PATHOPHYSIOLOGY OF RESPIRATION 2

Obstructive disorders

R. Benacka

Department of Pathophysiology,

Medical faculty, P.J. Safarik University

Košice

Respiratory diseases

- **Obstructive diseases (OPD)**

- restricted expiration
- ↓ FEV_1
- ↑ compliance, elasticity

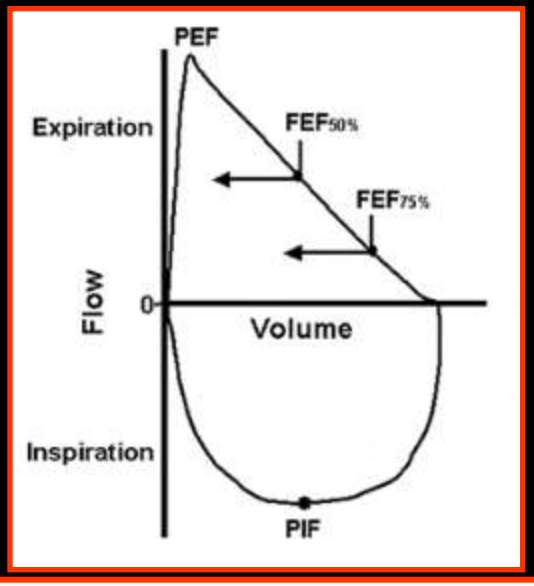
  - Chronic bronchitis
  - Emphysema
  - COPD (chronic obstructive pulmonary disease)
  - Asthma
  - Bronchiectasia
  - Cystic fibrosis
  - Athelectasia (not pure OPD)

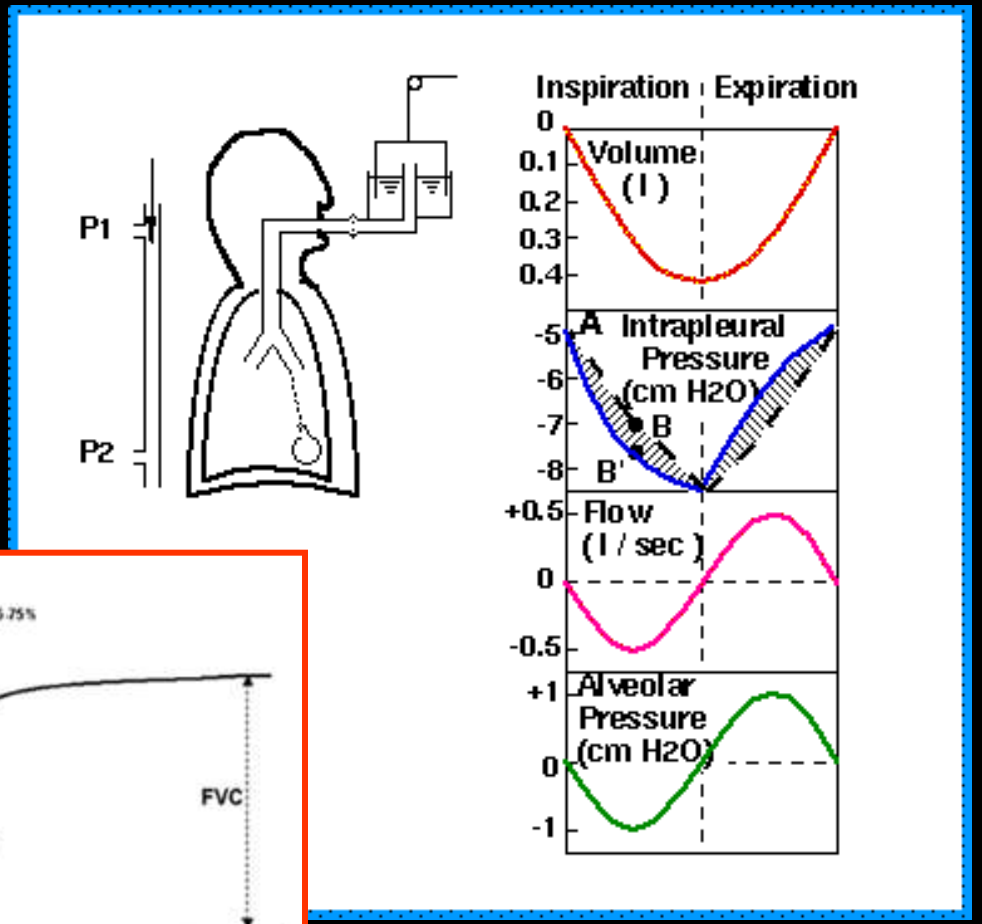
- **Restrictive diseases (RPD)**

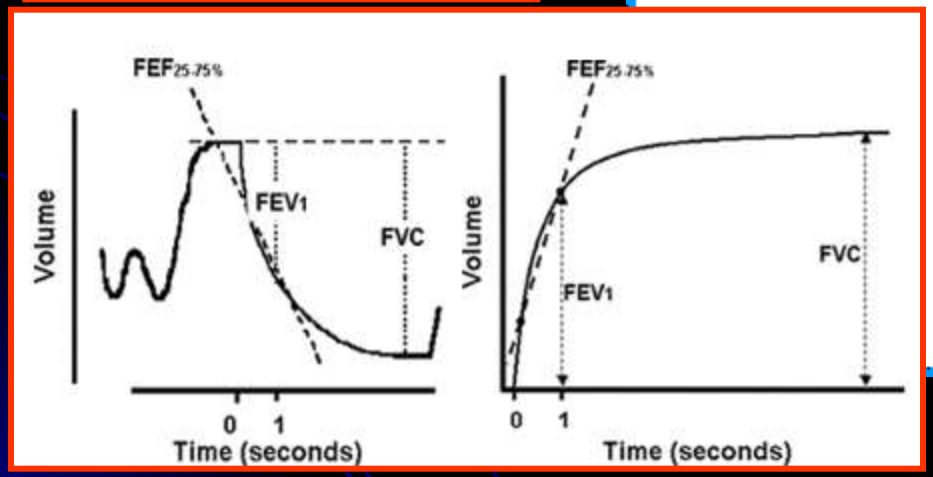
- restricted inspiration + expiration
- ↓ VC
- ↓ compliance, elasticity

  - Interstitial diseases: pneumonia
  - Fibrosis of lungs – pneumoconiosis, asbestosis, silicosis, beryliosis, farmers lungs
  - Restriction to breathing: pneumothorax, ribcage malformities, fracture, obesity

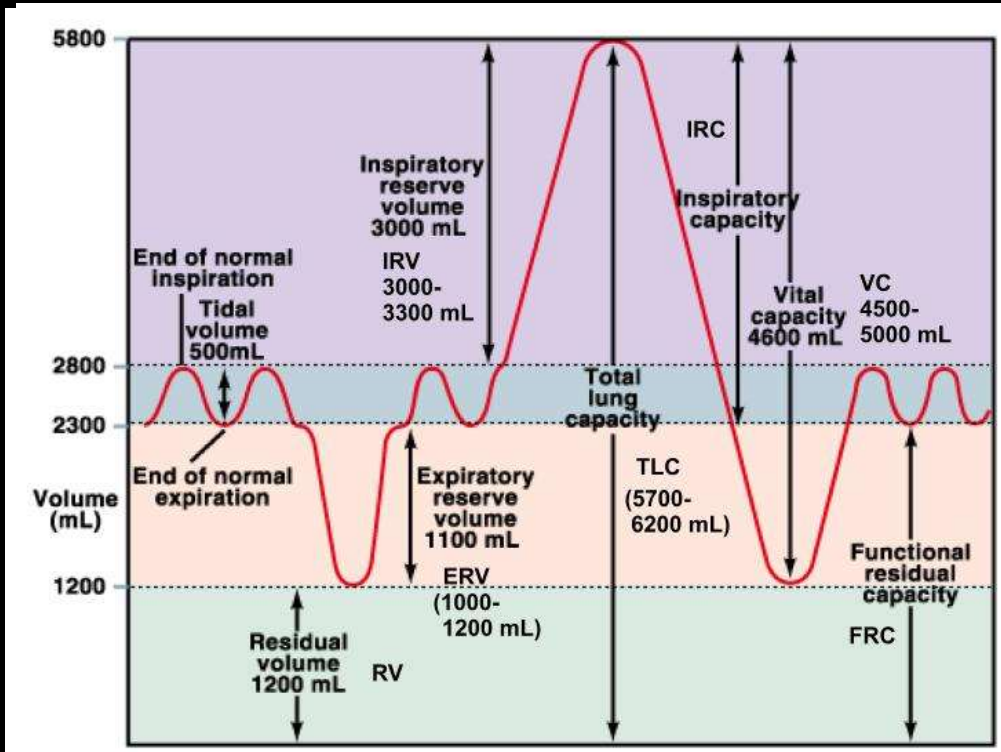
Ventilatory parameters

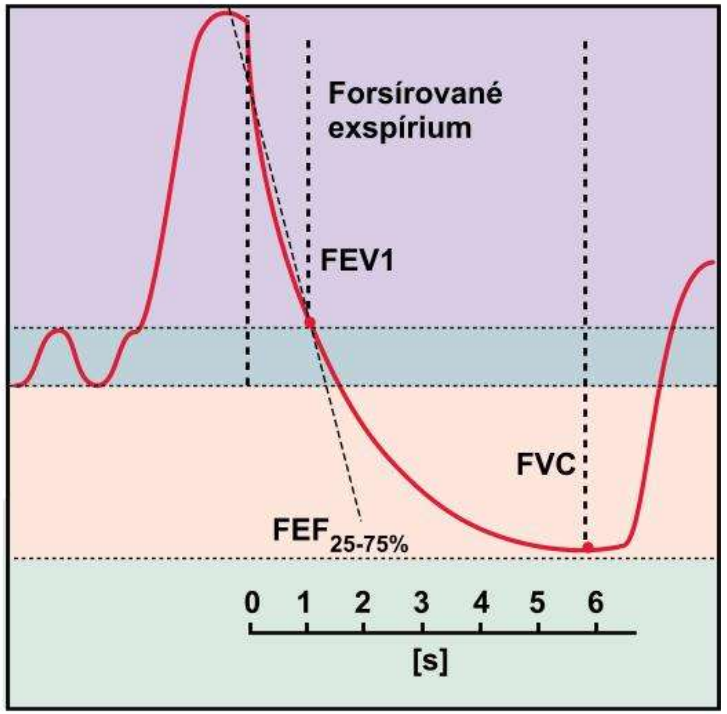




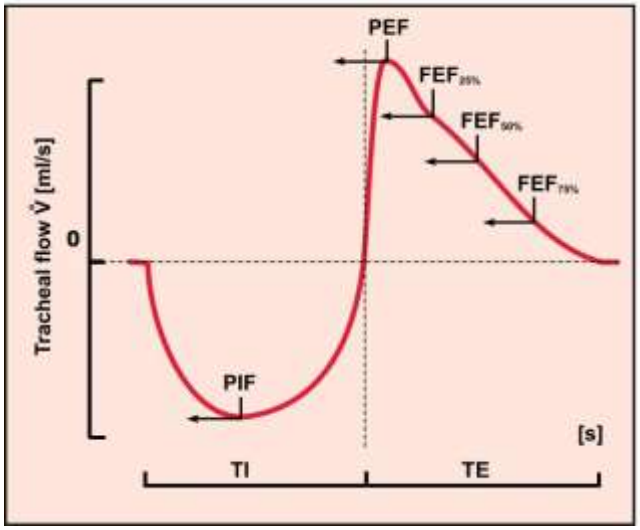


- FEV1 - % of the VC which is expelled in the first second. It should be at least 75%. The is reduced in obstructive disorders.

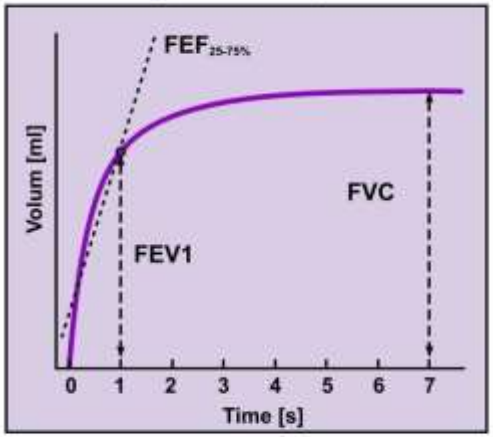




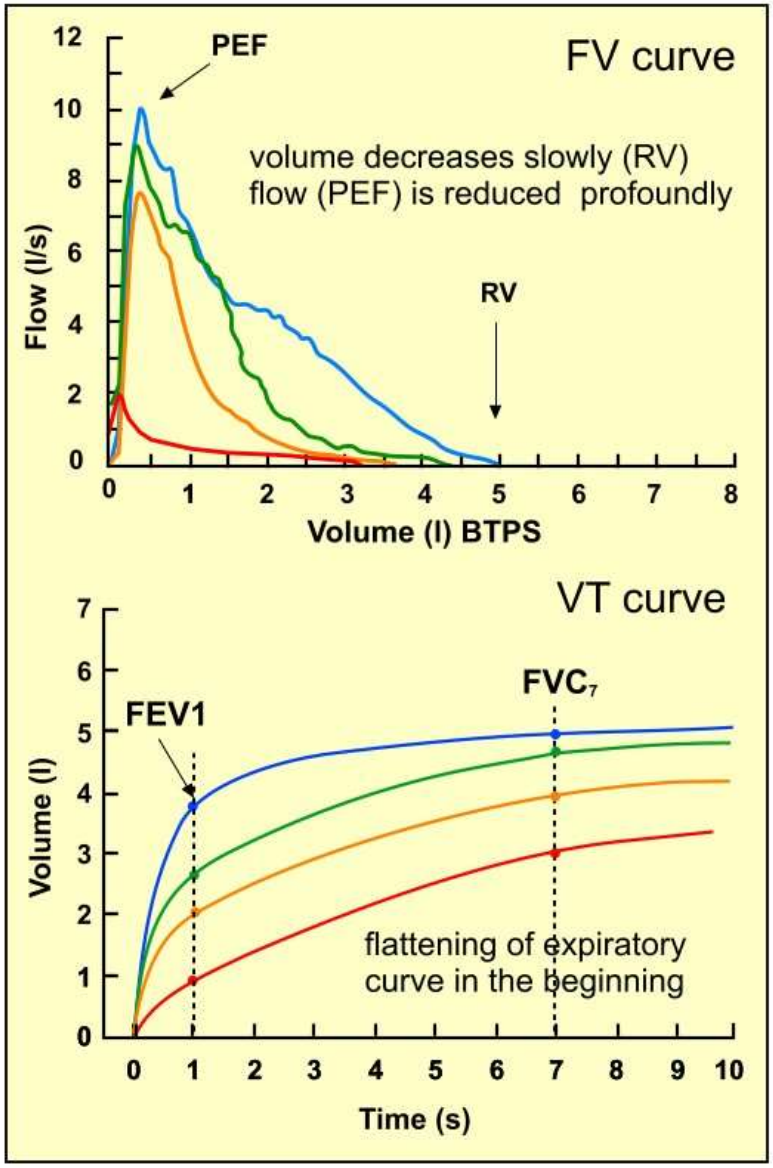
Krivka prietok - čas (flow - time)



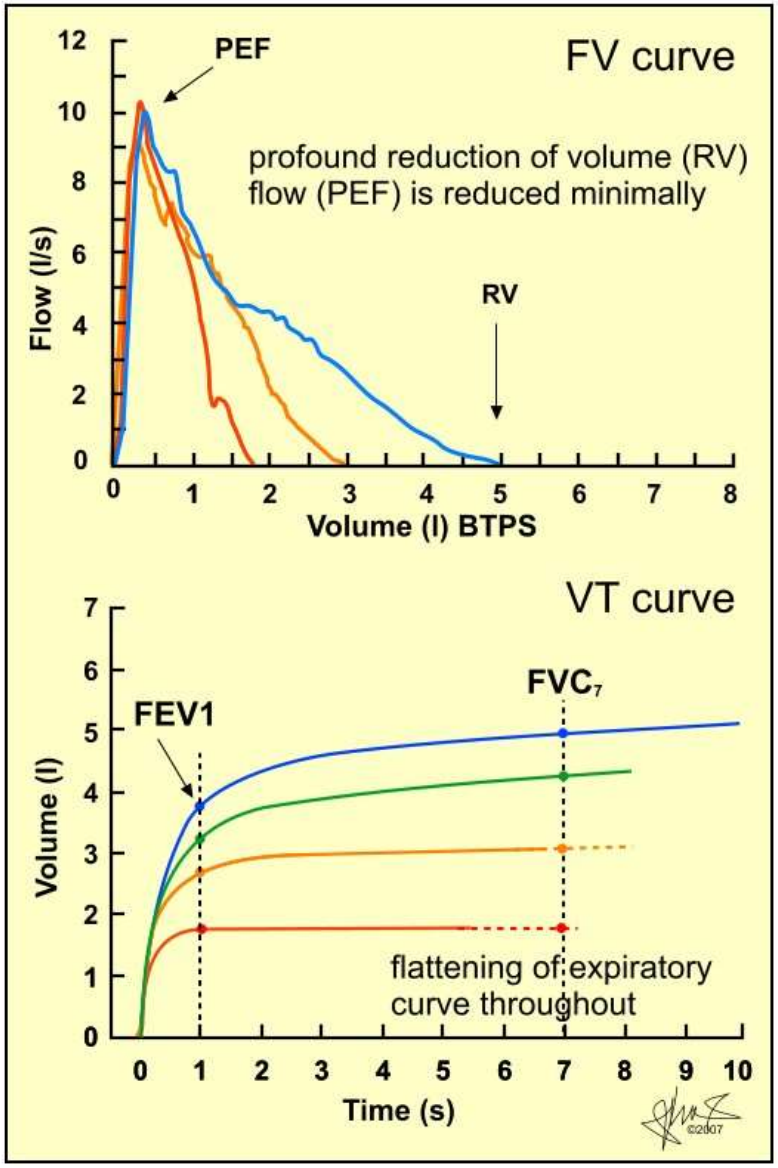
Krivka objem - čas (volume - time)



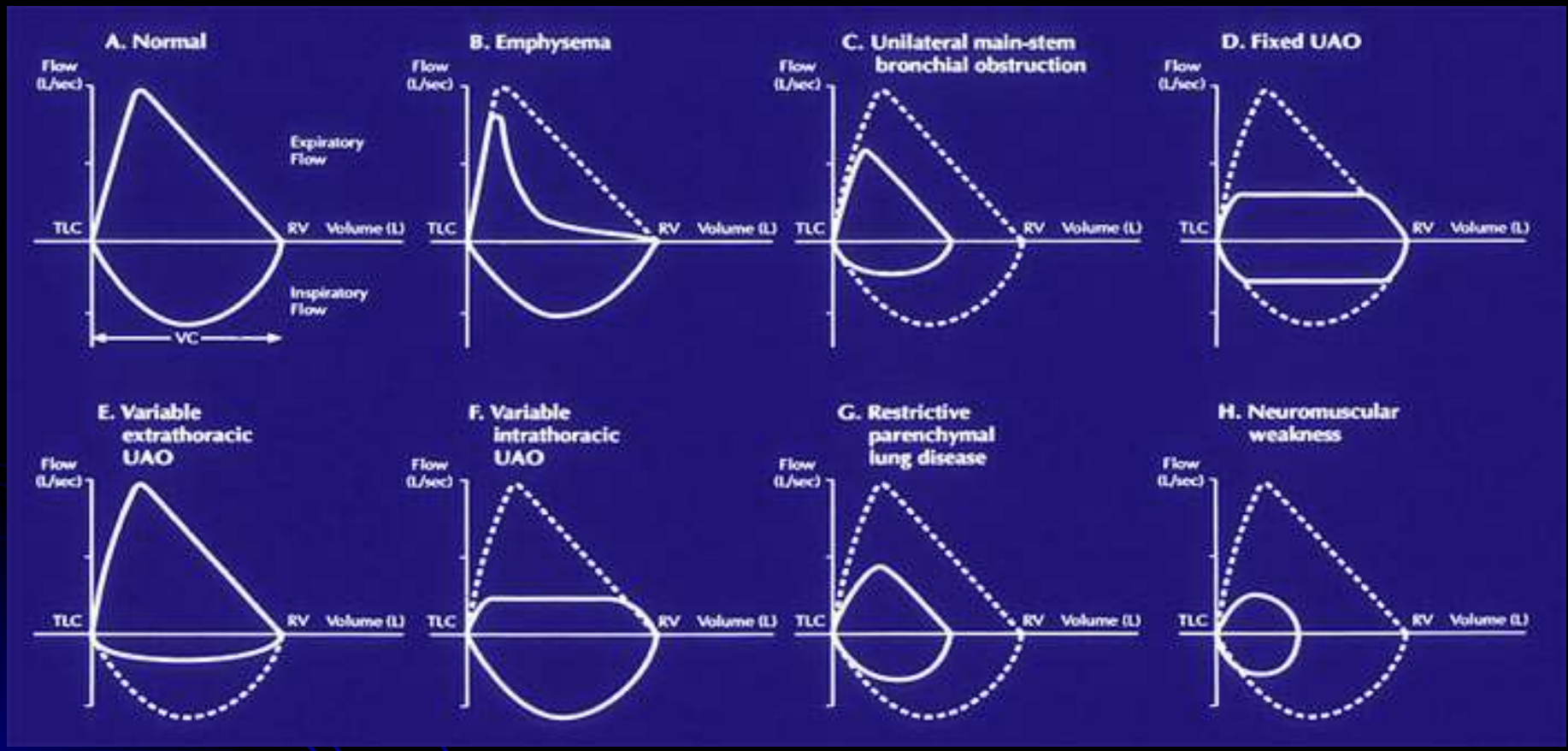
OBSTRUCTIVE DISORDERS



RESTRICTIVE DISORDERS

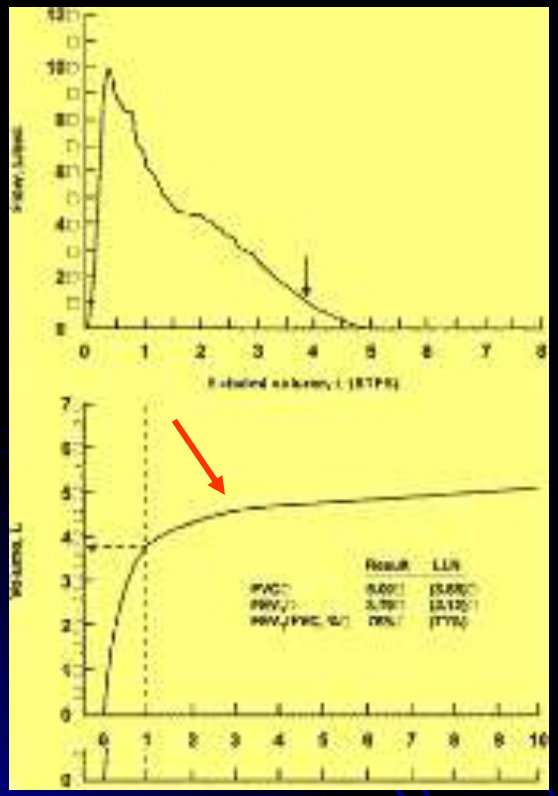


Volume- flow curves in various disorders



Findings in obstructive diseases

Flow-volume curve



Volum-time curve

- 1. flattening of FVC curve
- 2. FEV1/FVC (FEV6) <70% of control; drop is not linear to severity of disorders; FEV1decreases first, FVC later; in severe obstruction decrease of FVC
- 3. FEV1 < 80% of control
- 4. secrease of PEF, MEF, FEF
- 5. increase of Raw + RV

Patients with obstructive disorders

According to *Americal Thoracic Society; Am.J.Respir.Crit.Care Med. 1995; 152: S77-121*

Airflow obstruction

Chronic bronchitis (asymptomatic – early)

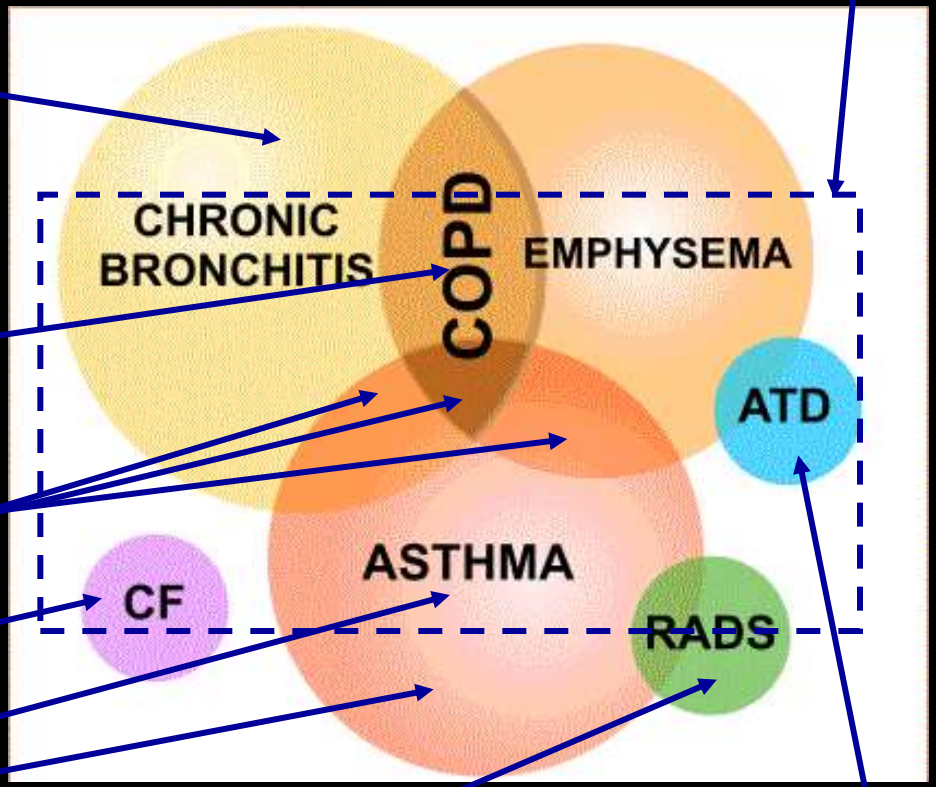
COPD (most common)

Asthmatic bronchitis
asthma + components of Bronchitis, emphysema

Cystic fibrosis

Reversible asthma

Spastic bronchitis

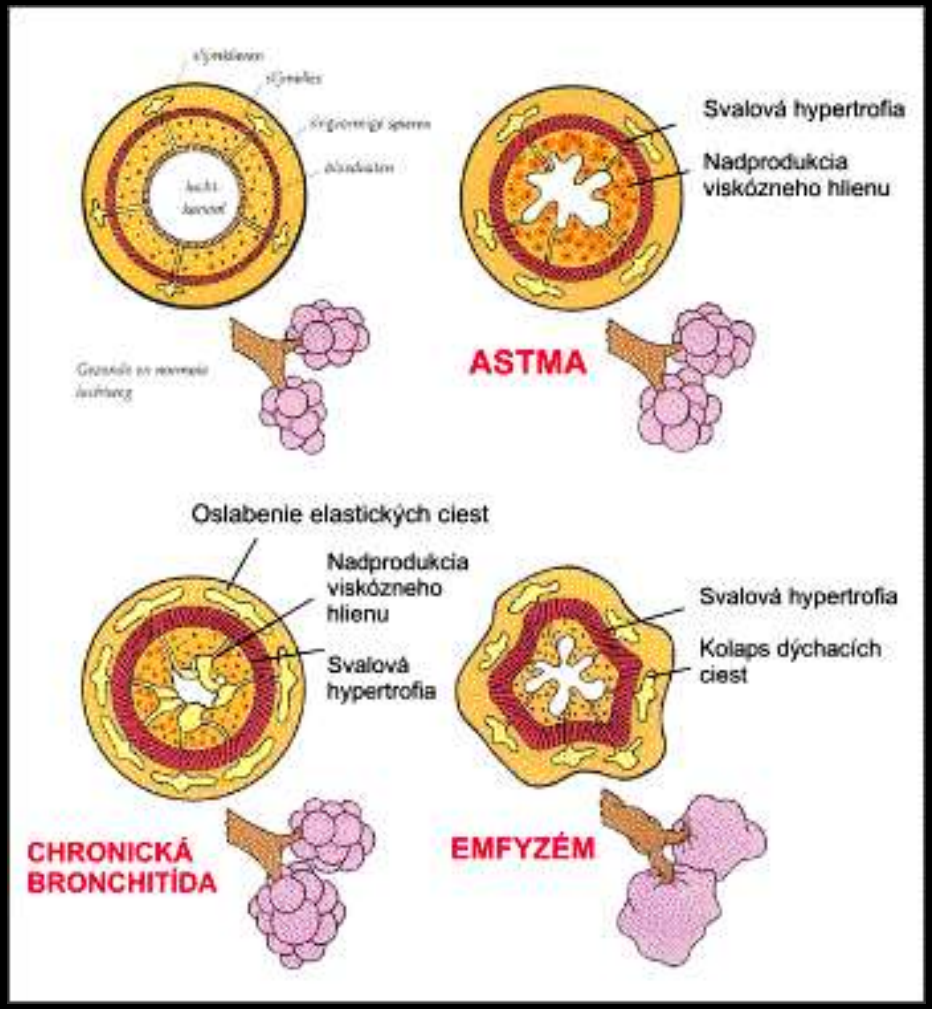


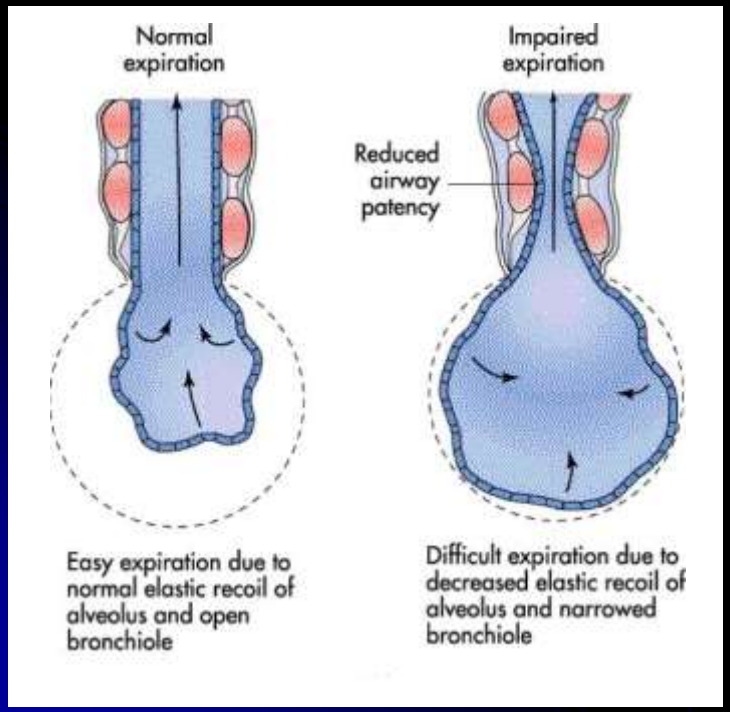
Reactive airways syndrome

Alpha- antitrypsin deficiency (familiar emphysema)

Pathogenesis of obstructive diseases

- Hyperplasia, metaplasia of mucous layer
- Hyperproduction of mucus
- Inflammation – cell infiltrates
- Thikening of muscle layer - spasms
- Airayw collapsibility – air trapping; expiratory limitation





Air trapping

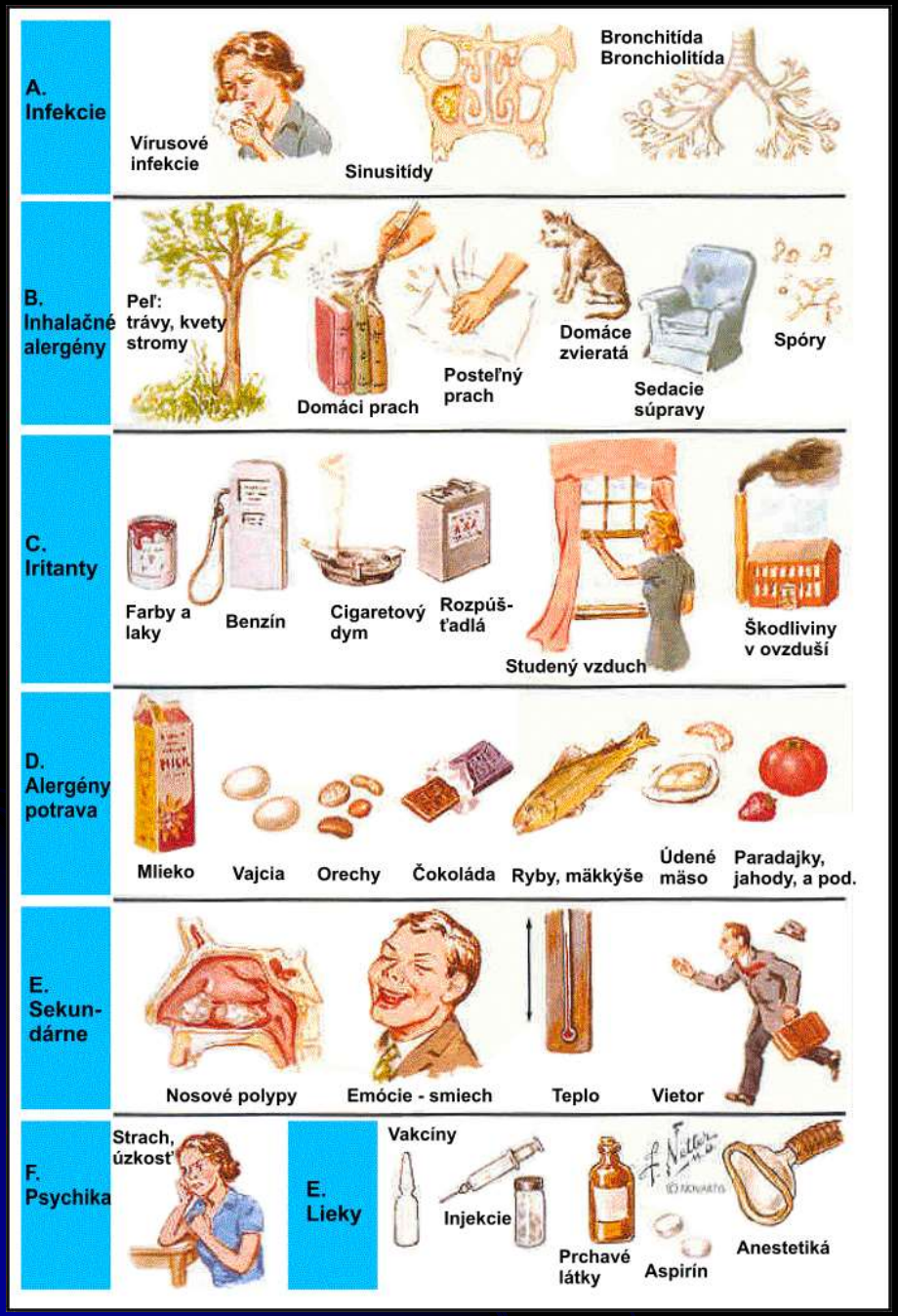
Asthma

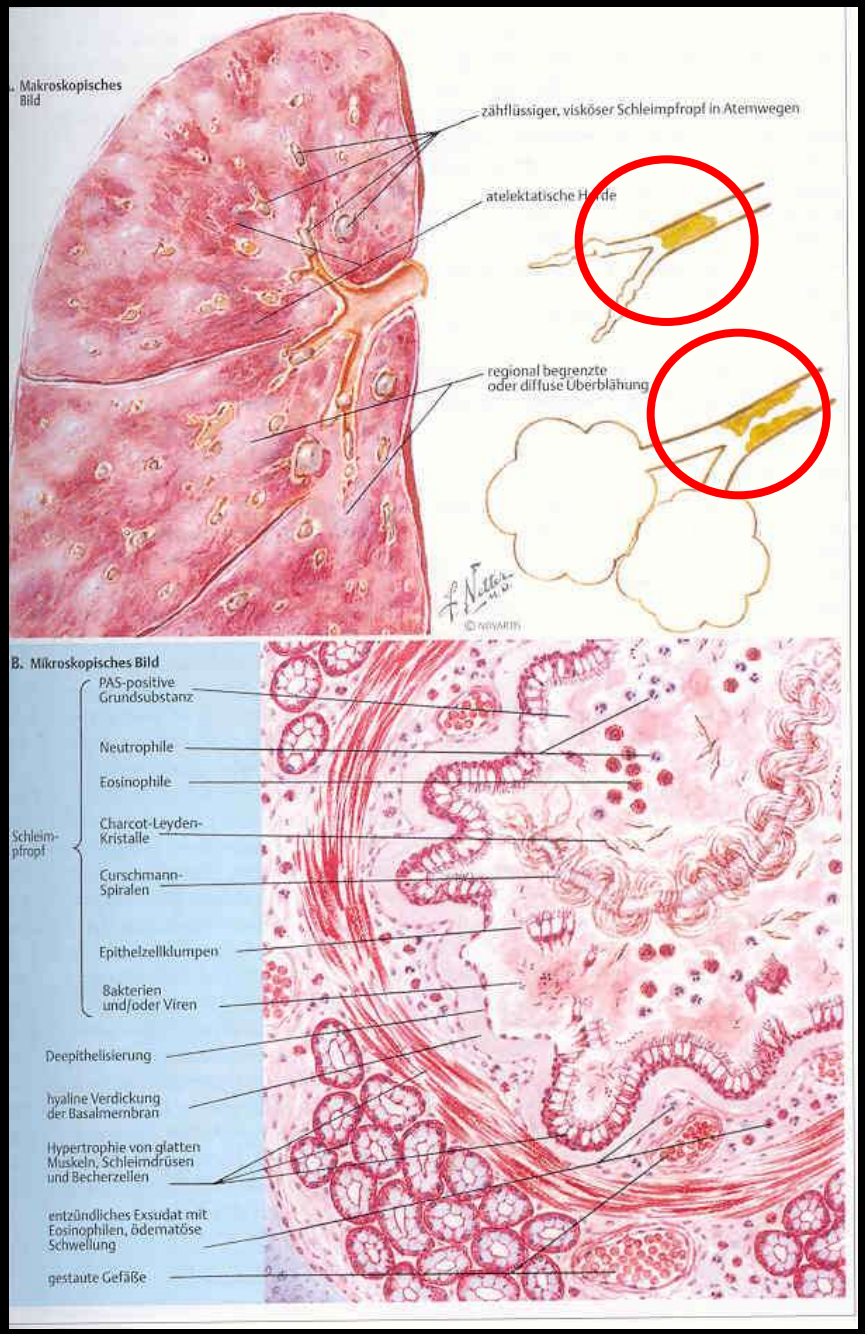
- **Definition:** Chronic inflammatory disease of bronchi leading to spasmatic occusion and hyperproduction of viscous mucus
- **Causes:** **a)** alergic – type I, type III (allergens, infections)

  b) non- allergic (neurogennic), psychogenic
- **Pathomechanism:**
- Mucosal hypertophy - hyperplasia of mucus producing cells
- Overproduction of very viscous mucus
- Hypertrophy of smooth muscles – narrowing of the lumen

Asthmatic crisis

- **Dyspnoea** - difficulty of breathing, weezing, catching for air
- **Cough** –difficult expectoration, viscous mucus
- **Cyanosis** – blue – coloring of face


A. Infekcie
Vírusové infekcie
Sinusitídy
Bronchitída
Bronchiolitída
B. Inhalačné alergény
Peľ: trávy, kvety stromy
Domáci prach
Posteľný prach
Domáce zvieratá
Sedacie súpravy
Spóry
C. Iritanty
Farby a laky
Benzín
Cigaretový dym
Rozpúšťadlá
Studený vzduch
Škodliviny v ovzduší
D. Alergény potrava
Mlieko
Vajcia
Orechy
Čokoláda
Ryby, mäkkýše
Údené mäso
Paradajky, jahody, a pod.
E. Sekundárne
Nosové polypy
Emócie - smiech
Teplo
Vietor
F. Psychika
Strach, úzkosť
E. Lieky
Vakcíny
Injekcie
Prchavé látky
Aspirín
Anestetiká


Makroskopisches Bild
zähflüssiger, viskoser Schleimpfropf in Atemwegen
atelektatische Herde
regional begrenzte oder diffuse Überblähung
B. Mikroskopisches Bild
Schleimpfropf
PAS-positive Grundsubstanz
Neutrophile
Eosinophile
Charcot-Leyden-Kristalle
Curschmann-Spiralen
Epithelzellklumpen
Bakterien und/oder Viren
Deepithelisierung
hyaline Verdickung der Basalmembran
Hypertrophie von glatten Muskeln, Schleimdrüsen und Becherzellen
entzündliches Exsudat mit Eosinophilen, ödematöse Schwellung
gestaute Gefäße

Asthmatic bronchitis

- overlap syndrome - features both asthma and CB
- Histologically eosinophilic bronchitis
- Clinically:
  - **CB with astma features:** exposure to tobacco + features of classic asthma, allergies, history of childhood asthma.
  - Asthma w/o CB: lack of a smoking history. Irreversible chronic airflow obstruction

Chronic bronchitis

- Badham (1808), Laennec (1827) classic description in early 19th century
- presence of a chronic productive cough for 3 months during each of 2 consecutive years
- 8 million people in US
- Histology:
  - Hypertrophy focal of the mucus-producing glands found in the mucosa of large cartilaginous airways
  - Airway smooth muscle hyperplasia, inflammation, and bronchial wall thickening
  - squamous metaplasia, imobilisation of cilia + abnormalities,
  - Neutrophilic infiltrates in the submucosa. Mononuclear inflammation in bronchioles
- Functional:
  - Lumen narrowing - mucous plugging, goblet cell metaplasia, + airway distortion due to fibrosis
  - Airway trapping – expiratory airflow limitation

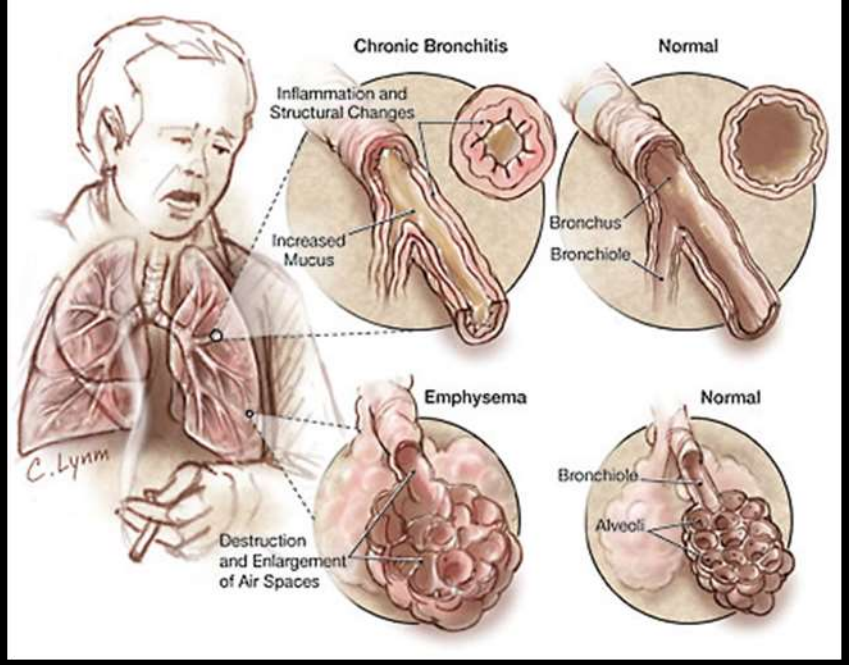
Chronic bronchitis

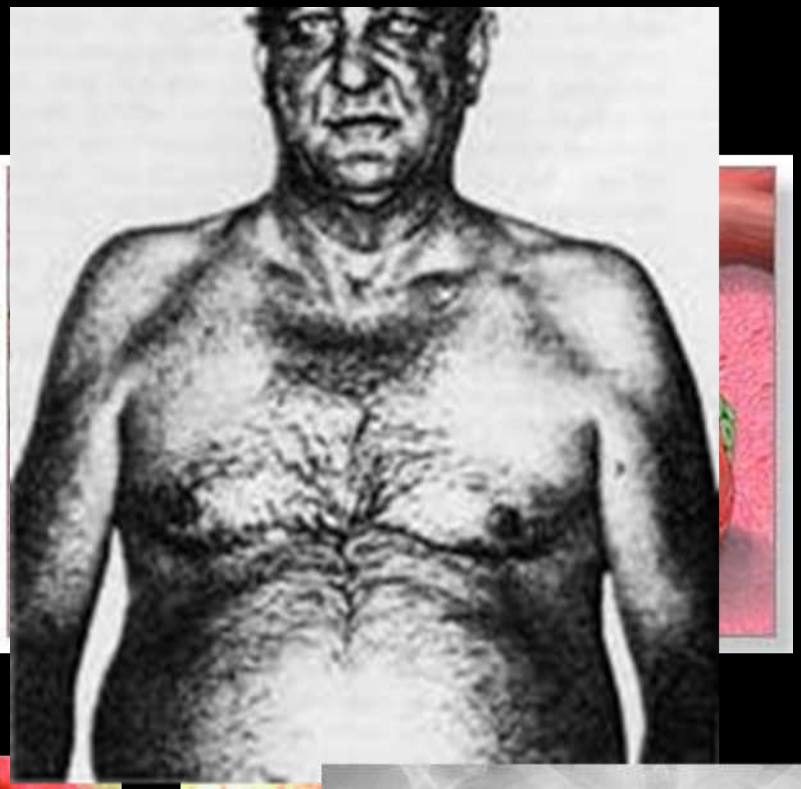
- Classification:
  - **Simple chronic bronchitis** - mucoid sputum production,
  - **Chronic mucopurulent bronchitis - p**ersistent or recurrent purulent sputum production in the absence of localized suppurative disease, such as bronchiectasis,
  - **Chronic bronchitis with obstruction -** distinguished from chronic infective asthma (long history of productive cough and late onset of wheezing, in asthma - long history of wheezing with late onset of productive cough).
- Reasons:
  - Remittent attacks of acute bacterial/ viral bronchitis
  - Gradually evolving
    - Cigarette smoking – the main reason (cigars, pipes), smoking marijuana
    - Air pollutants

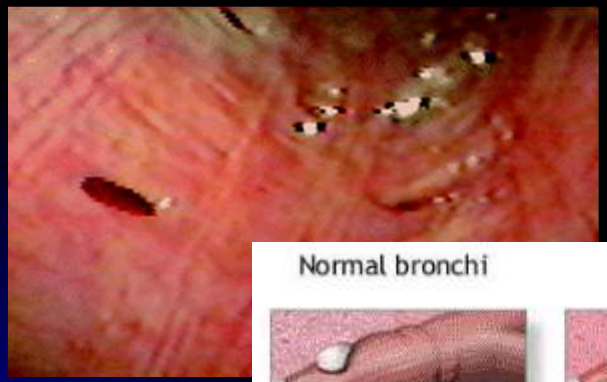
Chronic bronchitis

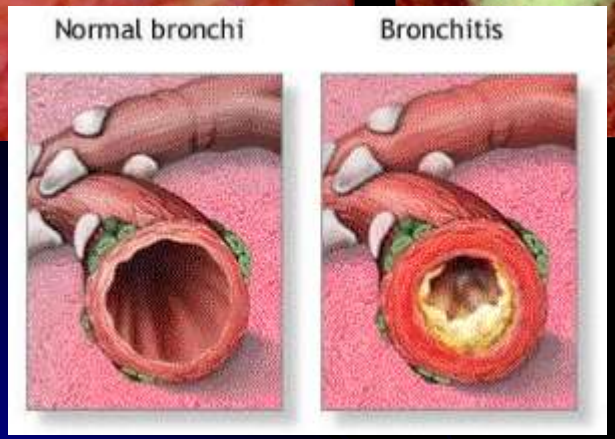
Causes

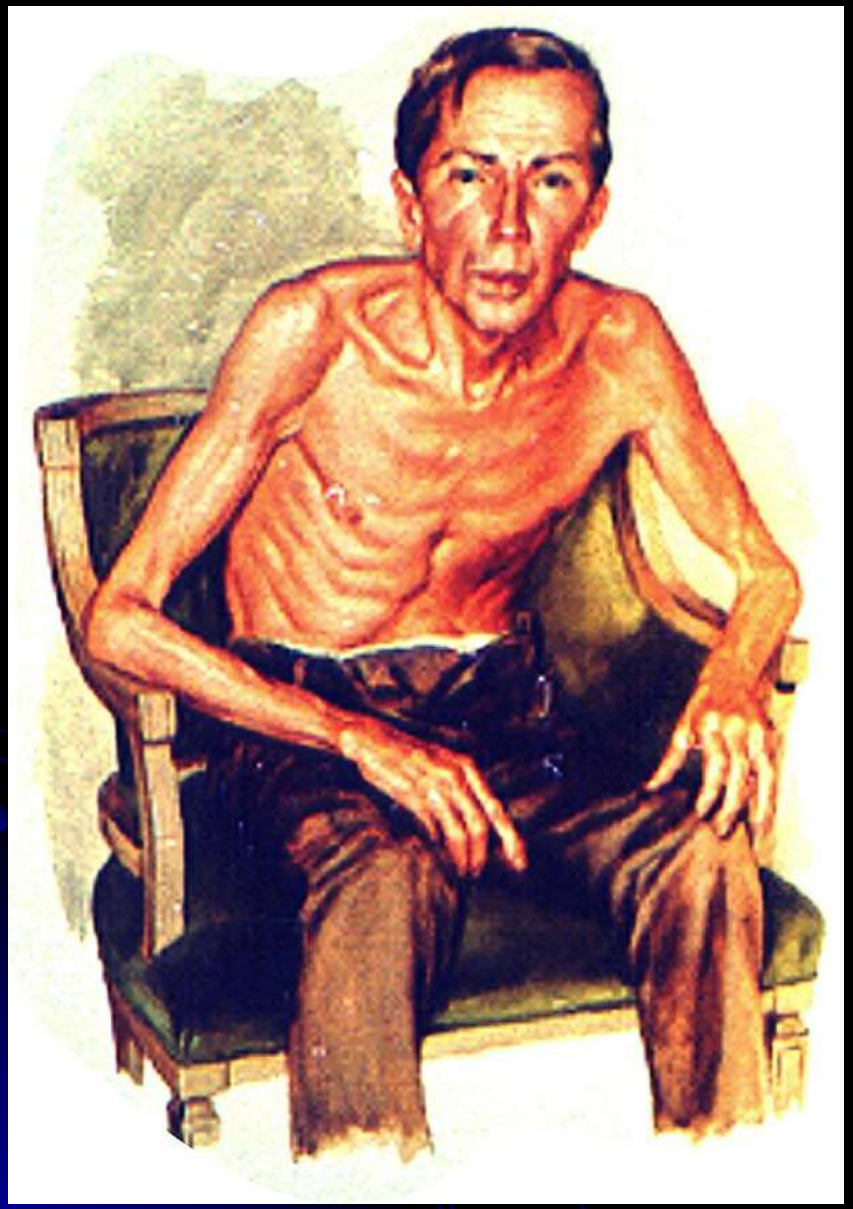
- Cigarette smoking
  - impairs ciliary movement, inhibits function of alveolar macrophages, and leads to hypertrophy and hyperplasia of mucus-secreting glands.
  - Smoking can also increase airway resistance via vagally mediated smooth muscle constriction.
  - Unless some other factor can be isolated as the irritant that produces the symptoms, the first step in dealing with chronic bronchitis is to stop smoking.
- Air pollution
  - US (1990): 50,000 to 120,000 premature deaths are associated with exposure to air pollutants."
  - Ozone (140 million) carbon monoxide, sulfur dioxide.


Chronic Bronchitis
Normal
Inflammation and
Structural Changes
Increased
Mucus
Bronchus
Bronchiole
Emphysema
Normal
Bronchiole
Alveoli
Destruction
and Enlargement
of Air Spaces
C.Lynn






Normal bronchi
Bronchitis



Emphysema

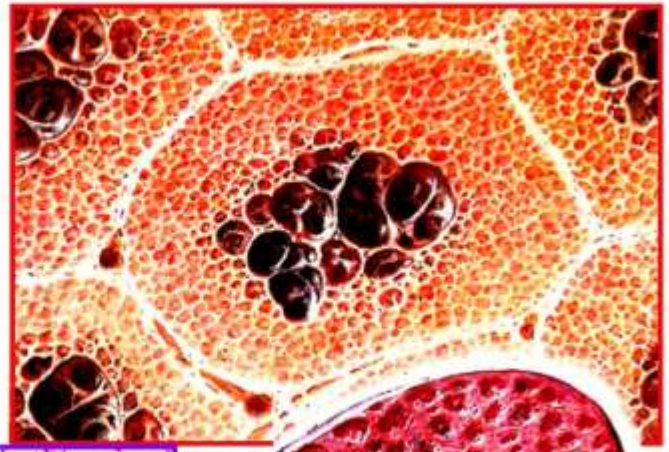
- **Definition:** *pathoanatomical:* abnormal, permanent enlargement and destruction of the air spaces distal to the terminal bronchioles without obvious fibrosis, progressively lose elasticity and eventual rupture of alveoli.
- **Occurence**: 2 million in US, most disabling pulmonary disease,more common in males than females
- Etiology:
  - Inherited susceptibility - hereditary emphysema – antitrypsin deficiency
  - Acquired in terminal stage of COPD – cigarette smoking
    - Smoking - mortality 20 x greater than nonsmokers, reduced to 5 x in smokers who have quit.
    - Air Pollution – suphur, chlorine, CO, ozone
- Pathogenesis: smoking -> damage of cilia in airways irritating agents stimulate chronic inflammation -> loss of elestin in parenchyme

Emphysema

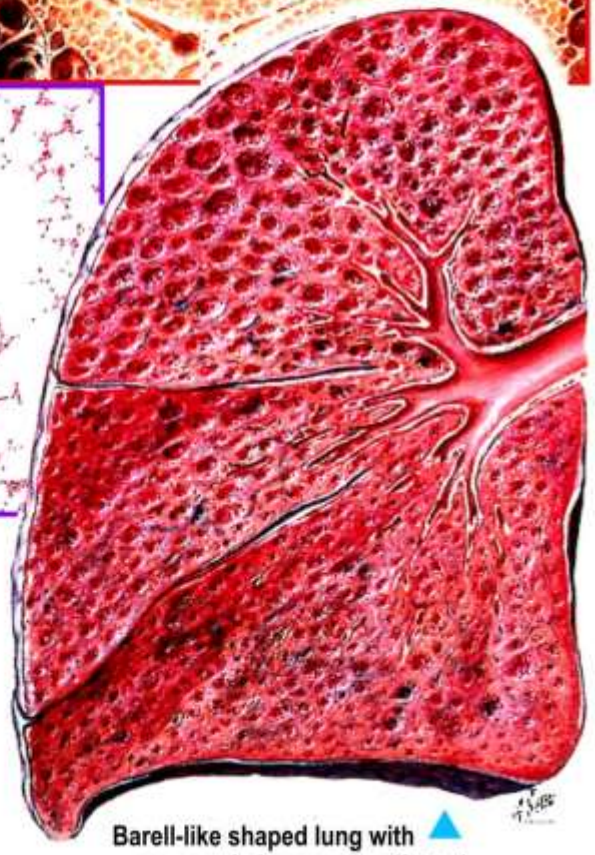
- Pathoanatomy:
  - Panlobular (panacinar)- all lung fields, particularly the bases, loss of all portions of the acinus from the respiratory bronchiole to the alveoli, typical for alpha-1-antitrypsin deficiency
  - Centrilobular (centriacinar) - upper lobes, loss of bronchioles in the proximal portion of the acinus, and alveolar ducts sparing of distal alveoli. in central portion of lungs, most typical for smokers
- Signs and Symptoms
  - Dyspnea upon exertion, wheezing, coughing
  - Pursed lip to maximize ventilation
  - Right heart failure- labored breathing, husky cough and labored heart rate ("Blue Bloaters")
  - Hypoxia, respiratory acidosis (↑ CO_2)
  - Mental vagueness, headache, twitching of fingers and eventual deep cyanosis
- Lab. Evaluation
  - ↑ TLV (Over expanded chest), ↑ RV, ↑ FEV 1%,
  - Diaphragm extended downwards and flattened
  - Respiratory muscles are weakened

Centriacinar emphysema

Distended and communicating sac-like spaces in central area of acini



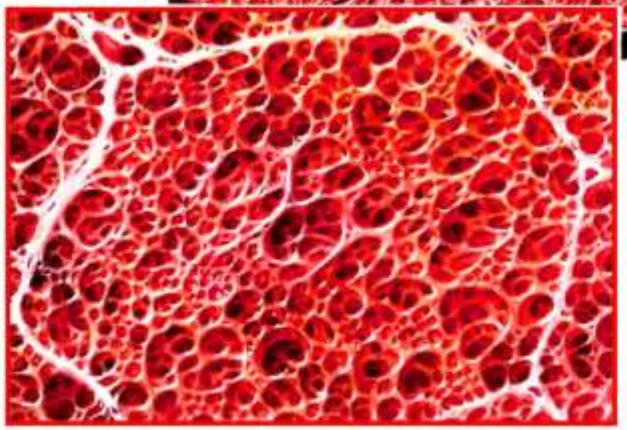
Distended airspaces with rupture of alvolar wall



Barell-like shaped lung with upper part being mostly affected

Panacinar emphysema

Dilated saccular airspaces in panlobular emphysema due to $\alpha 1$ - antitrypsin deficiency.
Barrel - like shape of lung with lower part being more affected



Diffusely enlarged saccular spaces of all portions of acini

COPD

- Definition: Progressive disease state characterized by the presence of airflow obstruction with disability of expiration
  - Clinically mixture of 3 separate diseases: **chronic bronchitis, emphysema, asthma.**
  - Other: cystic fibrosis, alpha-1 antitrypsin deficiency, bronchiectasis, bullous lung diseases
- Each case of COPD is unique in the blend of processes; 2 main types of the disease are recognized.
- Occurence: 4th leading cause of death; 10-15 (32) million diagnosed (US),

  Men more often than women; older than 40 years
- **Pathology:**
  - large (central) airways, the small (peripheral) bronchioles, lung parenchyma
  - Predominance of neutrophils and peribronchial distribution of fibrotic changes

COPD manifestations

- **CB predominant in COPD**
  - **Cough** – persists, worsens after UAW infection
  - **Sputum** - mucopurulent yellow, green, tan, or brown
  - Paroxysms of coughing+ expiratory wheezes + splitting pus
  - Cyanosis - carbon dioxide retention- advanced stages of CB; „**blue bloaters**" overweight + cyanosis
- Emphysema predominant
  - Exertional breathlessness - insidious in onset, not prone to carbon dioxide retention.
  - Barrel shaped chest, sounds are distant
  - Exhalation - prolonged and the lips are pursed during expiration - **"pink puffers."**
- **Endstage COPD**
  - Right heart failure (cor pulmonale)
  - Cough - change in sputum character and volume,
  - Breathlessness, wheeze, chest tightness can be triggered by cold, exposure to irritants, or high concentrations of pollutants

Diagnosis

- ***Spirometry*** **-** only criterion standard to demonstrate an obstructive defect -forced expiratory volume in 1 second/forced vital capacity (FEV1/ FVC)

  - FEV1/FVC defect is largely irreversible,
  - FEV1 fluctuates with bouts of bronchospasm.
  - *If ratio corrects with therapy, the diagnosis of "asthma"*

TABLE 2 Staging of COPD

FEV_1 actual/predicted	Degree of obstructive defect
>70%	Mild
60%-70%	Moderate
50%-60%	Moderately severe
34%-50%	Severe
<34%	Very severe

Key: COPD, chronic obstructive pulmonary disease.

Diagnosis

- ***Chest radiographs*** – in emphysema; in CB only increased interstitial markings (not specific for COPD or CB. In emphysema, is quite striking. Marked overdistention of the lung fields, flattened diaphragms, and increased retrosternal space are the obvious and classic findings.
- ***Sputum analysis*** Gram's staining, especially the CB type. Macrophages, neutrophils, T lymphocytes, and epithelial cells are seen in greater numbers in patients experiencing an exacerbation of the disease than they are in patients whose condition remains stable.
- ***CBC*** - evidence of eosinophilia - asthmatic bronchitis. In advanced cases of CB or emphysema, a secondary polycythemia. During exacerbations, leukocytosis and a left shift may indicate superimposed acute bronchitis or pneumonia.
- ***ECG*** - evidence of right atrial enlargement and/or right ventricular hypertrophy—right axis deviation and a posterior axis deviation.

Chronic bronchitis vs . emphysema

	Chronic bronchitis (Blue Boater)	Emphysema (Pink Puffer)
General appearance	Overweight, dusky, warm extremities	Thin, often emaciated Pursued-lip breathing – accesory muscles, anxious, cool extremities
Age onset	40-45 y	50-75 y
Symptoms	Cough – very prominent Sputum copious	Dyspnea, cought almost none Sputum scanty, clear
Acute exacerbations	Recurrent infections common	Occasional
Course Course	Cor pumonale; fast progr. to RHF, coma	During exacerbation & terminal illness cor pulmonale + RHF, prolonged course