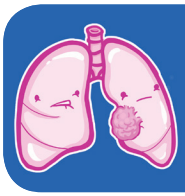

# NOTES
## OBSTRUCTIVE LUNG DISEASE

## GENERALLY, WHAT IS IT?

### PATHOLOGY & CAUSES

- Obstruction of airflow from lungs
- Increased resistance to airflow → air-trapping
- Classifications
  - Narrowing of lumen wall (e.g. asthma, chronic bronchitis)
  - Increasing pressure external to airway/loss of lung parenchyma (e.g. emphysema)
  - Obstruction of airway lumen (e.g. bronchiectasis, chronic bronchitis)

### COMPLICATIONS

- Cor pulmonale, right ventricular hypertrophy

### SIGNS & SYMPTOMS

- Cough, thick mucus, dyspnea, wheezing

### DIAGNOSIS

#### DIAGNOSTIC IMAGING

**Chest X-ray/CT scan**

#### LAB RESULTS

- Sputum culture
- Arterial blood gas (ABGs)

#### OTHER DIAGNOSTICS

**Spirometry/pulmonary function test (PFTs)**

- Tidal volume (TV)
  - Volume of air inspired, expired during quiet breathing
- Residual volume (RV)
  - Volume of air left in lung after maximal expiration
- Forced vital capacity (FVC)
  - Maximum volume of air that can be expired after maximal inspiratory effort
- Forced expiratory volume (FEV)
  - Volume of air forcibly exhaled per unit of time
- Peak expiratory flow rate (PEFR)
  - During FEV, maximum flow of expiration
- Functional residual capacity (FRC)
  - Volume of air left in lungs after quiet expiration

### TREATMENT

- See individual diseases

# ALPHA 1-ANTITRYPSIN (A1AT) DEFICIENCY

osms.it/a1at-deficiency

## PATHOLOGY & CAUSES

- Autosomal dominant (codominant) genetic disorder
  - Decreased production/absence of A1AT → overaction of proteases → damaged alveoli → damaged lungs, liver
- Lungs
  - Damaged alveoli inflammation → neutrophils secrete elastase → absence of/decreased A1AT → elastase overacts, inflames → increased breakdown of elastin → alveoli lose elasticity, integrity → chronic obstructive pulmonary disease (COPD)
- Liver
  - Genetic mutation → misfolded A1AT build up in endoplasmic reticulum of hepatocytes → kill hepatocytes → cirrhosis

### CAUSES

- Smoking
  - Earlier onset of COPD in individuals with A1AT deficiency
- Genetics
  - Serine protease inhibitor, clade A, member 1 (SERPINA1) encodes A1AT protein, located on long arm of chromosome 14
- Pi*M
  - Normal allele
- Pi*Z (most common)
  - Mutated/diseased allele
  - Misfolded A1AT proteins aggregate → stick in endoplasmic reticulum of hepatocytes → kill hepatocytes
- PiMZ
  - Heterozygous (one normal allele, one diseased allele)
  - Mutated gene contributes 10% normal amounts A1AT proteins
  - Heterozygous individuals have 60% normal levels (enough to protect lungs in non-smokers)
  - Increased risk of lung/liver disease
- PiZZ
  - Homozygous
  - Individuals only have 15–20% normal levels
  - Much higher risk of lung/liver disease
  - Can live without lung/liver disease if environmental exposures minimal
  - Infants can develop liver failure during first years of life
  - Individuals with no production of A1AT = no liver disease

### COMPLICATIONS

- COPD (emphysema, bronchiectasis, chronic bronchitis), hepatocellular carcinoma, liver cirrhosis, chronic hepatitis

## SIGNS & SYMPTOMS

- *COPD:* shortness of breath, wheezing, mucus production, chronic cough
- *Liver damage, cirrhosis, impaired liver function:* inability to make coagulation factors, hepatic encephalopathy, portal hypertension, esophageal varices, jaundice, hepatocellular carcinoma

# DIAGNOSIS

## DIAGNOSTIC IMAGING

### Liver ultrasound

### Chest X-ray/CT scan

- Hyperinflated/damaged lungs, basilar emphysema, panlobular emphysema
  - *Smoking:* apically distributed emphysema

## LAB RESULTS

- Serum A1AT levels
- Family history, genetic testing
- Liver biopsy

## OTHER DIAGNOSTICS

- PFT
  - Measure rate air exits lungs
- Periodic acid-Schiff (PAS)
  - Diastase-resistant pink globules in liver biopsy
  - Stains A1AT pink

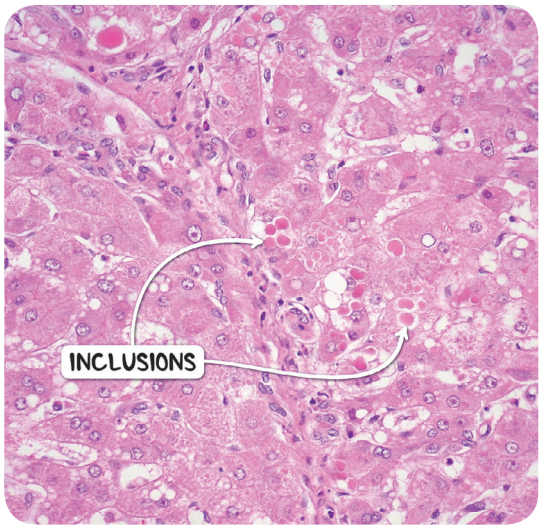


**Figure 126.1** The histological appearance of the liver in an individual with alpha 1-antitrypsin deficiency. There are globular inclusions within periportal hepatocytes.

# TREATMENT

## MEDICATIONS

- Augmentation therapy
  - Intravenous (IV) infusions of A1AT protein from plasma donors
  - Not curative, only slows progression
- Inhalers, supplemental oxygen
  - COPD
- Lactulose
  - Prevent hepatic encephalopathy
  - For liver cirrhosis

## SURGERY

- Liver transplant
  - Esp. homozygous infants, liver failure during first years
- Lung transplant

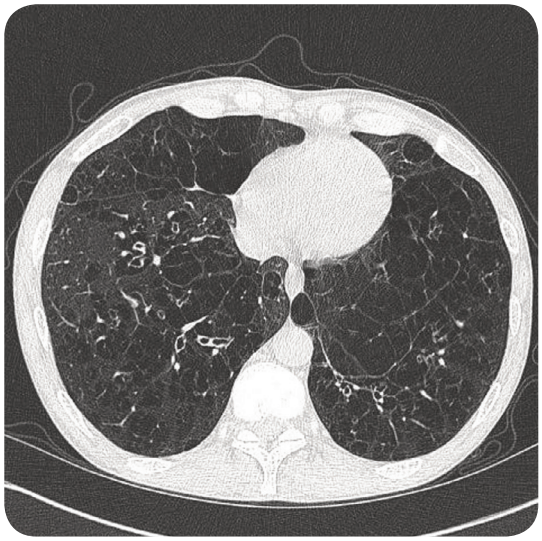

**Figure 126.2** A CT scan of the chest in the axial plane demonstrating panlobular emphysema as a consequence of alpha 1-antitrypsin deficiency.

# ASTHMA

osms.it/asthma

## PATHOLOGY & CAUSES

- Hyperresponsiveness disorder, reversible airflow obstruction
- Chronic inflammation, narrowing of airways
- Acute (Type 1 hypersensitivity reaction)
  - Initial sensitization to allergen → production of cluster of differentiation 4 (CD4), T helper 2 (Th2) cells → release interleukin 4 (IL4), interleukin 5 (IL5) → environmental trigger → eosinophils, mast cells release inflammatory mediators in bronchial walls (e.g. histamine, leukotrienes) → degradation of lipids, proteins, nucleic acids → tissue destruction → strong inflammatory reaction in bronchiolar walls → smooth muscle of bronchioles spasm, mucus in narrow airways increases → difficulty breathing
  - Vasodilation of pulmonary vasculature, increased capillary permeability → edema
  - Increased mucus production by goblet cells → impaired mucociliary function
- Chronic inflammation → scarring, fibrosis → thickening of epithelial basement membrane → permanently narrows airway
- Th2 cells release IL5 → attract, activate eosinophils
- Neutrophils release cytokines
  - Interleukin 8 (IL8)
  - More severe for individuals with neutrophilic asthma
- Triggers
  - Air pollution, cigarette smoke, dust, pet dander, cockroaches, mold, pollen, medications (e.g. aspirin, beta-blockers)

### TYPES

#### Extrinsic

- Type 1 hypersensitivity reaction triggered by extrinsic allergens (e.g. dust, mold)
- Individuals with atopic family history to allergies
- Atopic triad
  - Asthma, atopic dermatitis, allergic rhinitis

#### Intrinsic

- Nonimmune
- Viral infections, stress, exercise, smoking

## SIGNS & SYMPTOMS

- Coughing, chest tightness, dyspnea, difficulty breathing, wheezing, whistling during expiration
- Curschmann spirals in sputum
  - Spiral-shaped mucus plugs
  - Casts from small bronchi
  - Blocks air exchange, inhaled medications from reaching inflammation
- Charcot–Leyden crystals in sputum
  - Needle-shaped, formed from breakdown of eosinophils

## DIAGNOSIS

### OTHER DIAGNOSTICS

- Trigger test, spirometry, peak air flow
- Classifications based on frequency of symptoms (esp. night/morning), forced expiratory volume in one second (FEV1), PEFR, frequency of medication use (intermittent, mild persistent, moderate persistent, severe persistent)

## TREATMENT

### OTHER INTERVENTIONS

- No cure; treatments manage symptoms, prevent asthma attack
- Avoid triggers

## PHARMACOLOGICAL MANAGEMENT OF ASTHMA

| | | TREATMENTS |
|---|---|---|
| STEP 1 | Intermittent asthma | Preferred treatments: inhaled short–acting beta2–agonist (SABA) as needed (e.g. albuterol) |
| STEP 2 | Persistent asthma | Preferred treatments: low–dose inhaled corticosteroid (ICS) (e.g. fluticasone)<br><br>Alternative treatments: Cromolyn, leukotriene receptor antagonist (LTRA) (e.g. montelukast) or theophylline |
| STEP 3 | | Preferred treatments: low–dose inhaled corticosteroid (ICS) plus inhaled long–acting beta2–agonist (LABA)/ medium–dose inhaled corticosteroid (ICS)<br><br>Alternative treatments: Low–dose inhaled corticosteroid (ICS) plus leukotriene receptor antagonist (LTRA)/ theophylline/ zileuton |
| STEP 4 | | Preferred treatments: medium–dose inhaled corticosteroid (ICS) plus inhaled long–acting beta2–agonist (LABA) (e.g. salmeterol)<br><br>Alternative treatments: medium–dose inhaled corticosteroid (ICS) plus leukotriene receptor antagonist (LTRA)/ theophylline/ zileuton |
| STEP 5 | | Preferred treatments: high–dose inhaled corticosteroid (ICS) plus inhaled long–acting beta2–agonist (LABA), consider omalizumab for allergies |
| STEP 6 | | Preferred treatments: high–dose inhaled corticosteroid (ICS) plus inhaled long–acting beta2–agonist (LABA) plus oral corticosteroids, consider omalizumab for allergies |

## CLINICAL FEATURES OF ASTHMA VS. CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

| ASTHMA | COPD |
|---|---|
| Intermittent airflow obstruction | Progressively worsening airflow obstruction |
| Improved with bronchodilators and steroids | More permanent, less reversibility |
| Cellular inflammation (eosinophils, mast cells, t-cells) | Cellular inflammation (neutrophils, macrophages) |
| Airway remodeling | Emphysema frequent |
| | More common in > 50 year olds |

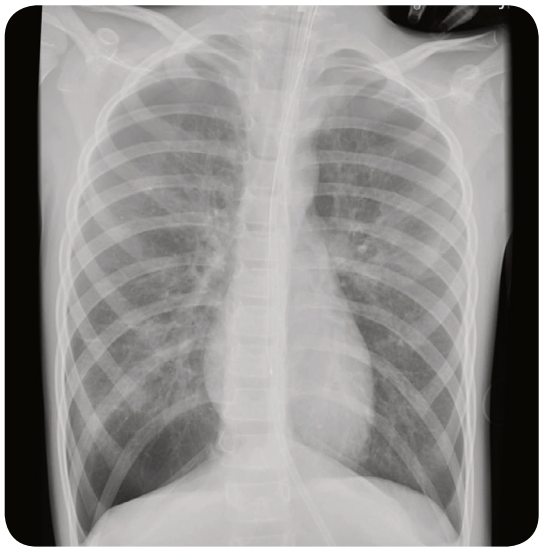

**Figure 126.3** A chest radiograph demonstrating hyperinflation in an individual with chronic asthma. There is a pneumothorax in the right lower zone.

# BRONCHIECTASIS

osms.it/bronchiectasis

## PATHOLOGY & CAUSES

- Chronic inflammation → permanent dilation of bronchi, bronchioles → destruction of airways
  - Damage to mucociliary "elevator" → mucus, bacteria accumulates

## CAUSES

### Chronic inflammation

- Primary ciliary dyskinesia
  - Absence of dynein arm in cilia → cilia move abnormally → mucus stuck in airways → bacteria in mucus multiply → pneumonia → chronic inflammation
- Cystic fibrosis (most common)
  - Mucus too sticky → hard for cilia to sweep → mucus accumulates → recurrent pneumonias → chronic inflammation, infection

### Airway obstruction

- E.g. tumor inside/outside airway, lodged foreign object
- Blockage prevents mucociliary escalator from clearing mucus → recurrent pneumonias → chronic inflammation

### Infections

- E.g. aspergillosis, tuberculosis, adenovirus, *Haemophilus influenzae*, *Staphylococcus aureus*; hypersensitivity response → inflammation
  - Chronic inflammation → immune cells, cytokines damage cilia, elastin fibers → airways dilated, clogged with mucus → fibroblasts deposit collagen → loss of elastin, buildup of collagen → lungs less elastic → more difficult for air to move smoothly → lung function declines → hypoxia → pulmonary arterioles constrict to divert blood away from damaged areas of lung → increased

pulmonary vascular resistance → right ventricular hypertrophy → cor pulmonale → inflammation of pleura

## SIGNS & SYMPTOMS

- Wheezing, productive cough, foul smelling mucus, dyspnea, hemoptysis, recurrent/persistent pneumonia, basilar crackles
- Long term hypoxia
  - Digital clubbing

## DIAGNOSIS

### DIAGNOSTIC IMAGING

#### CT scan

- Dilated bronchi/bronchioles

#### Chest X-ray

- Increased bronchial markings at lung periphery

### LAB RESULTS

- Sputum culture
- Genetic testing

### OTHER DIAGNOSTICS

- Spirometry
  - FEV1 decreased, FEV1/FVC ratio decreased
- Sweat test

## TREATMENT

### MEDICATIONS

- Bronchodilators; beta-2 agonists (e.g. albuterol)
- Inhaled corticosteroids (e.g. fluticasone
- Antibiotics
  - Recurrent pneumonias

### OTHER INTERVENTIONS

- Percussion, postural drainage
  - Recurrent pneumonias
- Pulmonary hygiene
- Adequate hydration

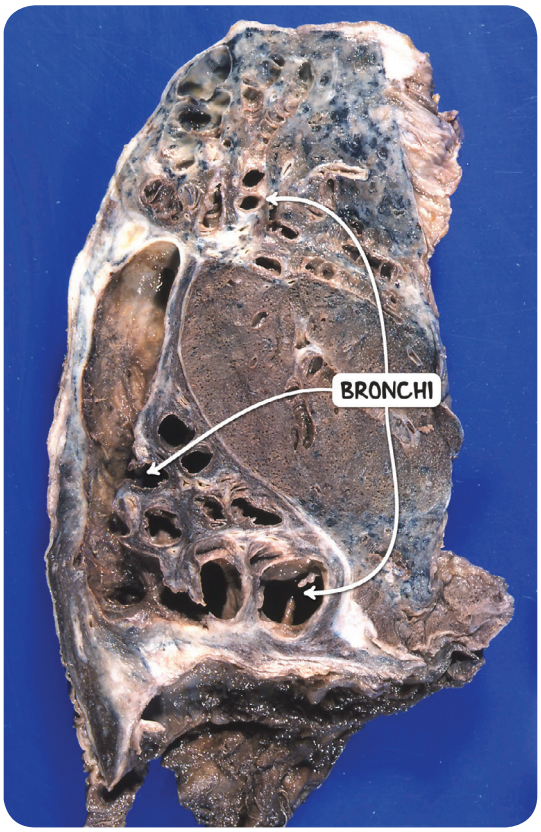


**Figure 126.4** The gross pathological appearance of the lungs in a case of severe bronchiectasis.

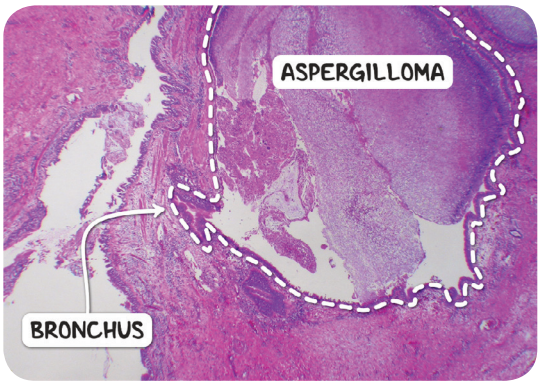


**Figure 126.5** The histological appearance of bronchiectasis complicated by fungal colonisation. There is a heavily dilated bronchus containing an aggregation of fungus known as an aspergilloma.

# CHRONIC BRONCHITIS

osms.it/chronic-bronchitis

## PATHOLOGY & CAUSES

- Preventable, progressive pulmonary disease
  - Chronic airway inflammation, limited airflow
  - Bronchial tubes in lungs inflame → productive cough
- Subset of COPD
- Exposure to irritants → hypertrophy/hyperplasia of bronchial mucous glands, goblet cells in bronchioles, cilia less mobile → increased mucus production, less movement → mucus plugs → obstruction in bronchioles → air-trapping → productive cough
- Blocked airflow, air-trapping → increased partial pressure of $CO_2$ in lungs → less $O_2$ reaches blood → cyanosis (if severe); individuals referred to as "blue bloaters"

### RISK FACTORS

- Smoking (primary cause), cystic fibrosis, sulfur, nitrogen dioxide, dust, silica, family history, genetic predisposition

### COMPLICATIONS

- Pulmonary hypertension, increased workload of right ventricle, cor pulmonale, infections distal to mucus blockages, fibrosis of terminal bronchioles, compensatory polycythemia

## SIGNS & SYMPTOMS

- Wheezing (due to mucus, narrow airway), crackles/rales (small airways pop open during air movement due to narrow passageway)
- Hypoxemia, hypercapnia (due to mucus plugs blocking air flow) → cyanosis → tissue hypoxia

## DIAGNOSIS

### DIAGNOSTIC IMAGING

#### Chest X-ray

- Large, horizontal heart, increased bronchial markings

### LAB RESULTS

- ABGs
  - Respiratory acidosis (arterial $PCO_2$ > 45mmHg, bicarbonate > 30mEq/L)

### OTHER DIAGNOSTICS

- Productive, mucinous cough
  - At least three months over two consecutive years
- PFTs
  - Increased TLC, air-trapping; decreased FVC1/FVC ratio
- Postmortem measurement
  - Reid index (measure ratio of thickness of bronchial mucinous glands, total thickness of airway, epithelium to cartilage)
  - > 40% (due to hyperplasia, hypertrophy of glands)

## TREATMENT

### MEDICATIONS

- Supplemental oxygen, bronchodilators, inhaled steroids, antibiotics
  - Manage symptoms
- Prophylactic vaccination against influenza, *Streptococcus pneumoniae* (*S. pneumoniae*)

### OTHER INTERVENTIONS

- Smoking cessation, pulmonary rehabilitation

# CYSTIC FIBROSIS (CF)

osms.it/cystic-fibrosis

## PATHOLOGY & CAUSES

- Autosomal-recessive multisystem disorder
  - Affects lungs, digestive system, reproductive system, sweat glands
- Caused by *CFTR* gene defect (located on long arm of chromosome 7)
  - Encodes cyclic adenosine monophosphate–regulated chloride channel cystic fibrosis transmembrane conductance regulator (CFTR)
  - *Various mutations:* including lack of protein production; protein trafficking defect, degradation within cellular endoplasmic reticulum, Golgi body
- Genetic defect → impaired sodium, chloride transport across epithelial cell surface → thick, tenacious secretions
  - *Classic triad:* ↑ sweat chloride levels, chronic sinopulmonary disease, pancreatic insufficiency
- Bronchi effects
  - Goblet cell hyperplasia, submucosal gland hypertrophy → production of viscous mucus, mucus plugging → airway inflammation → elastase released from neutrophils → tissue destruction → ↑ thickness of airway walls, bronchiectatic cysts, ventilation-perfusion mismatch → hypoxemia

### RISK FACTORS

- Family CF history; especially carrier parents
- ↑ incidence in white people of Northern, Central European descent

### COMPLICATIONS

- Chronic respiratory tract infections
  - *Common bacteria:* *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Haemophilus influenzae* (especially younger children)
  - Invasive fungal disease may occur → allergic bronchopulmonary aspergillosis (ABPA)
- Sinusitis
  - Related to chronic inflammation
- Significant hemoptysis
  - Related to enlarged, tortuous bronchial arteries
- Bronchiectasis
  - Due to mucus plugging
- Pneumothorax
  - Related to ruptured emphysematous bullae
- Secondary pulmonary hypertension
  - Related to small pulmonary artery hypertrophy
- Nasal polyps
  - Related to chronic inflammation
- Respiratory failure
- Non-pulmonary complications
  - Cirrhosis; gallstones; pancreatitis; heat exhaustion, dehydration; hypochloremic alkalosis (excessive salt-loss in sweat); rectal prolapse; infertility (azoospermia); fat-soluble vitamin deficiency; anemia; nail clubbing

## SIGNS & SYMPTOMS

- Highly variable presentation
  - Related to specific mutation, gene penetrance, environmental factors
- Specific pulmonary manifestations
  - Chronic, productive cough; dyspnea; ↑ anterior-posterior chest diameter; digital clubbing; basilar crackle; expiratory wheeze; generalized hyperresonance

# DIAGNOSIS

## DIAGNOSTIC IMAGING

### Prenatal ultrasound

- May detect hyperechogenic bowel, meconium peritonitis

### Chest X-ray

- Hyperinflation, air trapping, atelectasis, flattened diaphragm, peribronchial thickening, bronchovascular markings, peribronchial cuffing, parallel lines (related thickened bronchial walls—"tram tracks")

### CT scan

- Inspissated bronchial secretions; detects degree of bronchiectasis

## LAB RESULTS

- Genetic testing
- *CFTR* mutation identification
- Sweat chloride test
  - ↑ sweat chloride concentration
  - Pilocarpine administered → stimulate sweat; collected, analyzed for chloride content

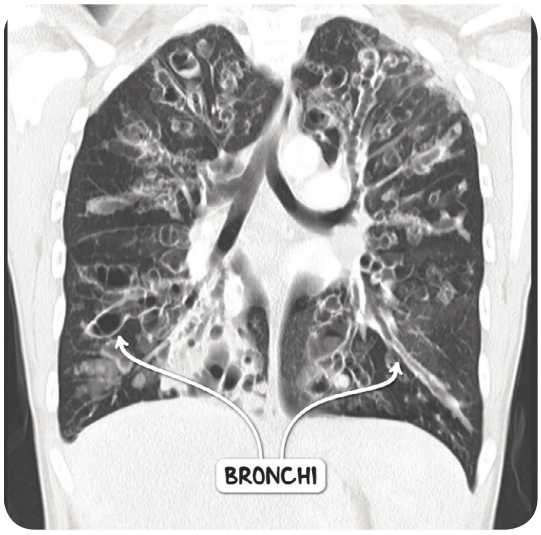


**Figure 126.7** A CT scan of the chest in the coronal plane demonstrating bilateral widespread bronchiectasis in a twenty five year old female with cystic fibrosis.

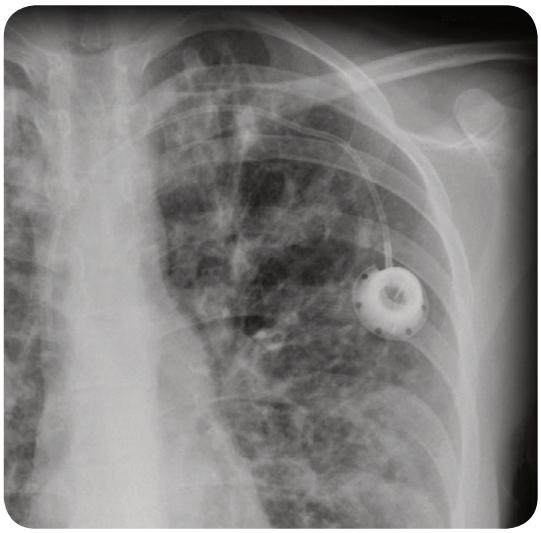

**Figure 126.6** A plain chest radiograph demonstrating tram-track opacities and ring shadows in an individual with cystic fibrosis. They are particularly well demonstrated in the left upper zone.

## OTHER DIAGNOSTICS

- Newborn screening
  - Detects CF in neonatal period; initiate early intervention
- Pulmonary function tests
  - ↓ FEV1 FEV1/FVC
  - ↑ residual volume to total lung capacity (RV/TLC) ratio
  - ↓ total lung capacity
  - ↓ vital capacity

# TREATMENT

## MEDICATIONS

- CFTR modulators
- Medications to clear respiratory secretions; inhaled hypertonic saline
- Anti-inflammatory medications (e.g. glucocorticoids)
- Antibiotics
  - Infections
- Bronchodilators
  - ↓ airflow obstruction
- Prevention
  - Annual influenza vaccine; pneumococcal vaccine

### SURGERY

- Lung transplantation
- Respiratory support
  - Respiratory failure → invasive ventilation

### OTHER INTERVENTIONS

- Address complications
- Chest physiotherapy
  - Mobilize retained secretions
- Respiratory support
  - Supplemental oxygen
  - Positive-pressure ventilation

# EMPHYSEMA

**osms.it/emphysema**

## PATHOLOGY & CAUSES

- COPD subset
  - Exposure to irritants → degrades elastin in alveoli, airways → air-trapping, poor gas exchange.
- Irritants (e.g. cigarette smoke) → attraction of inflammatory cells → release leukotrienes, chemical mediators (e.g. B4; IL8; TNF alpha/proteases, elastases/collagenases) → destroy collagen, elastin → lose elasticity → low pressure during expiration pulls walls of alveoli inward → collapse → air-trapping distal to collapse → septa breaks down → neighboring alveoli coalesce into larger air spaces → decreased surface area available for gas exchange
  - Loss of elastin → lungs more compliant (lungs expand, hold air)
  - Alveolar air sacs permanently enlarge, lose elasticity → exhaling difficult

### TYPES

#### Centriacinar/centrilobular emphysema

- Most common
- Damage to central/proximal alveoli of acinus sparing distal alveoli
  - Individuals who smoke (irritants can't reach distal alveoli); upper lobes of lungs

#### Panacinar emphysema

- Entire acinus uniformly affected
  - A1AT deficiency; lower lobes of lungs

#### Paraseptal emphysema

- Distal alveoli most affected
  - Lung tissue on periphery of lobules near interlobular septa
  - Ballooned alveoli on lung surface rupture → pneumothorax

### CAUSES

- Smoking, A1AT deficiency

### COMPLICATIONS

- Hypoxic vasoconstriction → cor pulmonale
  - Poor gas exchange → vessels vasoconstrict to shunt blood to better gas exchange → pulmonary hypertension → increased workload for right heart → right ventricular hypertrophy → cor pulmonale
- Hypoxemia
- Pneumothorax

## SIGNS & SYMPTOMS

- Barrel chest (air-trapping, hyperinflation of lungs), apparent respiratory distress with use of accessory muscles, tripod positioning, weight loss, exhaling slowly through pursed lips ("pink puffers"), hyperventilation
- Pursing lips increases pressure in airway → keeps airway from collapsing → weight loss
- Dyspnea, cough (with less sputum)

# DIAGNOSIS

## DIAGNOSTIC IMAGING

### Chest X-ray

- Increased anterior-posterior diameter, flattened diameter, increased lung field lucency (air-trapping)

## OTHER DIAGNOSTICS

- Increased TLC
- FVC decreased (esp. FEV1)

# TREATMENT

## MEDICATIONS

- Bronchodilators
- Inhaled steroids
- Combination inhalers
  - Bronchodilators + inhaled steroids
- Oral steroids
  - Adverse effects: oral candidiasis, weight gain, diabetes, osteoporosis
- Antibiotics (e.g. azithromycin prevents exacerbations)
- *Supplemental oxygen*

## SURGERY

- Lung volume reduction
  - Removal of areas of damaged lung tissue to create extra space in chest cavity for healthy lung tissue to expand
  - Can improve quality of life and prolong survival
- Lung transplant
- Bullectomy
  - Removal of bullae (large air spaces) to improve air flow

## OTHER INTERVENTIONS

- Pulmonary rehabilitation program
  - Customized education plan consisting of exercising training, nutrition advice, and lifestyle counseling

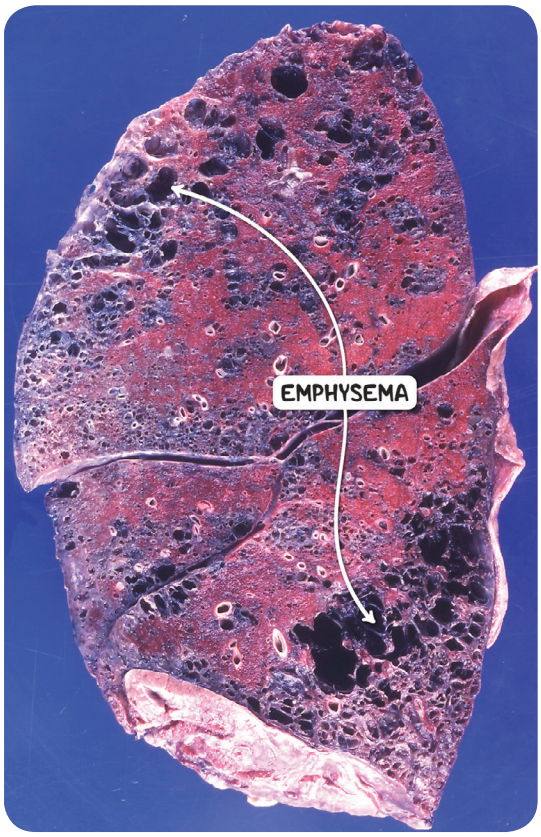


**Figure 126.8** The gross pathological appearance of emphysema. There are numerous dilated airspaces in a peripheral distribution.

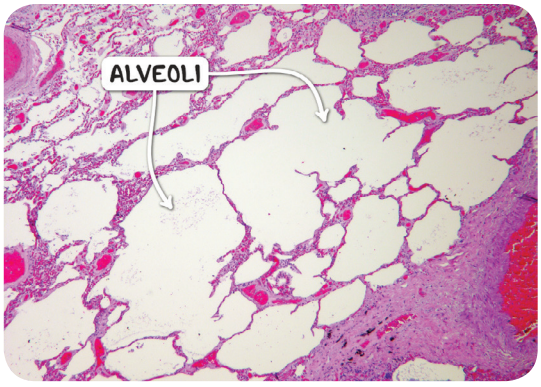


**Figure 126.9** The histological appearance of emphysema There are numerous hyperexpanded alveoli.

## COMPARISON OF SIGNS & SYMPTOMS: EMPHYSEMA VS. CHRONIC BRONCHITIS

| | EMPHYSEMA | CHRONIC BRONCHITIS |
|---|---|---|
| pH | Normal to ↑ | ↓ |
| $PaCO_2$ | Normal to ↓ | ↑ |
| $PaO_2$ | ↓ | ↓ |
| CYANOSIS | Absent | Present |
| HYPOXEMIA | Presents late | Presents early |
| DYSPNEA | Presents early | Presents late |
| APPEARANCE | Thin, leans forward when sitting, barrel chest, in apparent respiratory distress with use of accessory muscles<br><br>"Pink puffer" | Overweight, cyanotic, in no apparent respiratory distress with no apparent use of accessory muscles<br><br>"Blue bloater" |

**MNEMONIC: P vs. B**

**Emphysema vs. Bronchitis**

EmPhysema: Pink Puffer

Chronic Bronchitis: Blue Bloater