Respiratory

1. Dyspnoea
2. Cough
3. Obstructive vs. restrictive
4. Emphysema
5. Chronic bronchitis
6. Asthma
7. Bronchiectasis
8. Pneumonia
9. Pleural effusion
10. Pulmonary embolism
11. Interstitial lung disease
12. Lung cancer
13. Tuberculosis
14. Interpreting chest x-rays

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Dyspnoea

Definition[1,2]
Subjective sensation of SOB. An abnormal, uncomfortable awareness of respiration.

Types[1,2,5]

Acute dyspnoea
- ≤1 month

Chronic dyspnoea:
- >1 month

Exertional dyspnoea
- Dyspnoea on physical exertion

Orthopnoea
- Dyspnoea when supine due to redistribution of fluid in lung. Patient may need to be upright or propped on a number of pillows to sleep.

Paroxysmal nocturnal dyspnea
- Severe dyspnoea waking patient from sleep due to transudation of fluid and reabsorption of oedema to interstitial tissues and increase in work of breathing.

Differentials for acute dyspnoea[2]

Respiratory
- Asthma
- Bronchitis
- Pneumonia
- Pneumothorax
- Acute pulmonary oedema
- Pulmonary embolism
- ARDS
- Allergen exposure
- Foreign body obstruction

Cardiac
- Cardiac tamponade
- Shock

Other
- Psychogenic
- Haemolysis
- Rib fracture
- CO poisoning
- Metabolic acidosis

Differentials for chronic dyspnoea[2]

Respiratory
- Bronchiectasis
- COPD
- Chronic anaemia
- Infiltrative tumour
- Interstitial lung disease
- Pleural effusion
- Pulmonary hypertension

Cardiac
- Heart failure
- Pericardial effusion
- Restrictive pericarditis

Other
- Severe obesity
- Ankylosing spondylitis
- Kyphoscoliosis
- Neuromuscular disease

Questions to ask on history[1,2]

Onset?
Sudden or gradual, sporadic or in certain circumstances such as on exertion or exposure to an allergen or at rest
Duration?
Acute or chronic
Exercise tolerance?
Steps climbed/distance walked?
Effect on function?
NYHA classification scale
Exacerbating and relieving factors?
Use of puffers, resting, change of setting
Diurnal variation?
Asthma
Worse when lying flat?
Orthopneoa
How many pillows does the patient sleep with?
Orthopneoa
Does it ever wake patient from sleep gasping for breath?
Paroxysmal nocturnal dyspnoea
Associated symptoms?
Chest pain, swelling of ankles, panic or anxiety, cough

Possible associated symptoms/signs[2]

Wheeze
- Airway disease - asthma, COPD, anaphylaxis

Stridor
- Obstruction - foreign body, tumour, acute epiglottitis, anaphylaxis, trauma

Chest pain
- Cardiac event, pericarditis, pneumothorax, PE

Crackles
- Heart failure with pulmonary oedema, pneumonia, bronchiectasis, fibrosis

Cough with sputum production
- Pneumonia, bronchitis

Cough with haemoptyisis
- Pneumonia, bronchitis,, PE, malignancy

Oedema of ankles, sacrum

Examination[1,2]

Inspection
- Respiratory rate (brady <8bpm, tachy >25bpm)
- Cyanosis (peripheral in hands, central in tongue)
- Use of accessory muscles of respiration (sternocleidomastoids, scalene)
- Pursed lips breathing
  - COPD
- Increased anterioposterior diameter/barrel chest
  - COPD
- Elevated JVP (>5cm)
  - Heart failure
- Tracheal shift from midline
  - Pneumonthorax, pleural effusion

Percussion
- Dull note
  - Consolidation (pneumonia)
- Stony dull note
  - Fluid (pleural effusion)
- Hyperresonant note
  - Air trapping (COPD)

Auscultation
- Absent unilateral breath sounds
  - Pneumothorax
- Fine crackles
  - Interstitial LD
- Coarse crackles
  - Heart failure
- Inspiratory and expiratory crackles
  - Bronchiectasis
- Wheeze
  - Asthma
- Stridor
  - Upper airway obstruction
- S3 gallop
  - Heart failure
- Fixed S2 split
  - Pulmonary hypertension

Investigations[1,2]

CXR
- Pleural effusion (meniscus sign = curved upper margin)
- Pneumothorax (loss of lung markings, pleural reflection)
- Pneumonia (consolidation as indicated by opacification)
- Emphysema (lungs extend beyond rib VI, low and flat hemidiaphragms)

Lung Function Tests
- Peak flow meter (PEFR)
- Spirometry
  - Obstructive defect = ↓FEV1, ↓FEV1/FVC
  - Restrictive defect = ↓FEV1, ↓FVC, N/↑FEV1/FVC
- Lung volumes
  - Emphysema = ↑TLC, ↑RV
  - Restrictive defect = ↓TLC, ↓RV
- Diffusion capacity
  - Emphysema and ILD = ↓DLCO

ABGs
- Type I respiratory failure = PaO2 <8kPA, PaCO2 <6.0kPA
- Type II respiratory failure = PaO2 <8kPa, PaCO2 >6kPa
- Metabolic changes = acidosis

FBP
- Hb
  - Anaemia = 13.5g/100ml in M, 11.5g/100ml in F

Echocardiogram
- Ventricular and valvular function

ECG
- Electrical activity of the heart indicating ischaemia, heart failure

Pulse oximetry
- Oxygenation of haemaglobin

6 minute walk test
- At 6 minutes measure distance walked, oxygen saturation, heart rate, dyspnea score

Cardiopulmonary exercise testing
- Gas exchange
- Oxygen delivery and consumption
- Cardiac function

Acute management

Oxygen
- If hypoxic (oxygen not given for dyspnoea alone)

Address underlying cause

Spirometry[1,2]

DDx	FVC	FEV1	TLC	RV	DLCO
Emphysema	↓	↓	↑	↑	↓
Chronic bronchitis	↓	↓	=	↑	=
Asthma	↓	↓		↑	↑
Interstitial LD	↓		↓	↓	↓
Kyphoscoliosis	↓	↓	↓	=/↓	=
HF (early, ↑blood flow)	-	-	-	-	
HF (late, pulmonary oedema)	-	-	-	-	↓
PE	-	-	-	-	↓

Pathophysiology[3]

Respiration is regulated through the CNS.

The respiratory centre is composed of
- Dorsal respiratory group of the medulla (inspiration)
- Ventral respiratory group of the medulla (expiration)
- Pneumotaxic centre in the pons (rate and depth of breathing).

The respiratory centre transmits these efferent signals to muscles of respiration.

The ultimate goal of respiration is maintenance of O2, CO2 and H+ in the blood which occurs via afferent signals from
- Chemosensitive area of the medulla (CO2 and H+)
- Peripheral chemoreceptors of the carotid and aortic bodies (O2)

The sensation of dyspnoea arises from a mismatch between afferent and efferent signals. Factors that enter into the development of the sensation of dyspnoea
1. Abnormality of respiratory gases in the bodily fluids (primarily hypercapnia, secondarily hypoxia)
2. Amount of work that must be performed by respiratory muscles to provide adequate ventilation
3. State of mind (neurogenic/psychogenic)

NYHA Functional Classification Scale[4]

Class I (asymptomatic left ventricular dysfunction)
- No limitations, ordinary physical activity does not cause undue fatigue, dyspnoea or palpitations

Class II (mild CHF)
- Slight limitation of physical activity, ordinary physical activity results in fatigue, dyspnoea, palpations or angina

Class III (moderate CHF)
- Marked limitation of physical activity, less than ordinary activity leads to symptoms

Class IV (severe CHF)
- Unable to carry on any physical activity without discomfort, symptoms of CHF present at rest

Cough

Definition[2] Cough is deep inspiration followed by explosive expiration and is a defence mechanism which enables the airways to be cleared of secretions and foreign bodies. A common presenting symptom.

Classification:[5]
Acute cough: <3 weeks Sub-acute cough: 3-8 weeks Chronic cough: >8 weeks

History[2,5,6]
Cough
Onset and duration:
Acute cough

Acute cough with fever and symptoms of respiratory tract infection	Pneumonia, acute bronchitis

Chronic cough

Chronic cough with wheezing	Asthma
Chronic dry, irritating cough	Oesophageal reflux (acid irritation of lungs)
Chronic dry cough	ACE inhibitors (build-up of bradykinin)
Paroxysmal nocturnal cough	Cardiac failure, acid reflux (positional fluid shift)
Chronic cough productive of large volumes of purulent sputum	Bronchiectasis

Temporal changes in cough

Cough worse at night	Asthma, cardiac failure
Cough worse after food or drink	Oesophageal reflux, tracheo-oesophageal fistula

Character:

Barking	Inflammation, epiglottitis
Loud, brassy	Tracheal compression
Hollow, bovine	Recurrent laryngeal nerve palsy (inability of vocal cords to completely close)
Loose, productive	Chronic bronchitis, bronchiectasis, pneumonia (excessive bronchial secretions), post nasal drip
Dry, irritating	Chest infection, asthma, bronchial carcinoma, cardiac failure, interstitial lung disease, ACE inhibitor

Nb: Change in character of a chronic cough may signify development of a new and/or serious problem (infection, cancer)
Sputum
Enquire about volume, colour and character:

Large volume purulent (yellow or green)	Bronchiectasis, lobar pneumonia
Foul-smelling dark-coloured sputum	Lung abscess with anaerobic organisms
Pink, frothy	Pulmonary oedema (NOT sputum, originates from trachea)

Haemoptysis
Coughing up of blood.
May indicate serious underlying disease (e.g. malignancy) and always requires further investigation.
Other associated symptoms and signs
Dyspnoea, wheeze, chest pain, fever, hoarseness, night sweats
Complete full history, pertinently:
Past medical history (especially respiratory diseases), medications (ACE inhibitors), allergies (atopy), smoking history (pack years), environmental and occupational exposures (chemicals, dusts), travel history

Examination[2,5]
Respiratory examination
Inspection
- Sputum cup

Auscultation
- Crackles
- Wheeze
- Consolidation

Other
- Sinus tenderness
- Rhinitis

Investigations[5,6]
Sputum MC&S
- Gram stain for infectious causes

CXR
- If Hx and Ex do not clearly elucidate aetiology

Further testing to rule in/rule out diagnoses:
- Bronchodilator test (reversible airway obstruction)
- Lung function tests (reveal obstructive/restrictive/other defects)
- CT (lesions, masses in airway)
- Bronchoscopy

Common aetiologies[2,5,6]
- Post nasal drip (allergic, perennial non-allergic and vasomotor rhinitis, acute nasopharyngitis, sinusitis)
- URTI (pharyngitis, tracheitis)
- LRTI (bronchitis, pneumonia)
- Asthma
- Gastrooesophageal reflux
- Laryngopharyngeal reflux
- ACE inhibitors
- Structural changes (bronchiectasis, tumours, interstitial lung disease)
- Occupational or environmental exposures (smoke, pollen, dusts, chemicals)

Pathophysiology[2,5]

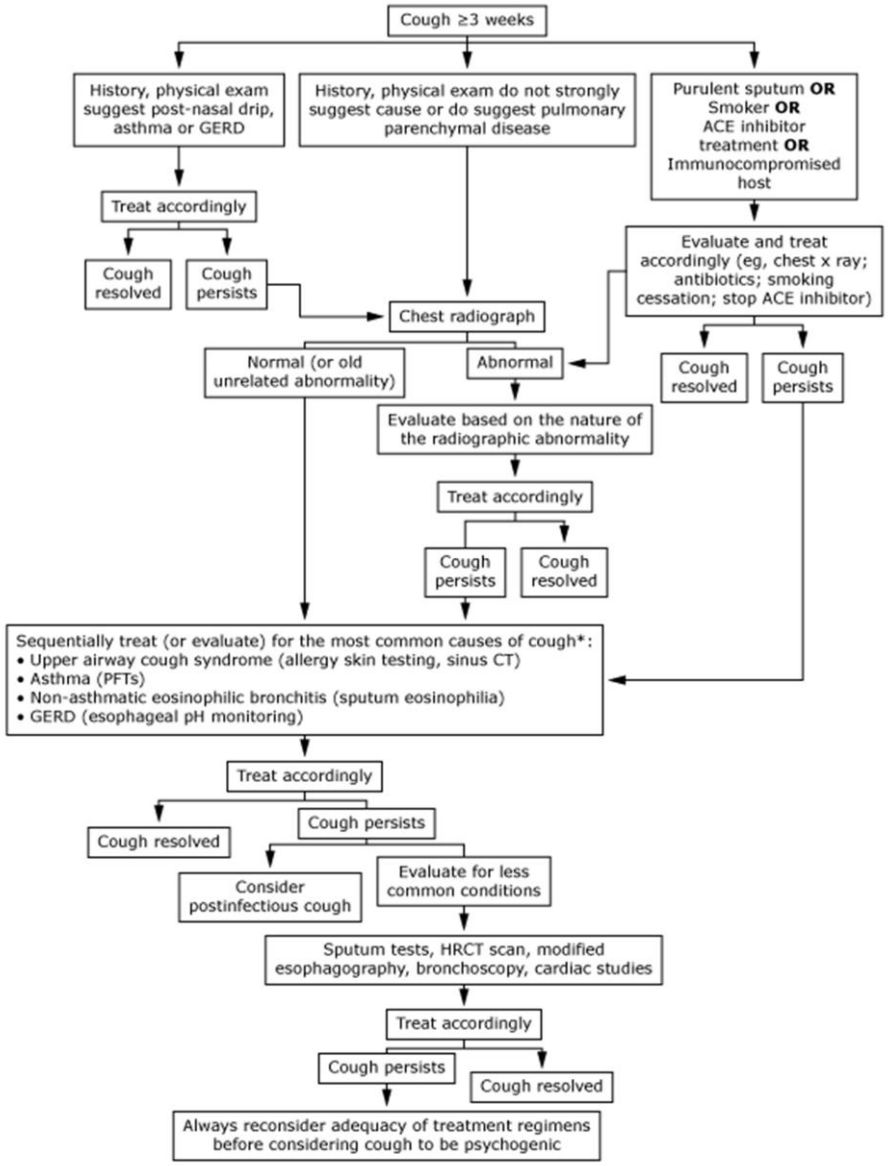
Coughing

- Deep inspiration is followed by explosive expiration.
- Increased flow rates of air (may approach the speed of sound)
- Defense mechanism (clearance of foreign bodies/secretions from airways)

Pathway

- Chemical cough receptors
  - Located in epithelium of the respiratory tracts, pericardium, oesophagus, diaphragm, stomach.
  - Stimuli include temperature, acid, other chemical irritants
  - Stimulation activates of cough reflex through transient receptor potential vanilloid type 1 (TRPV1) and transient receptor potential ankyrin type 1 (TRPA) ion channel classes.
- Mechanical cough receptors
  - Located in larynx, trachea, bronchial tree
  - Stimuli include touch and displacement
- Reflex arc
  - Stimulation of cough receptor → afferent impulse → vagus n → medullary cough centre → efferent impulse → vagus, phrenic, spinal motor n → expiratory musculature → cough
  - There is also some descending input from higher cortical centres

Algorithm for sub-acute and chronic cough



a: Silverstri RC, Weinberger SE. Evaluation of subacute and chronic cough in adults. In Barnes PJ, King TE, Hollingsworth H, editors. UpToDate. Waltham: UpToDate ; 2011.

Acute management[5]

Empiric treatment is directed at common causes of cough.

Removal of stimuli

- Avoidance of stimuli (smoking, occupational exposures, environmental pollutants), cessation of ACE inhibitors

Antibiotics

- If infective aetiology is suspected
- Empirical treatment according to TGA

Anti-histamines and decongestants

- First generation combination anti-histamine and decongestant
- Where post-nasal drip is suspected

Inhaled glucocorticoids

- Where chronic inflammation is suspected or obstructive defect is present

Anti-cholinergics

- Ipratropium bromide
- Blocks efferent limb of cough reflex and decreases cough receptor stimulus

Bronchodilators

- If obstructive defect is found on LFTs

Protein pump inhibitor

- Where GORD is suspected

Anti-tussives

- Symptomatic relief only where aetiology cannot be identified
- Peripherally acting antitussives (work on peripheral cough receptors) such as Benzonatate.
- Centrally acting antitussives (↑ threshold of impulse required to activate medullary cough centre) which may be opioid (e.g. Codeine) or non-opioid (Dextromethorphan)

Obstructive vs. restrictive lung disease

Note: obstructive and restrictive lung diseases often co-exist giving a mixed picture

Obstructive lung disease

Pathophysiology[1,5,6,8,9]
Increased resistance to airflow due to partial or complete obstruction of the airways at any level of the respiratory tract resulting in decrease in maximal expiratory air flow.

Aetiology[5,6]
- Asthma
- Emphysema (COPD
- Chronic bronchitis (COPD)
- Bronchiectasis

Presentation[1,2,5]
Typical presentation: dyspnoea, productive cough, wheeze
Fever and systemic signs (if infective exacerbation)
Typical history: smoking (COPD), past medical history (respiratory tract infections - bronchiectasis, atopy – asthma)

Examination[1,2,5]
Inspection: Barrel chest, pursed lips breathing, use of accessory muscles of inspiration and indrawing of intercostal muscles, cachexia and weight loss, no clubbing
Palpation: reduced chest expansion
Percussion: hyperresonant percussion note
Auscultation: reduced air entry, wheeze
Other: signs of RHF

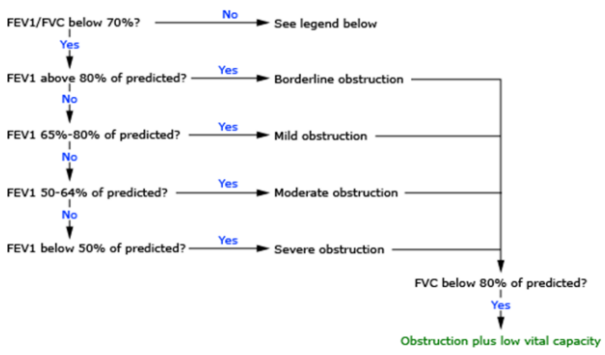
Investigations[2,5,6]
CXR:
- Hyperinflation, decreased peripheral vascular markings, bullae in lung parenchyma

Lung function tests:
Obstructive defect
- FEV1 <80% of predicted, FEV1/FVC: 0.7
- Bronchodilator test
  - Reversible: asthma
  - Irreversible: COPD
  - Often mixed component present

Increased lung volumes
- ↑TLC, ↑RV

DLCO
- ↓ DLCO= emphysema
- Normal DLCO = chronic bronchitis

Spirometry



b: Enright PL. Interpretation of office spirometry: obstructive pattern. In Stoller JK, Hollingswroth H, editors. UpToDate. Waltham: UpToDate; 2011.

Restrictive lung disease

Pathophysiology[5,6,9,10]
Decreased expansion of lung parenchyma due to chronic inflammation of the lung resulting in damage to alveolar wall and surrounding structures. Leads to decreased viable lung for gas exchange and tissue scarring and fibrosis resulting in restriction of movement of the lung.

Aetiology[5]
Interstitial lung disease:
Idiopathic pulmonary fibrosis: sarcoidosis, vasculitides, haemorrhagic syndromes, auto-immune disorders
Exposures: silicates, carbon, metals, dusts, birds
Medications: antibiotics, anti-inflammatories, anti-arrythmics, chemotherapeutic agents
Chest wall disorders: kyphoscoliosis, obesity, polio, pleural disease

Presentation[5]
Typical presentation: dyspnoea and non-productive cough
May also present with: haemoptysis, wheezing, extra-pulmonary signs (reflecting underlying aetiology)
Typical history: smoking, occupational/environmental exposures (dusts, chemicals)

Examination[2,5]
Inspection: clubbing
Palpation: reduced chest expansion
Percussion: normal
Auscultation: fine or late pan-inspiratory crackles
Other: signs of RHF (cor pulmonale from pulmonary hypertension), associated extrapulmonary signs (reflecting underlying aetiology)

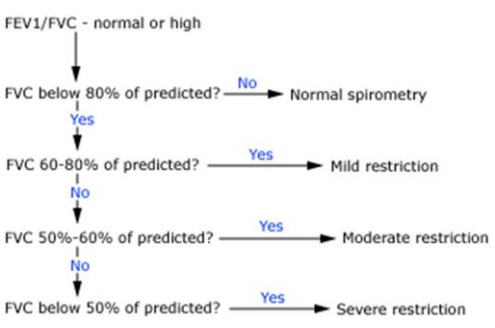
Investigations[5]
CXR:
- Reticular or reticular nodular infiltrates, diminished lung volumes, hilar and mediastinal lymphadenopathy, (sarcoid), pleural disease, honeycomb lung (IPF)

Lung function tests:
Restrictive defect
- ↓FEV1, ↓FVC, normal/↑ FEV1/FVC

Decreased lung volumes
- ↓VC, ↓TLC

Decreased DLCO
↓SaO2 (decreases with walking)

Spirometry



c: Enright PL. Interpretation of office spirometry: obstructive pattern. In Stoller JK, Hollingswroth H, editors. UpToDate. Waltham: UpToDate; 2011.

Emphysema

Definition[1,2,5] Histological diagnosis of pathological and permanent dilatation (increase in size) of the air spaces distal to terminal bronchioles with destruction of the alveolar walls. A subtype of chronic obstructive pulmonary disease (COPD).

Presentation[1,2,5]

Typical presentation:

- Dyspnoea (persistent and exertional)
- Cough (intermittently or daily)
- Sputum production (absent or scant)
- No haemoptysis

History of presentation complaint:

- Dyspnoea: gradual onset (years), ask about exertion required to precipitate dyspnea, rate on NYHA scale
- Cough: ask about onset and duration, character, sputum production, haemoptysis

Acute exacerbation:

- Ask about recent changes in symptoms from normal day-to-day symptoms
- Ask about any identifiable precipitants

Respiratory history:

- Smoking history: age of initiation, amount, pack years, high risk if heavy smoker especially if >70 pack years
- Past medical history: frequent respiratory infections
- Personal history or family medical history: alpha1-antitrypsin deficiency, emphysema or other respiratory diseases

Investigations[2,5,6]

Lung function tests:

- Obstructive defect:
  - FEV1 <80% of predicted
  - FEV1/FVC: 0.7
  - Irreversible (some reversibility may be present on bronchodilator test)
- ↑ TLC, ↑RV
- ↓ DLCO

CXR:

- Hyperinflation: >6 anterior ribs seen above diaphragm in mid-clavicular line, flat hemidiaphragms, narrow cardiac shadow
- Large central pulmonary arteries
- Decreased peripheral vascular markings
- Increased radiolucency of lungs
- Bullae in lung parenchyma (radiolucent areas >1cm diameter surrounded by arcuate hairline shadows)
- Cardiomegaly (if cor pulmonale)

CT:

- Loss of markings of alveolar walls
- Pancinar: lung bases, genearlized paucity of vascular structures
- Centrilobular: upper lobes, holes seen in centre of secondary pulmonary lobules

ABGs:

- Low PaO2
- May have high PaCo2 (CO2 retention)

V/Q Scan:

- V/Q mismatch
  - High V/Q (ventilatory compensation of undamaged lung)

Examination[1,2,5]

"Pink puffers"

Inspection:

- Dyspnoea
- Barrel chest (increased AP diameter, hyperinflation)
- Pursed lip breathing (increases end expiratory pressure to open airways to minimize air trapping)
- Use of accessory muscles of inspiration (SCM, scalenes)
- In-drawing of lower intercostal muscles in inspiration
- May show signs of cachexia and weight loss
- No clubbing

Palpation:

- Reduced chest expansion

Percussion:

- Hyperresonant percussion note

Auscultation:

- Decreased breath sounds/air entry

↑ Forced expiratory time

Acute exacerbation may show:

- Fever
- Tachypnoea
- Cough
- Sputum production
- Early inspiratory crackles

In pre-terminal state, signs of right heart failure may be present:

- Elevated JVP
- Peripheral oedema
- Increased P2, splitting of S2
- Hepatospenlomegaly
- Early inspiratory crackles

Management[5,7]

Pharmacotherapy:

- Long acting B2 agonists (e.g. salmeterol, eformoterol)
- Inhaled anticholingergics (e.g. tiotropium bromide)
- Combination inhalers (ICS and LABA, e.g.salmeterol/beclometasone, eformoterol/fluticasone)
- Theophylline (very occasionally used)

Steroids:

- 2 week high oral steroid trial to assess reversibility.
- >15% in FEV1 indicates clinical benefit from steroids.
- Avoid long term steroid use

Non-invasive positive pressure ventilation (PPV)

Pulmonary rehabilitation progarm

- 6 week exercise training and education

Home oxygen therapy

- Oxygen must be given with care in hypoxia as CO2 retention results in insensitivity of respiratory centres to CO2 = dependence on hypoxia for respiratory drive.
- Supplementary oxygen may therefore result in suppression of respiratory drive and respiratory failure

Reduction of risk factors:

- Smoking cessation, exercise, nutrition, obesity

Preventative medicine:

- Influenza vaccination, pneumococcal vaccination

Acute exacerbations:

- Antibiotics if infective exacerbation
- May require hospitalization

Aetiology[1,5,6]

Development of COPD:

- A complex process that is not completely understood but is thought to be multifactorial (genetic, biological, behavioural).

Smoking:

- Most common cause of COPD in developed world is exposure to tobacco smoke. 50% of chronic smokers develop COPD and almost all COPD patients have significant smoke exposure recorded.

Environmental exposures:

- Occupational dusts, chemicals, air pollution

Genetic alpha1-antitrypsin deficiency:

- Alpha1-antitrypsin is a protease inhibitor. Its deficiency results in loss of inhibition of proteases (such as elastase) which are then able to digest alveolar walls resulting in alveolar destruction as seen in emphysema. Alpha1-antitrypsin deficiency shows a histologically distinct pattern of emphysema (panacinar rather than centrilobular).

Exacerbations of COPD:

- An acute exacerbation is diagnosed on signs and symptoms and may be supported by spirometry showing decreases in FEV1, FVC and PEF due at least in part to airway inflammation.
- Triggered primarily by infection (viral and bacterial) and airborne pollutants.
- Bacterial pathogens are responsible for 50-70% of acute exacerbations.
    - Most common organisms: Haemophilus influenzae, Streptococcus penumoniae, Moxarella catarrhalis.
    - Other pathogens: atypical bacteria Mycoplasma and Chlamydia pneumoniae, respiratory viruses rhinovirus, influenza, respiratory syncytial virus, parainfluenza virus and human metapneumovirus.
- Other precipitants are environmental pollutants: Smoke, particular matter, sulfur dioxide, nitrogen dioxide, ozone

Pathophysiology[5,6,8,9]

Smoking:

Smoke results in

- Impaired integrity of normally tight junctions between epithelial cells of the lung
- Inflammation including action of neutrophil elastase (protease which digests CT)

Results in

- Destruction of the alveolar walls
- Loss of alveolar surface area for gas exchange and decreased elastic recoil
- Increased tendency of the airways to collapse in expiration
- Air outflow limitation and hyperinflation and dyspnoea.

Smoking typically displays centriblobular emphysema

- Most affects respiratory bronchioles and alveolar ducts
- Typically seen in the upper lobes of the lung.

Alpha1-anti-trypsin deficiency:

Alpha1-anti trypsin is a protease inhibitor

- Genetic deficiency in alpha1-antitrypsin protease inhibitor
- Unchecked action of proteases on connective tissue
- Alveolar destruction

Alpha1-antitrypsin deficiency typically displays panacinar emphysema

- Destruction through the acinus
- Seen typically in the lower lobes of the lung.

Acute exacerbation:

- "Acute on chronic" inflammatory response
- Increases in airway inflammatory cells and proteins
- Exacerbated obstructive defect and airflow limitation to expiration.
- Worsening of dyspnoea, cough, sputum production beyond normal baseline
- Acute exacerbations become more frequent and severe as COPD progresses and may of themselves accelerate COPD progression.

Epidemiology[10]

Prevalence of COPD:

- 2.9% of population (591,000) in 2004-05
- F (1.6%) >M (1.3%) in 2004-05
- M > F in >85 age group due to dramatic increase in male prevalence rates >75 years
- Disease of older age groups

Mortality from COPD:

- Mortality from COPD most marked >75 years
- 4% (4,761) deaths in 2006

Morbidity from COPD:

- 34% of patients with COPD reported some disability due to the condition in 2003

Services use from COPD:

- <1% of GP encounters for COPD in 2007-08
- 52,560 hospitalisations for COPD in 2006-07

Complications[5,6,8,9]

Pulmonary hypertension

- Blood vessel constriction from hypoxia
- Blood vessel loss from alveolar destruction

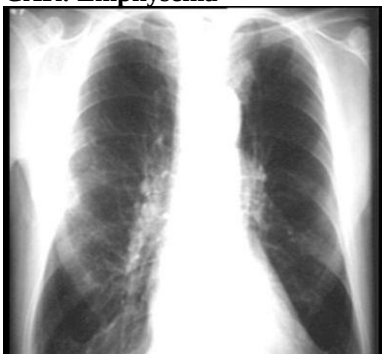
Cor pulmonale

- Right heart failure from pulmonary hypertension

Abnormal ventilatory response

- CO2 retention results in blunted response to hypercapnia
- Switch to hypoxia driven respiratory drive.

CXR: Emphysema



- Hyperinflation
- Reduced vascular markings
- Prominent pulmonary vessels (pulmonary hypertension)

d: Medscape (US). Chronic Obstructive Pulmonary Disease and Emphysema in Emergency Medicine Workup [Internet]. New York, NY: WebMD LCC; 2011 [updated 2011 Jan 4; cited 2011 Jun 10]. Available from: http://emedicine.medscape.com/article/80714

Chronic bronchitis

Definition[5] A clinical diagnosis of daily sputum production for three months of the year for two consecutive years. A subtype of chronic obstructive pulmonary disease (COPD).

Presentation[1,2,5]

Typical presentation:

- Chronic loose cough
- Chronic sputum production (mucoid or muco-purulent)
- Dyspnoea
- Wheeze
- No haemoptysis
- History of recurrent respiratory infection

History of presentation complaint:

- Dyspnoea: ask about exertion required to precipitate dyspnoea, rate on NYHA scale
- Cough: ask about onset and duration, character
- Sputum production: ask about frequency, volume, character, colour, smell
- Impact on function: ask about mobility, communication, activities of daily living, occupational

Acute exacerbation:

- Ask about recent changes in symptoms from normal day-to-day symptoms
- Ask about any identifiable precipitants (exposure to illness, environmental exposures, etc.)

Respiratory history

- Smoking history: age of initiation, amount, high risk if heavy smoker especially if >70 pack years
- Exposures: dusts, chemicals, air pollution
- Past medical history: respiratory infections
- Family history: COPD, other respiratory diseases

Examination[1,2,5]

"Blue bloaters"

Inspection:

- Cyanosis
- Oedema (from right ventricular failure)
- No clubbing

Palpation:

- Reduced chest expansion

Percussion:

- Hyperresonant percussion note

Auscultation:

- Reduced breath sounds/air entry
- End expiratory or low pitched wheeze
- Early inspiratory crackles

Acute exacerbation may show:

- Fever
- Tachypnoea
- Cough
- Sputum production (change in volume/character)

In pre-terminal state may have signs of right heart failure:

- Elevated JVP
- Peripheral oedema
- Increased P2, splitting of S2
- Hepatosplenomegaly

Investigations[2,5,6]

Lung function tests:

- Obstructive defect:
  - FEV1: <80% of predicted
  - FEV1/FVC: 0.7
  - Irreversible (some reversibility may be present on bronchodilator test)
- ↑ TLC, ↑RV
- ↓ DLCO

CXR:

- Hyperinflation: >6 anterior ribs seen above diaphragm in mid-clavicular line, flat hemidiaphragms, narrow cardiac shadow
- Large central pulmonary arteries
- Decreased peripheral vascular markings
- Increased radiolucency of lungs
- Bullae (radiolucent areas >1cm diameter surrounded by arcuate hairline shadows)
- Cardiomegaly (if cor pulmonale)

CT:

- Loss of markings of alveolar walls
- Pancinar: lung bases, generalized paucity of vascular structures
- Centrilobular: upper lobes, holes seen in centre of secondary pulmonary lobules

ABGs:

- Low PaO2
- May have high PaCo2 (CO_2 retention)

V/Q Scan:

- V/Q mismatch
  - High V/Q (ventilatory compensation) undamaged lung

Management[5,7]

Pharmacotherapy:

- Long acting B2 agonists (e.g. salmeterol, eformoterol)
- Inhaled anticholingergics (e.g. tiotropium bromide)
- Combination inhalers (ICS and LABA, e.g.salmeterol/beclometasone, eformoterol/fluticasone)
- Theophylline (very occasionally used)

Steroids:

- 2 week high oral steroid trial to assess reversibility.
- >15% in FEV1 indicates clinical benefit
- Avoid long term steroid use

Non-invasive positive pressure ventilation (PPV)

Pulmonary rehabilitation progarm

- 6 week exercise training and education

Home oxygen therapy

- Oxygen must be given with care in hypoxia as CO_2 retention results in insensitivity of respiratory centres to CO_2 = dependence on hypoxia for respiratory drive.
- Supplementary oxygen may therefore result in suppression of respiratory drive and respiratory failure

Reduction of risk factors:

- Smoking cessation, exercise, nutrition, obesity

Preventative medicine:

- Influenza vaccination, pneumococcal vaccination

Acute exacerbations:

- Antibiotics if infective exacerbation
- May require hospitalization

Aetiology[1,5,6]

Development of COPD

- A complex process that is not completely understood but is thought to be multifactorial (genetic, biological, behavioural).
- Smoking:
  - Most common cause of COPD in developed world is exposure to tobacco smoke. 50% of chronic smokers develop COPD and almost all COPD patients have significant smoke exposure recorded.
- Environmental exposures:
  - Occupational dusts, chemicals, air pollution
- Recurrent bronchial infection

Exacerbations of COPD

- An acute exacerbation is diagnosed on signs and symptoms and may be supported by spirometry showing decreases in FEV1, FVC and PEF due at least in part to airway inflammation.
- Triggered primarily by infection (viral and bacterial) and airborne pollutants.
- Bacterial pathogens are responsible for 50-70% of acute exacerbations.
  - Most common organisms: Haemophilus influenzae, Streptococcus penumoniae, Moxarella catarrhalis.
  - Other pathogens: atypical bacteria Mycoplasma and Chlamydia pneumoniae, respiratory viruses rhinovirus, influenza, respiratory syncytial virus, parainfluenza virus and human metapneumovirus.
- Other precipitants are environmental pollutants: Smoke, particular matter, sulfur dioxide, nitrogen dioxide, ozone

Pathophysiology[5,6,8,9]

Chronic bronchitis:

- Hypertrophy and hyperplasia of airway mucous glands and increased numbers of globlet cells and hypersecretion of mucous into the bronchial tree
  - Cough and excessive sputum prodution
  - Mucous plugging in the lumen of the airways
- Chronic mucosal and submucosal inflammation
  - Smooth muscle hypertrophy
- Airway obstruction
  - Obstructive defect: ↓FEV1 and ↓FEV1/FVC
- Loss of ventilation in regions distal to the obstruction
  - Dypsnoea
- Decreased mucociliary clearance
  - Increased risk for pathogens to stimulate the lower respiratory tract
  - Increased risk of infection
- Infection further initiates inflammation
  - Inflammatory oedema
  - Mucuous gland activity
  - Exacerbates obstructive defect and baseline symptomatology.

Acute exacerbation:

- "Acute on chronic" inflammatory response
- Increases in airway inflammatory cells and proteins
- Exacerbated obstructive defect and airflow limitation to expiration.
- Worsening of dyspnoea, cough, sputum production beyond normal baseline symptomatology.
- Acute exacerbations become more frequent and severe as COPD progresses and may of themselves accelerate COPD progression.

Epidemiology[10]

Prevalence of COPD:

- 2.9% of population (591,000) in 2004-05
- F (1.6%) >M (1.3%) in 2004-05
- M > F in >85 age group due to dramatic increase in male prevalence rates >75 years
- Disease of older age groups

Mortality from COPD:

- Mortality from COPD most marked >75 years
- 4% (4,761) deaths in 2006

Morbidity from COPD:

- 34% of patients with COPD reported some disability due to the condition in 2003
- 12.1% of patients with COPD reported severe/profound disability (core activities of communication, mobility and self-care) in 2003

Services use from COPD:

- <1% of GP encounters for COPD in 2007-08
- 52,560 hospitalisations (0.7% of separations) for COPD in 2006-07

Asthma

Definition[12,13] A disease characterized by recurrent episodes of reversible airway obstruction due to bronchial hyperresponsiveness to stimuli, and contributed to by underlying chronic processes of mucosal inflammation and excess mucous production.

History[2,6,12]

Typical history:
- Intermittent episodes of dyspnoea, wheeze, chest tightness, cough, sputum production, nocturnal waking

Time course
- Episodic with duration minutes-hours

Relieving factors
- Rest, removing self from situation
- Use of bronchodilators

Exacerbating factors
- Symptoms in relation to work (ask about exposure to allergens, chemicals, ask if symptoms better at weekends or holidays)
- Symptoms in relation to home (ask about carpets, pets, dust, feather pillows, clutter)

Precipitating factors
- Cold air, exercise, emotion, allergens (dust mites, pollen, animals), infection, smoking, pollution, NSAIDs, beta-blockers

Character
- Diurnal variation (decreased peak flow in morning which can precipitate attack despite normal peak flow at other times of day)

Functional capacity
- Exercise tolerance, disturbed sleep (nights per week), days off per week from work or school

Past medical history
- Atopic disease (eczema, hay fever, allergies)

Medication history and adherence
- Asthma drugs, NSAIDs, beta-blockers

Family history
- Asthma, other atopic disease

Smoking history

Investigations[6, 14]

Diagnosis made on
- History of typical symptoms
- Spirometry showing reversible airflow obstruction
  - Baseline FEV1 >1.7 L and post-bronchodilator FEV1 at least 12% higher than baseline

Other investigations if indicated by uncertain Dx
- Serial PEF
  - PEF varies by ≥20% for 3/7 over several weeks or PEF ↑≥20% in response to Rx
- CXR
  - Hyperinflation
- Bronchial challenge test
  - Nebulised metacholine or histamine induces bronchoconstriction (which occurs at low threshold in asthmatics)
- Allergy tests

Examination[1,2,3,6]

Signs of asthma attack
- Wheezing
- Dry or productive cough
- Tachypnoea, tachycardia
- Use of accessory muscles of expiration (rectus abdominus, external obliques, internal obliques)
- Hyperinflated chest (increased AP diameter, high shoulders, decreased liver dullness)
- Inspiratory and expiratory wheeze
- Decreased chest wall movement symetrically
- Hyperresonnance on percussion
- Reduced air entry
- Added sound wheeze

Bedside spirometry:
- Prolonged expiration (↓PEFR, ↓FEV1)

Additional signs of severe asthma attack
- Inability to speak due to dyspnoea, drowsiness (hypercapnia), cyanosis, tachycardia (>130bpm), pulsus paradoxus (>20mmHg), tachypnoea (>25breaths/min) reduced breath sounds

Differentials of acute asthma attack[6]
- Pulmonary oedema (“cardiac asthma”)
- Bronchitis
- Pulmonary embolism
- Upper airway obstruction
- Pneumonia
- COPD
- Pneumothorax

Management[14]

Acute management of asthma attack
- Oxygen (elevated CO2 means severe disease requiring intubation)
- SABA
- Evaluate if adrenalin is indicated
- Initiate treatment with other agents as indicated by response to initial treatment and severity

Long term management of asthma

Asthma Action Plan (individualized treatment algorithm)

Classes of medications:
- Relievers: direct bronchodilators taken for relief of acute attack
  - Short acting beta-2 agonists (SABA)
  - Long acting beta-2 agonists (LABA)
- Preventers: anti-inflammatories taken regularly to reduce symptoms and prevent exacerbations
  - Inhaled glucocorticoids (ICS)
  - Leukotriene receptor antagonists (LTRA)
  - Cromones
  - Anti-IgE

Aetiology[6,14]

Risk factors

- Atopy (strongest risk factor, genetic predisposition to develop IgE-mediated response to aeroallergens, as indicated by positive skin prick test)
- Wheezing before 3 years of age
- Allergic rhinitis
- Environmental tobacco exposure
- Residential exposure (pets, gas cooking, damp housing, mold exposure)
- Perinatal risk factors (preterm delivery, maternal smoking, antenatal chemical exposure)
- Occupational risk factors (cleaning, farming)
- Respiratory infections before 1 year of age (pneumonia, RSV, otitis media, croup)
- Medications (acetaminophen, aspirin, oestrogen, beta-blockers)
- Genetic (possible associations with genes encoding GPRA protein, PTGDR receptor, ADAM33, CH13L1, CHIT1)

Pathophysiology[3]

Acute asthma

Constriction of smooth muscles of bronchioles causing obstruction and acute difficulty in breathing.

Bronchoconstriction caused by hypersensitivity to stimuli (younger people typically exhibit allergic hypersensitivty to pollen, etc where older people have nonallergenic hypersensitivity such as irritants in pollution)

Allergic asthma

- Atopic individual has tendency to form excessive IgE antibodies which are attached to mast cells of lung near bronchioles and small bronchi to cause allergic reaction upon interaction with antigen
- Exposure to antigen results in IgE cross-linking resulting in mast cell activation and degranulation
- Degranulation releases histamine, leukotrienes, eosinophilic chemotactic factor and bradykinin
- Pro-inflammatory markers produces oedema in small bronchiolar walls, mucous secretion into lumen of bronchioles and contraction of bronchiole smooth muscle combining to cause airway resistance.

Bronchioles have the tendency to dilate in inspiration and collapse in expiration. The reduced bronchiolar diameter in asthma thus results in further bronchiolar occlusion in expiration which results in

- Decreased PEFR and FEV1

Chronic expiratory difficulty results in increased FRC and RV and manifests clinically as hyperinflation of lungs, barrel chest.

Chronic asthma

Persistent changes from asthma can include

- Accumulation of leukotrienes and prostaglandins
- Over time, smooth muscle hyperptrophy and hyperplasia
- Vascular congestion and oedema
- Mucous gland hyperplasia and hypersecretion
- Epithelial cell injury
- Accumulation of mucous (mucous gland hyperplasia)
- Angiogenesis
- Sub-basement fibrosis

Results in persistent chronic inflammatory state and hyperproduction of mucous.

Natural history of asthma

- Most childhood asthmatics either remit or greatly improve in adulthood.
- Some childhood asthma will progress to chronic asthma in adulthood.

Classification of asthma

Table 1. **Classification of asthma in a patient with untreated, newly diagnosed asthma**

	Daytime asthma symptoms	Night-time asthma symptoms	Exacerbations	Spirometry
Intermittent	Less than weekly	Less than 2 per month	• Infrequent • Brief	FEV_1 at least 80% predicted FEV_1 variability less than 20%
Mild persistent	More than weekly and less than daily	More than 2 per month but not weekly	• Occasional • May affect activity or sleep	FEV_1 at least 80% predicted FEV_1 variability 20–30%
Moderate persistent	Daily	Weekly or more often	• Occasional • May affect activity or sleep	FEV_1 60–80% predicted FEV_1 variability more than 30%
Severe persistent	• Daily • Physical activity is restricted	Frequent	Frequent	FEV_1 60% predicted or less FEV_1 variability more than 30%

e: National Asthma Council Australia. Asthma Management Handbook 2006 [Internet]. Melbourne, VIC (Australia): National Asthma Council Australia Ltd; 2006 [cited 2011 Jun 10]. Available from: http://www.nationalasthma.org.au/cms/images/stories/amh2006_web_5.pdf

Epidemiology[12,13]

Prevalence

- 10.2% prevalence in Australia
- Most common reported long term condition in those aged 0-14 yrs.
- 12% prevalence in age group 0-14 yrs.
- 9% prevalence in age group ≥25 yrs
- M>F (13%>10%) prevalence 0-14 yrs
- F>M (12%>8%) prevalence ≥15 yrs
- 15% prevalence in Indigenous

Mortality

- 402 deaths attributable to asthma in 2006 (0.3% of deaths in 2006)

Health service use

- $606 million health expenditure 2004-5 (1.2% of all health care)

Bronchiectasis

Definition[2,,10,15] Pathological permanent dilatation and distortion of the bronchi resulting in impaired clearance of mucous characterised by chronic cough and persistent infection.

Presentation[2,5,6]

Ask about history of:

- Chronic cough and purulent sputum (often since childhood, quantify amount when well vs. unwell)
- Severe bacterial infections (pneumonia, TB, pertussis, measles)
- History of recurrent infections (pneumonia, sinusitis)
- Past admissions to hospital
- Past medical history of respiratory conditions (cystic fibrosis, asthma, COPD)
- Medication use (bronchodilators, ICS, etc)

Ask specifically about symptoms of:

- Cough (chronic, productive)
- Sputum (voluminous, purulent, foul-smelling sputum)
- Haemoptysis
- Pleuritic chest pain
- Dyspnoea
- Systemic symptoms of infection: fever, LOW and LOA

Other

- Family history of respiratory tract disease
- Smoking history

Effects on function and activities of daily living

Examination[2,5,6]

Vital signs:

- Fever

General inspection:

- Moist cough
- Sputum cup (voluminous, purulent, foul smelling, blood)
- Cachexia

Inspection :

- Clubbing
- Cyanosis (if severe disease)

Auscultation:

- Coarse late inspiratory or pan-inspiratory crackles (localized or diffuse)
- Wheeze

If very severe, clinical signs of cor pulmonale may be present.

Investigations[2,5,6]

CXR

- Cystic shadows (dilated bronchi)
- Thickened bronchial walls (tram-tracking)

Sputum culture

- Haemophilus influenzae
- Streptococcus pneumoniae
- Staphylococcus aureus
- Pseduomonas aeruginosa

Bronchoscopy

- Tumour, foreign body, bronchial stenosis

Spirometry

- Obstructive pattern (common)
  - FEV1 <80% of predicted, FEV1/FVC: 0.7
  - Assess reversibility (bronchodilator test)
- Restrictive
  - ↓FEV1, ↓FVC, normal FEV1/FVC

CT chest

- To confirm diagnosis and extent of disease

Tests to confirm aetiology

- Genetic studies for CF

Differentials[5,6]

Chronic bronchitis Acute bronchitis

Management[5,6]

Antibiotics

- Sensitivities as taken from sputum culture.

Bronchodilators and ICS

- If co-existing COPD, asthma, CF
- If reversible component identified in spirometry
- Inhaled mannitol

Chest physiotherapy

- Postural drainage (aid mucous drainage and sputum expectoration)
- Pulmonary rehabilitation (improve exercise tolerance)

Surgical excision

- If localised disease or severe haemoptysis (embolization)

Prophylaxis

- Longterm antibiotics have little proven efficacy
- Predisposes to individual and population resistance and other side effects such as antibiotic associated diarrhea, etc.

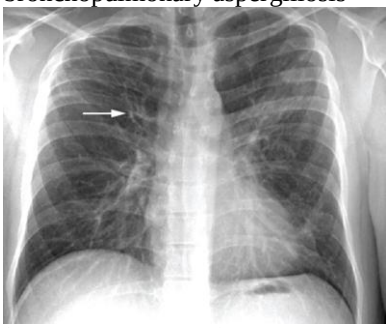
Vaccinations

- Yearly influenza, pneumococcal, Haemophilus

Cessation of smoking

Management of any associated complications

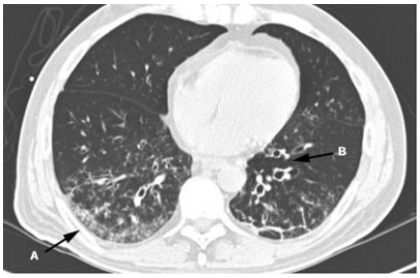
CXR: Central bronchiectasis from allergic bronchopulmonary aspergillosis



f: Barker AF. Clinical manifestations and diagnosis of bronchiectasis in adults. Bronchiectasis PA. In King TE, Hollingsworth H, editors. UpToDate. Waltham: UpToDate; 2011.

PA view showing dilation and thickening of airways RUL (arrow). Cellular debris and mucous seen in airways of LUL.

CT: Bronchiectasis



g: Barker AF. Clinical manifestations and diagnosis of bronchiectasis in adults. Tree-in-bud. In King TE, Hollingsworth H, editors. UpToDate. Waltham: UpToDate; 2011.

Typical "tree in bud" linear branch markings of small airways (A) and dilated and thickened airways (B).

Aetiology[5,6,10]

Causes:

- Congenital
  - Cystic fibrosis, Young's syndrome, primary ciliary dyskinesia, Kartagener's syndrome.
- Post-infection
  - Measles, pertussis, bronchiolitis, pneumonia, tuberculosis, HIV.
- Other
  - Bronchial obstruction (retained foreign body, tumour, anatomical obstruction, recurrent aspiration), immune deficiency, allergic bronchopulmonary aspergillosis, hypogammaglobulinaemia, rheumatoid arthritis, ulcerative colitis
- Idiopathic.

Risk factors:

- Congenital cystic disease of the lung
- Bronchial stenosis (tracheobronchomalacia)
- Compression of bronchi
- Subglottic hemangioma

Associated conditions:

- Congenital conditions
  - Marfan's syndrome, pulmonary sequestration, cartilage deficiency, tracheobronchomegaly, cystic fibrosis, primary cilary dyskinesia
- Post-infectious
  - Pseudomonas aeruginosa, Haemophilus influenzae, Mycobacterium tuberculosis, Aspergillus, measles virus, influenza virus, adenovirus, HIV.
- Sequelae of toxic aspiration
  - Chlorine, foreign body, heroin overdose
- Rheumatic conditions
  - SLE, rheumatoid arthritis, Sjogren's syndrome, relapsing polychondritis
- Immunodeficiency
  - Hypogammaglobulinemia, chemotherapy, malignancy, immune modulation
- Other
  - Inflammatory bowel disease, Young's syndrome (secondary ciliary dyskinesia), yellow nail syndrome

Pathophysiology[5,6,15]

- Chronic, recurrent or severe infection in the airways
- Destruction of bronchial wall → bronchial dilatation and impaired mucociliary function.
- Impaired clearance of secretions → accumulate and predispose to bacterial infection.
- Inflammation from infection → further mucous production and damage to bronchial walls →self-propagating cycle.

Causes of trauma to the airway

- Chronic or recurrent infection in the airways (especially childhood)
- Severe infection (pneumonia, tuberculosis, pertussis, measles), in particular suppurative infection in an obstructed bronchus.
- Tumour, foreign body in airway
- Congenital

Mnemonic for aetiology: "BRONCHIECTASIS"

Bronchial cyst
Repeated gastric acid aspiration
Or due to foreign bodies
Necrotizing pneumonia
Chemical corrosive substances
Hypogammaglobulinemia
Immotile cilia syndrome
Eosinophilia (pulmonary)
Cystic fibrosis
Tuberculosis (primary)
Atopic bronchial asthma
Streptococcal pneumonia
In Young's syndrome
Staphylococcal pneumonia

Complications[6,10]

- Pneumonia
- Pleural effusion
- Pneumothorax
- Haemoptysis
- Cerebral abscess
- Amyloidosis

Epidemiology[10,15]

- Not usually a primary condition but a consequence of other respiratory disease
- More common in F>M
- More common in older age groups
- More common in Indigenous Australians (14/1,000 Indigenous children)
- Few deaths directly attributed to bronchiectasis (80 males and 153 females in 2006)
- More deaths with bronchiectasis as an associated cause (120 males and 188 females in 2006)
- 80% of deaths from bronchiectasis >70 years, average age 77 years

Pneumonia

Definition[1,2,5,6] A lower respiratory tract infection characterized by inflammation of the lung and exudation into the alveoli and manifested clinically with systemic and respiratory signs and symptoms and radiological changes on chest x-ray.

Classifications/subtypes[1,2,5,6]

By setting:
- Community acquired (presents in community) or nosocomial (presents >48 hours after admission to hospital)

By host:
- Normal immunity vs. immunocompromised, normal lung vs. abnormal lung (COPD, bronchiectasis, etc)

By anatomy
- Lobar pneumonia, segemental pneumonia or lobular pneumonia

By organism
- Typical (S. pneumoniae, H influenzae, S. aureus, GAS, Moraxella catarrhalis, anaerobes, aerobic GNB)
- Atypical (Legionella, M. pnuemoniae, C. pneumonaie, C psittaci)

Other
- Aspiration pneumonia (high risk in those with stroke, myasthenia, bulbar palsies, decreased consciousness - drunk, post-ictal), oesophageal disease (achalasia, reflux)

Presentation[1,2,5,6]

Typical symptoms (sudden onset - days):
- Fevers and rigors
- Malaise
- Anorexia
- Dyspnoea
- Cough
- Sputum production
- Haemoptysis
- Pleuritic chest pain

Obtain history:
- Past respiratory history (underlying CF, COPD, etc.)
- Past medical history (immunocompromisation, Haemophilus and Pneumococus immunization history if elderly)
- Medications and allergies
- Smoking history
- Recent travel (unexpected pathogens)
- Recent exposure to illness

Examination[1,2,5,6]

Vital signs:
- Fever
- Tachypnea
- Tachycardia
- Hypotension

Inspection:
- Cyanosis
- Confusion or altered mental state (elderly)

Palpation:
- Increased tactile fremitus
- Reduced chest expansion

Percussion:
- Dull percussion note

Auscultation:
- Bronchial breathing
- Medium, late or pan-inspiratory crackles
- Pleural rub
- Increased vocal fremitus

Investigations[1,2,5,6]

CXR
- Consolidation (radiopaque density, typically sharply demarcated in lobar pneumonia)
  - RML pneumonia (loss of R cardiac border)
  - RLL pneumonia (loss of R hemidiaphragm)
  - LLL pneumonia (loss of L hemidiaphragm)
- Interstitial infiltrates (poorly defined opacities)
- Cavitations (radiolucent shadow)

Negative CXR may be present in:
- Initial stages of infection
- PCP
- Neutropenia
- Dehydration

Bloods (FBC, U&E, LFTs, CRP)
- Raised WCC, raised CRP may be seen

Blood culture
- MC&S (5-10% yield)
- IgM/IgG serology for Mycoplasma, Legionella, Chlamydia

Sputum culture
- MC&S (40% yield)

Urinary antigen
- Pneumococcal, Legionalla

ABGs
- Indicated if oxygen saturation <92%

Bronchoscopy and bronchoalveolar lavage (BAL)
- If patient is immunocompromised, high risk or unresolving

Management[1,2,5,6,16]

Supportive therapy
- Oxygen (maintain oxygen saturation ≥94%)
- IV fluids (as required)
- Analgesia (as required)

Antibiotics

Empirical therapy:
- Streptococcus pneumonia, Haemophilus influenzae, Mycoplasma pneumoniae
  - Amoxicillin, Clarithromycin
- Legionella
  - Amoxicillin, Clarithromycin and Rifampcin
- PCP
  - Co-trimoxazole
- Pseudomonas
  - Anti-pseudomonal penicillin (Ticarcillin or Piperacillin) or 3rd generation cephalosporin

Targeted therapy:
- According to culture and sensitivities

Prevention:

High risk patients (elderly, immunocompromised, respiratory disease)

Vaccines:
- Influenza, Pneumococcus, Haemophilus

Aetiology[1,5,6]

Causes:

	Community acquired	*Nosocomial*	*Immunocompromised*
Bacteria	Most common • Streptococcus pneumoniae • Haemophilus influenza • Mycoplasma pneumoniae Others • Staphylococcus aureus • Legionella • Moraxella catarrhalis • Chlamydophila Rare • Gram negative bacilli • Coxiella burnetti • Anaerobes	Most common • Gram negative enterobacteriacae • Staphylococcus aureus Others • Pseudomonas • Klebsiella • Bacteroides • Clostridia	• Streptococcus pneumonia • Haemophilus influenzae • Staphylococcus aureus • Moraxella catarrhalis • Mycoplasma pneumoniae • Gram negative bacilli • Mycobacteria
Viruses	• Influenza • Parainfluenza • Adenovirus		• CMV • HSV
Fungi			• Pneumocystis jeroveci (formerly carinii)

Risk factors:

Smoking
Alcohol
Toxic inhalation
Pulmonary oedema
Uremia
Malnutrition
Immunosuppressive agents
Mechanical airway obstruction
Cystic fibrosis
Bronchiectasis
COPD
Chronic bronchitis
Previous pneumonia
Immotile cilia syndrome
Kartagener's syndrome (ciliary dysfunction, situs inversis, sinusitis, bronchiectasis)
Young's syndrome (azoospermia, sinusitis, pneumonia)
Alteration in level of consciousness (aspiration)

Epidemiology[10]

Mortality

- 2% (2,715) of deaths in Australia from influenza or pneumonia in 2006
- 14.1% death rate in males
- 10.2% death rate in females
- Death most likely in COPD and elderly

Hospitalizations

- >50 years age group showed highest rate of hospitalizations.
- Rise in pneumonia hospitalizations in seasonal flu period (late autumn to late spring)

Pneumonia severity index (PSI)

Online access: http://www.debug.net.au/pharmacy/calculator.html

Divides patients into classes:

- I: oral antibiotics, outpatient
- II-III: IV antibiotics, outpatient or 24 hour admission
- IV-V: antibiotics inpatient, may require ICU

CURB-65

Confusion (abbreviated mental test ≤8)
Urea (>7mmol/L)
Respiratory rate (≥30 breaths/min)
Blood pressure <90mmHg systolic and/or <60mmHg diastolic
65 years or older

Scoring

- 0-1: outpatient,
- 2: hospital admission,
- 3-5: hospital admission, consider ICU

Pathophysiology[5,6]

Lower respiratory tract is sterile despite day to day exposure to pathogens and particulate matter due to

- Innate (non-specific) immune function
- Acquired (specific) immune function

Pneumonia occurs when the virulence of an organism is able to overcome the host immune system due to

- Host factors (e.g. immunocompromisation)
- Pathogen factors (e.g. high virulence factors).

Transmission to lung

- Microaspiration (most common)
- Haematogenous spread
- Direct local spread
- Macroaspiration

Differentials[5,6]

Infectious:

- URTI, sinusitis, pharyngitis, acute bronchitis

Non-infectious:

- Pulmonary embolism, chronic HF, bronchial carcinoma, inflammatory lung disease

Unresolving pneumonia

Pneumonia should improve within 24 hours of Rx

- Subjectively "feeling better", resolving fever

If no improvement, consider

- Wrong antibiotic (e.g. different organism, poor compliance, poor absorption)
- Wrong diagnosis (e.g. cancer, pulmonary embolism)
- Complication (e.g. empyema)

Pleural effusion

Definition[2] A collection of fluid in the pleural space (between the parietal and visceral pleura). Fluid may consist of blood (haemothorax), lymph (chylothorax) or pus (empyema).

Classification[1,2]

Transudate: <30g protein per litre of fluid

Exudate: >30g protein per litre of fluid

Presentation[1,2]

Often asymptomatic

If symptomatic:

- Dyspnoea
- Pleuritic chest pain

Associated clinical features of pleural effusion are important in determining likely aetiology:

- Cough, sputum production
- Haemoptysis
- Fever
- Night sweats, weight loss (signs of malignancy)

Take a full respiratory history considering possible risk factors for pleural effusion:

- Occupational exposures
- Smoking
- Personal history of malignancy
- Family history of malignancy
- Medication history

Examination[2]

- Trachea displaced away from effusion
- Apex beat displaced away from effusion
- Reduced chest expansion on affected side
- Stony dull percussion note over fluid
- Reduced or absent breath sounds.
- Bronchial breath sounds may be present above the level of the effusion (compression of lung)
- Pleural friction rub
- Reduced vocal resonance

Investigations[1,5,9]

CXR

- Blunt costophrenic angle (loss of adjacent aerated lung for contrast)
- Water dense shadows with curved concave upper border ("meniscus sign")
- Trachea and heart border may be deviated away from effusion

Pleural fluid aspiration (thoracentesis)

- Diagnostic (may also be therapeutic)
- Performed under ultrasound guidance
- Needle with syringe inserted 1-2 intercostal spaces below upper border of pleural effusion (as percussed)

MC&S

Pleural fluid sent to laboratory for:

- Clinical chemistry (protein, glucose, pH, LDH, amylase)
- Bacteriology (microscopy, culture, staining)
- Cytology
- Immunology (rheumatoid factor, ANA, complement)

Pleural biopsy

- If inconclusive pleural fluid analysis
- Performed under CT or thorascopic guidance

Pleural fluid observation[5]

Colour of fluid

Clear	Normal
Pale yellow (straw)	Transudate, some exudates
Red (bloody)	Malignancy, benign asbestos pleural effusion, postcardiac injury syndrome, pulmonary infarction in absence of trauma
White (milky)	Chylothorax, cholesterol effusion
Brown	Long-standing blood effusion, rupture of amoebic liver abscess
Black	Aspergillosis
Yellow-green	Rheumatoid pleurisy
Dark green	Biliothorax
Colour of enteral tube feeding	Feeding tube has entered pleural space
Colour of central venous catheter infusate	Extravascular catheter migration

Character of fluid

Pus	Empyema
Viscous	Mesothelioma
Debris	Rheumatoid pleurisy
Turbid	Inflammatory exudate, lipid effusion
Anchovy paste	Amoebic liver abscess

Odour of fluid

Putrid	Anaerobic empyema
Ammonia	Urinothorax

Pleural fluid analysis[5]

Normal pleural fluid

- pH 7.60-7.64
- <1000WBC/mm3
- LDH <50% of plasma
- Glucose similar to that of plasma

Diagnostic yield from pleural fluid analysis

Empyema	Observation (pus, putrid odour); culture
Malignancy	Positive cytology
Lupus pleuritis	LE cells present; pleural fluid serum ANA >1.0
Tuberculosis pleurisy	Positive AFB stain, culture
Oesophageal rupture	High salivary amylase, pleural fluid acidosis (can be as low as 6.0)
Fungal pleurisy	Positive KOH stain, culture
Chylothorax	Triglycerides (>100mg/dL); lipoprotein electrophoresis (chylomicrons)
Haemothorax	Haematocrit (pleural fluid/blood >0.5)
Urinothorax	Creatinine (pleural fluid/serum >1.0)
Peritoneal dialysis	Protein (<1g/dL); glucose (300-400mg/dL)
Extravascular migration of central venous catheter	Observation (milky if lipid infusion); pleural fluid/serum glucose >1.0
Rheumatoid pleurisy	Characteristic cytology

Management[1,5]

Therapeutic drainage

- Pleural fluid aspiration under U/S guidance
- Intercostal drain (alternative)
- Repeated drainage may be necessary

Pleurodesis

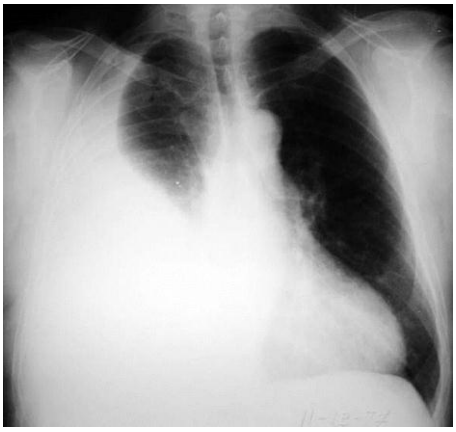
- Indicated in recurrent effusions
- Obliteration of pleural space by adhesion of pleural surfaces
- Chemical pleurodesis
  - Talc, tetracyclines or bleomycin
- Surgical pleurodesis
  - If persistent collections
- Pleural catheter (tunneled)

Epidemiology

Most common causes of pleural effusion are:

- Congestive heart failure with pulmonary oedema
- Malignancy (lung cancer)
- Pulmonary embolus
- Tuberculosis
- Pneumonia
- Parapneumonic effusion
- Pancreatitis

CXR: Pleural effusion



h: Chandrasekhar AJ. Chest X-Ray Atlas: Pleural Effusion Case 1. [Internet]. Chicago, IL (US): Loyola University Chicago Stretch School of Medicine; 2002 [updated 2006 Jan 3; cited 2011 Jun 10]; Available from: http://www.meddean.luc.edu/lumen/meded/medicine/pulmonar/cxr/atlas/cxratlas_f.htm

- Loss of costophrenic angle
- Loss of right cardiac border
- Loss of diaphragmatic border
- Meniscus (seen maximally in axilla)

Aetiology[5,9]

Pleural effusion is a clinical manifestation that is indicative of underlying disease.

Causes of transudate (<30g protein/L) pleural effusion:

- Increased venous pressure (cardiac failure, fluid overload, constrictive pericarditis)
- Hypoproteinaemia (nephrotic syndrome, chronic liver disease, malabsorption)
- Hypothyroidism
- Meigs syndrome (ovarian fibroma which causes pleural effusion and ascites)

Causes of exudate (>30g protein/L) pleural effusion:

- Pneumonia
- Malignancy (bronchial carcinoma, metastatic carcinoma, mesothelioma)
- Tuberculosis
- Pulmonary infarction
- Subphrenic abscess
- Acute pancreatitis
- Connective tissue disorders (rheumatoid arthritis, SLE)
- Drugs (methysergide, cytotoxics)
- Irradiation
- Trauma

Causes of haemothorax:

- Chest trauma
- Rupture of pleural adhesion with blood vessel

Causes of chylothorax

- Trauma to thoracic duct
- Surgical instrumentation of thoracic duct
- Carcinoma or lymphoma of thoracic duct

Causes of empyema:

- Pneumonia
- Lung abscess
- Bronchiectasis
- Tuberculosis
- Penetrating chest trauma

Pathophysiology[5,9]

A small amount of fluid (0.13ml/kg of body mass) is usually present in the pleural space to allow frictionless movement of two pleural surfaces (visceral and parietal) against each other during respiration. This volume is maintained through the balance of oncotic and hydrostatic pressures and lymphatic drainage.

The interplay of several mechanisms can result in the formation of a pleural effusion:

- Change in permeability of pleura
- ↓intravascular oncotic pressure (e.g. hypoproteinaemia)
- ↑ permeability of capillaries or disruption in vascular integrity of capillaries
- ↑ hydrostatic pressure in capillaries of systemic or pulmonary circulation
- ↓ pressure in pleural space resulting in decreased expansion
- ↓ or absent lymphatic drainage due to obstruction or rupture of vessel, typically of thoracic duct
- ↑ amount and migration of peritoneal fluid across the diaphragm
- Presence of pulmonary oedema resulting in migration of fluid across visceral pleura
- ↑ pleural fluid oncotic pressure

This can result in increased pleural fluid formation and/or decreased pleural fluid clearance resulting in collection of fluid in the pleural space and pleural effusion.

Pulmonary embolism

Definition[1,25] Pulmonary embolism is the obstruction of a pulmonary artery or one of its branches by a material that has originated from elsewhere in the body. Emboli are most commonly formed by blood clots, but may also be due to fat, air or amniotic fluid embolism.

Classification[5] *Acute* (patient develops clinical features immediately following obstruction of pulmonary vessel) or *chronic* (patient develops clinical features, typically progressive dyspnoea, over years). Acute pulmonary embolism can be sub-classified as *massive* (causing hypotension <90mmHg systolic or <40mmHg diastolic for >15 minutes, medical emergency) or *sub-massive* (all other acute pulmonary embolisms not meeting criteria for massive acute pulmonary embolism)

Presentation[1,2,5]

Pulmonary embolism is often asymptomatic

Common symptoms reported:

- Dyspnoea (severe, sudden onset)
- Pleuritic chest pain
- Cough
- Wheezing
- Orthopnoea
- Calf or thigh pain
- Calf or thigh swelling
- Dizziness
- Syncope
- Haemoptysis

Note

- Pulmonary embolism is often asymptomatic
- Clinical features PE are nonspecific

Ask about

- Risk factors
- Past history of thromboembolism
- Family history of thromboembolism

Examination[1,2,5]

Signs on general inspection

- Tachycardia
- Tachypnoea
- Cyanosis
- Hypotension
- Fever (if infarction)

Signs on auscultation

- Decreased breath sounds
- Crackles (rales)
- Pleural friction rub (if infarction)

Signs of massive pulmonary embolism

- Elevated JVP
- Right ventricular gallop
- Right ventricular heave
- Tricuspid regurgitation murmur (pansystolic)
- Loud P2 in second heart sound

Signs of deep vein thrombosis

- Tenderness
- Oedema
- Erythema

Investigations[1,5]

Essential as PE cannot be diagnosed on Hx and Ex alone.

Bloods

- FBC, U&E, coagulation picture

D-dimer

- High sensitivity (useful to rule out PE if negative)
- Low specificity (not useful to rule in PE even if positive)
- Detects fibrin degradation product in blood
- Positive in: PE, inflammation, thrombosis, post-op, infection, malignancy

ABG

- Hyperventilation (low PaO2 and PaCo2)

CXR

- May be normal
- May show oligaemia, dilated pulmonary vessels, linear atelectasis (collapse), pleural effusion, opacities (wedge-shaped, cavitation)

ECG

- May be normal
- Tachycardia (most common)
- RBBB
- Right ventricular strain
- Right axis deviation
- AF
- Classical "SI QIII TIII" pattern (deep S waves in I, Q waves in III, inverted T waves in III)

CT pulmonary angiography (CTPA)

- High sensitivity and specificity

V/Q scan

- V/Q Mismatch
  - Decreased perfusion, normal ventilation
  - Useful only if previously normal lung (indeterminate in lung disease)

Echocardiogram

- Right heart strain

Management[1,5]

Immediate management

- Oxygen 100%
- Analgesia (morphine)
- Anti-emetic
- Establish IV access
- Assess haemodynamic stability
- Colloid infusion +/- adrenalin if hypotensive (systolic <90mmHg)

Anti-coagulation

- To prevent further blood clot
- Warfarin if systolic >90mmHg
- IV heparin (LMW or unfractioned), bolus first then infusion, infusion as guided by APTT

Thrombolysis

- Dissolve existing blood clot
- High risk patients (large or unstable PE)
- Streptokinase or recombinant tissue plasminogen activator (rTPA)

Inferior vena cava filter

- Limited indications
- Should be used in co-therapy with anticoagulation

Prevention

- Early mobilization post-op
- TED stockings (anti-thromoboembolic)
- LMW Heparin prophylaxis
- Anticoagulation if recurrent PE

Aetiology[1,5]

Causes

- Thrombus
  - Deep venous thrombosis (most common cause)
  - 50-80% from distal vein below the popliteal veins
  - Others from proximal iliac, femoral and popliteal veins
- Air
- Fat
- Amniotic fluid
- Malignant cells
- Parasites

Risk factors

- Deep vein thrombosis (50%)
- Immobilization (decreased mobility, bedbound, stroke, paresis, paralysis)
- Recent surgery (<3 months, particularly if abdominal or pelvic, hip or knee replacement)
- Thrombophilia
- Malignancy
- Recent central venous instrumentation (<3 months)
- Hormonal risk factors (pregnancy, post partum, oral contraceptive pill, hormone replacement therapy)
- Previous pulmonary embolism
- Chronic heart disease
- Obesity (BMI >29)
- Smoking (>25 cigarettes/day)
- Hypertension

Pathophysiology[5]

- Spontaneous emboli (most typically thrombus from the deep venous system of the lower limbs)
- Venous system → right heart → pulmonary vessels
- Large thrombi lodge at bifurcation of the pulmonary artery or its branches
- Results in obstruction to blood flow
- Infarction in10% (especially patients with pre-existing respiratory disease)

Symptoms

Pleuritic chest pain

- Inflammatory response of parietal pleura to thrombus

Dyspnoea

- Atelectasis (pulmonary collapse) from obstruction by thrombus and release of inflammatory mediators
- Impaired gas exchange from functional intrapulmonary shunting and changes in surfactant function

Right ventricular failure

- ↑ pulmonary pressure

Hypotension

- ↓ cardiac output due to increase pulmonary resistance = ↓ right ventricular outflow = ↓ left ventricular inflow.

Differentials[5]

- AMI
- Pneumonia
- Aortic dissection
- Pneumothorax
- Cardiac tamponade
- Septicaemia

Epidemiology[5,17]

Incidence

- Likely underestimated (commonly asymptomatic and undiagnosed)

Mortality

- 0.2% of all deaths in Australia in 2008 (ABS)
- Untreated mortality rate is 30%
- Treated mortality rate is 2-8%
- Recurrent embolism is most common cause of death

Morbidity

- Morbidity is common amongst survivors
- Pulmonary hypertension (acute PE)

Mnemonics/extra notes[9]

Virchow's triad

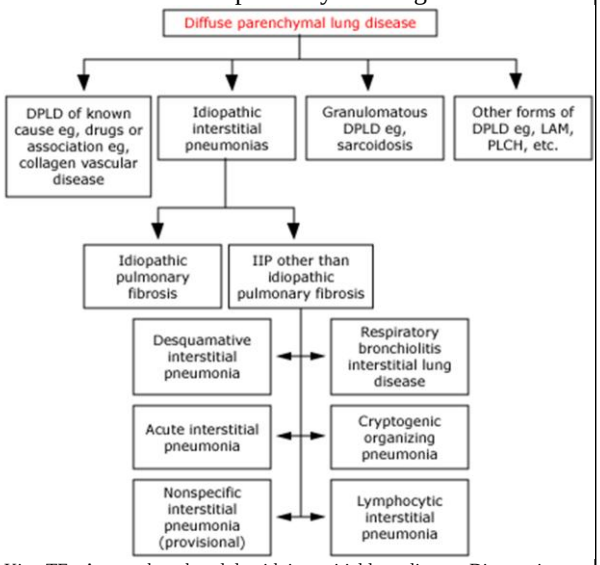
Factors contributing to venous thrombosis:

1. Hypercoagulabilty (thrombophilia, hormonal factors)
2. Haemodynamic changes (stasis, turbulence, other changes to blood flow)
3. Endothelial injury or dysfunction (hypertension, etc)

Interstitial Lung Disease

Definition[5,11] A heterogenous group of diffuse parenchymal lung diseases that are classified together because of similar clinical, radiographic or pathological features.

Classification Diffuse parenchymal lung diseases



i: King TE. Approach to the adult with interstitial lung disease: Diagnostic testing. Diffuse parenchymal lung diseases . In Flaherty KR, Hollingsworth H, editors. UpToDate. Waltham: UpToDate; 2010.

Presentation[5]

Typical presentation:

- Dyspnoea (exertional, progressive over months-years)
- Cough (non-productive)

May also present with:

- Haemoptysis
- Wheezing
- Extra-pulmonary symptoms (reflecting underlying aetiology: joint, skin, muscles, GIT)

History:

- Exposures:
  - Occupational and environmental (metals, silica, carbon, organic dusts, chemicals, other inhaled agents)
- Medication history
  - Antibiotics, anti-arrythmics, anti-inflammatories, cytotoxics
- Past medical history
  - Respiratory history, autoimmune disorders, connective tissue disease, malignancy
- Family medical history
  - Interstitial lung disease, autoimmune disorders
- Smoking history:
  - Current (Goodpasture's syndrome)
  - History of smoking (pulmonary Langerhans' cell histiocytosis, desquamative interstitial pneumonitis, idiopathic pulmonary fibrosis)

Epidemiology[10,11,18]

Prevalence and incidence

- Idiopathic pulmonary fibrosis and sarcoidosis are the most common ILDs

Mortality

- Lung diseases due to external agents accounted for 0.9% of deaths in Australia in 2008

Investigations[5]

Bloods and serology

Findings may include:

- Leukopenia, leukocytosis, eosinophilia, thrombocytopenia, haemolytic anaemia, normocytic anaemia, hypercalcemia, elevated LDH hypogammaglobulinaemia, hypergammaglobulinaemia, anti-GBM antibody, RF, ANA

CXR

Normal in 10% (false negative rate) of ILD diagnosed on biopsy

Findings may include:

- Reticular or reticulonodular infiltrates (nodular densities and shadowing), diminished lung volume, alveolar infiltrates, hilar and mediastinal lymphadenopathy, pneumothorax, pleural disease, miliary disease, honeycomb lung

Anatomical location may provide hint to aetiology:

- Upper zones: Sarcoidosis, silicosis, berylliosis, coal miner's pneumoconiosis, histiocytosis X, chronic hypersensitivity pneumonitis, tuberculosis
- Lower zones: rheumatoid arthritis, asbestosis, scleroderma, radiation, drugs (busulphan, bleomycin, nitrofurantoin, methotrexate, amiodarone), idiopathic

HRCT (high resolution computerized tomography)

Greater sensitivity and specificity

- Can help stage ILD

Findings may include:

- Air space opacities, reticular opacities, nodules, isolated lung cysts

Lung function tests

- Decreased lung volume (decreased IC, VC, TLC)
- Decreased DLCO
- Restrictive defect (decreased FEV1 and FVC, normal FEV1/FVC)
- Variable obstructive defect may be seen

Lung biopsy

Gold standard diagnostic tool in ILD

Types:

- Transbronchial lung biopsy during bronchoscopy (sarcoid), thorascopic biopsy or open lung biopsy (IPF)

Bronchoscopy with bronchoalveolar lavage

May reveal

- Infectious agents, antigens, antibodies, small molecules (dusts, particles), malignant cells, inflammatory cells (eosinophils, macrophages)
- Inflammatory cell differential can suggest aetiology

Examination[2,5]

Inspection

- Clubbing

Auscultation

- Fine late or pan-inspiratory crackles

Signs of RHF

- Advanced pulmonary fibrosis → pulmonary HTN → cor pulmonale
- Accentuated P2, right sided heave, congestive hepatomegaly, ankle and sacral oedema, raised JVP

Associated signs

- May be present due to associated illness

Differentials[5]

Pneumonia CCF Asthma COPD

Management[5]

Aetiology

- Identify aetiology through Ix and eliminate aetiology as appropriate (e.g. removal of agent in exposures, immunosuppressive therapy in autoimmune diseases)

Corticosteroids

- High dose and taper for response
- If unresponsive to aetiological removal/if not possible
- Prevent progression
- Typically does not alter existing disease
- Decline in respiratory function in absence

Supplemental oxygen

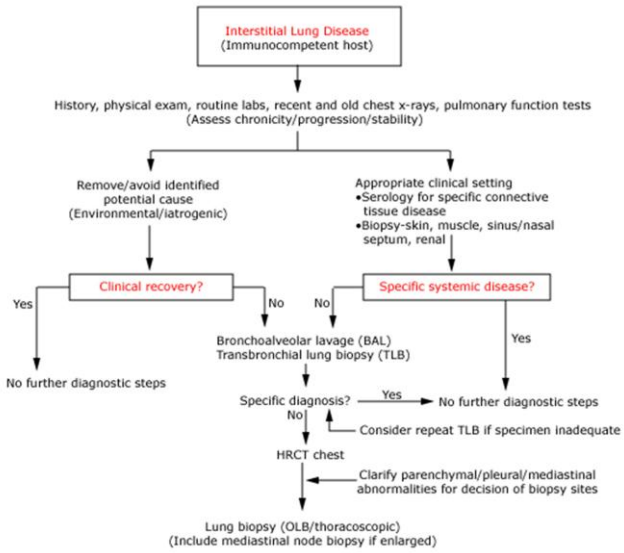
Lung transplantation

Pathophysiology[5,6,9,10]

Aetiological factors → chronic inflammation of the lung with polymorphonuclear leukocytes, B lymphocytes, T lymphocytes, macrophages → inflammatory damage to alveolar wall and surrounding structures → scarring and fibrosis → decreased viable lung for gas exchange, restriction of movement of the lung (restrictive defect) and decreased lung volumes and may result in a variable obstructive pattern.

Specific mechanism and pattern of defect depends on aetiology.

Algorithm to approach patient with interstitial lung disease



j: King TE. Approach to the adult with interstitial lung disease: clinical evaluation. Approach to patient with ILD. In Flaherty KR, Hollingsworth H, editors. UpToDate. Waltham: UpToDate; 2010.

Aetiology[5]

Primary diseases associated with ILD:

Sarcoidosis	Amyloidosis	Chronic gastric aspiration
Pulmonary Langerhans cell histiocytosis	Vasculitides (Wegener's granulomatosis, Churg-Strauss syndrome)	Haemorrhagic syndromes (Goodpasture's syndrome, idiopathic pulmonary haemosiderosis)
Lymphangeio-leiomyomatosis	Neurofibromatosis	Lymphangitic carcinomatosis
Chronic pulmonary oedema	Chronic uraemia	Respiratory bronchiolitis
Alveolar proteinosis	Pulmonary veno-occlusive syndrome	Hermansky-Pudlak syndrome
Gaucher's disease	Neimann-Pick disease	

Occupational/environmental exposures associated with ILD:

Silicates	**Carbon**	**Metals**	**Organic inhaled agents**	**Other inhaled agents**
Silica (silicosis)	Coal dust (coal worker's pneumoconiosis)	Tin (stannosis)	Thermophilic fungi (Macropolyspora faenia, Thermactinomyces vulgaris, Thermactinomyces sacchari)	Synthetic fibres (orlon, polyester, nylon, acrylic)
Asbestos (asbestosis)	Graphite (carbon pneumoconiosis)	Aluminium	True fungi (Aspergillus, Cryptostroma cortcale, Aureobasidiu pullulans, Penicillium)	Vinyl and polyvinyl chloride
Talc (talcosis)		Hard metal dusts	Bacteria (Bacillus subtilis, Bacillus cereus)	Gases (oxygen, nitrogen oxide, sulphur dioxide, chlorine, methyl isocyanate)
Beryllium (berylliosis)		Iron ("siderosis", "arc welder's lung")	Animal proteins	Fumes (zinc, copper, manganese, cadmium, iron, magnesium, nickel, brass, selenium, tin, antimony oxides)
		Barium (baritosis)		Vapours (hydrocarbons, toluene diisocyanate, mercury)
		Antimony		Aerosols (oils, fats, pyrethrum)
		Hematite ("siderosilicosis")		
		Mixed dusts of silver and iron oxide ("argyrosiderosis")		

Drugs associated with ILD:

Antibiotics	**Anti-inflammatories**	**Anti-arrhythmics**	**Illicit drugs**	**Chemotherapeutic agents**
Nitrofurantoin	Gold	Tocainide	Heroin	Antibiotics (Bleomycin, Mitocymcin C)
Sulfasalazine	Penicillamine	Amiodarone	Cocaine	Alkylating agents (Busulfan, Cyclophosphamide, Chlorambucil, Melphalan)
Minocycline	NSAIDs		Methadone	Anti-metabolites (Azathioprine, Cytosine arabinoside, Nethotrexate)
Ethambutol	Lefluonomide		Hydrochloride	Eoposide
			Propoxyphene	Paclitaxel
			Hydrochloride	Thalidomide
			Talc	Alpha interferon

Drugs associated with SLE:

Procainamide hydrochloride	Isoniazid	Hydralazine hydrochloride	Hydantoin	Penicillamine

Lung cancer

Definition[5] Malignancy that originates in the airways or pulmonary parenchyma

Classifications/subtypes[5]
Broad clinical classification into:
Small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC)

Presentation[5]
Typical presentation:
Absence of symptoms until local spread or metastases is common
Advanced disease seen in majority of clinical presentations
75% of patients have ≥1 symptom at diagnosis

- Cough (45-75%)
- Weight loss (46-68%)
- Dyspnoea (37-58%)
- Chest pain (27-49%)
- Haemoptysis (27-29%)
- Bone pain (20-21%)
- Hoarseness (8-18%)

Other features in presentation may include:

- Pleural effusion
- Recurrent pneumonia
- Superior vena cava syndrome (fullness in head, dyspnoea commonly, may have cough, pain, dysphagia)
- Extrathoracic metastases (liver, bone, adrenal gland, brain)
- Paraneoplastic syndromes (hypercalcaemia, SIADH, neurological manifestations, haematological manifestations, hypertrophic osteoarthropathy, dermatomyositis and polymyositis, Cushing's syndrome

History taking:

- Smoking history: pack years, current/past smoker
- Exposure history: occupational and environmental (asbestos, dusts, chemicals, metals)
- Past medical history: radiation, past malignancy, lung conditions and infections
- Family medical history: lung cancer, other malignancies

Investigations[5]
CXR (raises suspicion of lung cancer)

- Mass or nodule
- Hilar and mediastinal adenopathy
- May also see: cavitations (rare), lobar atelectasis, pleural effusion

Tissue diagnosis (required to confirm Dx and determine histology)

- FNA under CT or fluoroscopic guidance (transthoracic needle aspiration)
- Resection of lesion
- Thoracentesis (if pleural effusion)
- Bronchial washings or brushings
- Sputum cytology

Lymph node biopsy (diagnose SCLC vs. NSCLC)

- Transbronchial biopsy
- Thorascopy
- Mediastinoscopy or mediastinotomy

CT (staging – more sensitive than CXR)

- Lung mass
- Adenopathy

Bone scan

- Bony metastases (can assist in staging)

Examination[2,5]
Many patients have no signs on examination.
Inspection

- Cachexia
- Haemoptysis in sputum cup
- Clubbing
- Hypertrophyic pulmonary osteoarthropathy (not SCLC)

Palpation

- Lymphadenopathy (supraclavicular, axillary)

Auscultation

- Fixed inspiratory wheeze

Other

- Pleural effusion
- Pneumonia
- Less commonly: signs of focal emphysema, atelectasis, bronchitis, bronchiectasis

Signs of metastases

- Bony tenderness of ribs (bone), hepatomegaly (liver), confusion, fits, focal neurological signs (brain)

Management[5]
NSCLC
<u>Stage I and stage II</u>
Surgical resection offers best long term survival rate and cure
Suitability according to pre-operative staging (resectability), performance status regarding comorbidities, pulmonary function (operability).
Post-operative adjuvant chemotherapy improves survival (NSCLC stage II)
Radiotherapy can be provided for non-surgical candidates and may include stereotactic radiosurgery, radiofrequency ablation , photodynamic therapy (primary treatment in superficial airway lesions)
<u>Stage III</u>
Combined radiotherapy and chemotherapy with some role for surgical resection
<u>Stage IV</u>
Palliative symptomatic treatment (not curative).
Types may include chemotherapy, molecular targeted therapy, radiotherapy, surgery
SCLC
<u>Limited stage disease</u>
Combination chemotherapy and radiotherapy
Usually not surgical resection unless solitary pulmonary nodule with no lymph node involvement or metastases
<u>Extensive stage disease</u>
Chemotherapy alone (initial)
<u>Prophylactic radiation therapy</u>
Both limited and extensive stage disease
↓ incidence of brain metastases and ↑ survival

Differentials[5]
Lung mass: tuberculosis, granulomatous (sarcoidosis, Wegener's), fungal (histoplasmosis, coccidiomycosis, Cryptococcus)

Aetiology[5]

Risk factors

Smoking

- Primary risk factor, accounts for 90% of lung cancers, 20x ↑ risk for a patient with 40 pack years compared to non-smoker
- Passive smoking also ↑ risk.

Radiation

- Radiation therapy ↑ the risk of a primary lung cancer in those being treated for other malignancies (especially ipsilateral lung)

Environmental toxins (act as carcinogens)

- Second hand smoke, asbestos, radon, metals (arsenic, chromium, nickel), ionizing radiation, polycyclic aromatic hydrocarbons

Pulmonary fibrosis

- 7x risk

Genetic factors

- Familial risk clearly established
- Specific genetic markers (oncogenes – EML4-ALK fusion gene, K-ras oncogene, HER2 oncogene, Bcl-2 gene, tumour suppressor genes – p53) have been implicated but are still being investigated

Pathophysiology[5]

WHO classification for primary lung cancer:

Histological types (WHO)

- Small cell carcinoma (13%)
- Adenocarcinoma (including bronchioalveolar carcinoma) (38%)
- Squamous cell carcinoma (20%)
- Large cell carcinoma (5%)
- Other non-small cell carcinomas that cannot be further classified (18%)
- Other (6%)

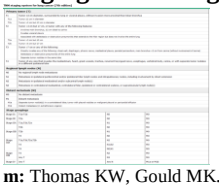
Clinically, NSCLC is made up of adenocarcinoma, squamous cell carcinoma and large cell carcinoma.

- 95% of lung cancers are SCLC or NSCLC.

Symptomatology

- Direct effects of the tumour (chest pain, haemoptysis),
- Local effects of tumour (phrenic nerve irritation causing cough, mass effects causing hoarse voice)
- Local spread
- Metastatic spread (bony metastases causing bone pain)

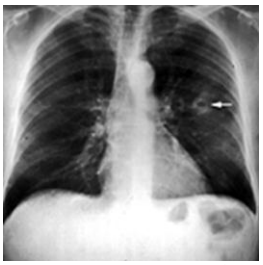
Staging: TNM staging for lung cancer (see online reference for full-sized copy)



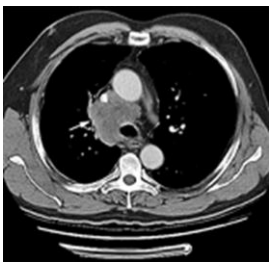
m: Thomas KW, Gould MK. Diagnosis and staging of non-small cell lung cancer. TSN staging system for lung cancer (7th edition). In Jett JR, Wilson KC, editors. UpToDate. Waltham: UpToDate; 2011.

Approach to possible lung cancer

Ask yourself	*Ask the patient*
Is it lung cancer? (Biopsy)	What do they think is going on?
What type of lung cancer is it? (Pathology)	What would they like to happen?
Has it spread? Local? Distant? Paraeoplastic? (Consider investigations – LFTs, U&Es, Ca)	What are they scared of? Prognosis? Cause of death?
What is the best treatment? Curative? Palliative?	
Are they fit for their treatment? Heart? Lungs?	



k: Midthun DE. Overview of the risk factors, pathology, and clinical manifestations of lung cancer. Large cell carcinoma. In Jett JR, Ross ME, editors. UpToDate. Waltham: UpToDate; 2011.



l: Midthun DE. Overview of the risk factors, pathology, and clinical manifestations of lung cancer. Small cell carcinoma. In Jett JR, Ross ME, editors. UpToDate. Waltham: UpToDate; 2011.

Epidemiology[19,20]

Prevalence and incidence

- Most commonly Dx cancer in Australia
- Dramatic ↑ in relative incidence of adenocarcinoma and corresponding ↓ in incidence of other types of NSCLC and SCLC

Mortality

- Most common cause of cancer death worldwide
- Most common cause of death in M
- Third most common cause of death in F
- ATSI>non-ATSI rates of mortality from lung cancer
- 5th most common premature cause of death in Australia
- 4th leading cause of all deaths in Australia in 2009
- 5 year survival rate: 10% males, 12% females

Tuberculosis

Differentials[5] Sarcoidosis, Malignancy, Histoplasmosis, Coccoidosis (USA)

Classification[5,21]

Active disease:

- Uncontrolled disease by Mycobacterium tuberculosis causing clinical features and infectivity.

Latent disease:

- Absence of active disease through control by cell mediated immunity but persisting infection with Mycobacterium tuberculosis bacilli.
- Clinical features are absent and patient is not infectious.

Primary disease:

- Active disease upon infection with M. tuberculosis

Reactivation disease:

- Active disease years after infection with M. tuberculosis

Disseminated disease:

- Dissemination of bacilli → haematogenous → military TB in distal organs

Presentation[5]

Primary tuberculosis

- Most common presentation of primary disease: fever (low grade, typically 14-21 days duration)
- Other symptoms in primary disease (<25%): chest pain, pleuritic chest pain , bronchial lymphadenopathy, arthralgia, pharyngitis

Reactivation tuberculosis

- Classical symptoms of reactivation disease: night sweats, malaise, cough (non-productive or scant productive, ↑ in morning, progresses to productive of yellow-green sputum and continuous), haemoptysis (due to caseous sloughing, endobronchial erosion, blood typically in small amounts), weight loss
- Reaction disease may also have: chest pain, dyspnoea

Ask about

- Recent travel to places where tuberculosis is endemic
- Contact with people with known tuberculosis
- Past tuberculosis infection or BCG vaccination
- HIV/AIDs status

Management[5,16]

Antibiotic treatment

- Long term, combination therapy:
- Therapeutic Guidelines: Antibiotics
  Isoniazid 300mg, po, daily for 6/12 PLUS
  Rifampcin 600mg, po, daily for 6/12 PLUS
  Ethambutol 15mg/kg, po, daily for 2/12 PLUS
  Pyrazinamide 25-40mg/kg up to 2mg, po, daily for 2/12
- Consider susceptibilities when prescribing regimen.

Side effects:

- Isoniazid: Hepatitis, neuropathy, pyridoxine deficit, agranulocytosis.
- Rifampcin: Hepatitis, orange discolouration of urine and tears, inactivation of oral contrapcetive pill, flu-like symptoms. Cease if rise in bilirubin.
- Ethambutol: Optic neuritis
- Pyrazinamide: Hepatitis, arthralgia. Contraindicated in acute gout and porphyria.

Prevention

- Bacillus Calmette-Guerin (BCG) vaccine (live attenuated)

Examination[2,5]

Physical findings are non-specific and often absent in mild or moderate disease.

Inspection

- Febrile, finger clubbing

Chest examination

- Typically no abnormal findings on chest examination
- Signs of pleural effusion may be present
  - Displaced trachea and apex beat away from the effusion, reduced chest expansion, stony dull percussion note, reduced or absent breath sounds, reduced vocal resonance
- Signs of pleural thickening may be present
  - Dull percussion note and decreased fremitus
- Inspiratory or post-tussive (post-cough) crackles
- Consolidation if large area of lung involved
  - Dull percussion, ↓ expansion, bronchial breathing

Disseminated disease

- May have abnormal findings according to site of military tuberculosis if disseminated disease
  - E.g. hepatosplenomegaly, meningitis, lymphadenopathy, dyspnoea, pleural effusion

Investigations[5]

Bloods

- FBC typically shows no changes
- Advanced disease: normocytic anaemia, leukocytosis, monocytosis

CXR

Primary tuberculosis:

- Hilar adenopathy (seen within 1/52-8/52)
- Pleural effusion (1/3 of patients within first 3-4/12)
- Pulmonary infiltrates (peri-hilar, pleural effusion)
- Right middle lobe collapse
- Focal shadowing
- Solitary nodules

Reactivation tuberculosis:

- 80-90% → apical-posterior segment of upper lobes
- Pulmonary infiltrates
- Cavitations (unlike primary disease)
- No lymphadenopathy (unlike primary disease)
- Air fluid level may be visible
- Fibrosis and calcification may be seen

CT scan

- More sensitive than CXR (esp. for small apical lesions)
- May visualize cavities, centrilobular lesions, nodules, branching linear densities (“tree in bud” appearance)

MC&S

- Clinical samples (sputum, pleural fluid, as indicated urine, pus, peritoneal fluid, bone marrow, CSF) should be tested for M. tuberculosis acid fast bacilli.
- Caseating granulomata is classical of disease.

Mantoux test (tuberculin skin test)

- Intradermal injection of TB antigen with recording of cell-mediated response after 48-72 hours.
- Positive test indicates immunity (previous infection or BCG vacc, ↑ positive indicates active infection).

Interferon gamma testing (Quantiferon-TB/T-spot-TB)

- Measures delayed hypersensitivity reaction to exposure to Mycobacterium tuberculosis.

Aetiology[5,21]

Cause

- Mycobacterium tuberculosis
- Anaerobic, slow growing pathogen (20-24 hours), difficult to identify (acid fast bacilli) due to mycolic acid surface coating with no true outer membrane of cell envelope which makes it difficult for gram staining (stains gram positive). Acid fast stain (Ziehl-Neelsen stain) used instead.
- Virulence factors include mycolic acid glycolipids and trehalose dimycolate 'cord factor' (form granulomas), catalase-peroxidase and lipoarabinomannan (resist oxidative stress response from host, induce cytokines) .

Risk factors

- Immunosuppression (HIV, AIDs, end stage renal disease, diabetes mellitus, malignant lymphoma, corticosteroids, TNF-alpha inhibitors, old age due to decreased cell mediated immunity)
- Low socioeconomic status, overcrowding, poor access to healthcare
- Family history of tuberculosis

Pathophysiology[5,21]

Inhalation of Mycobacterium tuberculosis bacilli and deposition in the lungs can result in several outcomes

- Clearance of the organism
- Chronic latent infection
- Rapidly progressive active disease (primary disease)
- Active diseases years after infection (reactivation disease)

Primary disease

- Uncommon (5-10%), high risk in patients with AIDs
- Bacilli are deposited in the alveoli → evade the innate immune system → proliferate inside alveolar macrophages → kill the cells
- Infected alveolar macrophages produce cytokines, chemokines → recruit phagocytes, macrophages, neutrophils → form nodular granuloma (tuberculoma)
- Uncontrolled replication →infection of lymph nodes →lymphadenopathy
- Ghon's complex = infection from expansion of tubercle from alveoli to lung parenchyma and lymph nodes
- Primary infection occurs until cell mediated immune response occurs (typically 2-6 weeks following infection)
- If no CMI → progressive lung destruction → haematogenous spread → dissemination (spleen, liver, kidneys, brain, joints) → military tuberculosis (millet seed appearance)
- If caseating lesions invade into the airway → host is infectious to others.
- Resolution of disease → healing by fibrosis around tuberculous lesions
- Complete eradication of Mycobacterium tuberculosis is rare and latency most commonly occurs

Reactivation disease

- Proliferation of latent bacteria
- Most commonly in immunocompromised patients.
- Reactivation disease is typically more localized (apex of lung with disseminated disease uncommon) with less involvement of lymph nodes and less caseation.

Epidemiology[5,21]

Worldwide

- 2nd most common infectious cause of death worldwide
- 8 million new cases of active TB/year
- 1.7 million TB deaths/year
- Magnified by concurrent epidemic of HIV

Australia

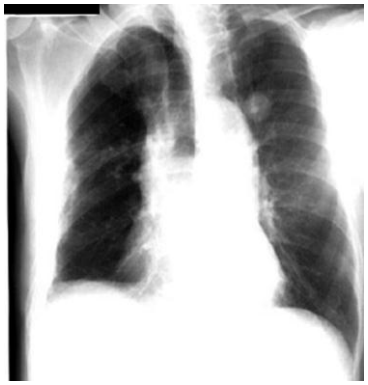
- 1000 notifications/year
- Most cases due to latent re-activation in patients infected in birth countries (migrants or refugees) or in childhood (Australia)
- 85% of notifications for TB in overseas-born Australians
- Reactivation tuberculosis is the most common type of TB infection seen = 90% of non-HIV adult cases

Trends

- Decline observed in 20th century however resurgence in 1990s due to rise in HIV co-infection, drug resistance and poor management of control programs.

CXR: Tuberculosis

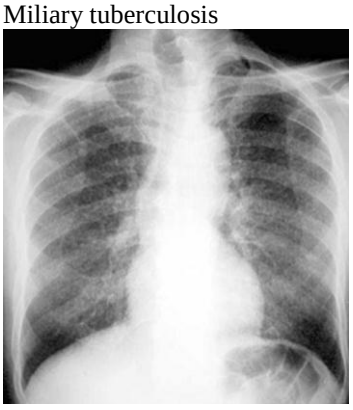
Tuberculoma



n: Chandrasekhar AJ. Chest X-Ray Atlas: Tuberculoma. [Internet]. Chicago, IL (US): Loyola University Chicago Stretch School of Medicine; 2002 [updated 2006 Jan 3; cited 2011 Jun 10]; Available from: http://www.meddean.luc.edu/lumen/meded/medicine/pulmonar/cxr/atlas/cxratlas_f.htm

CXR: Tuberculosis

Miliary tuberculosis



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Interpreting chest x-rays

XR[9,22]

X-ray is a radiological imaging technique which is painless, fast and easy.

5 Roentgen densities seen:

From most black (exposed) to most white (blocked)

1. Gas
2. Fat
3. Soft tissue
4. Bone
5. Metal

Radiation dose

- X-ray: 0.2mSv
- Annual background radiation dose: 2.6mSv

Process

- X-ray source and x-ray receiving plate
- Stand with chest against x-ray plate (PA) or if unable to stand lie on a table (AP).
- Patient takes a deep breath and holds inspiration whilst x-ray is taken.

Indications for CXR[9,22]

- Chest pain
- Cough
- Dyspnoea
- Other cardiovascular complaints
- Other respiratory complaints
- Septic screen
- Abdominal pain (if suspected cardiac/thoracic origin)
- Rib fractures
- Diagnostic
- Monitoring (resolution of pneumonia, etc)

Signs on CXR[9]

- Silhouette sign
  - Loss of lung/soft tissue interface
  - Implies two areas of similar radiodensity
  - Caused by pathology where normal air in lung is displaced/replaced
  - E.g. Silhouette sign seen in right middle lobe pneumonia where consolidation results in loss of right heart border

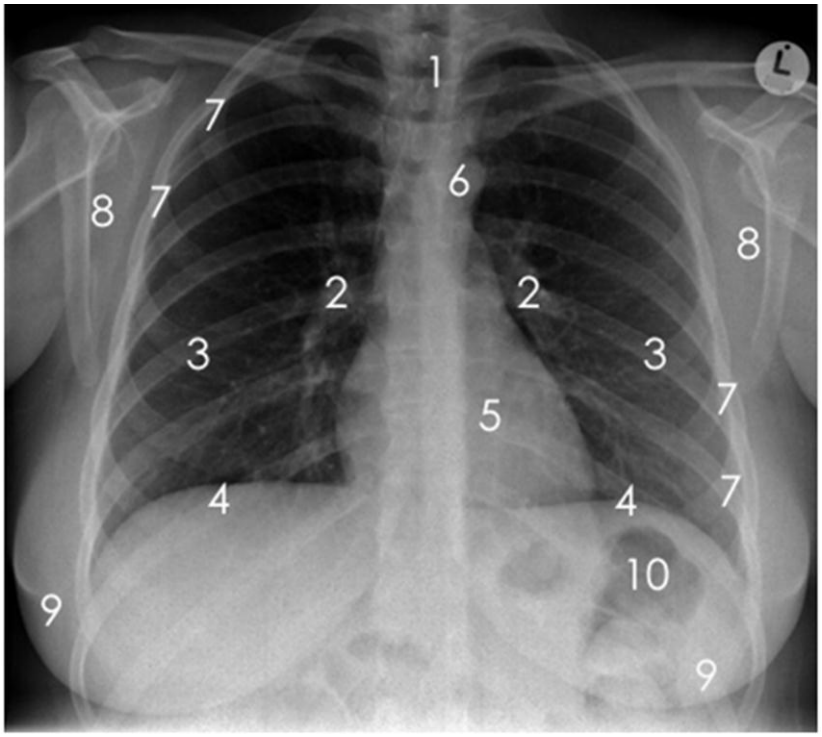
Systematic interpretation of CXRs[9]

- ABCDE
  - A: Airways (bronchi, lung, pleura)
  - B: Bones (ribs, clavicles, scapula)
  - C: Circulation (heart, vessels, mediastinum)
  - D: Diaphragm
  - E: Soft tissue (breast) and other (lines, tubes, artefacts)
- Outside chest to inside chest

General points for interpretation of CXR[9,23]

- Refer to lung zones (e.g. left upper zone of lung) rather than lobes
- Compare left to right side

Normal CXR[23]



Visible structures

1. Trachea
2. Hilum
3. Lung
4. Hemi-diaphragm
5. Heart
6. Aortic knuckle
7. Ribs
8. Scapula
9. Breast
10. Stomach

Obscured or invisible structures (typically only visible on CXR when abnormal)

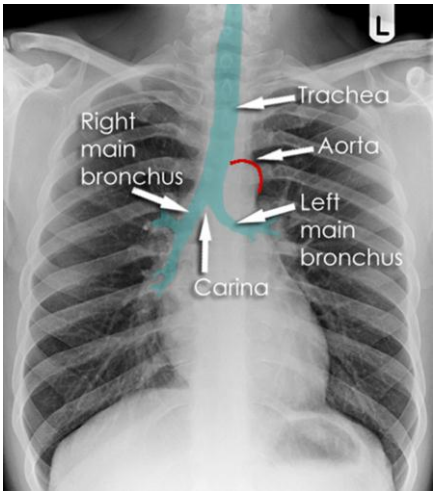
- Sternum
- Oesophagus
- Spine
- Pleural
- Lung fissures
- Aorta

p: Lloyd-Jones G. Chest X-ray tutorials [Internet]. Salisbury (United Kingdom): 2007 [updated 2011; cited 2011 Aug 26]. Available from: http://radiologymasterclass.co.uk/tutorials/tutorials.html

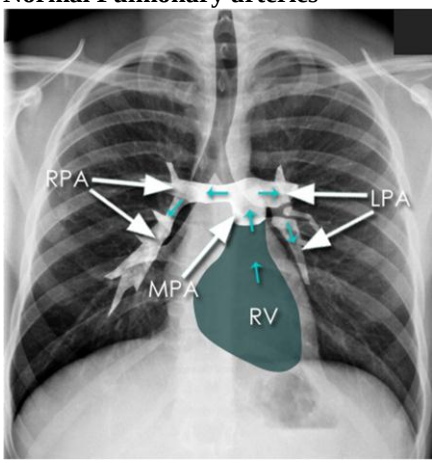
Interpreting a CXR[9,22,23]

1. Identify the CXR
   - Correct patient name, date of birth, UMRN, gender.
   - Correct date and time of CXR.
2. Technical aspects
   - Rotation
     - Centred CXR will have symmetrical distance between L and R sternoclavicular joint and central spinous process of vertebrae
   - Penetrance
     - Optimal penetration: vertebral bodies are just visible
     - Under-penetration: vertebral bodies cannot be visualized
     - Over-penetration: vertebral bodies are distinctly visible, lung markings are poorly seen and lungs are very black
   - Patient position
     - Label should denote PA/AP/lateral and erect/supine/decubitus/sitting
     - PA (posterior-anterior)
       - Usual position
       - X-ray source posterior to patient and receiving x-ray plate anterior to patient (patient stands hugging plate against chest)
       - Scapulae are clear of lungs on PA
       - All are erect CXR
     - AP
       - May be taken if patient is unable (too ill, etc) to stand for PA view
       - All supine are AP, AP may also be done sitting or standing
     - Lung volume
       - CXR requires full inspiration to be held whilst film is being taken to visualize lung abnormalities
       - Normal inspiration should see diaphragm at 6^{th} rib anteriorly or 8-10^{th} rib posteriorly
3. Skin and soft tissue
   - Body habitus
     - Is patient obese or very thin?
   - Breast
     - Can breast shadow be seen?
     - Mastectomy?
4. Pleura
   - Thick or thin?
   - Fluid or air in pleural space?
   - Mass or nodules in pleural space?
   - Asbestosis/mesothelioma?
5. Bones
   - Consider: ribs, clavicles, scapula, vertebrae
   - Symmetrical? (scoliosis, chest deformity)
   - Dislocations, fractures? (rib fracture: "arrowhead")
6. Heart
   - Cardiothoracic ratio
     - Width of heart: width of thorax
     - <50%: normal
     - >50%: cardiomegaly
     - Cardiomegaly can only be Dx on PA film as AP film magnifies heart due to divergence. Only assessment that can be made from AP film is cardiothoracic ratio <50% is normal.
   - Heart borders
     - Should be well defined
     - Loss of heart borders
       - Consolidation (lobar pneumonia)
7. Lungs
   - ↑ opacification
     - Pulmonary oedema (diffuse opacification)
     - Interstitial lung disease (reticular white line markings)
     - Nodular (small, white, round markings)
   - ↓ opacification
     - Emphysema (↓of lung markings, very black lung)
   - ↑ lung volume
     - Hyperinflation (COPD)
   - ↓ lung volume
     - Atelectasis
   - Fluid level
     - Pulmonary effusion (meniscus seen)
   - Peripheral lung markings
     - Should be visible to chest wall
     - If not visible (pneumothorax)
   - Hila
     - Left hilum should be higher than right (heart)
     - Hilar lymphadenopathy?
   - Fissures
     - Right lung
       - 3 lobes (U, M, L)
       - Horizontal fissure (U/M lobes)
       - Oblique fissure (M/L lobes)
     - Left lung
       - 2 lobes (U, L)
       - Oblique fissure (U/L lobes)
     - Horizontal fissures seen on frontal view
     - Oblique fissures seen on lateral view
8. Hemidiaphragms
   - Right hemidiaphragm should be higher than left hemidiaphragm (due to liver on right side)
   - Costophrenic angles
     - Should be sharp and well-defined
     - Abnormalities
       - Blunt/flattened hemi-diaphragm (pleural effusion, hyperinflation)
       - Hemidiaphragm lower than expected (hyperinflation in COPD)
       - Hemidiaphragm higher than expected (poor inspiration on x-ray)
   - Free gas under diaphragm
     - Perforated hollow viscous (e.g. small bowel perforation)
9. Mediastinum
   - Consider: tracheal, oesophagus
   - Deviated from midline
     - Tension pneumothorax (deviated away from affected lung)
     - Atelectasis (deviated towards affected lung)
10. Abdomen
    - Stomach and bowel
      - Gas?
11. Other
    - Lines
      - Chest drain
      - Central line (to lower superior vena cava)
      - Endotracheal tubes
      - Gastric tubes

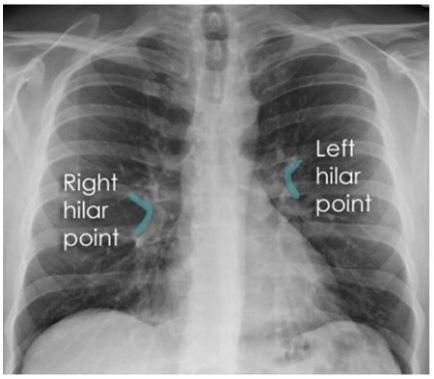
Normal Trachea and bronchi[p]



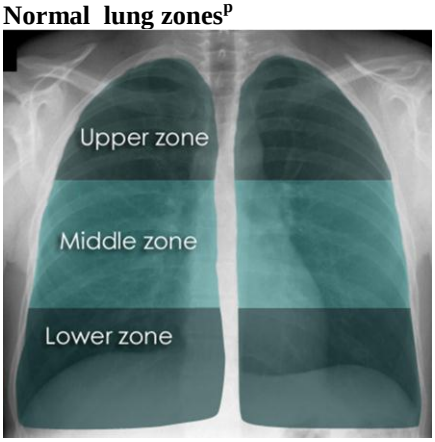
Normal Pulmonary arteries[p]



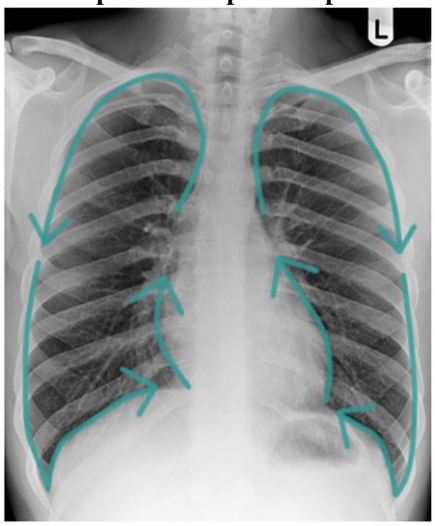
Normal hila[p]



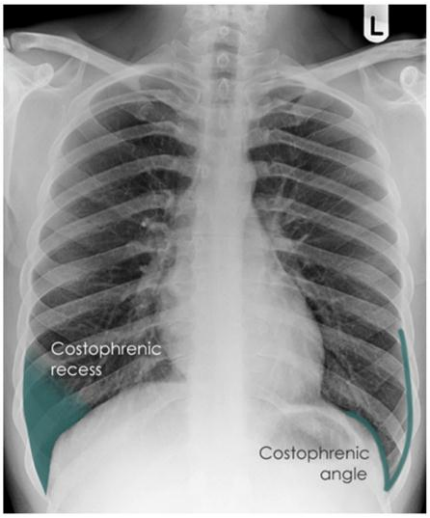
Normal lung zones[p]



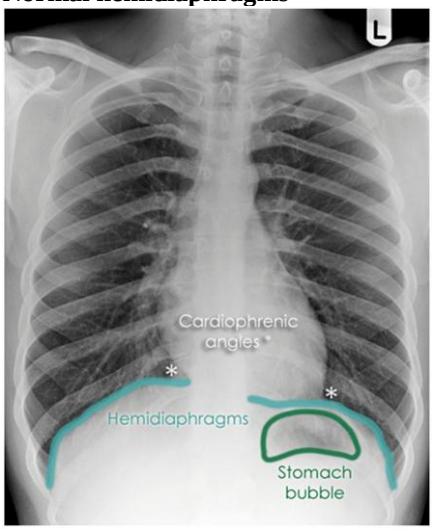
Normal pleura and pleural spaces[p]



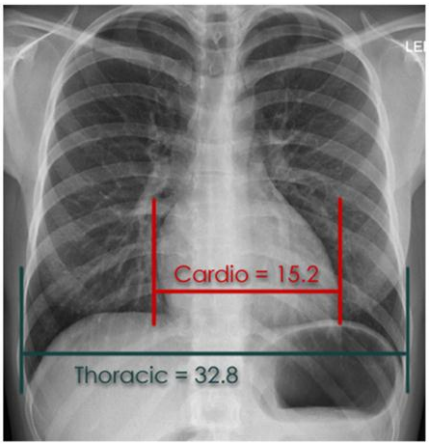
Normal costophrenic angle and recess[p]



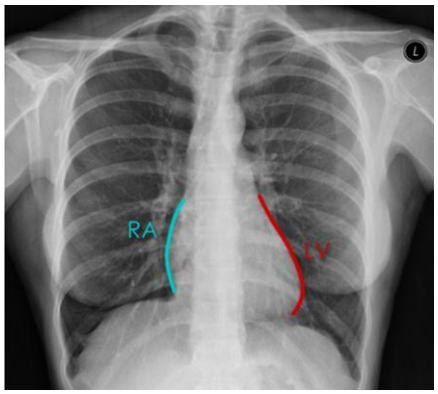
Normal hemidiaphragms[p]



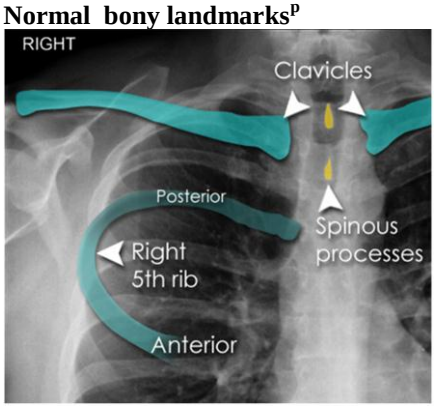
Normal heart size[p]



Normal cardiac contours[p]

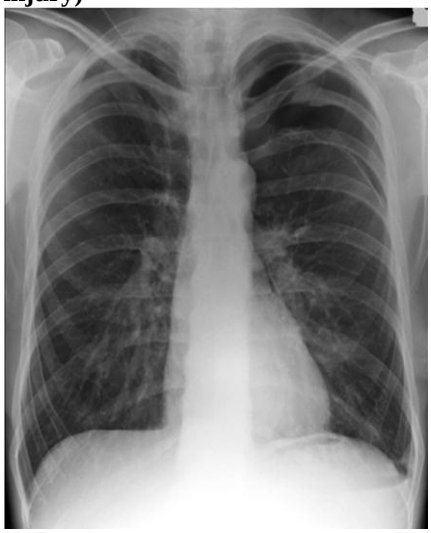


Normal bony landmarks[p]

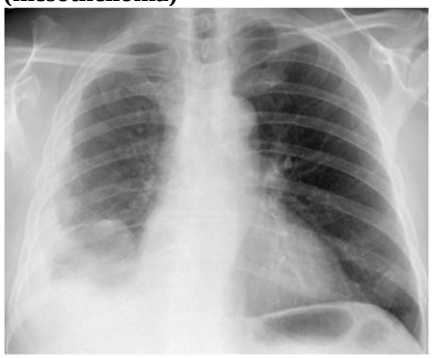


p: Lloyd-Jones G. Chest X-ray tutorials [Internet]. Salisbury (United Kingdom): 2007 [updated 2011; cited 2011 Aug 26]. Available from: http://radiologymasterclass.co.uk/tutorials/tutorials.html

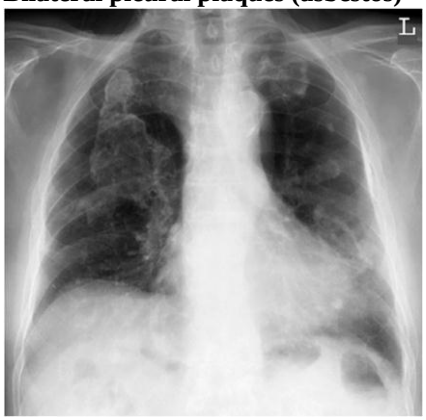
Left pneumothorax (traumatic injury)[p]



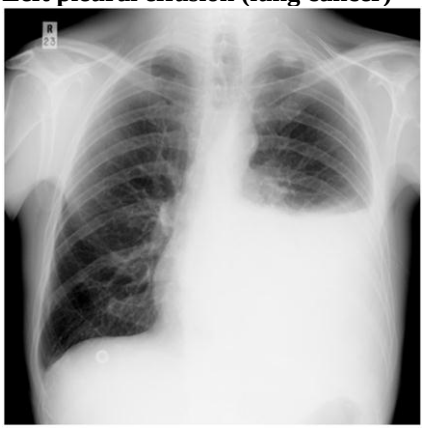
Right pleural thickening (mesothelioma) [p]



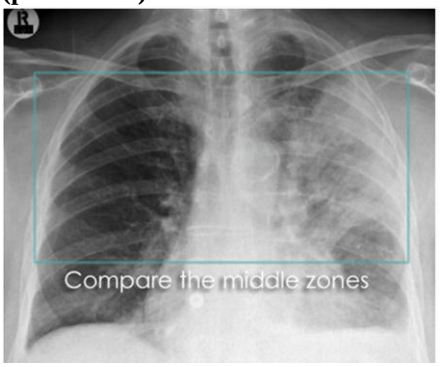
Bilateral pleural plaques (asbestos)[p]



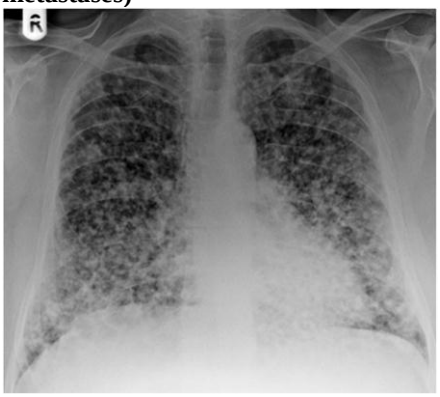
Left pleural effusion (lung cancer)[p]



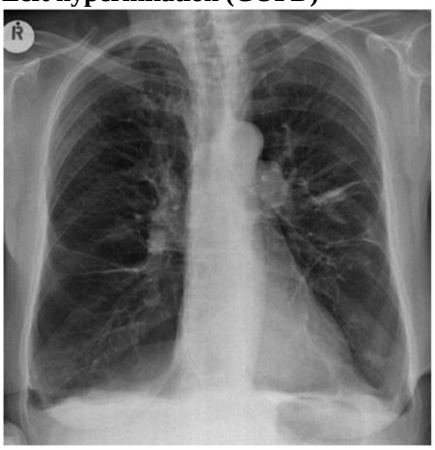
Left middle zone consolidation (pneumonia)[p]



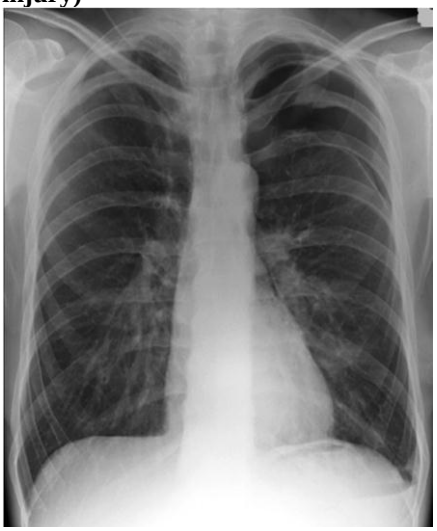
Bilateral lung nodules (pulmonary metastases)[p]



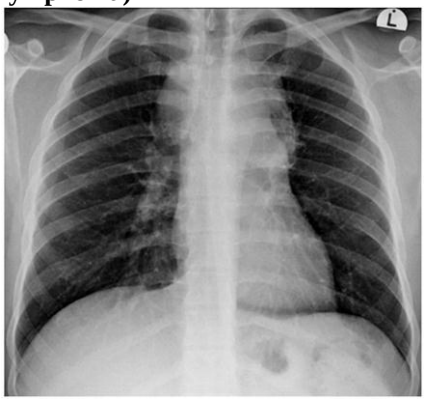
Left hyperinflation (COPD)[p]



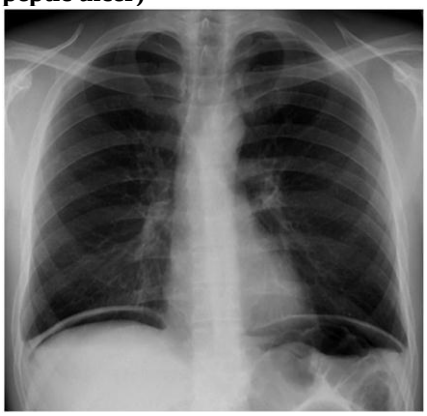
Left pneumothorax (traumatic injury)[p]



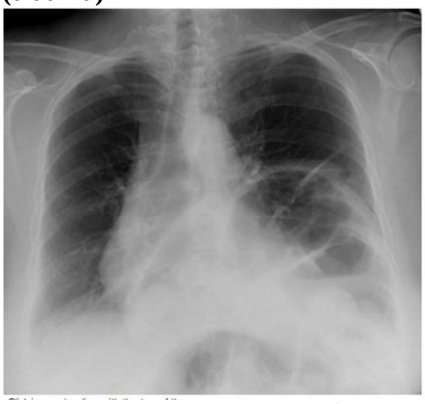
Mediastinal mass (Hodgkin's lymphoma)[p]



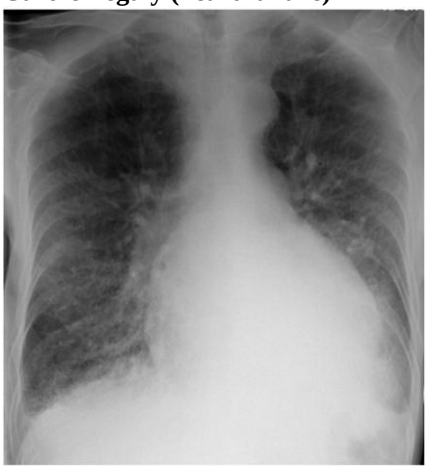
Pneumoperitoneum (ruptured peptic ulcer)[p]



Left diaphragmatic rupture (trauma)[p]



Cardiomegaly (heart failure)[p]



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