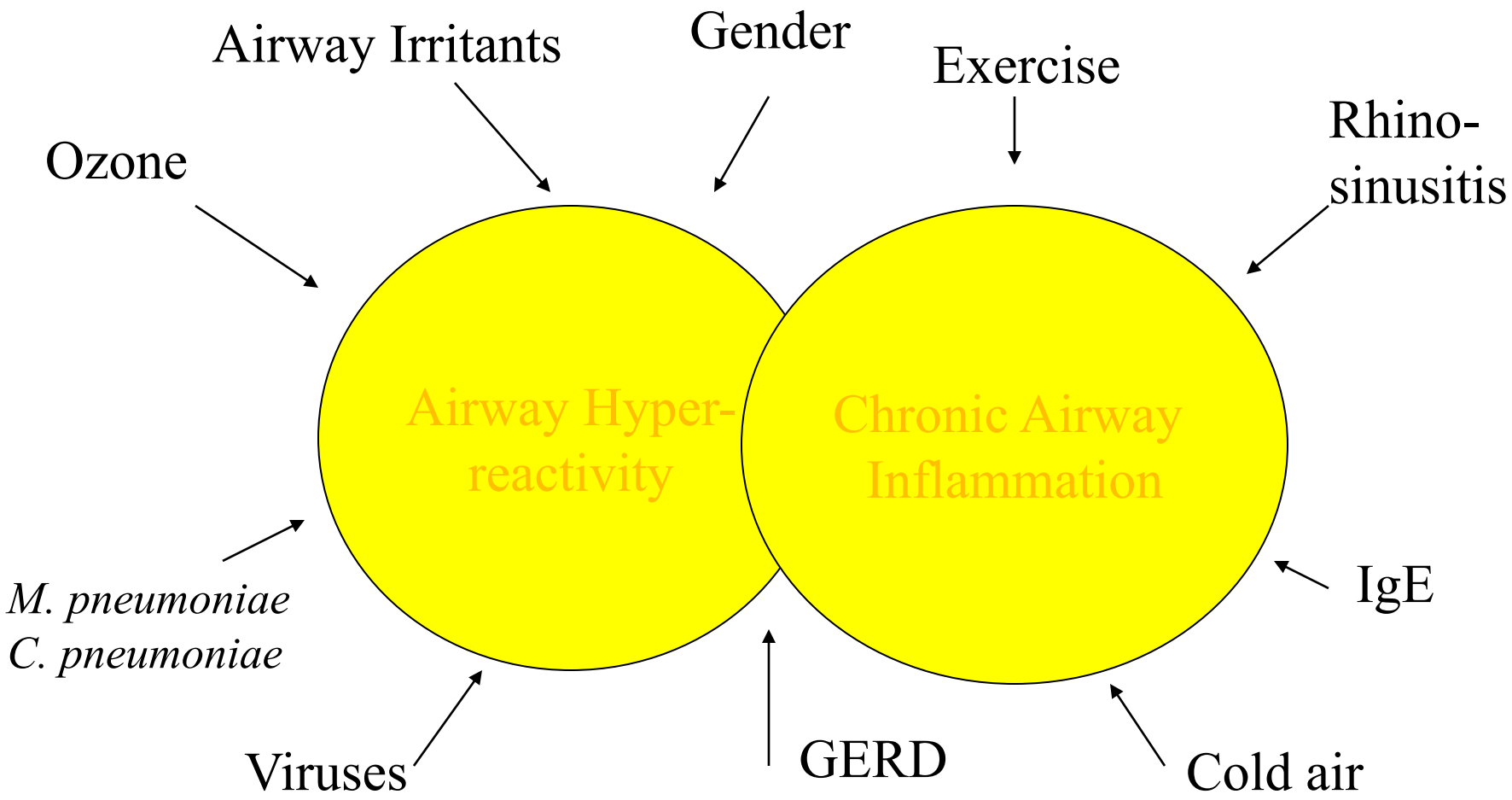
Asthma



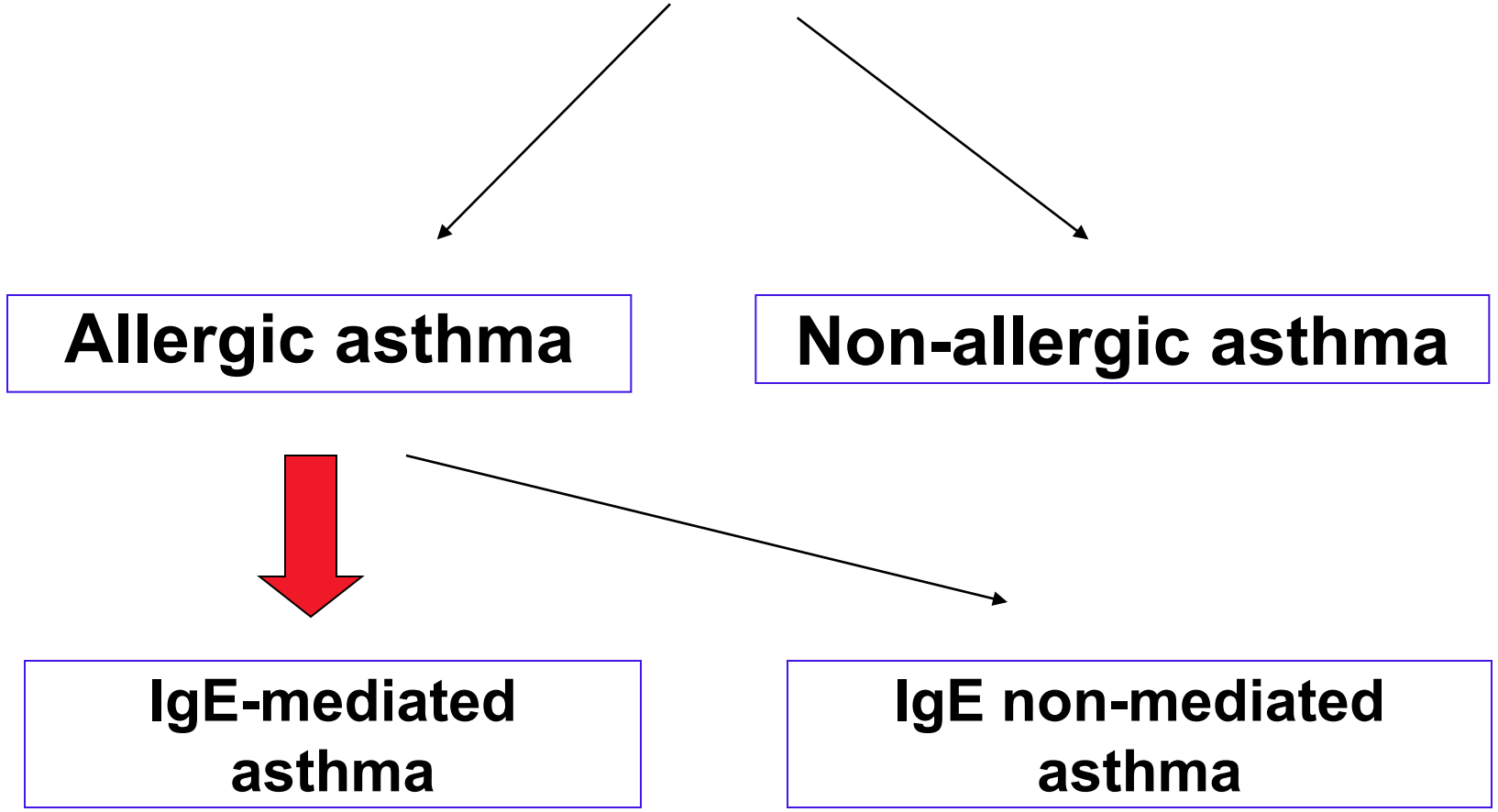
Asthma bronchiale

- **Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role.**
- **The chronic inflammation causes an associated increase in airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning.**
- **These episodes are usually associated with widespread but variable airway obstruction that is often reversible either spontaneously or with treatment.**

Asthma Pathogenesis



Types of asthma

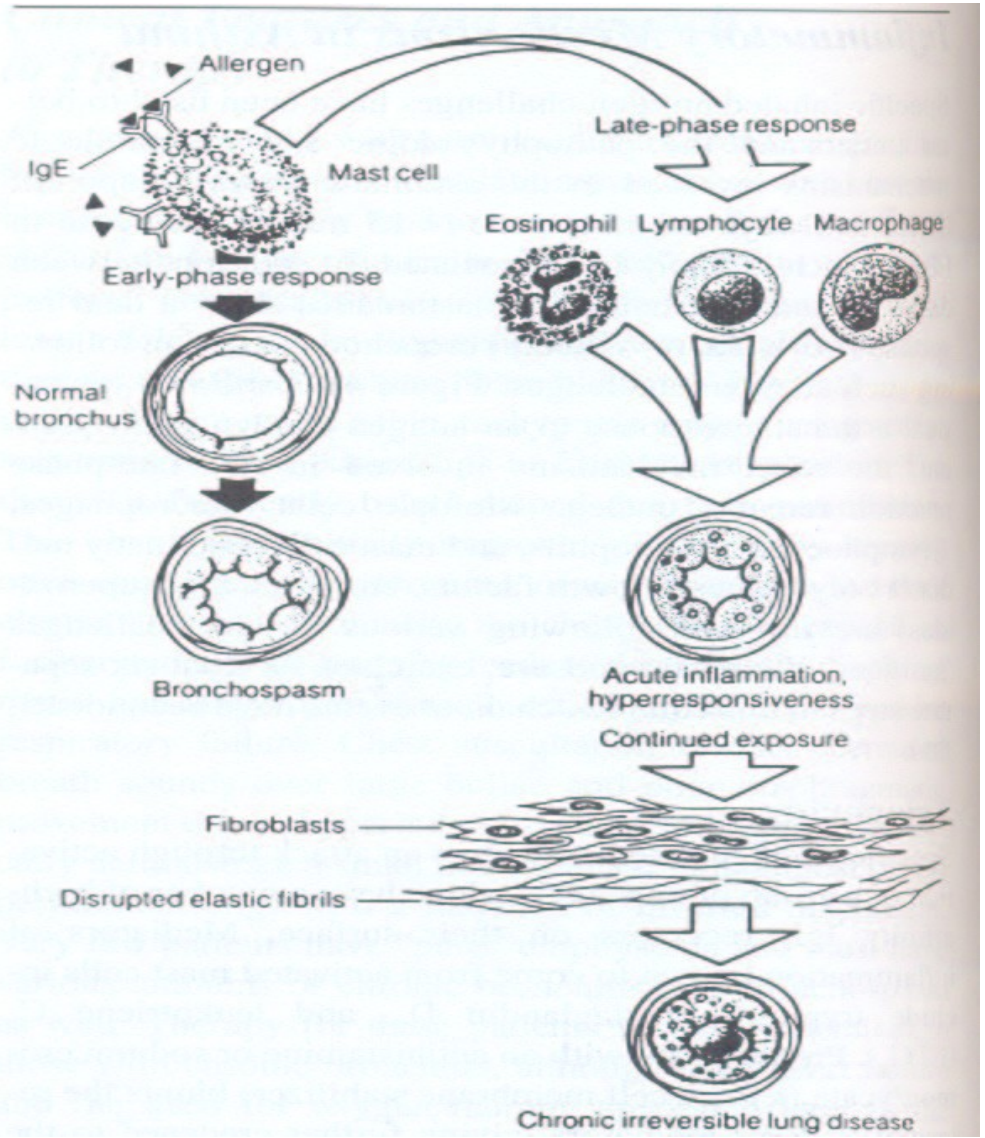


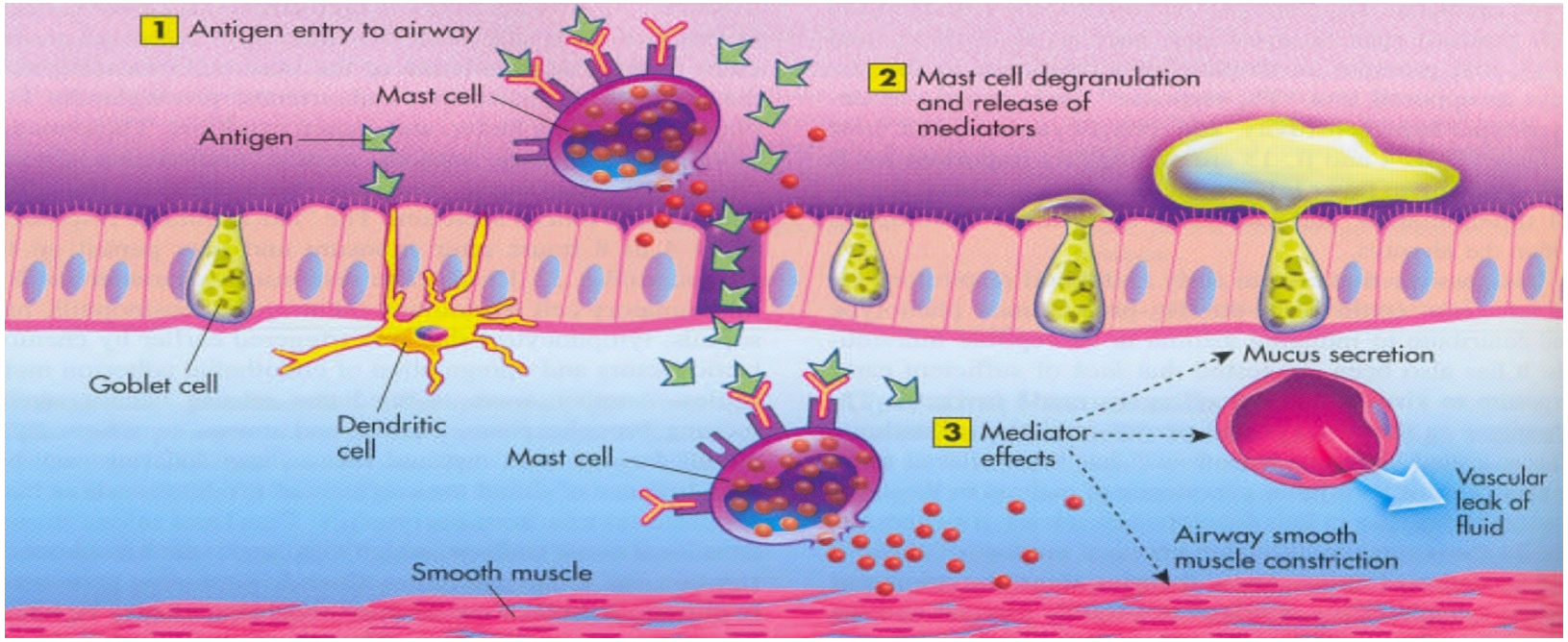
Allergic asthma

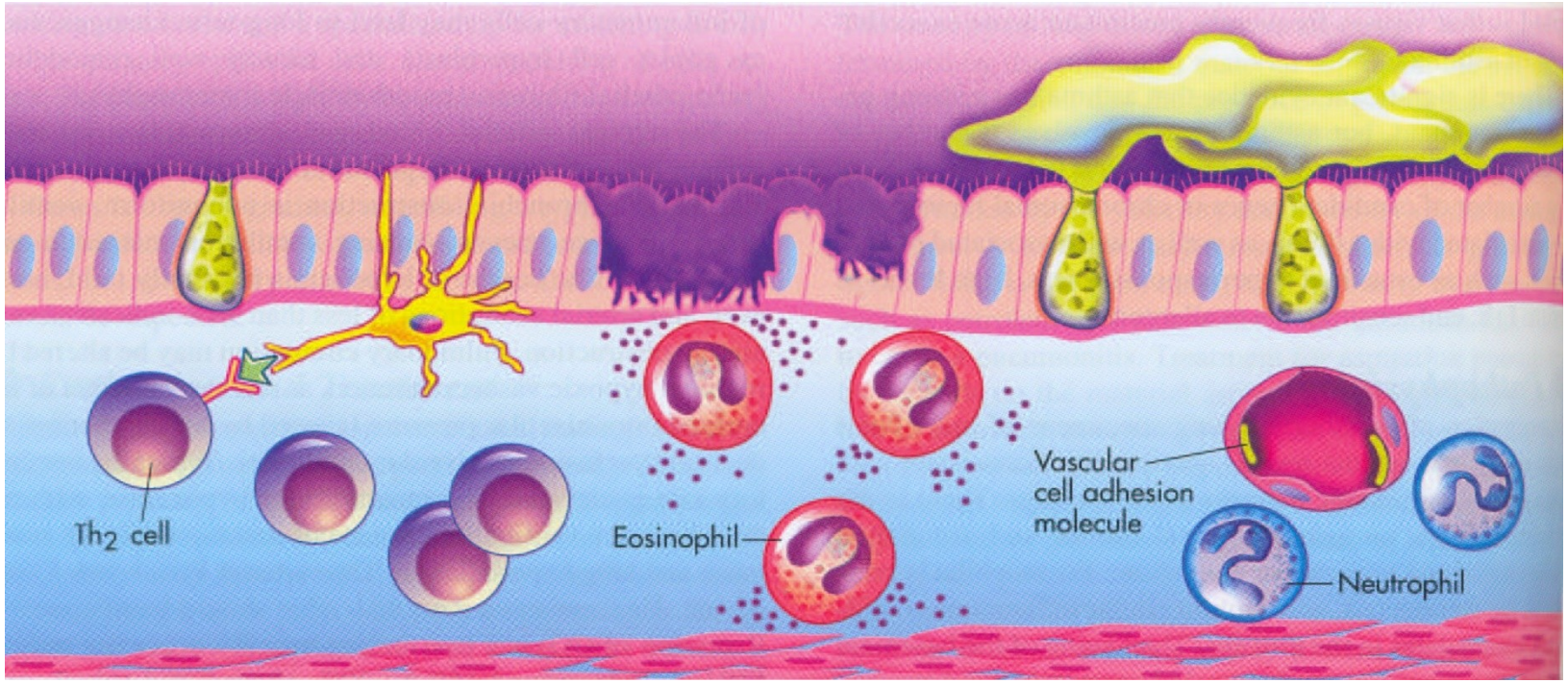
Asthma response

Early phase

Late phase




1 Antigen entry to airway
Mast cell
Antigen
2 Mast cell degranulation and release of mediators
Goblet cell
Dendritic cell
Mast cell
3 Mediator effects
Mucus secretion
Vascular leak of fluid
Airway smooth muscle constriction
Smooth muscle


Th2 cell
Eosinophil
Vascular cell adhesion molecule
Neutrophil

Asthma classification based on severity

- Mild intermitent
- Mild persistent
- Moderate persistent
- Severe persistent

Determining Asthma Severity

Asthma – clinical manifestations

- **During full remision**
  - Individuals are asymptomatic and pulmonary function tests are normal.
- **During partial remision**

  There are no clinical symptoms but pulmonary function tests are abnormal

- **During attacks**
  - Individuals are dyspneic and respiratory effort is marked
  - Breath sounds are ecreased except for considerable wheezing, dyspnea, non-productive coughing, tachycardia and tachypnea occur

Asthma - pulmonary function

- Spirometry shows decreases in expiratory flow rate, forced expiratory volume (FEV), and forced vital capacity (FVC)
- FRC and total lung capacity (TLC) are increased.
- Blood gas analysis shows hypoxemia with early respiratory alkalosis or late respiratory acidosis.

Treatment

Goals:

- To reverse of acute attacks
- To control recurrent attacks
- To reduce bronchial inflammation and the associated hyperreactivity
- + elimination of allergens (if it is possible)

Drugs:

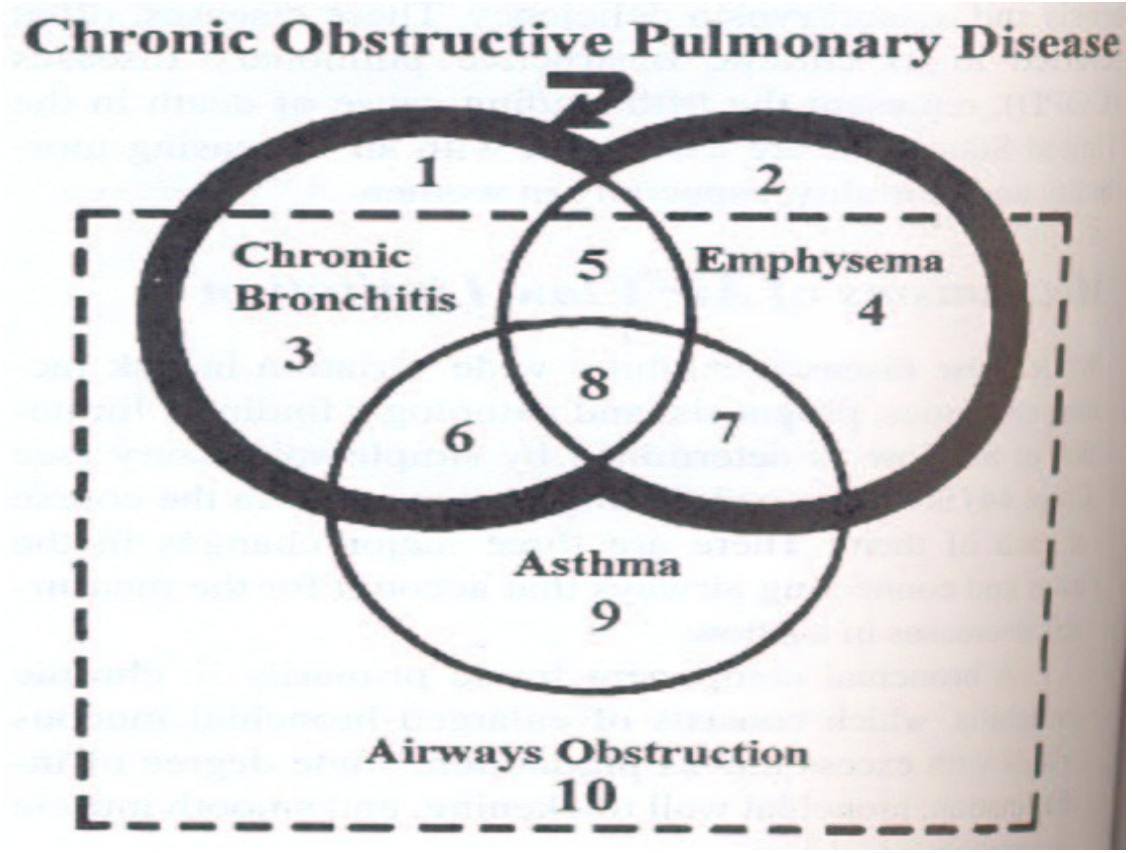
- Allergen´s immunotherapy
- Bronchodilator (Beta agonists, Anticholinergic agents, Theophylline)
- Immunosuppressant (corticosteroids)
- Others (Leukotriene modifiers, antihistamine, e.g.)

Chronic obstructive pulmonary disease (COPD)

- COPD is defined as pathologic lung changes consistent with emphysema or chronic bronchitis.
- It is syndrome characterized by abnormal tests of expiratory airflow that do not change markedly over time, and without a reversible response to pharmacological agents.

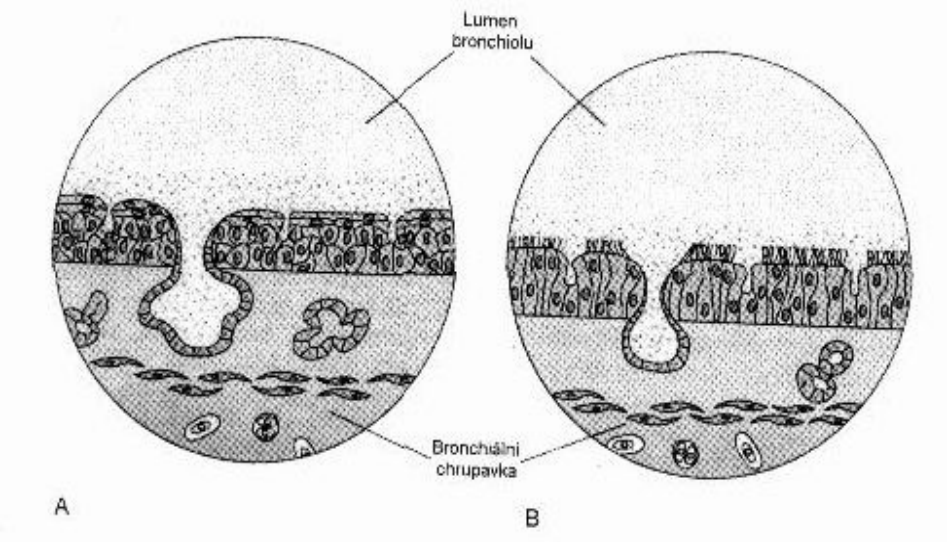
- 5-20% adult population
- Most frequently in men
- The fifth leading cause of death

The complex, heterogenous overlapping of the three primary diagnoses include under diseases of air flow limitation is present on the next picture:



1. Chronic bronchitis

- Chronic bronchitis is defined as hypersecretion of mucus and chronic productive cough that continues for at least 3 months of years for at least 2 consecutive years.
- Incidence is increased in smokers (up to twentyfold) and even more so in workers exposed to air pollution.
- It is a major health problem for the elderly population. Repeated infections are common.



Chronic bronchitis - etiology

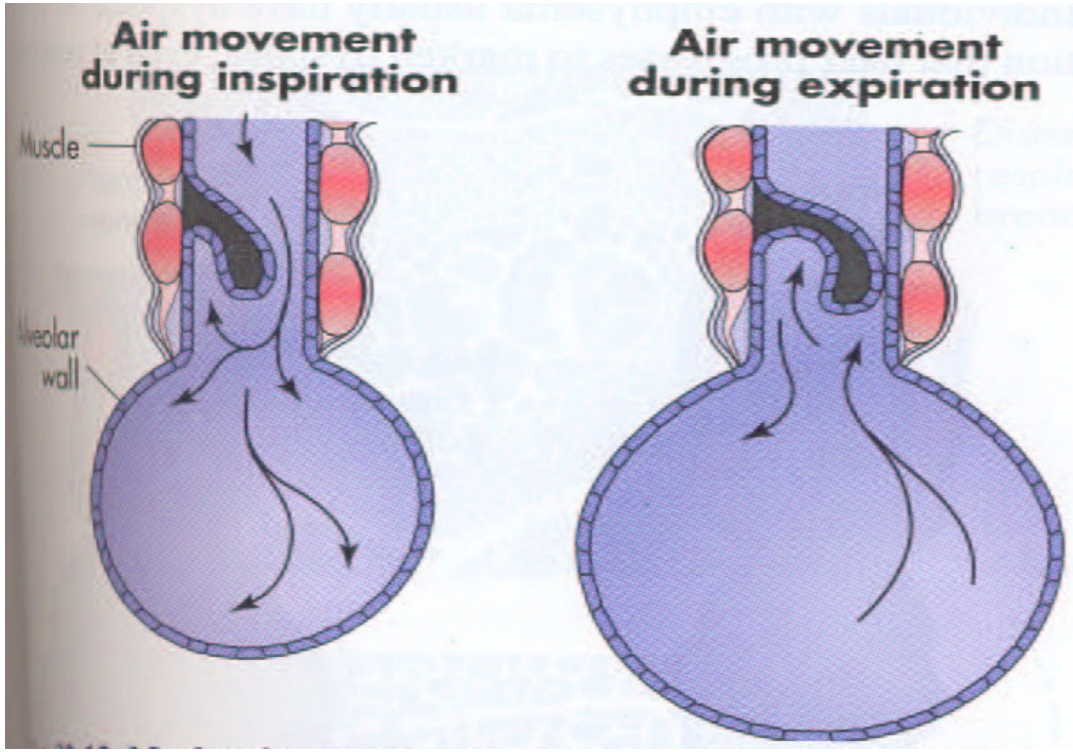
- It is primarily caused by cigarette smoke, both active and passive smoking have been implicated

- Other risk factors:
  - profesional exposition
  - air pollution
  - repeated infections of airways
  - genetics

Chronic bronchitis - morphology

- Inspired irritants not only increase mucus production but also increase the size and number of mucous glands and goblet cells in airway epithelium
- The mucus produced is thicker and more tenacious than normal. This sticky mucus coating makes it much more likely that bacteria, such as H. influenze and S. pneumoniae, will become embedded in the airway secretions, there they reproduce rapidly.
- Ciliary function is impaired, reducing mucus clearance further. The lung´s defense mechanisms are tehrefore compromised, increasing susceptibility to pulmonary infection and injury.
- The bronchial walls become inflamed and thickened from edema and accumulation of inflammatory cells.

- Initially chronic bronchitis affects only the larger bronchi, but eventually all airways are involved.
- The thick mucus and hypertrophied bronchial smooth muscle obstruct the airways and lead to closure, particularly during expiration, when the airways are narrowed.
- The airways collapse early in expiration, trapping gas in the distal portions of the lung.
- Obstruction eventually leads to ventilation-perfusion mismatch, hypoventilation (increased $PaCO_2$) and hypoxemia.



Chronic bronchitis – clinical manifestations

- Individuals usually have a productive cough („smoker´s cough“) and evidence of airway obstruction is shown by spirometry

- Bronchitis patients are often described as „blue bloaters“ due to their tendency to exhibit both hypoxemia and right heart failure with peripheral edema in spite of only moderate obstructive changes on pulmonary functional tests.

- Acute episodes (e.g. after infection) result in marked hypoxemia that leads to polycytemia and cyanosis (blueness) associated with an increase in pulmonary artery pressure, impairing right ventricular function, and significant jugular venous distension and ankle edema (bloated)

Chronic bronchitis – evaluation and treatment

- Diagnosis is made on the basis of physical examination, chest radiograph, pulmonary function tests and blood gas analyses.
- The best „treatment“ is prevention, because pathological changes are not reversible.
- If the individuals stops smoking, disease progression can be halted
- Therapy: - bronchodilators
  - expectorans
  - chest physical therapy
  - steroids
  - antibiotics

Chronic bronchitis: low-flow oxygen therapy

- It is administered with care to individuals with severe hypoxemia and CO2 retention
- Because of teh chronic elevation of PaCO2, the central chemoreceptors no longer act as the primary stimulus for breathing.
- This role is taken over by the peripheral chemoreceptors, which are sensitive to changes in PaO2.
- Peripheral chemoreceptors do not stimulate breathing if the PaO2 is much more than 60 mmHg.
- Therefore, if oxygen therapy causes PaO2 to exceed 60 mmHg, the stimulus to breathe is lost, PaCO2 increases, and apnea results.
- If inadequate oxygenation cannot be achieved without resulting in respiratory depression, the individual must be mechanically ventilated)

2. Emphysema

- It is abnormal permanent enlargement of gas-exchange airways (acini) accompanied by destruction of alveolar walls and without obvious fibrosis.
- In emphysema, obstruction results from changes in lung tissues, rather than mucus production and inflammation, as in chronic bronchitis.
- The major mechanism of airflow limitation is loss of elastic recoil.

Types of emphysema

- Three distinctive types of alveolar destruction have been described, according to the portion of the acinus first involved with disease:

1) Centrilobular (centriacinar):

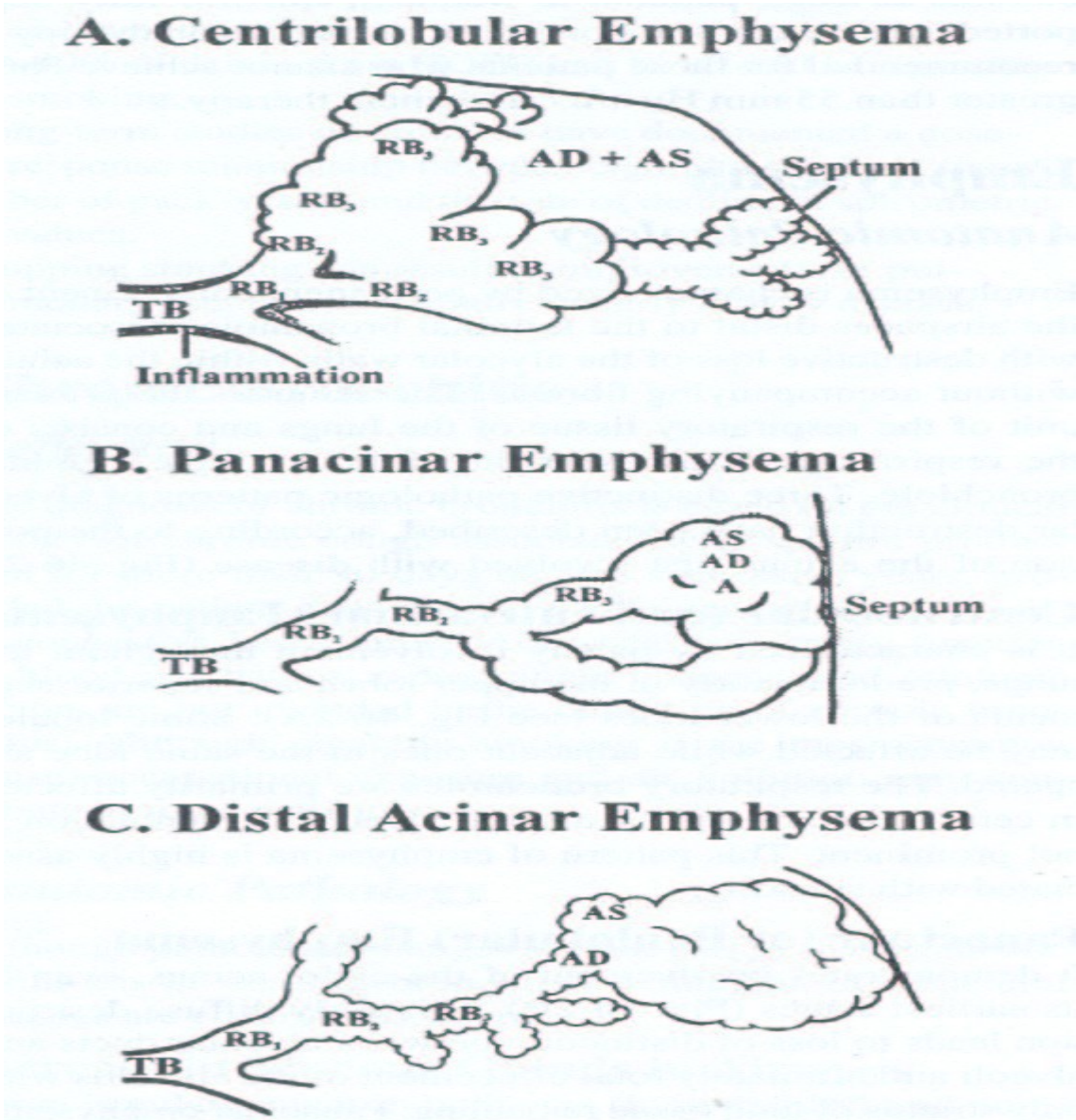
- septal destruction occurs in the respiratory bronchioles and alveolar ducts, usually in the upper lobes of the lung. The alveolar sac (alveoli distal to the respiratory bronchiole) remains intact. It tends to occur in smokers with chronic bronchitis.

2) Panacinar (panlobular):

- It involves the entire acinus with damage more randomly distributed and involving the lower lobes of the lung. It tends to occur in patients with α1-antitrypsin deficiency.

3) Distal acinar (subpleural):

- It is typically seen in a young adult with a history of a spontaneous pneumothorax.


A. Centrilobular Emphysema
RB3
AD + AS
Septum
RB3
RB3
RB2
RB3
RB1
RB2
TB
Inflammation
B. Panacinar Emphysema
AS
AD
A
RB3
RB2
RB1
Septum
TB
C. Distal Acinar Emphysema
AS
AD
RB2
RB2
RB1
TB

Types of emphysema

- **Primary emphysema:**
  - it is commonly linked to an inherited deficiency of the enzyme α1-antitrypsin that is a major component of α1-globulin, a plasma protein.
  - Normally it inhibits the action of many proteolytic enzymes.
  - Individuals with deficiency of this enzyme (AR) have an increased likelihood of developing emphysema because proteolysis in lung tissues is not inhibited.

- **Secondary emphysema:**
  - It is also caused by an inability of the body to inhibit proteolytic enzymes in the lung. It results from an insult to the lungs from inhaled toxins, such as cigarette smoke and air pollution.

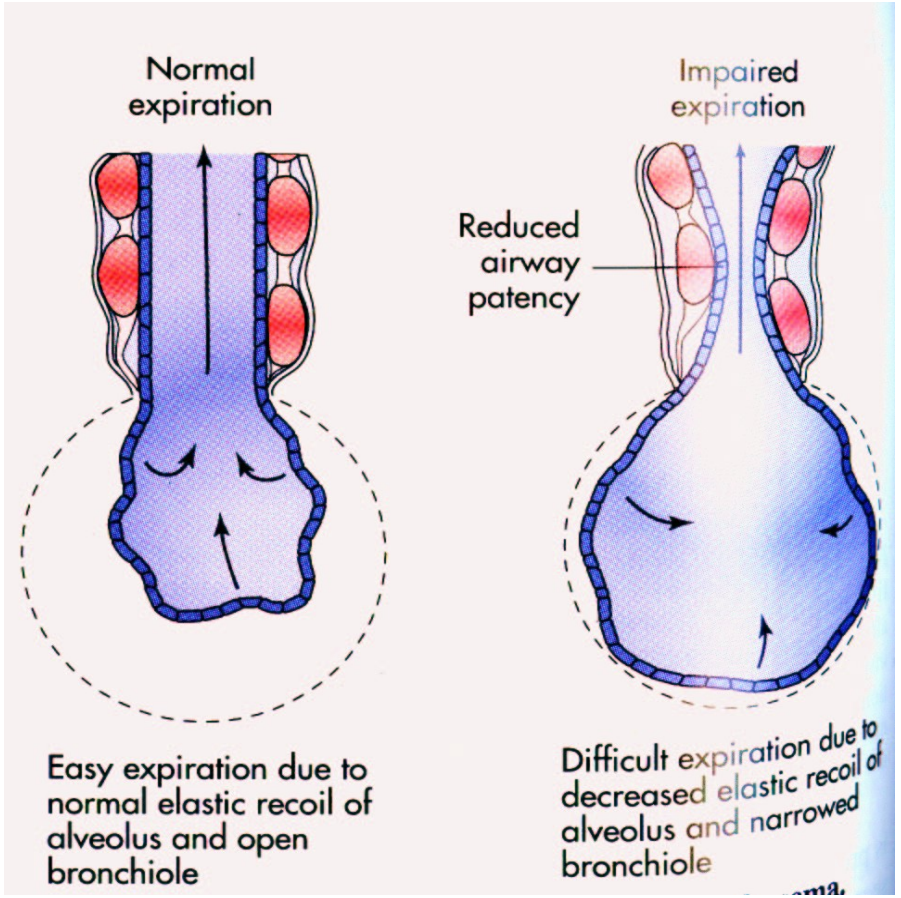
Pathophysiology of emphysema

- Emphysema begins with destruction of alveolar septa

- It is postulated that inhaled oxidants, such as those in cigarette smoke and air pollution, tip the normal balance of elastases (proteolytic enzymes) and antielastases (such as α1-antitrypsin) such that elastin is destroyed at an increased rate
- Expiration becomes difficult because loss of elastic recoil reduces the volume of air that can be expired passively.
- Hyperinflation of alveoli causes large air spaces (bullae) and air spaces adjacent to pleura (blebs) to develop.
- The combination of increased RV in the alveoli and diminished caliber of the bronchioles causes part of each inspiration to be trapped in the acinus.

Mechanisms of air trapping in emphysema

Damaged or destroyed alveolar walls no longer support and hold open the airways, and alveoli lose their property of passive elastic recoil.
Both of the se factors contribute to collapse during expiration.



Emphysema – clinical manifestations

- Patients with emphysema are able to maintain a higher alveolar minute ventilation than those with chronic bronchitis. Thus they tend to have a higher PaO_2 and lower $PaCO_2$ and have classically been referred to as „pink puffers“
- Physical examination often reveals a thin, tachypneic patient using accessory muscles and pursed lips to facilitate respiration. The thorax is barrel-shaped due to hyperinflation.
- There is little cough and very little sputum production (in „pure“ emphysema)

Emphysema – evaluation

- **Pulmonary function tests:**

  - indicate **obstruction to gas flow during expiration**
  - airway collapse and air trapping lead to a **decrease in FVC and FEV1** and an **increase in FRC, RV, and TLC.**
  - **diffusing capacity is decreased** because destruction of the alveolocapillary membrane

- **Arterial blood gas measurements are usually normal** until latge in the disease

Emphysema – approach to therapy

- Smoking cessation is the most important intervention
- Inhaled anticholinergic agets
- β2-adrenergic agonists
- Steroids
- Low-flow oxygen therapy in selected individuals
- Lung transplant can be considered

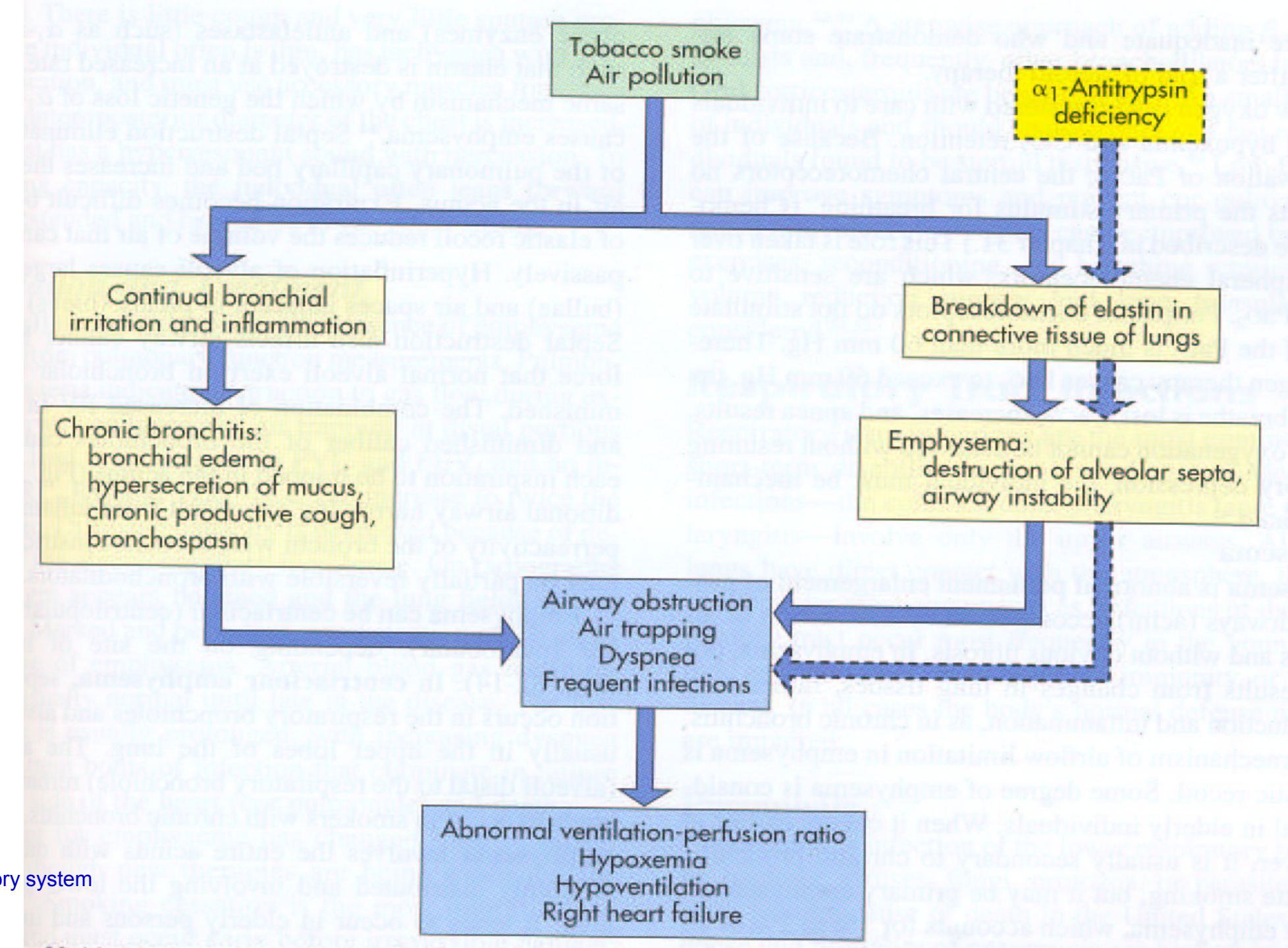

Tobacco smoke
Air pollution
α1-Antitrypsin deficiency
Continual bronchial irritation and inflammation
Breakdown of elastin in connective tissue of lungs
Chronic bronchitis:
bronchial edema,
hypersecretion of mucus,
chronic productive cough,
bronchospasm
Emphysema:
destruction of alveolar septa,
airway instability
Airway obstruction
Air trapping
Dyspnea
Frequent infections
Abnormal ventilation-perfusion ratio
Hypoxemia
Hypoventilation
Right heart failure

Table 32-4 Clinical Manifestations of Chronic Obstructive Lung Disease

Clinical Manifestations	Bronchitis	Emphysema
Productive cough	Classic sign	Late in course with infection
Dyspnea	Late in course	Common
Wheezing	Intermittent	Minimal
History of smoking	Common	Common
Barrel chest	Occasionally	Classic
Prolonged expiration	Always present	Always present
Cyanosis	Common	Uncommon
Chronic hypoventilation	Common	Late in course
Polycythemia	Common	Late in course
Cor pulmonale	Common	Late in course

Cyansis

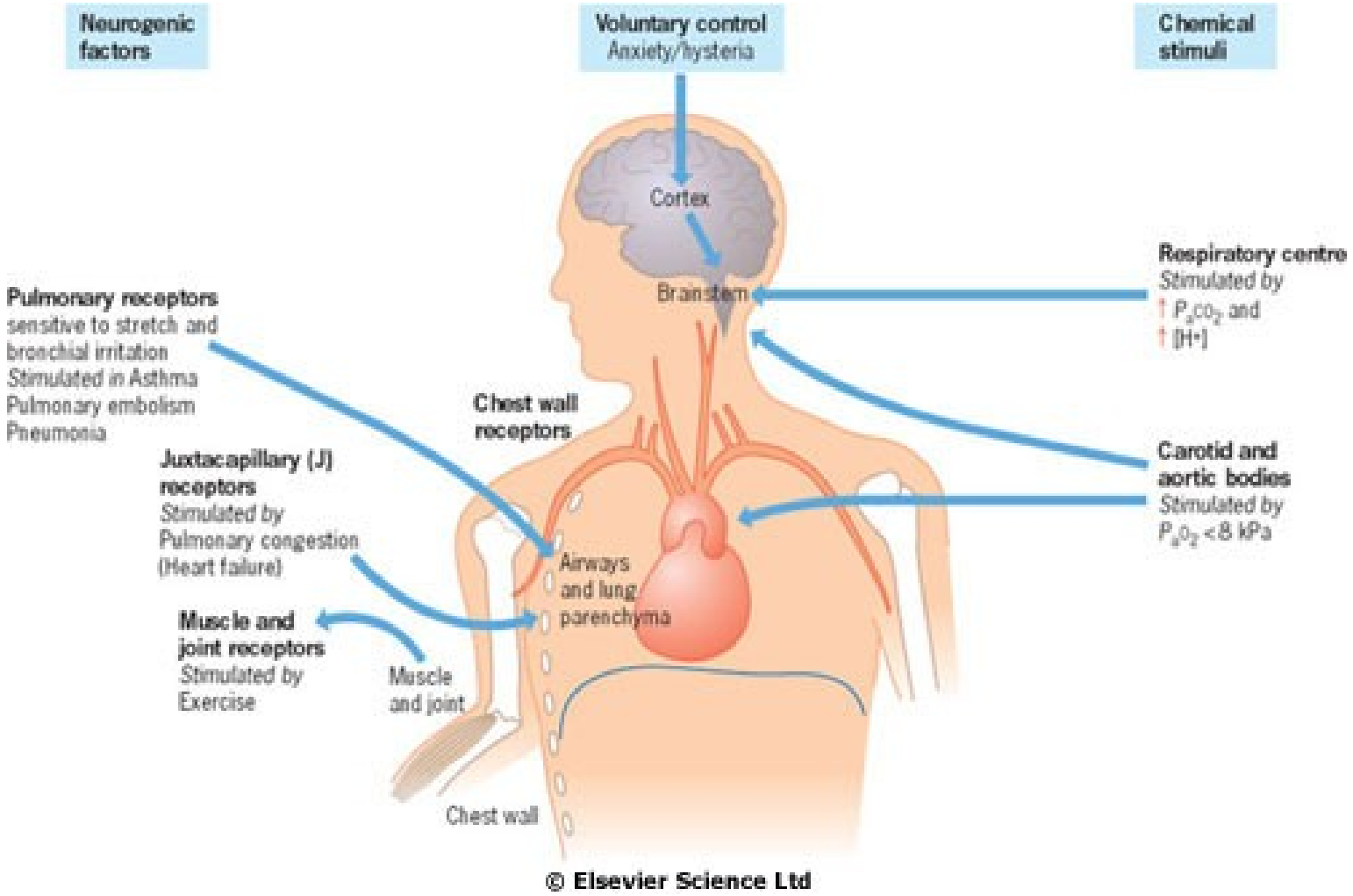
- Reduced hemoglobin higher than 50 g/l

- Hemoglobin

  Normal – 120-160 g/l (F), 130-180 g/l (M)

  Anemia – less than 110 g/l,
  Severe anemia – less than 79 g/l

MUNI
MED

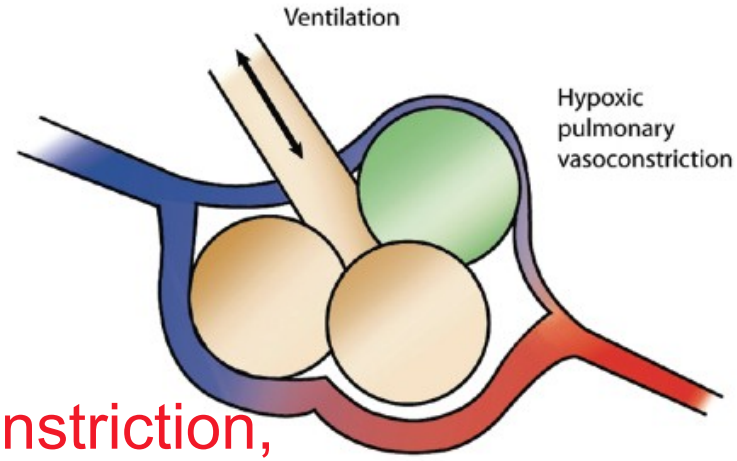

Neurogenic factors
Voluntary control
Anxiety/hysteria
Chemical stimuli
Cortex
Brainstem
Respiratory centre
Stimulated by
↑ P_aCO_2 and
↑ [H+]
Pulmonary receptors
sensitive to stretch and bronchial irritation
Stimulated in Asthma
Pulmonary embolism
Pneumonia
Chest wall receptors
Juxtacapillary (J) receptors
Stimulated by
Pulmonary congestion
(Heart failure)
Carotid and aortic bodies
Stimulated by
P_aO_2 <8 kPa
Airways and lung parenchyma
Muscle and joint receptors
Stimulated by
Exercise
Muscle and joint
Chest wall
© Elsevier Science Ltd

Hypoxic drive

- Traditional theory, obsolete
- Global respiratory insufficieny (hypoxemia + hypercapnia) disables stimulation based on pCO_2
- Respiration stimulated by hypoxemia
- Administration of oxygen may cause depression of the respiratory center (leading to critical hypercapnia)

MUNI
MED

Ventilation-perfusion mismatch



- Current theory
- Low pO_2 causes pulmonary vasoconstriction
  (redistribution of perfusion to a ventilated area)
- Administration of oxygen will reverse pulmonary vasoconstriction, however, a poorly ventilated alveolus does not ventilate CO_2
- Oxygen also leads to a shift of the dissociation curve to the right (release of CO_2 from hemoglobin – Haldane effect), which is not ventilated, increasing pCO_2
- Oxygen administration is safe if oxygenation is titrated to reach 88%-92% saturation

MUNI
MED

Interstitial lung diseases

- There are a large number of diseases that affect the interstitium of the lung

  ⇓

  it is connective tissue present between the alveolar epithelium and capillary endothelium

- Some of these diseases have known etiology, e.g. occupational diseases

- Others are diseases of unknown etiology

  - most frequent of these are idiopatic pulmonary fibrosis

  (diffuse interstitial fibrosis), pulmonary fibrosis associated with collagen-vascular diseases, and sarcoidosis.

Nozological units

Idiopatic pulmonary fibrosis

- Diseases unknown etiology, non-specific fibrotic change in lung. The diagnosis is to some extent one of exclusion.

Sarcoidosis

- One of the most common. It is multi-systém granulomatous disease that involves lung, lymph nodes, salivary glands, and liver. Specific type is called erythema nodosum

Occupational intersticial diseases

- Exposure to occupational and environmental inhalants for a long time can lead to develop lung disease. Workers in industries with heavy exposure to silica dust, asbestos particles, and welding fumes are generally aware of the risk of their occupation.

Occupational diseases

Diseases	Cause
Azbestosis	Azbestos particlesl
Aspergilosis	Mould -
Berryliosis	Berrylium´s compouds
Lung of breeder of birds	Birds´ antigens
Pneumoconiosis	Coal
Farmer´s lung	Grain´s mould
Silicosis	Silica dust
Welder´s lung	Welding fumes

Clinical manifestations

Subjective symptoms

- dyspnoe
- cough

Objective signs

- tachypnoe
- crackles
- clubbing
- cyanosis
- cor pulmonale

Laboratory findings

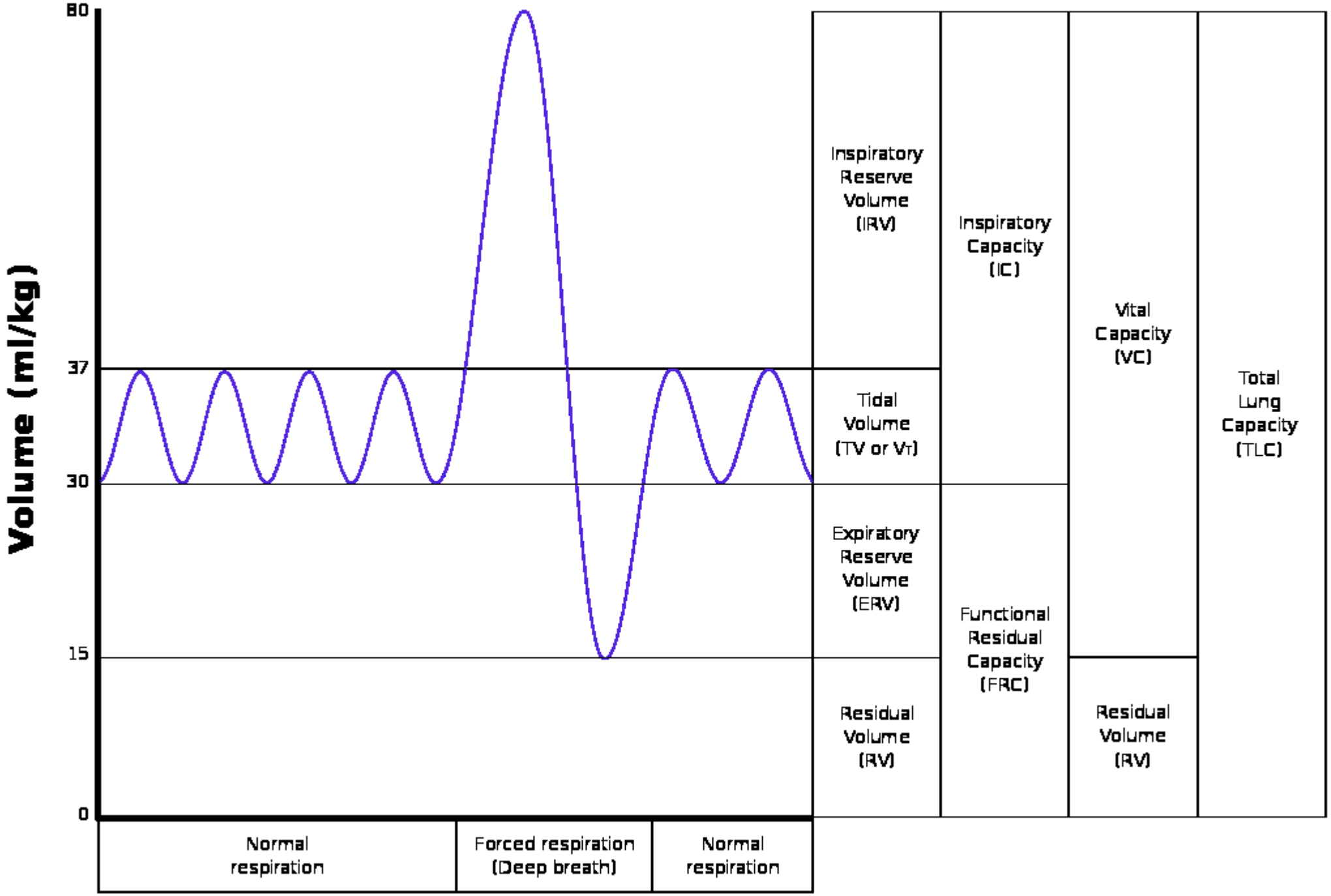
- Decrease PaO_2
- normal $PaCO_2$
- ECG- cor pulmonale
- Spirometry - restrictive pattern (VC, normal ratio FEV1/FVC)
- Decrease diffusion capacity of the lung for carbon monooxide

Therapy

- It depends on etiology (if it is known)
- Stopping the occupational exposure
- Antibiotics
- Diseases of unknown etiology (sarcoidosis, idiop. pulmonary fibrosis) corticosteroids
- Oxygen therapy

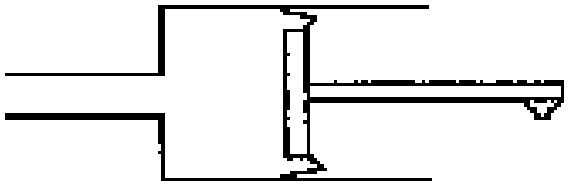
MUNI
MED

Spirometry

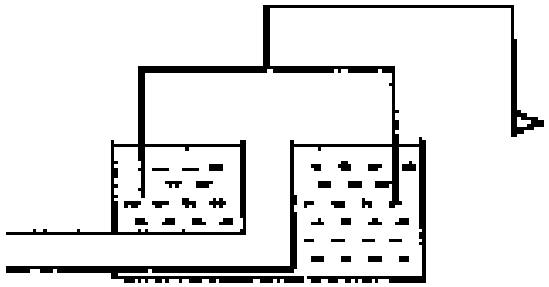

Volume (ml/kg)
80
37
30
15
0
Inspiratory Reserve Volume (IRV)
Tidal Volume (TV or VT)
Expiratory Reserve Volume (ERV)
Residual Volume (RV)
Inspiratory Capacity (IC)
Functional Residual Capacity (FRC)
Vital Capacity (VC)
Residual Volume (RV)
Total Lung Capacity (TLC)
Normal respiration
Forced respiration (Deep breath)
Normal respiration

Types of spirometers

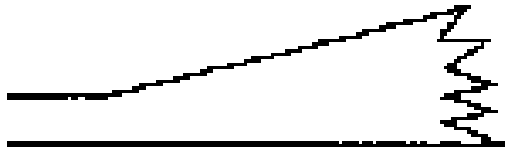
Rolling Seal



Water Sealed

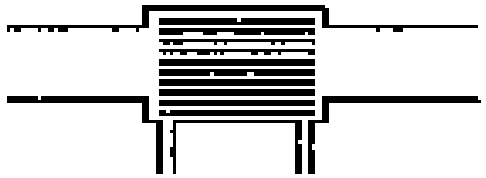


Bellows

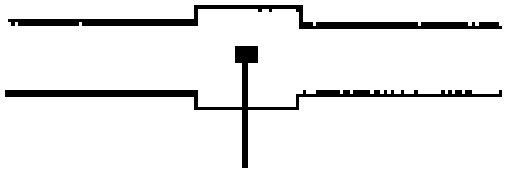


Flow Sensors

Pneumotach



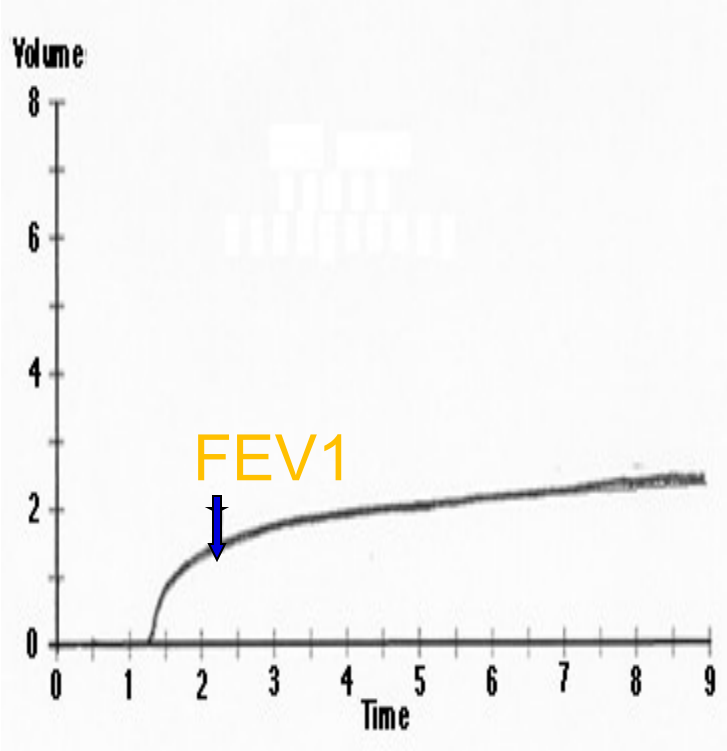
Hot-Wire



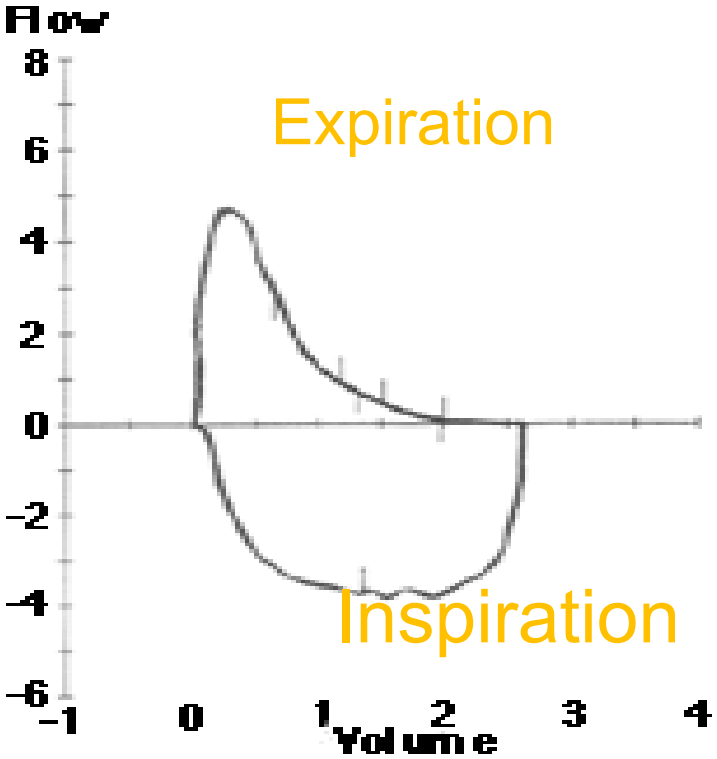
Turbine

MUNI MED

Graphs



Volume-time



Flow-volume

Lung Volume Patterns

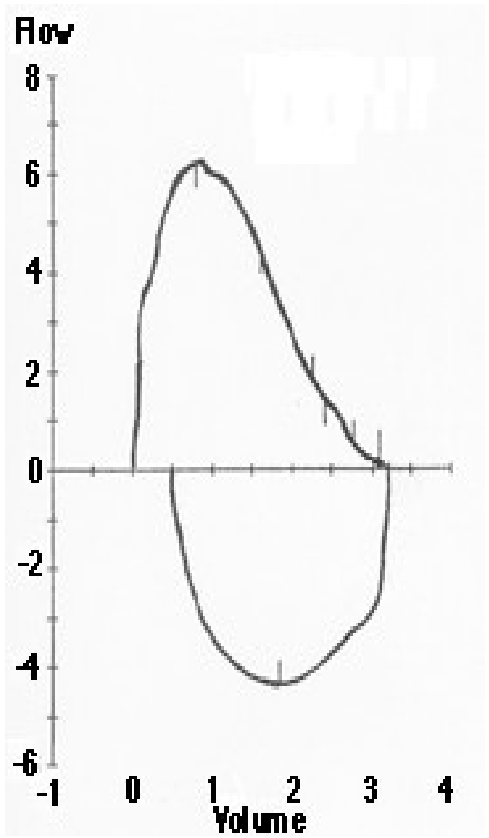
- **Obstructive Disease**: Characterized by hyperinflation and gas trapping (increased TLC and RV/TLC)

- **Restrictive Disease**: Characterized by generalized reduction in lung volume (decreased TLC, RV and FRC)

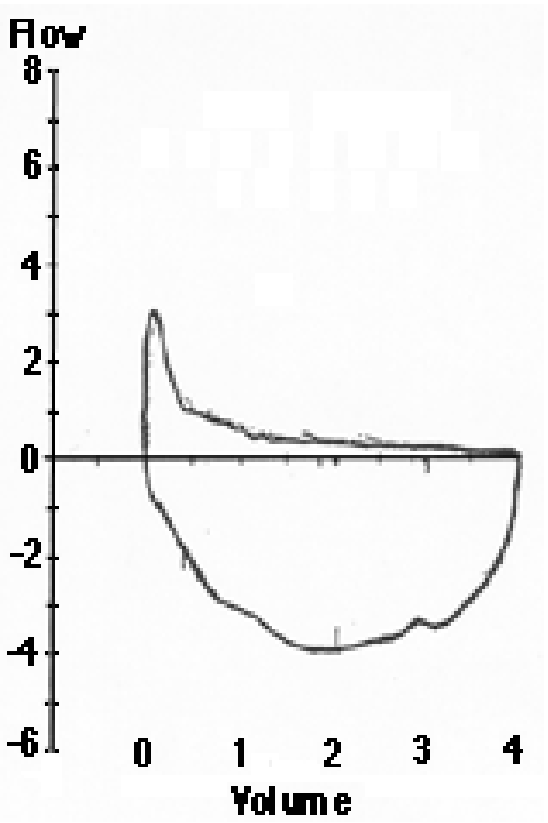
MUNI
MED

Flow-volume graphs

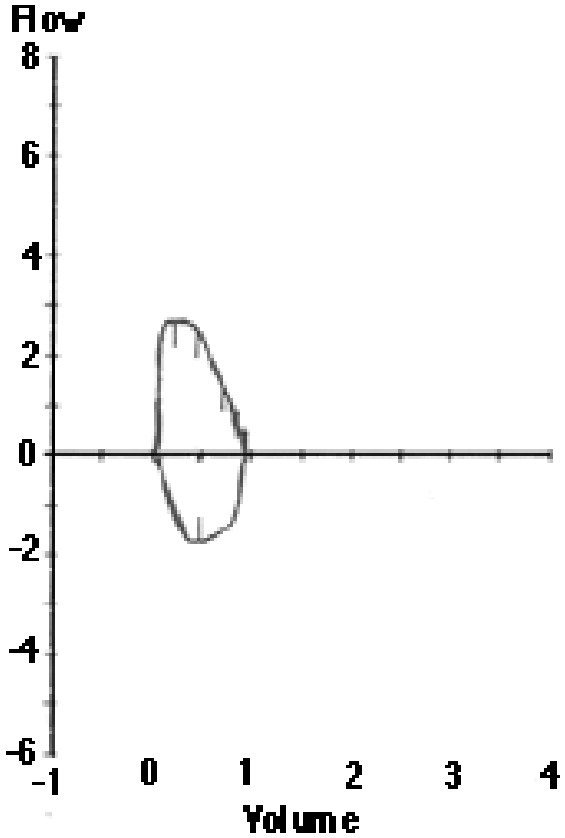
Normal

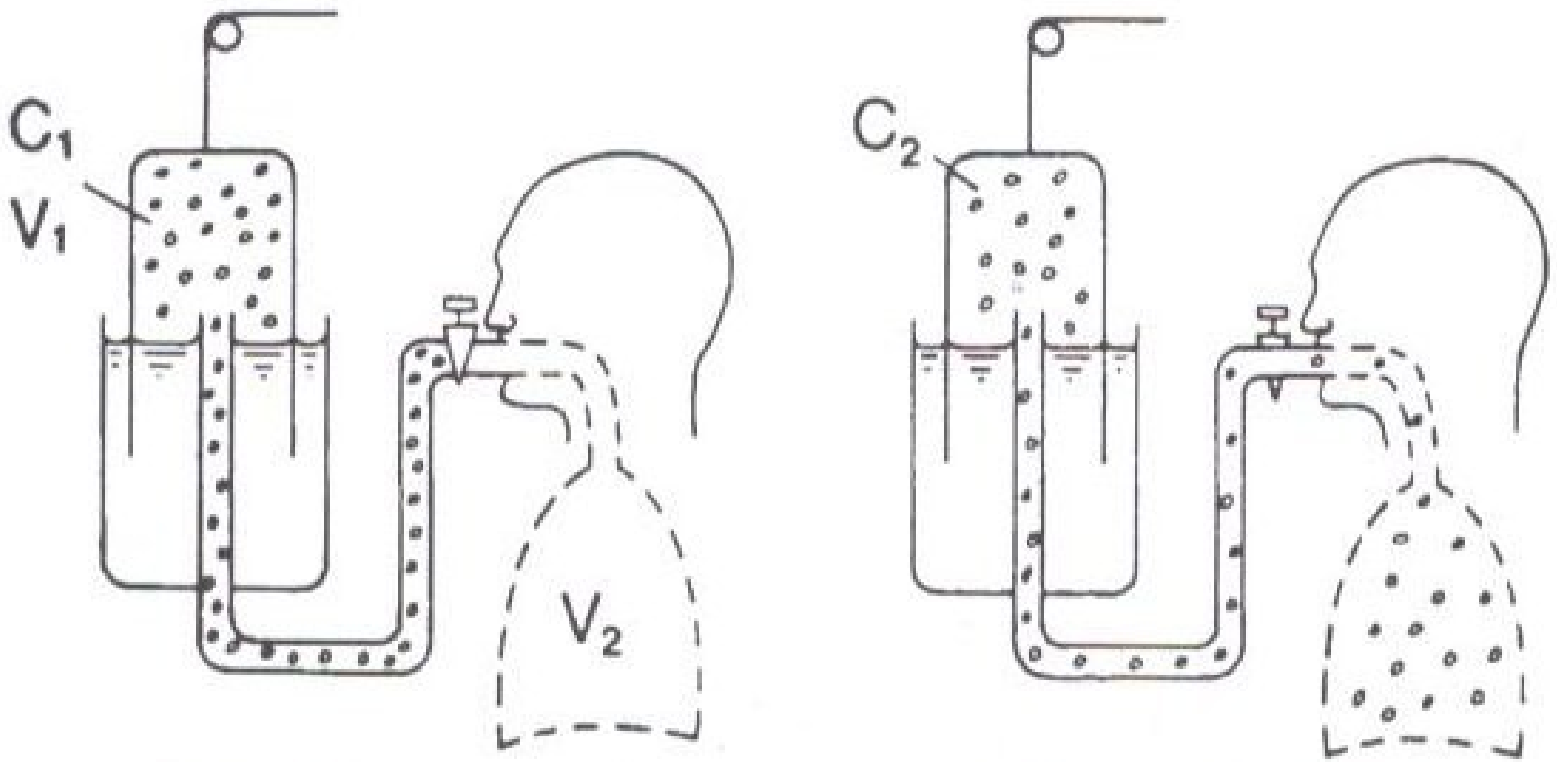


Obstructive



Restrictive





Před ekvilibrací

Po ekvilibraci

$$C_1 * V_1 = C_2 * (V_1 + V_2)$$