RESPIRATORY DISEASE

CONTENTS

CLINICAL ASPECTS

ANATOMY

- Right main bronchus is more vertical → ↑ risk of aspiration.
  - Divides into upper and intermediate bronchi.
  - Intermediate bronchi further divide into middle and lower lobe bronchi.

- Left main bronchus divides into the upper and lower lobe bronchi
  - Lingular branch of the upper lobe bronchus may be affected by bronchiectasis
  - All bronchis divide into segmental and sub-segmental branches.
  - At the acinus, the terminal bronchus sub-divides into bronchioles to supply alveoli.

- Left lung is divided into upper and lower lobes by the oblique fissure.
  - This runs from the 4th vertebra to the 6th costochondral junction anteriorly.

- The right lung is divided into upper, middle and lower lobes, by the additional presence of the horizontal fissure.
  - Begins at the oblique fissure in the mid-clavicular line
  - Runs anteriorly to the sternal edge of the 4th costochondral cartilage.

- Diaphragm is a muscular sheet with a central tendon on which the pericardium sits.
  - On inspiration the diaphragm descends, causing the cardiac shadow to narrow and elongate.
  - On expiration, the cardiac shadow broadens.
  - Beware a false positive cardiomegaly if the patient fails to inspire adequately on chest x-ray.
  - Conversely, cardiomegaly may be missed in a hyperinflated lung.
  - Innervation = phrenic nerve (C3, C4, C5)
  - Paralysis to one side causes a paradoxical motion (e.g. diaphragm ascends on inspiration)

- On chest x-ray (CXR):
  - Abnormalities found posteriorly on examination point to pathology in the lower lobes.
  - Masses should be described in relation to upper or lower zones of the lung (not lobes)
  - A lateral CXR will show the position of the oblique fissure, allowing identification of lobes.
  - Upper lobe collapse will cause tracheal deviation.
  - Lower lobe collapse will cause mediastinal shift. (Left lobe collapses behind the heart)
  - Middle lobe collapse shows a triangle adjacent to the right heart, with loss of border.

- Divisions of the pulmonary arteries follow those of the bronchi to the lung parenchyma.
  - Pulmonary venules will eventually drain into 4 pulmonary veins
  - In heart failure, look for upper lobe venous diversion
  - In pulmonary hypertension, look for narrowing of peripheral arteries (*pruning*) and reduced flow to the peripheries of the lungs (*oligaemia*)
  - Major pulmonary embolus (PE) can cause oligaemia to a whole zone.

- An extensive lymphatic system can be infiltrated by cancer cells → blockage
  - *Lymphangitis carcinomatosis* causes lymphatics to be seen as fine lines adjacent to the peripheral lung borders (Kerley B lines)
  - The lymphatics of the lungs drain into the thoracic duct – runs posteriorly to the root of the neck
  - Trauma or malignancy can cause blockage of the duct and leakage of lymph (*Chylothorax*)

PULMONARY PHYSIOLOGY

- To achieve gas exchange, there needs to be:
  - Adequate ventilation of the alveoli
  - Matching of ventilation (V) and perfusion (Q)
  - Diffusion of gases between alveoli and the capillary bed
  - Carriage of gases in the blood.

- Other functions of the lung include modification of drugs and hormones (e.g. AT I to AT II), and to act as a physical (e.g. cilia) & immunological (e.g. macrophages, IgA) barrier to noxious/pathogenic agents.

- Ventilation:
  - Inspiration is an active process, whereas expiration depends mainly on elastic recoil.
  - Ribs move up and out, and the diaphragm descends on inspiration.
  - Abdominal muscles and accessory muscles may be utilised under excess stress or a rise in airflow resistance (e.g. chronic bronchitis or emphysema)
  - Impairment of ventilation causes a $\uparrow pCO_2$, and can be caused by:
    - Respiratory muscle weakness (Guillain-Barré syndrome)
    - Diaphragmatic weakness (phrenic nerve palsy)
    - Thoracic spine and rib disorders (kyphoscoliosis)

- The respiratory centre in the brainstem controls respiration, and is altered by neurogenic (e.g. pain/anxiety) and chemical stimuli.
  - PaO_2 11-13 kPa 80-100 mmHg
  - $PaCO_2$ 4.8-6.0 kPa 35-45 mmHg
  - pH 7.35-7.44
  - HCO_3^- 22-30 mmol/l

- These ranges are maintained by a pulmonary blood flow (Q) of 5 litres/min, and a ventilation (V) of 6 litres/min.
  - Tidal volume is about 500 ml, which is divided into alveolar ventilation and dead-space air ventilation (150 ml).
  - Dead-space air is predominantly in the larger airwars, but PE can lead to an increase in dead-space air.

- Chemical stimuli of respiration is achieved predominantly via the hypercapnic drive ($\uparrow PaCO_2$)
  - In patients with chronic bronchitis or emphysema, sensitivity to $\Delta PaCO_2$ are lost, and the individual relies on his hypoxic drive ($PaO_2 < 8$ kPa)
  - Administration of high inspired oxygen is therefore dangerous.
  - Acidosis ($\uparrow [H^+]$) stimulates respiration (e.g. Kussmaul's respiration seen as "deep sighing" in metabolic acidosis)
  - Opiates and sedatives can depress the respiratory centre, while other drugs (e.g. aspirin) stimulate it.
  - Other stimuli include PE and sepsis.

- Ventilation-perfusion matching:
  - V > Q at the apices → bronchoconstriction
  - Q > V at the lung bases → vasoconstriction of arterioles

- In diseases affecting lung parenchyma (e.g. fibrosing alveolitis, atelectasis or collapse), this local control breaks down resulting in perfusion without ventilation.
- This results in hypoxaemia = the hallmark sign of V/Q mismatching.
- In contrast to local defects in blood-flow mechanism causing hypoxia, global defects in ventilation tend to cause hypercapnia.
- V/Q scanning is used to identify pulmonary emboli, with multiple defects often seen in areas remote from a CXR abnormality, or the side with pleuritic pain.

- Oxygen is transported in the blood as oxyhaemaglobin.
  - Its pressure-saturation characteristics are such that at normally a large fall in pressure causes a small change in saturation.
  - However under hypoxic conditions (e.g. in working tissue where PO_2 < 5.3 kPa or 40 mmHg), a small fall in pressure causes a large fall in saturation, as oxygen is released from haemoglobin and delivered to the tissues.
  - Under conditions such as ↑ temperature, acidosis or hypercarbia, the O_2-saturation curve shifts to the right causing a decreased affinitity of Hb for O_2 → more oxygen released to tissues.

COMMON SYMPTOMS

- Breathlessness = a subjective description of sensation.
  - Should not be confused with dyspnoea or tachypnoea.
  - Need to clarify degree of disability caused by breathlessness
  - NYHA dyspnoea scale:
    - Class O
    - Class I
    - Class II
    - Class IIIa
    - Class IIIb
    - Class IV

  - Need to determine:
    - Nature of onset?
    - How long?
    - Does it vary with time?
    - What effects their breathing? (e.g. summer or "morning dipping" in asthmatics)

- Wheeze – a frequent symptom of patients with airflow obstruction
  - Diurnal/seasonal variation suggests asthma
  - Heart failure can produce wheeze (e.g. cardiac asthma)
  - Must exclude an inspiratory stridor implying an extra-thoracic airflow obstruction

- Cough – either in association with breathlessness or on its own.
  - Most often caused by a recent infection
  - Mycoplasma can cause a prolonged dry cough (<4 weeks), but persistence may reflect bronchial hypersensitivity from asthma.
  - Productive cough:
    - Clear mucoid sputum in smokers
    - Yellow/green sputum in patients with infection
    - Yellow mucus plugs expectorated in bronchopulmonary aspergillosis

- Large volume of sputum typically associated in bronchiectasis.

- Causes of cough:
  - URTI/LRTI
  - Asthma
  - Rhinitis, chronic sinusitis
  - Oesophageal reflux
  - COPD
  - Smoking
  - 1° or 2° lung tumour
  - LVF
  - ACE inhibitors
  - Bronchiectasis
  - Ear wax, foreign body in ear canal
  - Radiotherapy
  - Alveolitis
  - Sarcoidosis
  - Aspiration
  - Cystic Fibrosis
  - Laryngeal carcinoma
  - Diaphragmatic abscess

- Haemoptysis causes:
  - Bronchial disease – carcinoma or bronchiectasis
  - Parenchymal disease – TB, pneumonia, actinomyces/aspergilloma fungal infections
  - Lung vascular disease – PE, pulmonary infarct, polyarteritis nodosa, or Goodpasture's.
  - Physical cause – trauma, or Mallory-Weiss equivalent.
  - Exclude haematemesis or bleeding from nasopharynx.

- Chest pain (non-anginal):
  - Pleuritic? (sharp, worse on inspiration or coughing)
  - Rib fracture? (sudden onset, h_x of trauma, pain on movement, local chest wall tenderness)
  - Musculoskeletal? (exacerbated by movement, but not by inspiration)
  - Pericardial pain?
  - Other causes include Herpes-Zoster, which is often misdiagnosed until the appearance of the characteristic rash.

PEAK EXPIRATORY FLOW RATE (PEFR) TEST

- Standard test for airflow obstruction; result depends on age, height and gender
- Interpret result by comparing it with a predicted value.
- Low values obtained by poor technique or respiratory muscle weakness.
- Normal or increased values may be seen in *restrictive* lung disorders.

- Technique:
  - Re-set the peak flow meter, and add a clean mouthpiece.
  - Hold the device and take a deep breath in.
  - Place the mouthpiece in the mouth, and wrap lips around it to make a good seal.
  - Breath out *as hard and as fast as you can.*
  - Record measurement 3 times, and use patient's best value.

- Diurnal variation in bronchomotor tone causes bronchoconstriction. This is exaggerated in asthmatic patients, and is seen as severe "morning dipping".

- Spirometry provides more information such as the forced expiratory volume in one second (FEV_1) and the forced vital capacity (FVC)
  - Obstruction (e.g. asthma) will give a $\downarrow$ FEV_1/FVC ratio.
  - Restriction (e.g. pulmonary fibrosis) will give an increased or unchanged FEV_1/FVC ratio.

COMMON DRUGS

- β_2-agonist Bronchodilators
  - Salbutamol and terbutaline are commonly used
  - Work directly on the β_2 receptors within airways, causing smooth muscle relaxation
  - Metered dose inhalers (MDIs) are commonly used.
  - Patients must be educated in the use of MDIs, and technique must be checked:
    - Shake inhaler
    - Fully expire
    - Place inhaler in mouth, and "fire" at the start of inspiration
    - Continue to full inspiration
    - Hold breath, then repeat as prescribed.
  - Spacer devices (e.g. volumatic/nebuhaler), or dry powder systems (e.g rotacaps/turbohalers).
  - If oral doses are used, they must be larger than the inhaled dose → ↑ s/e
  - Side effects include tremor, anxiety and palpitations.

- Theophyllines
  - Antagonise intracellular PDE (phosphodiesterase), preventing breakdown of cAMP
  - Promotes smooth muscle relaxation.
  - Nocturnal administration may alleviate early morning dipping.
  - Need to monitor blood levels.
  - Side effects include:
    - Nausea
    - Abdominal pain
    - Palpitations
    - Arrhythmias (if overdosed by i.v. therapy)
    - Insomnia
    - Anxiety
    - Convulsions (if overdosed by i.v. therapy)

- Anticholinergics – prevents bronchoconstriction
  - Ipratropium Bromide is most commonly used
  - Given by inhalation route, since poorly absorbed from the GI tract.

- Corticosteroids – suppresses the inflammatory response
  - Beclomethasone or budenoside should be given on a *regular* basis to patients with reversible airflow limitation, in conjunction with bronchodilators.
  - S/e = oropharyngeal candidiasis with dysphonia
  - Oral R_x reserved for those with chronic asthma that is unresponsive to inhaled therapy.
    - <10 mg Prednisolone, to reduce adrenal suppression and long-term side-effect such as osteoporosis and cataracts.
    - Also used vs. other respiratory conditions such as vasculitis or sarcoidosis.

- Disodium Chromoglycate
  - Stabilises mast cells, to prevent histamine release
  - Used as prophylaxis in young people with asthma or atopy.
  - Administered as a dry powder inhaler.
  - No major side-effects.

- Antitussives – suppresses a cough, but beware pooling of secretions and a hypostatic pneumonia.
  - "Simple lictus" has a soothing nature useful vs. mild irritative coughs
  - Opioids are the most effective, working on both lung and central brain receptors
  - Codeine or phosphcodeine elixir are 1st line treatments; use morphine if there is pain as well.

INFECTIVE DISORDERS

CLASSIFICATION

- Pneumonia
  - An acute, infective, respiratory illness
  - Typified by fever, cough, dyspoea, and a new infiltrate on CXR
  - Production of purulent sputum → bronchopneumonia
  - If localised to one area, clearly demarcated on CXR → lobar pneumonia by *Strep. pneumoniae*

- Atypical pneumonia
  - Erythromycin or tetracycline responsive pneumonia (includes *Legionella* pneumonia)
  - Non-bacterial pneumonia (includes viruses & *Mycoplasma*, excludes *Legionella*)
  - Often present with extra-pulmonary symptoms:
    - Headache
    - Jaundice
    - Diarrhoea

- Aspiration pneumonia
  - Following vomiting or reflux
  - Gastric contents cause an infective and chemical (acidic) pneumonia
  - Common in alcoholics, stroke victims, and those with impaired mental function.

- Pneumonitis
  - Implies a new, diffuse pulmonary process. May or may not be infective.
  - Fine bilateral shadows on CXR
  - Typically caused by viruses (e.g. adenovirus), or CMV in the immunocompromised.

- Acute bronchitis
  - Acute infection of the bronchial tree
  - Productive cough and mucopurulent sputum, ± fever.
  - No new CXR abnormalities
  - Usually caused by the same bacteria that cause pneumonia.

- Acute Tracheitis (Tracheobronchitis)
  - Typically viral (e.g. parainfluenza)
  - Patient complains of a painful, rasping cough, in the anterior chest
  - Commonly no fever
  - CXR usually normal
  - Need to exclude stridor caused by a foreign body, and bacterial epiglottitis.

COMMUNITY ACQUIRED PNEUMONIA

- Increasingly common with age, and in debilitated individuals.
- Mortality is 6-20%

- Caused by microscopic aspiration of bacteria from the nasopharynx, nose or oesophagus
  - 45% of normal adults aspirate during sleep! (radioisotope tracer studies)
  - bacteria enter trachea and reproduce → bronchial ± parenchymal infection
  - the bacterial flora of the nasopharynx and throat, will determine the causative organism

❖ Pneumoncoccal and *Haemophilus* pneumonia

- Most common cause of community acquired pneumonia (50-80%)
- Often part of the commensal flora in the nasopharynx
- Elderly, alcoholics and immunocompromised are at higher risk
- Conversely, *Haemophilus influenzae* is an uncommon cause of pneumonia.
- Abrupt onset if lobar pneumonia; more gradual onset in bronchopneumonia

- Symptoms:
  - Fever (usually high)
  - Shaking chills
  - Rigors imply bacteraemia
  - Productive cough
  - Pleuritic chest pain
  - Dyspnoea
  - Acute confusional state in elderly
  - Headache is unusual (cf. atypical pneumonias)
- Signs:
  - Pyrexia & toxic appearance
  - Flushed and distressed
  - Tachypnoea + use of accessory muscles
  - Central cyanosis (if severe)
  - Crackles over affected lung area
  - Bronchial breathing
  - Pleural rub (occasional)
  - Labial herpes simplex reactivation

- Investigations:
  - CXR – for type and extent of involvement
  - ABG – to determine appropriate O_2 therapy
  - FBC
  - Blood Cultures – to isolate pathogen, and target R_x
  - U&E – hyponatraemia is typical of Legionella infection; ↑ urea is a poor prognostic sign
  - LFT – often abnormal in *atypical* pneumonias
  - Serology (serum)
  - Sputum microbiology
  - Pneumococcal antigen test from sputum and urine specimens
  - Legionella antigen from urine specimen

- R_x:
  - ↑ concentrations of humidified O_2
  - tracheal aspiration and physiotherapy in patients producing sputum
  - 3rd generation cephalosporins (e.g. cefotaxime or ceftriaxone)
  - Quinalones (ciprofloxacin or norfloxacin) are not effective vs. *Strep. pneumoniae*
  - Erythromycin is 1st choice in the community. Beware ↑ resistance (10-15%).

- Prognosis:
  - Pneumococcal pneumonia has a 5% mortality. Rises to 75% if ICU care needed.
  - Poor prognostic signs:
    - Respiratory rate > 30 min^{-1}
    - Diastolic b.p. < 60 mmHg
    - Urea > 7 mmol/left

- Complications:
  - Respiratory failure
    - ↑ pCO_2, a ↓ pO_2 (<70 mmHg), or an exhausted patient are indications for ventilation

- Empyema
- Pericarditis
- Meningitis
- Endocarditis
- Arthritis
- Bacterial peritonitis
  - Beware the patient with a persistent fever, despite antibiotics.

➢ Patients who are asplenic or have sickle cell anaemia are at a risk of an overwhelming pneumococcal infection.
- Require immunisation and lifelong prophylaxis.

❖ **Staphylococcal pneumonia:**
➢ Occurs as a super-infection following influenza
➢ Extremely high mortality
➢ Patients deteriorate rapidly
➢ Respiratory failure, ↑ fever, and general features of sepsis
➢ Sputum analysis = gram +ve cocci in intracellular clusters
➢ Evidence for maximum anti-staphylococcal R_x:
- 2g Flucloxacillin, 4 hourly
- Vancomycin for MRSA

❖ **Legionnaire's disease:**
➢ Caused by *Legionella pneumophila* – a gram negative, pleomorphic rod.

➢ Transmission is through inhalation of an infected aerosol (water droplets)
- Transmission is promoted by crowding, moisture and humidity
- Particularly common in Spanish holiday resorts by ↓ sanitation in shower heads and air conditioner systems.

➢ 31% community acquired, 4% nosocomial, and 64% imported infections.
- Chronic chest disease, smoking, immunosuppression, and age are risk factors.
- Transplant surgery is a risk factor in nosocomial infections

➢ Inhalation of dead organisms results in **Pontene fever**:
- 90% attack rate, 1-2 days incubation
- Mild symptomology, that includes fever and myalgia
- Clears quickly without treatment
- ↓ ↓ ↓ mortality

➢ Inhalation of live organisms results in severe **pneumonia**:
- <5% attack rate
- 2-10 days incubation
- Sudden onset SOB + tachypnoea (30-40 min^{-1})
- Localised pleural chest pain, can refer to shoulder or abdominal wall
- Painful cough (dry → productive of sputum)
- Severe vomiting and diarrhoea → hypovolaemia and shock.
- Malaise + headache
- High fever → mental confusion
- *Hyponatraemia and proteinuria accompanies symptoms of pneumonia*

- Rapid deterioration to a multi-systems disease (lungs → liver & kidneys)
- 20% mortality (rises to 40% if the diagnosis is late)

- Diagnosis from bronchial washings.
  - ↓ respiratory movement, ? pleural rub
  - ? pleural effusion (look for stony dullness and persistent pyrexia)
  - consolidation after 48 hours, with ↑ pitched bronchial breath sounds
  - coarse crepitations on resolution (indicated liquefaction of alveolar exudates)
  - *immunofluorescence*

- Treatment = 0.5 - 1g erythromycin q.d.s. + 600mg rifampicin b.d.
  - Use a fluoroquinalone, if there is a penicillin allergy.

❖ **Mycoplasma pneumonia:**
- An atypical pneumonia
- Fever, malaise and headache will precede the respiratory symptoms
- Most common in 5-20 year olds. But can affect the whole family.
- Tends to occur in 4-yearly cycles

- Clinical features:
  - Unproductive cough without lobar involvement
  - Haemoptysis possible
  - Tracheobronchitis ± pharyngitis (sore throat and retrosternal chest pain)
  - Mild to moderate fever (37.5 – 38.0 °C)

- R_x = tetracycline and erythromycin

- Complications:
  - Myringitis – inflammation of the eardrum (15%)
  - Maculopapular skin rashes (15%)
  - Meningoencephalitis and other neurological problems (<10%)
  - 50% will develop *cold haemagglutinins* (= cross reaction with the I antigen of red cells), after 10 days of illness.

❖ **Influenza:**
- Caused by influenza viruses A and B
- Common infection, and its remarkable antigenic variation allows for multiple re-infection
- Incubation period is 1-3 days
- Immunization and amantadine (anti-viral) prophylaxis reduces attack rates
- R_x = neuro-aminidase inhibitors is effective, and may reduce transmission

- Clinical features:
  - Abrupt onset (lasts 3 days)
  - Feverishness, chills, headaches, myalgia, malaise and anorexia
  - Painful eye movements
  - Burning sensation in eyes
  - Sense of photophobia
  - Dry cough
  - Clear nasal discharge
  - Throat may be reddened
  - Small lymph nodes often palpable in the neck.

- Pregnancy and cardiovascular disease are also risk factors

- Severe influenza
  - Super-infection with *Staph. aureus*
  - Increased mortality in elderly

❖ **Other Viruses:**
- Adenoviruses
- Measles
- CMV in immunocompromised.

NOSOCOMIAL PNEUMONIA

❖ Usually caused by gram negative organisms
- Use of broad-spectrum antibiotics changes the commensal flora of the nasopharynx, predominantly to gram –ve species.
- This change can occur independent of infection in patients with NG- or ET-tubes.
- Use of H_2-antagonists increases stomach pH, allowing proliferation of gram –ve bacteria.

❖ Clinical features are similar to those of community-acquired pneumonias
❖ Lobar and atypical pneumonias are rare, except for *Legionella sp.*
❖ R_x = cefotaxime, or ceftazidime if *Pseudomonas* is suspected.

❖ Aspiration Pneumonia
- Relatively common, after inhalation of gastric or pharyngeal contents.
- Anaerobes are more commonly implicated → use metronidazole or carbapenem.

PNEUMONIA IN THE IMMUNOCOMPROMISED

❖ Any new respiratory symptom or new infiltrate on CXR should be urgently investigated.
- The time from the 1st cough to death is 5-7 days with CMV or *Aspergillus* pneumonia

❖ More important to ascertain the aetiology, since *Pneumocystis, Pseudomonas, Aspergillus, Nocardia, Mycobacterium tuberculae*, and CMV are often implicated..
- Bronchoscopy, bronchoalveolar lavage, CT and percutaneous biopsy of the chest are useful, if performed rapidly.

❖ Begin empirical treatment immediately, until results of culture and sensitivity arrive.
❖ Get expert advice!

LUNG ABSCESS

❖ Some pneumonias will develop into an abscess.
❖ Typically involved are:
- *Staph. aureus*
- Anaerobes
- *Klebsiella pneumoniae*
- Fungal infections (e.g. *Aspergillus*)

❖ Look for a large circular lesion with cavitation, and an air/fluid level on CXR
❖ R_x = long term (for 2-4 months) antibiotics/antifungals, with postural drainage.

TUBERCULOSIS

- Caused by *Mycobacterium tuberculosis* or atypical mycobacteria.
- Around one third of the world's population is currently infected by *M. tuberculosis*
- Rates are rising as a result of AIDS and deterioration of social conditions in inner cities.
- Infection commonly occurs in childhood in developing countries.
- At risk are:
  - Elderly
  - Immunocompromised
  - Homeless
  - Alcoholics

- Infections are acquired by inhalation of infected droplets
  - Most infectious are patients with cavitary pulmonary TB with sputum containing visible acid-fast bacilli, who are coughing.
  - *People not coughing are essentially non-infectious*

- Clinical features:
  - Chronic, mildly productive cough
  - Fever
  - Weight loss

- Diagnosis:
  - CXR shows asymmetrical upper lobe or apex of lower lobe infiltrates, with cavitation
  - 3 samples of sputum collection for microscopy and culture
    - obtained on separate days, in the morning
  - Bronchoscopy with washings/brushings can verify the diagnosis.

  - Skin testing allows an assessment of population prevalence, and the infection status of relatives/contacts of a TB patient.
    - Mantoux test (intermediate strength is commonly used, 1 in1000)
    - Heaf test is easier to grade, but more specialised.
    - Beware false negatives in immunocompromised, malnourished individuals, and patients with sarcoidosis.
    - A florid positive test implies not simply prior exposure, but also disease.

- Treatment:
  - 10% in the UK have frank resistance to one of the 1st line drugs
  - 4% to two or more drugs (multi-drug resistant TB)
  - Rifampicin + Isoniazid & Pyrazinamide
    - Isoniazid can cause *pellagra* (mixed peripheral neuropathy and hyperpigmentation)
    - Co-administer pyridoxine (vitamin B_6)
  - Indications for a 4th drug are:
    - Life threatening disease (e.g. meningitis)
    - Immunocompromised patients
    - Previously treated TB with relapse
    - Region of origin has ↑ resistance (e.g. Phillipines, Vietnam, Cambodia, New York)
    - Contact with patients known to have MDR-TB
  - 6 months of treatment is appropriate in uncomplicated cases, with pyrazinamide and ethambutol being stopped after 2 months.
  - If patient is compliant, the relapse rate after 6 month R_x, is <3%
  - Mortality rate is 10-15%

CHRONIC PULMONARY & BRONCHIAL SEPSIS

- TB, sarcoidosis, lung cysts, and ankylosing spondylitis cause cavities
  - Within these cavities bacteria and fungi can thrive
  - Cavities usually communicate with the bronchial tree, allowing organisms to enter and pus to leave.

- **Aspergilloma** – most common inhabitant of a tuberculous cavity
  - Once inhaled, will reproduce to form a fungal ball (= aspergilloma)
  - Not invasive, but produces toxins that cause symptomology
    - Productive cough
    - Haemoptysis
    - Clubbing in 30%
  - R_x is difficult, since drugs do not penetrate the aspergilloma easily
  - Surgery has many complications

- **Bronchiectasis** (means dilatation of the bronchi)
  - Causes include:
    - Congenital or genetic (e.g. cystic fibrosis)
    - Childhood infection (e.g. whooping cough)
    - Bronchial obstruction (e.g. overlooked foreign body)
    - Allergic disease (e.g. allergic bronchopulmonary aspergillosis)
    - Autoimmune disease (e.g. 1° biliary cirrhosis)

  - *Dry* bronchiectasis:
    - Usually asymptomatic
    - Identified on CXR by curly or ring shadows in the lung
    - Commonest presentation is haemoptysis → suspicion of cancer is natural.
    - Bronchoscopy is usually normal
    - Confirm diagnosis by a high quality CT scan of the chest.

  - *Wet* bronchiectasis:
    - Presents with a chronic productive cough
    - Large volume of grossly purulent sputum
    - No fever
    - Co-existent sinusitis
    - Worse in the morning
    - Clubbing if the disease is chronic
    - Usually caused by same organisms that cause pneumonia.
    - *Pseudomonas aeruginosa* may appear later in antibiotic treated patients.

  - Management:
    - Antibiotics for exacerbations (occasionally need admission for i.v. R_x).
    - Physiotherapy with postural drainage
    - Mucolytics
    - If just one lobe is involved, and respiratory function is good → surgical resection.

  - Complications:
    - Cor pulmonale (from pulmonary fibrosis)
    - Brain abscess.

TUMOURS

BRONCHIAL CARCINOMA

- Most common cause of malignancy in ♂; incidence has plateaued.
- Second to breast carcinoma in ♀; incidence still rising because of Δ in smoke habits.
- ♂ : ♀ ratio is 3 : 4.1
- Common in urban areas → associated with atmospheric pollution.
- Main risk factors are:
  - SMOKING + chemical/occupational exposure (e.g. asbestos and radon)

- *Non-small cell (squamous) carcinoma*
  - Squamous carcinoma accounts for just under 50% of all 1° malignancies
  - Squamous Metaplasia → carcinoma in situ → invasive carcinoma.
  - Usually central in origin, and frequently cavitates.
  - Peripheral lesions may invade the chest wall
  - Distant metastases are frequent
  - Commonly cause hypercalcaemia through bone destruction or parathyroid hormone-related peptide (PTHrP)
  - Managed using radiotherapy and surgical resection (20-25% 5-year survival).
  - Chemotherapy is of no use

- *Small cell carcinoma*
  - 30% of lung cancers
  - *Oat cell* carcinoma arise from the APUD system (amine precursor uptake decarboxylase)
  - Neurosecretory granules common
  - Tumour releases peptides with hormonal activity (e.g. ADH, ACTH)
  - Arise centrally
  - Grow rapidly, and disseminate early
  - Debulked using radiotherapy and surgery. Good response to chemotherapy thereafter.

- *Large cell carcinoma*
  - Undifferentiated tumours
  - 25% of lung cancers
  - Arise centrally
  - Metastasise early
  - Poorer prognosis
  - Radiotherapy offers palliation, and surgery is less effective than with squamous cell carcinoma.
  - Chemotherapy is of no use.

- *Adenocarcinoma*
  - Account for 10% of lung cancers
  - Occur peripherally, or in areas of lung scarring
  - Seen in smokers and non-smokers
  - Frequently seen as a consequence of asbestos exposure
  - No cavitation
  - Local invasion of the pleural space common
  - If biopsied, it is hard to differentiate 1° from 2° malignancy arising from another adenocarcinoma elsewhere (e.g. GI-tract)
  - Poor response to chemotherapy and radiotherapy, though some palliation may be achieved.
  - Surgery offers poor survival chances.

- Local clinical features:
  - Persistent cough or breathlessness
  - ? Coexistent chronic bronchitis and emphysema
  - ? manifests as infection with signs of collapse/consolidation
  - Beware an infection that is slow to clear or is recurrent
  - Ill-defined or pleuritic chest pain?
  - Severe unremitting pain → local invasion of the chest wall, ribs or vertebra.
  - Haemoptysis from endobronchial erosion into blood vessels
  - Central tumour with hilar involvement can obstruct the superior vena cava
    - Facial swelling, headache and dilated chest wall veins
  - Phrenic nerve damage → elevated (hemi)-diaphragm, with paradoxical movement. (elevation on inspiration)

- Pancoast's syndrome:
  - Apical tumour invades the lower portion of the brachial plexus (C7-T1)
  - Pain along medial border of the hand & arm
  - Weakness of the intrinsic muscles of the hand
  - Wasting of the thenar and hypothenar eminences
  - Horner's Syndrome may also occur as a result of damage to the sympathetic outflow through T1.
  - Subclavian veins may be infiltrated, causing thrombosis.

- Distant symptoms:
  - Secondary disease from distant metastasis to the:
  - Brain → fits, hemiparesis
  - Bone → pain, pathological fracture
  - Liver → hepatomegaly
  - Lymph nodes or elsewhere
  - Most likely in small cell carcinomas.

- Non-metastatic manifestations of malignancy:
  - Anorexia
  - Weight loss
  - Dermatomyositis, Eaton Lambert syndrome, polymyopathy
  - Hypercalcaemia, hyponatraemia
  - Gynaecomastia
  - Clubbing
  - Hypertrophic osteoarthropathy (HPOA)
  - Peripheral neuropathy
  - Encephalopathy & cerebellar degeneration

- Investigations:
  - CXR (plain PA, as well as lateral)
    - Irregular pulmonary mass, with possible cavitation
    - Partial or complete collapse of a lobe
    - A hilar mass
    - A pleural effusion with any of the above
    - Sequential enlargement → always compare with previous films.
  - CT scan – for diagnosis and staging
  - Sputum cytology

        - Use nebulised saline and physiotherapy to obtain a sample
        - Positive sample *makes* the diagnosis, but a negative one will not rule out carcinoma.
    - Bronchoscopy
        - Allows visualisation of a centrally located endotracheal tumour
        - Allows collection of biopsy, brushings of lavage.
    - Pleural aspirate of an effusion
    - FNAC (CT or USS guided)
    - Thoracoscopy may be used in mediastinal disease.

- Surgical Constraints:
    - What is the cell type? Non-small cell carcinoma is amenable to surgery
    - Is the tumour confined to the lung? Metastasis contra-indicates sugery
    - Is the tumour technically respectable? Too close to the carina? More than one lobe?
    - Lung function? $FEV_1 < 1½$ litres is unsuitable for surgery.
    - Quality of life? Concomitant disease (e.g. coronary artery disease)?

- Radiotherapy:
    - Can be used for debulking.
    - Useful in palliation of haemoptysis, bone metastases, and SVC obstruction.
    - S/e = radiation pneumonitis, and progressive fibrosis leading to breathlessness.

- Chemotherapy:
    - Improves outlook in small cell carcinoma
    - Increases median survival from 2 months to 12 months.
    - Occasionally achieves long-term remission.

ALVEOLAR CELL CARCINOMA

- Very rare, slow growing tumour
- Unrelated to smoking
- Arises in areas of damaged lung
- Histological appearance of malignant cells growing along bronchi
- Presents with:
  - Breathlessness
  - Bronchorrhoea (large volumes of sputum)
  - Single/multiple areas of consolidation on CXR
- Sputum cytology may be positive, but differentiation from an adenocarcinoma is hard
- FNAC or surgical biopsy is therefore needed
- Surgical resection early on offers good results

BRONCHIAL ADENOMA

- Uncommon and benign endobronchial tumours
- Arise from the APUD system
- Most present in young adulthood (♂:♀ =1)
- Produce local effects:
  - Airway obstruction
  - Collapse
  - Distal infection (recurrent, non-resolving)
  - Cough
  - Haemoptysis
  - Unilateral wheeze
- Carcinoid syndrome is a rare manifestation (secretion of 5-hydroxytryptamine analogues)
- Rarely becomes malignant
- Usually not detectable on CXR, unless there is collapse → diagnose using bronchoscopy.
- Surgical resection is curative.

METASTATIC DISEASE

- The lung is a common site for secondary deposits of carcinoma.
- The pleura is particularly affected, with a pleural effusion developing.
- 1° malignancies tend to have an ill-defined border on CXR, with streaky shadowing.
- In contrast, 2° tumours may have a "cannon-ball" appearance, with a smooth rounded opacity.
- Lymphomas can cause diffuse disease in the lung.
  - Can block the thoracic duct → chylothorax
  - Can cause mediastinal lymph node enlargement.

SOLITARY PULMONARY NODULE

- 40% represent a malignant process – most are bronchial adenomas or 2° deposits.
- 60% are benign – TB, non-infective (Wegener's) granulomas.
- Always compare with previous CXRs.
- FNAC is more useful than bronchoscopy, since nodules are usually parenchymal.
- Surgical resection is often required, before the diagnosis can be established.

LYMPHANGITIS CARCINOMATOSIS

- Malignant cells grow along the lymphatic channels of the lungs.
  - Can be a consequence of disseminating bronchial carcinoma
  - Or breast carcinoma in women
  - Gastric and pancreatic carcinoma are also implicated.

- Patients present with intense breathlessness + a dry cough.
- Examination may reveal a few fine basal crackles?
- CXR may show streaky, fine basal shadows with Kerley B lines.
- No specific R_x; opiates may alleviate breathlessness.

CHRONIC AIRFLOW OBSTRUCTION

CHRONIC BRONCHITIS & EMPHYSEMA

- Chronic bronchitis is *pathologically* an increase in bronchial wall thickness, with hyperplasia & hypertrophy of the mucous glands.
  - Excess mucous secretions, and wall thickening cause obstruction to airflow
  - *Clinically*, the patient must have at least a 2 year h_x of a productive cough on most days, for a minimum of 3 months of each year.

- Emphysema – pathological destruction of the acinus.
  - *Centrilobular*:
    - Commonest
    - Associated with smoking
    - Affects upper zones of the lungs
    - Proximal part of the acinus is destroyed
  - *Panacinar:*
    - Associated with α_1-antritrypsin deficiency (autosomal recessive, 1 in 5000)
    - Smoking, which activates proteases, exacerbates the condition
    - Can progress to respiratory failure in 4th-5th decade of life
    - Predominantly affects the lower zones of the lungs.

- Risk factors:
  - Smoking
  - Male
  - Living in urban areas
  - ↓ Social class
  - Air pollution

- Symptoms:
  - Productive smoker's cough – clear mucoid sputum
  - Progressive breathlessness
  - "colds going to the chest" – infective exacerbations with purulent sputum
  - worsened by cold, pollution, fog, and upon waking.
    - Always consider asthma, if there is chronic and marked diurnal variation.
  - No clubbing – cf. bronchiectasis

- Signs of Type 1 Respiratory Failure: (Pink Puffer)
  - ↑ respiratory drive - tachypnoea
  - Hypoxic & hypocarbic
  - O_2 desaturation on exercise
  - Pursed lips
  - Use of accessory muscles
  - Indrawing of intercostal muscles
  - Wheeze & rhonci
  - Hyperinflated chest

- Signs of Type 2 Respiratory Failure: (Blue Bloater)
  - ↓ respiratory drive - hypoventilation
  - Hypoxic, but hypercarbic
  - Right heart failure (peripheral oedema)
  - Confusion, drowsiness
  - Papilloedema
  - Cyanosis
  - Wheeze & rhonci
  - Hepatic congestion
  - Warm peripheries, bounding pulse

- Investigations:
  - CXR:
    - Hyperinflation
    - Upper zone bullae
    - Lower zone bullae in α_1-antitrypsin deficiency
    - Pulmonary conus & pruning of pulmonary vasculature → pulmonary hypertension
  - Lung Function Tests:
    - ↓ PEFR
    - ↓ FEV_1
    - ↓ FEV_1/FVC ratio
    - ↑ TLC (total lung capacity)
    - reduced or normal transfer factor (depending on degree of emphysema)
  - ↑ Hb – 2° erythrocytosis
  - ECG – "P"- pulmonale, right ventricular hypertrophy
  - ABGs

- Management:
  - Greatest impact of halting progression = quit smoking
  - Regular exercise can maintain function
  - Influenza vaccination - ↓ acute deteriorations
  - ↓flow O_2 (≈24%), for >15 hours per day
  - Bronchodilators – salbutamol (β_2-agonist) or ipratropium bromide (anti-cholinergic)
  - Theophyllines
    - ↑ dose in smokers, drinkers, or those taking anticonvulsants (enzyme induction)
    - ↓ dose in hepatic/cardiac failure, and elderly
    - ↓ dose in patients taking cimetidine, allopurinol, erythromycin, and propranolol
  - Corticosteroids
    - Trial to exclude reversible airflow obstruction
    - i.e. >15% improvement of PEFR or FEV_1/FVC ratio after a 14 day course of 30 mg/day prednisolone.
    - Continue inhaled steroids, if reversible airflow obstruction proven.

- Complications:
  - Acute infective episodes
  - Respiratory failure
  - Cor pulmonale
  - Pneumothorax
  - Pulmonary embolus (in immobile patients)

- Acute infective episodes:
  - Very commonly treated unnecessarily by antibiotics.
  - Exacerbation may be the result of a pneumothorax, heart failure, stress or non-compliance
  - Exacerbation may be viral in origin
  - Sputum cultures may be positive *Strep. pneumoniae* or *H. influenzae* – but these can be commensal
  - Yellow/green sputum may be normal in some patients (especially in the morning)
  - A small ↑ WCC may reflect water depletion or stress, rather than infection
  - Always determine the following before R_x antibiotics:
    - Evidence for pneumonia (e.g. new CXR abnormality)?

        - Severe exacerbation - ↑ dyspnoea *and* ↑ sputum volume *and* purulent sputum?
    - Management of acute exacerbations:
        - Early diagnosis
        - Appropriate antibiotics:
            - Oral cephalosporins
            - Amoxycillin or C.O.-amoxiclav
            - Erythromycin (if allergic, or an atypical infection)
        - Maintain or ↑ bronchodilators by use of a nebuliser
        - Short course of ↑ dose of corticosteroids
        - Admit to hospital if not responding

- Respiratory failure:
    - In an acute situation renal compensations would not have occurred, so there will be a respiratory acidosis (caused by CO_2 retention)
    - Treat any heart failure and correct any hypovolaemia – to impove tissue O_2 delivery
    - Discontinue any sedatives
    - 24% oxygen therapy in Type 2 respiratory failure.
    - Can be increased to 28% with the use of **doxapram** (a respiratory stimulant)
        - Close monitoring needed, since overdose leads to convulsions.

- Cor pulmonale:
    - Heart failure, 2° to lung disease
    - Pulmonary hypertension causes right ventricular and atrial hypertrophy
    - Fluid retention, ↑ JVP
    - Peripheral oedema
    - ↑ breathlessness

- Only 30% of patients with severe COPD and cor pulmonale will survive 5 years
    - At high risk of IHD, and lung cancer if they continue smoking.

ASTHMA

- ↑ prevalence – accounts for 2000 deaths per year in the UK
- Hypersensitivity of bronchi → widespread reversible narrowing of airways.
- 5% of children, and 2% of adults affected.
- Occupational risks include: polyurethane (toluene di-isocyanate) and textiles (cotton, byssinosis) industries.

- Intrinsic asthma:
    - Non-atopic
    - Late onset
    - Chronic condition with little seasonal variation
    - Nasal polyps
    - Aspirin sensitivity
    - Variable response to β_2-agonist bronchodilators
    - No response to mast cell stabilisers (disodium chromoglycate)
- Extrinisc asthma:
    - Atopic
    - Positive family h_x
    - ↑ IgE + blood eosinophilia
    - Early onset
    - Intermittent, seasonal nature
    - Sputum production
    - No nasal polyps or sensitivity to aspirin
    - Good response to bronchodilators and mast cell stabilisers

- Pathophysiology:
  - Immediate hypersensitivity reaction produced by the binding of IgE (on mast cells) to antigen.
    - Causes mast cell degranulation, with release of histamine and *eosinophil chemotactic factor of anaphylaxis*
    - Through the action of PL-A_2, arachadonic acid is transformed into inflammatory mediators such as prostaglandins and leukotrienes (by the COx and lipo-oxygenase pathways)
    - LT-D_4 is the most potent broncho-constrictor
    - Platelet activation factor also implicated.
    - Culminates in chemotaxis of eosinophils, T-lymphocytes and macrophages.
    - Δs in calcium regulation → bronchoconstriction.
  - A delayed immune reaction also takes place.
  - Final pathological features:
    - Severe mucus plugging (yellow – packed with eosinophils and epithelial cells)
    - Basement membrane thickening in the bronchi
    - Mucosal and sub-mucosal thickening
    - Eosinophil/neutrophil infiltration
    - Vasodilatation
    - Mucus gland hyperplasia
    - If chronic → irreversible changes.

- Symptoms:
  - SOB
  - Wheeze
  - Diurnal/seasonal variation (a.m. and ↑ pollen counts)
  - Productive cough with mucus plugs – consider bronchopulmonary aspergillosis

- Signs:
  - Distress
  - Central cyanosis
  - Tachypnoea
  - Use of accessory muscles
  - Tachycardia – may be the result of overuse of β_2-agonists
  - Pulsus paradox
  - Widespread inspiratory and expiratory wheezes
  - Inability to speak?
  - Δ in consciousness – muscle fatigue, profound hypoxia, hypercarbia?
  - Silent chest – mucus plugging hinders airflow further?

- Diagnosis – prove a >15% revsersibility of airflow obstruction
  - Use a 1-2 week trial of corticosteroids
  - Exclude differential for wheeze – e.g. heart failure, PE, foreign body/tumour obstruction.
  - Rare causes:
    - Tropical eosinophilia
    - Churg-Strauss Syndrome (eosinophilic syndrome)
    - Carcinoid syndrome

- Investigations:
  - Spirometry (↓ FEV_1, FVC)
  - Monitor with symptom diaries
  - Lung function tests (hyperinflation, ↑ TLC)
  - Normal ABGs (? hypoxaemia during acute attacks)
  - CXR – hyperinflation? Collapse caused by mucus plugs? Segmental/lobar atelectasis?
  - Mild eosinophilia in young, extrinisic asthmatics
  - Positive skin tests to multiple allergens.

- Managing acute asthma (*Status asthmaticus*)
  - Progressive deterioration over several hours or days, usually in response to a definite trigger (e.g. chest infection, or NSAIDs)
  - Occasionally, *brittle* asthma = abrupt onset, and life-threatening.
  - **Must perform:**
    - **PEFR** – gross ↓ (<100 ml/min)
    - **CXR** – hyperinflation/atelectasis/collapse? Pneumothorax excluded?
    - **ABGs** – hypoxaemia, hypocarbia & alkalosis. Normocarbia is an ominous sign.
  - ↑ dose oxygen therapy (60%)
  - 2.5 – 5 mg **salbutamol** via nebuliser, every 3-6 hours
  - Nebulised **ipratropium bromide**
  - Correct any dehydration
  - If admission necessary
    - i.v. bolus of **hydrocortisone** (3-6 mg/kg)
    - 40-60 mg oral prednisolone in divided doses

  - 0.5 mg/kg infusion of **aminophylline**
    - If the patient is not already taking oral theophyllines, then a bolus of 5 mg/kg can be given over 20-30 minutes
    - Titrate dose to maintain blood levels between 10-20 mg/l
    - Reduce dose in patients with hepatic or cardiac disease

  - Avoid sedation
  - Use appropriate antibiotics, if evidence of a bacterial infection.
  - Intubation and artificial ventilation if further deterioration with signs of exhaustion and mental changes.

- Emergency treatment of acute asthma:
  - Assess severity rapidly:
    - **P**ulse (<115 min^{-1})
    - ***P***O_2 (< 60 mmHg, 8 kPa)*; **P***CO_2 (> 41 mmHg, 5.5 kPa)
    - **P**EFR (<130 ml/min, or unrecordable)
    - **P**aradox
    - **P**neumothorax
    - **P**anic (inability to speak complete sentences in a breath, or at all)
    - ↓ O_2 saturation (<93%)
    - Cyanosis
    - Silent chest, ↓ consciousness

- R_x:
  - ↑ flow oxygen
  - nebulised salbutamol (5 mg)
  - i.v. hydrocortisone (200 mg)
- Investigate = request CXR to exclude a pneumothorax
- Reassess frequently; call for senior help early.

❖ Managing chronic asthma:
- Regular outpatients/asthma clinic follow-up.
- Education on self-monitoring, and adjustment of inhaler usage/dose.
- Symptomatic relief using β_2-agonists, theophyllines and anticholinergics.
- Prophylactic relief using corticosteroids and disodium chromoglycate.
- Following an acute attack:
  - Prescribe a reducing course of steroids over a few weeks, or substitute with inhaled steroids.
  - Ensure this is done in conjunction with the patient carefully monitoring their symptoms and airflow limitation with a home peak flow meter.
  - Advise patient to contact GP and reduce steroid dose no further, if asthma deteriorates.

❖ Complications:
- Pneumothorax
- Lung collapse from mucus plugging.

❖ Most asthmatics are children, whose symptoms will improve or disappear spontaneously with maturity. Late onset indicated chronicity and difficulty treating.

❖ 33% of deaths occur within a couple of hours of the onset of attach. Two-thirds of these deaths are potentially preventable, given adequate assessment and treatment!

PULMONARY EOSINOPHILIA

❖ A blood eosinophilia with pulmonary infiltrates
- Pulmonary infiltrates are often transient and peripheral on CXR

❖ Symptoms = SOB and a cough

❖ Asthmatics develop hypersensitivity to *Aspergillus fumigatus* (a ubiquitous fungus)
- Causes allergic bronchopulmonary aspergillosis
- Patients have green "rubbery" mucus plugs + fever
- Recurrent pulmonary infiltrates on CXR (upper lobe shadowing) give the diagnosis in asthmatics.
- ↑ IgE levels, and +ve precipitins to *Apergillus*.
- R_x = oral corticosteroids vs. acute attacks.

❖ Other causes of pulmonary eosinophilia:
- Drug induced (e.g. sulphonamides, nitrofurantoin, hydralazine)
- Helminthic infection (e.g. *Ascaris lumbricoides*, Loeffler's syndrome)
- Fungi (e.g. *Aspergillus, Candida*)
- Cryptogenic (e.g. eosinophilic pneumonia)
- Granulomatosis (e.g. Churg-Strauss syndrome)

INTERSTITIAL LUNG DISEASE

CRYPTOGENIC FIBROSING ALVEOLITIS

- Unknown aetiology, occurring in middle-age
- ♂>♀
- Inflammatory response within alveoli (predominantly polymorph leucocytes)
- Progresses to pulmonary fibrosis
- **Hamman-Rich syndrome** – rare acute form; death within a few months.
- Gradual onset SOB + cough

- Signs:
  - *Clubbing*
  - Fine, late inspiratory crackles at the lung bases
  - Tachypnoea?
  - Cyanosis (end-stage)

- Investigations:
  - Lung function tests show a *restrictive* pattern
  - ABGs show hypoxia with hypocarbia → increased respiratory drive
  - CXR – bi-basal shadowing with *honeycombing*
  - Autoantibodies ☑ (e.g. rheumatoid factor)

- R_x = corticosteroids and immunosuppressives (no proven benefit)

EXTRINSIC ALLERGIC ALVEOLITIS

- Bird fancier's lung:
  - People keeping pigeons or budgerigars
  - Pathology = formation of granuloma with subsequent fibrosis
  - Damaged initiated by a particular antibody. (Precipitins +ve)
  - Lung function tests show a *restrictive* pattern, with ↓ lung volumes & ↓ transfer factor.

- Pigeon fancier's lung:
  - Episodic exposure, with an acute illness several hours after each exposure.
  - Fever
  - Cough + SOB
  - Myalgia
  - o/e – lung crackles

- Budgerigar fancier's lung
  - Exposure is more constant → progressive breathlessness and cough

- Other causes include: paraquat poison, (100%) oxygen, and radiation.

- Culminates in severe *upper lobe* fibrosis with cavitation
  - Inspiratory crackles and wheeze
  - *Uncommon* finger clubbing (cf. cryptogenic fibrosing alveolitis)

- Management = antigen avoidance + corticosteroids.

SARCOIDOSIS

- Unknown aetiology affecting young adults
- ♀>♂
- Afro-Carribeans > Caucasians

- Pathology:
  - T-cell activation with granuloma formation
  - No central necrosis (cf. TB)
  - Characterised by ↑ levels of angiotensin-converting enzyme (ACE)
  - **Anergy** is found with ↓ peripheral T-cell immunity
  - Pulmonary fibrosis occurs as the disease progresses.

- Clinical features:
  - Blindness, 2° to uveitis
  - Erythema nodosum, keloid and lupus pernio = skin manifestations
  - Neuritis, space-occupying lesions or sterile meningitis = CNS involvements
  - Pyrexia of unknown origin (PUO)

- Most common site is the lung. 3 classifications:
  - I – hilar lymphadenopathy alone; erythema nodosum?
  - II – hilar lymphadenopathy and pulmonary infiltrate.
  - III – pulmonary infiltrate with fibrosis

- Investigations:
  - CXR:
    - Stage I = hilar shadowing
    - Stages II and III = parenchymal shadowing in both lung fields
  - ↑ serum ACE
  - Lung function tests - ↓ transfer factor, and a *restrictive* pattern.
  - If active disease → gallium lung scan reveals widespread uptake
  - Hypercalciurea?
  - Hypercalcaemia?
  - Broncho-alveolar lavage - ↑ T-lymphocytes
  - Anergy to intradermal tuberculin testing
  - **Kweim test** – sarcoid tissue injected intra-dermally, and biopsied 6 weeks later
    - +ve = typical non-caseating granuloma
    - may be negative during Stage I of the disease.

- Management:
  - Stage I cases mainly resolve spontaneously
  - Corticosteroids, if progressive disease, ↓ pulmonary function or extra-thoracic symptoms

WEGENER'S GRANULOMATOSIS

- Widespread granulomatous angiitis of lungs, kidneys and upper respiratory tract.
- ♂>♀
- Symptoms:
  - Haemoptysis
  - SOB
  - Pleuritic pain
  - General malaise
  - ↓ grade pyrexia

- Signs:
  - Bilateral pulmonary nodules, that may cavitate.
  - *No* hilar lymphadenopathy
  - **Anti-neutrophil cytoplasmic antibodies (ANCA)** ☑ (consistent with vasculitis)

- Renal involvement determines outcome
- R_x = corticosteroids & Cyclophosphamide achieves remission in most patients.

GOODPASTURE'S SYNDROME

- A disease of young men
- Presents with pulmonary haemorrhage and glomerulonephritis
- **Antiglomerular basement membrane antibodies** ☑
- R_x:
  - Dialysis
  - Plasma exchange to remove the antibody
  - Cytotoxic therapy

OTHER CAUSES OF PULMONARY FIBROSIS

- Drugs:
  - Cytotoxic drugs (e.g. bleomycin, MTX) – 1st indication is ↓ transfer factor
  - Amiodarone
  - Nitrofurantoin

- Autoimmune Disease:
  - Rheumatoid arthritis (with strongly +ve rheumatoid factor)
    - diffuse fibrosis
    - nodular fibrosis – particularly with pneumoconiosis; *Caplan's* syndrome
    - focal fibrosis
  - Systemic sclerosis
  - SLE – pleurisy, vasculitis
  - Ankylosing spondylitis – upper lobe fibrosis

- Occupational:
  - *Pneumoconiosis* = spectrum of fine mottling to progressive fibrosis, or nodular.
  - *Asbestosis* – basal, pleural calcification; associated with mesothelioma and bronchial carcinoma.
  - *Silicosis* – "eggshell" calcification in hilar nodes

MISCELLANEOUS RESPIRATORY DISEASE

SLEEP APNOEA SYNDROME

- The absence of gas flow at the mouth/nose for 10 seconds, during sleep.
  - >30 episodes per night

- Obstructive apnoea:
  - No airflow despite chest wall movement
  - More common
  - Associated with obesity, hypertension and daytime somnolence
  - H_x of noisy snoring

- Central apnoea
  - No chest wall movement.
  - Snore less
  - Night-time wakening
  - Not obese
  - Morning headaches
  - Intellectual deterioration
  - Pulmonary hypertension and RHF may supervene

- Need to be monitored while asleep, in special units.
- R_x = weight reduction, and protryptalline (a TCA)

ADULT (ACUTE) RESPIRATORY DISTRESS SYNDROME

- ARDS has a ↑ mortality once established
- ARDS is characterised by:
  - Progressive hypoxaemia
  - Reduced lung compliance
  - Normal left atrial pressure
  - Widespread bilateral pulmonary infiltrates

- Initial damage = pulmonary capillary endothelium
  - ↑ permeability + leak of plasma and red cells into the interstitium/alveoli

- Causes:
  - Sepsis
  - Trauma
  - Aspiration
  - Smoking
  - Disseminated intravascular coagulapathy (DIC)

- Management = special care & ICU
  - Maintain tissue oxygenation using ventilation methods that minimse ongoing damage to the lungs.
  - Remove/treat the initial trigger.
  - Fluid balance (prevent overload)
  - Inotropic agents.

PLEURAL DISEASE

- Parietal pleura lines the thoracic cavity and mediastinum
- Visceral pleura covers the lungs
  - Rich in blood vessels and lymphatics
  - No pain fibres
- The pressure within the space is *negative* ($\approx$ -5 cm H_2O)

PLEURITIC PAIN

- Major causes:
  - Infection
  - PE
  - Malignancy
  - Trauma (e.g. fractured ribs from a cough fracture)

- Pain should be relieved, to prevent splinting of the ribcage
  - Poor respiratory effort and cough → hypostatic pneumonia/respiratory failure
  - Use NSAIDs to relieve bone pain and inflammation
  - Strong opiates can cause respiratory depression.

PLEURAL EFFUSION

- An effusion is detected clinically above 500ml
  - May be loculated in the transverse fissure
  - Analyse for protein, glucose and amylase.
  - Send to microbiology: gram stain, culture, and examination for TB
  - Cytology for malignancy (e.g. lymphoma or malignancy)

- Transudates = protein < 20 g/l
  - Congestive cardiac failure
  - Hypoalbuminaemia
  - Nephrotic syndrome
  - Constrictive pericarditis
  - Hypothyroidism
  - Meig's Syndrome (right pleural effusion with ovarian fibroma)
- Exudates = protein > 30 g/l
  - Infection (including TB)
  - Malignancy (bronchogenis carcinoma, lymphangitis carcinomatosis, mesothelioma)
  - Connective tissue disease (e.g. rheumatoid, SLE)
  - Pulmonary infarction

- Signs:
  - Decreased chest expansion
  - Stony dullness on percussion
  - ↓ tactile vocal fremitis and breath sounds.
  - Above the effusion line, where the lung is compressed → bronchial breathing?
  - Blunting of the costo-diaphragmatic recesses.
  - An absolutely horizontal upper lung border, indicates a pneumothorax.

- Management:
  - Make an aetiological diagnosis by aspiration.
  - Small effusions may simply be aspirated
  - Essential in a small haemothorax – prevents organisation, fibrosis and adhesions.
    - Also blood is a good culture medium for bacterial colonisation
  - A chylothorax is caused by obstruction of the thoracic duct.
  - Large effusions require an intercostal drain.
  - Rapid aspiration can lead to distress, and may cause pulmonary oedema.
  - For recurrent effusions caused by malignancy, tetracycline is used as a sclerosing agent to cause *pleurodesis* (adhesions to obliterate the pleural space)

INFECTION OF THE PLEURAL SPACE

- Pleurisy:
  - A sharp chest pain on inspiration, with features of infection.
  - Caused by lobar pneumonia, or viral infections (e.g. Coxsackie B)
  - Investigations = CXR and WCC
  - Manage with analgesia and antibiotics if appropriate.

- Parapneumonic Effusions:
  - Simple = -ve culture, and resolved without loculation or drainage
  - Complicated = + culture/gram stain, loculates and required drainage.
  - > 50% of patients with pneumococcal pneumonia will develop a pleural effusion
    - need to ascertain whether it is a simple or complicated effusion
    - assess pH or glucose of pleural aspirate
    - pH < 7.2 or glucose <2.5 μmol/l → complicated effusion

- Empyema:
  - Can be in the absence of a preceding chest infection
  - Subacute course (over weeks) of weakness, anorexia and weight loss.
  - Little or no fever.
  - Foul smelling and purulent pleural fluid. Often coloured opaque.
  - R_x = antibiotics + chest drainage (occasionally needs open surgical drainage)
  - Most common organisms = Gram –ve ae robes (e.g. *E. coli*) and anaerobes.
  - Treat rapidly to prevent:
    - Loculation
    - Subsequent restrictive pulmonary disease
    - ↓ Lung movement

- Tuberculous Empyema
  - Relatively common manifestation of post-1° TB
  - Symptoms:
    - Breathlessness (can be SOB at rest, if effusion is very large)
    - Fever
    - Weight loss
    - Chest pain
  - Exudate contains: ↓ sugar, ↓ yield bacilli, but ↑ lymphocytes.
  - Pleural fluid contains mycobacteria in 20% of patients
  - Pleural biopsy is more sensitive (95%)
    - Granulomata seen histologically

PNEUMOTHORAX

- Presents with SOB and chest pain.
- Commonly spontaneous in young males, or 2° to trauma.
- ↑ resonance on percussion, with ↓ breath sounds
- Frequently diagnosed on CXR
- Leak often closes spontaneously → manage simply by aspirating
  - Insertion of a chest drain is mandatory if patient needs ventilation
- Can seriously compromise breathing in asthmatics or patients with chronic bronchitis.
- *Tension* pneumothorax is a medical emergency:
  - Increasingly severe SOB
  - Cyanosis
  - Deviated trachea
  - Absence of breath sounds on one side.
  - Required immediate intrathoracic decompression.

ASBSESTOSIS

- Exposure leads to basal pulmonary fibrosis + pleural plaques & calcification.

- H_x of working in shipyards with boilers, or in demolition, or as laggers.

- Signs:
  - Clubbing
  - Breathlessness
  - Cough
  - CXR shows predominantly basal Δ.
  - Asbestos bodies usually present in the sputum, if severe disease.

- Frequently leads to bronchial carcinoma or mesothelioma (particularly in smokers)

- **Mesothelioma**:
  - Occurs after minimal exposure to blue asbestos (*crocidolite*)
  - Develops many years later
  - Presents with chest wall pain, and breathlessness.
  - CXR – lung gradually encased in malignant tissue + fibrosis
    - Effusion also present
    - USS helps delineate tumour from fluid.
  - Biopsy will confirm the diagnosis.
    - s/e = development of nodules along the course of the biopsy track.
  - Tumour can spread through the diaphragm.
  - Distant metastases are rare
  - No curative treatment → R_x = specialist analgesia.