

RESPIRATORY NOTES

LUNG FUNCTION

A decrease in *diffusion capacity* (DLCO) indicates interstitial lung disease.

Forced Expiratory Flow (FEF) 25%-75% primarily reflects the status of the small airways and is more sensitive than the FEV1 for identifying early airway obstruction. It is impaired in bronchiolitis obliterans, smokers, and in patients with lung and heart transplant.

Functional residual capacity is measured at the end point of respiration. FRC is raised due to increased air trapping in bronchiectasis.

Residual Volume is equal to Total Lung Capacity minus Vital Capacity.
Residual Volume is usually 20% of the TLC.

Restrictive lung disorders are characterised by reduced FEV1 & FVC, FEV1/FVC >70%, reduced TLC & RV and reduced TLCO.

Causes of **restrictive lung defect** are :

- neurogenic or psychogenic causes
- abnormalities of the thoracic wall
- stiff parenchyma (pulmonary fibrosis)
- loss of lung tissue, e.g. pneumonectomy
- displacement

Obstructive lung disorders are characterised by reduced FEV1 & FVC, FEV1/FVC < 70%, raised TLC & RV (gas trapping) and reduced TLCO (emphysema) or normal or raised TLCO (asthmatics).

Occupational asthma is defined as asthma induced or aggravated by work. 3-6% of all asthma cases are suspected to be occupational related.

The highest groups at risk include: spray painters (isocyanate)
plastic makers (resins)
farmers (grain dust)
bakers (flour)

The main objective test in occupational asthma is the two-hourly serial measurement of peak flow for at least two weeks while at work and two weeks while away from work. Full blood count may show eosinophilia. Specific IgE may be raised but it tends to disappear within six months if not exposed to the suspected substance.

The **British Thoracic Society Asthma guidelines** are as follows:

Step 1: PRN use of inhaled short-acting beta agonists

Step 2: regular inhaled steroids

Step 3: high-dose inhaled steroids, or low-dose inhaled steroids plus long-acting beta agonist

Step 4: high-dose inhaled steroid and regular bronchodilators (sustained release

theophylline, inhaled ipatropium, oral long-acting beta agonist, high-dose inhaled bronchodilators, cromoglycate / nedocromil)
Step 5: addition of regular steroid tablets

Severity of emphysema is defined by the British Thoracic Society (BTS) in relation to **FEV1**, not FEV1:FVC ratio. Mild is 60-80% predicted; moderate 40-60% and severe <40%.

Severe COPD is diagnosed if the FEV1 is less or equal to 30% predicted.

In infective exacerbations of **COPD**, *Streptococcus pneumoniae* and *Haemophilus influenzae*, as well as *Moraxella* are the commonest organisms.

ALVEOLAR DISEASE

Extrinsic allergic alveolitis causes a neutrophilia due to cell mediation and eosinophils are normal. Bronchoalveolar lavage shows lymphocytes and mast cells. EAA is a delayed hypersensitivity reaction which may be immune complex (III) mediated or cell mediated (type IV) in chronic disease. Precipitins to micropolyspora faeni in farmer's lung or aspergillus are seen. Upper zone fibrosis and crackles can be heard. Symptoms are typically of breathlessness but not wheeze.

Extrinsic Allergic Alveolitis is a type III or type IV response. There is no eosinophilia. IgG and lymphocytes are involved in immune response.

Antigens of micropolyspora faeni and thermoactinomyces are 0.5-5 microns (not mm). These constitute inhaled antigens which may be detected as precipitins. Haemoptysis is uncommon but can occur. The acute form takes about 6 hours for sensitisation to the inhaled antigen. The chronic form may take weeks. The chronic form is characterized by gradual development of cough, dyspnea, malaise, anorexia, and weight loss.

Particle distribution in the lungs parallels the distribution of ventilation; ventilation is greater in the dependent lung bases than in the apices. With chronic exposure, the upper zones are more severely affected.

As in extrinsic allergic alveolitis, haemoptysis and wheeze are uncommon in **cryptogenic fibrosing alveolitis**. Dry cough and breathlessness is common. Rheumatoid factor and anti nuclear antibody may be raised. Neutrophils are raised in CFA, Rheumatoid arthritis and asbestosis. Lymphocytes are raised in granulomatous and drug induced lung disease.

CYSTIC FIBROSIS

Cystic Fibrosis The abnormality is the chloride transporter, which is encoded by the cystic fibrosis transmembrane conductance regulator (CFTR) gene, and is cAMP driven. The commonest CFTR gene mutation is due to deletion of 3 base pairs affecting the delta 508 position (phenylalanine) on chromosome 7 (mnemonic : cystic seven). The condition is autosomal recessive.

Pulmonary disease develops over a few months after birth. Common infective organisms are pneumococcus, Haemophilus influenzae and Pseudomonas aeruginosa. Pseudomonas cepacia is rare but major as the infection is serious. Pneumothorax is relatively common over the age of 10 years (5%).

Diabetes (20% of patients) occurs due to occlusion and fibrosis of pancreatic ducts. Pancreatic gland occlusion causes malabsorption (diarrhoea). Occlusion of intrahepatic ducts cause cirrhosis and obstruction of bile ducts (pale stools)

The **sweat test** remains the gold standard for confirming the diagnosis of cystic fibrosis. A chloride value of **>60 mmol/l** is considered **positive**, between 40 and 60 mmol/l equivocal and less than 40 mmol/l negative.

PULMONARY FIBROSIS & BRONCHIECTASIS

The causes of **upper zone fibrosis** in the lung are

TB

Extrinsic allergic alveolitis

ankylosing spondylitis

radiation

sarcoidosis

silicosis

Causes of **lower zone lung fibrosis** are:

Asbestosis

bronchiectasis

cryptogenic fibrosing alveolitis

drugs

Drugs which can cause lung fibrosis.

Busulphan, bleomycin and methotrexate (cytotoxic agents),

Amiodarone, azathioprine, antibiotics (nitrofurantoin, sulfasalazine), penicillamine, gold, phenytoin.

The causes of **bronchiectasis** are:

chronic obstruction e.g. tumour

Kartagener's syndrome (impaired ciliary motility)

cystic fibrosis

whooping cough/pertussis

tuberculosis

smoking

LUNG CARCINOMA

The overall survival is 20% and 5 year survival is 6% for all lung cancers. Small cell lung cancer has the worst outcome.

Squamous cell carcinoma accounts for approximately one-third of all cases of bronchogenic carcinomas. Unlike adenocarcinoma, it is strongly linked with a history of cigarette smoking. Its histogenesis may be related to chronic inflammation and

injury of the bronchial epithelium, which leads to replacement of the normal ciliated columnar epithelium by a squamous epithelium.

Squamous cell carcinomas tend to form firm, nonencapsulated, sharply circumscribed masses located in the main, lobar or segmental bronchi. Larger tumors often outgrow their vascular supply and may have central areas of hemorrhage, necrosis or cavitation.

SIADH is most commonly seen with small cell carcinoma rather than non-small cell carcinoma.

HPOA and **hypercalcaemia** without bone metastasis is more common in squamous cell carcinoma.

Small cell lung cancer has a propensity to spread early. Surgical resection is not a part of the routine treatment. Patients diagnosed following biopsy are treated by combined radiotherapy and chemotherapy.

Chemotherapy has been used in **non small cell lung cancer** but has not been proven to prolong survival (controlled trials).

Adverse prognostic factors in small cell lung cancer are:

Extensive metastatic disease

weight loss >10%

hyponatraemia < 132 mmol/l

ALP > 1.5 times normal

LDH > 1.5 times normal

Contraindications for surgical resection of bronchial lung tumour:

FEV1 is less than 1.5L

Mediastinal LN >1cm

Staging >IIIB

Nerve involvement is present (rec laryngeal)

Malignant pleural effusion is present

Malignant mesothelioma is a pleural (not pulmonary) malignancy in which there is almost always a history of asbestos contact. Radiotherapy reduces seeding and invasion through percutaneous biopsy sites.

Median survival is approximately 12 months. Pleural fluid provides a diagnosis less than 50% of the time, and even multiple pleural biopsies can be negative in some cases due to a florid fibrotic reaction.

PLEURAL FLUID

Causes of **transudate** are:

Congestive heart failure

Nephrotic syndrome

Cirrhosis

Hypoalbuminaemia Urinothorax

Peritoneal dialysis
Atelectasis (early)

Causes of **exudate** are :

Infection (Bacterial, viral, or parasitic)
Malignancy
Connective tissue disease
Chylothorax
Pancreatitis
Postcardiotomy syndrome
Drug-induced (eg, by amiodarone)
Esophageal rupture
Uremia
Subdiaphragmatic abscess

Light's criteria (suggests exudate) is satisfied if
pleural fluid protein/serum protein ratio greater than 0.5
Pleural fluid lactate dehydrogenase (LDH)/serum LDH ratio greater than 0.6
Pleural fluid LDH greater than two-thirds the upper limit of normal for serum LDH (a cut-off value of 200 IU./L was used previously)

Any **pleural effusion** associated with bacterial pneumonia, lung abscess or bronchiectasis is a parapneumonic effusion. *Streptococcus* infection is common. These effusions can be monitored by the pH:
pH<7 - absolute indication to insert an intercostal drain
pH>7.20 - usually does not need drainage
pH 7-7.20 - should be monitored.

MISCELLANEOUS

Allergic Broncho Pulmonary Aspergillosis: commoner among asthmatics
Eosinophilia and high IgE levels are suggestive
RAST test for antibodies towards *Aspergillus* confirms the diagnosis.

Acute respiratory distress syndrome is characterised by hypoxaemia, reduced lung compliance, pulmonary hypertension and pulmonary infiltrates on chest X ray. There is damage to the capillary endothelial cell linings resulting in oedema leakage of proteins cells into interstitial alveolar spaces. It is associated with profound hypoxia and increased vascular permeability (causing a V/Q mismatch). A normal PCWP differentiates the condition from pulmonary oedema. It does not respond to steroids.

Aspergillomas are masses of fungal mycelia that grow in preexisting lung cavities. *Haemoptysis* is a common symptom. They do not require treatment with either anti-fungals or steroids and are not associated with bronchiectasis (unlike allergic bronchopulmonary aspergillosis).

Alpha 1 antitrypsin is a glycoprotein synthesized in the liver and comprises 90% of the serum alpha 1 globulin seen on electrophoresis. It is an anti-protease which inhibits neutrophil elastase.

The production of alpha1 antiprotease is controlled by a pair of genes at the protease inhibitor (Pi) locus. The phenotypes are **M, S or Z**. The most common (90%) allele is **M** (PiM), and homozygous individuals (MM) produce normal amounts of alpha1 antiprotease (serum levels of 20-53 mmol/L).

Deficient levels of alpha1 antiprotease are associated with allele **Z** (**MZ** or **ZZ**). Serum levels of the enzyme greater than 11 mmol/L appear to be protective against emphysema. Emphysema develops in most (but not all) individuals with serum levels less than 9 mmol/L.

Byssinosis is caused by cotton dust, and is commoner among smokers. Immunologically, it is different from farmer's lung but is more akin to occupational asthma – wheeze occurs after exposure to cotton and hemp. The condition typically worse on Mondays when work begins and lung function stabilises throughout the week. The CXR is normal, unlike *extrinsic allergic alveolitis*, where mottling is seen on CXR (interstitial pneumonitis).

Churg-Strauss syndrome (triad of 1) asthma, 2) hypereosinophilia, and 3) necrotizing vasculitis) can present with gastrointestinal involvement may sometimes present as bloody diarrhea or simulating ulcerative colitis and is caused by bowel ischemia.

Desquamative interstitial pneumonia (DIP) is a distinct clinical and pathologic entity. It affects cigarette smokers in their 30s or 40s. Most patients present with dyspnea. DIP differs histopathologically from usual interstitial pneumonia (UIP) in that it tends to be diffuse and uniform in appearance.

Goodpasture's syndrome is due to the presence of circulating anti-glomerular basement membrane antibodies (anti-GBM antibodies).

Hypereosinophilic syndrome is a rare condition where there is an idiopathic eosinophil count of $> 15 \times 10^9/\text{dl}$. It generally affects young men ages 20-50. Thrombotic tendency, neurological involvement and restrictive cardiomyopathy occur. There is response to steroids.

Apart from obesity, **obstructive sleep apnoea** is associated with acromegaly, hypothyroidism, jaw and craniofacial abnormalities, and alcohol. During the sleep study or polysomnography, a cessation of breathing for 10 seconds with desaturation in oxygen saturation would help to confirm **obstructive sleep apnoea**. The hallmark clinical symptom of OSA is excessive snoring.

Long Term Oxygen Therapy is indicated when $\text{pO}_2 < 8\text{kPa}$ when there is polycythaemia or pulmonary hypertension.

In uncomplicated COPD, it is indicated when $\text{pO}_2 < 7.2\text{kPa}$. Patients without chronic hypoxaemia and not on LTOT, should be considered for ambulatory oxygen therapy if they show evidence of exercise oxygen desaturation (a fall of SaO_2 of at least 4% below 90%)

Kartagener's syndrome is hereditary. It comprises a triad of: situs inversus (transposition) of the viscera, abnormal frontal sinuses producing sinusitis and bronchiectasis, and immobility of the cilia.

Symptoms and signs are dyspnoea, productive cough, recurrent respiratory infections, rheumatoid arthritis, renal abnormalities, malformations of renal vessels and anomalous subclavian artery. There is also otitis media, nasal speech, conductive hearing loss, anosmia or clubbing.

Lofgren's syndrome is a self limiting subset of **sarcoidosis**. It consists of the triad of fever, bilateral hilar lymphadenopathy and erythema nodosum. Therefore, the prognosis is good and steroids are not required.

Legionella pneumophila is an obligate aerobic gram negative bacilli. The natural habitat of the bacterium is water and it is spread through contaminated aerosols. The incubation period is 2-10 days and the spectrum of the disease varies from asymptomatic seroconversion to severe life-threatening pneumonia. Symptoms such as headache, fever, rigors, myalgias and lethargy are frequent.

Erythromycin or *doxycycline* are the drugs of choice and treatment should be continued for at least 3 weeks. *Rifampicin* (600mg) should be added to the treatment in patients who are severely ill or who have cavitation.

Mycobacterium avium complex (MAC) is a saprophyte which is found in soil, water, dust etc. It typically affects middle age and old men with underlying lung diseases such as COPD, old TB, bronchiectasis. It is associated radiographic evidence of disease (cavities etc), and diagnosis should be made after isolation in three sputum samples. Extrapulmonary disease is seen typically in immunosuppressed patients. Recommended treatment is with rifampicin and ethambutol for 24 months.

Mycoplasma pneumonia is the commonest atypical pneumonia. Approximately 15% of pneumonias in adults are due to *Mycoplasma pneumoniae*. Transmission occurs from person to person by infected droplets. The incubation period is 9-21 days. The incidence is higher during the winter months. Fever, chills, cough and headache are early symptoms. Dyspnoea, chest pain and haemoptysis are rare. Small pleural effusions may occur but are rare. Cold agglutinins are usually present in a titre greater than 1:32.

The acute mortality in **pneumocystis pneumonia** is usually 10%. Dry cough, fever and tachypnoea are typical in PCP. The organism lies in the alveolar space (foam), causing hypoxia and a low transfer factor. Typically there are no crackles, although it may occasionally be present. The duration of treatment recommended for patients with AIDS is 21 days. Non-AIDS patients with PCP generally respond to therapy within four to five days.

Primary pulmonary hypertension presents mostly after age 30s, and more commonly affects women. There is right heart failure and treatment includes prostaglandin analogues (iloprost, epoprostenol), sildenafil, bosentan and calcium channel blockers.

Psittacosis is a systemic illness with primarily pulmonary manifestations. The diagnosis is suggested by exposure to birds. The rash (Horder's spots) and

splenomegaly are characteristic. Diagnosis can be made by a four-fold increase in the complement-fixing antibodies. *Tetracycline* for 2 weeks is the treatment of choice.

Causes of **phrenic nerve palsy** are:

- pneumonia
- pleurisy
- aortic aneurysm
- substernal goiter
- neoplasms
- thoracic surgery
- herpes zoster infection
- vasculitis
- diabetes

A protein of >35 g/L suggests an exudate.

Sarcoidosis can cause many changes on the CXR:

- unilateral or bilateral hilar lymphadenopathy
- diffuse parenchymal changes
- eggshell calcification
- pleural effusions
- nodules

A prolonged history of epistaxis and sinusitis is commonly found in **Wegener's granulomatosis**. Breathlessness with a raised KCO suggestive of alveolar haemorrhage Causes of pulmonary haemorrhage and renal failure include Wegener's granulomatosis, microscopic polyangiitis and systemic lupus erythematosus (SLE).