A JOURNEY INTO MRCP(UK)

RESPIRATORY SYSTEM

PLATINUM NOTES

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PREFACE

The journey of MRCP(UK) is not just about knowledge, books or post-nominals. It is as much about the aspirations & honour, as about the validation of exemplary medical professionals. It is a story written by blood, sweat, endless hours of sheer hard work, uncountable episodes of nervous breakdown & getting back up again.

Modern times demand modern methods of warfare. The Covid-19 pandemic shifted the perpetual war of human survival from international borders to Hospitals. Medical personnel, especially Doctors, became the new Army. We lost many of our brethren, young & enthusiastic doctors & nurses, with years of promising careers ahead, left unfulfilled. We lost our family & friends too. Although this is a never-ending war, we succeeded in controlling it to much extent.

Now the responsibility of learning, perfecting and practicing the art of medicine lies on your valiant shoulders. You, who've chosen this path to heal and minimize human suffering. You, who have decided to value the pain and diseases of fellow humans above your own. Persevere and dedicate your life and time to it, as if it were your breath. It shall pay you back not only by realizing your material desires but also by self-realization.

Medicine, the most glorious fusion of art & science, is yours to learn, research and progress now. I wish you all the very best in all your future endeavours. May the gods of healing always be by your side.

Director

Crack Medicine

How To Use This Book

JUST READ IT.

Lung: Basic Clinical Sciences

The bronchi divide 23 times.
The initial 16 branches or so are known as the conducting zone and do not take part in gas exchange.
Generation 17-23 contain alveoli and take part in gas exchange.
Gas exchange can occur in the final seven branches of the bronchoalveolar tree.
The Angle of Louis (also known as the Sternal Angle or Angle of Ludwig) corresponds to T4/T5 vertebral bodies, which is the location at which the trachea bifurcates to the mainstem bronchi (carina).
Cartilage disappears from the terminal bronchioles onwards.

Anatomical dead space in the lung

The part of Respiratory tract which is not involved in respiration.
The normal anatomical dead space is approximately 150 ml.
The dead space can be increased in diseases that cause an additional physiological deadspace, where parts of the lung do not take part in gas exchange (eg pneumonia)

Azygos lobe of the lung

Azygos lobe is seen in about 0.5% of routine chest X-rays and is a normal variant.
It is seen as a 'reverse comma sign' behind the medial end of the right clavicle.

Phrenic nerve:

The diaphragm is innervated by the phrenic nerve (C3,4,5).
Causes of phrenic nerve palsy:
Thoracic surgery (invasion by an adjacent tumour)
Infection (it may also be stretched by an aortic aneurysm)
Guillain-Barre Syndrome.

Diagnosis of unilateral paralysis:
Suggested by asymmetric elevation of the affected hemidiaphragm on X-ray,
Confirmed fluoroscopically by observing paradoxical diaphragmatic motion on sniff and cough
(During a forced inspiratory manoeuvre (the 'sniff test), the unaffected hemidiaphragm descends forcefully, increasing intra-abdominal pressure and pushes the paralysed hemidiaphragm cephalad (paradoxical motion)).
In patients with normal lungs, unilateral paralysis is usually asymptomatic and rarely requires treatment.
Fluoroscopy is inaccurate for the diagnosis of bilateral paralysis.

The Transitions of Respiratory Epithelium

The epithelium that lines the majority of the conducting portion of the respiratory tract is Pseudostratified columnar epithelium with cilia and goblet cells.
From trachea to primary bronchus: Pseudostratified.
Secondary bronchus: simple columnar.
Large bronchiole, Small bronchiole & Terminal bronchiole: simple Cuboidal.

Pulmonary surfactant

Surfactant is a mixture of **Phospholipids** (Single best answer if asked to select one), carbohydrates and proteins
Released by type 2 Pneumocytes
The main functioning component in surfactants is Lecithin or DiPalmitoylPhosphatidylCholine(DPPC) which reduce alveolar surface tension. Lecithin makes up more than 75% of the phospholipids covering the air-liquid interface in pulmonary alveoli.
First detectable around 28 weeks.
As alveoli decrease in size, surfactant helps prevent the alveoli from collapsing.
Reduces the muscular force needed to expand the lungs (i.e. decreases the work of breathing) lowers the elastic recoil at low lung volumes and thus helps to prevent the alveoli from collapsing at the end of each expiration.
Because of surfactant, the pressure difference across the pleura required to inflate the lungs is usually no more than about 4 cmH_2O.

The normal pulmonary circulation is characterised by low pressures, low flow rates, high compliance vessels.
Resting pulmonary blood flow in an adult is around 5 L/min.
The V:Q(Ventilation:Perfusion) ratio is higher in the apical than the basal segments.
While a single small airway provides more resistance than a single large airway, resistance to airflow depends on the number of parallel pathways present. For this reason, the large and particularly the medium-sized airways provide greater resistance to flow than do the more numerous small airways.

Control of respiration

medullary respiratory centre
apneustic centre (lower pons)
pneumotaxic centre (upper pons)
central Chemoreceptors: raised [H+] in ECF stimulates respiration
peripheral Chemoreceptors: carotid + aortic bodies, respond to raised pCO2 & [H+], lesser extent low pO_2
pulmonary receptors
stretch receptors: lung distension causes slowing of respiratory rate (Hering-Bruer reflex)
irritant receptor: leading to bronchoconstriction
juxtacapillary receptors, stimulated by stretching of the microvasculature

Peripheral chemoreceptors are known to transmit information via the glossopharyngeal and vagus nerves regarding changes of carbon dioxide in the blood. Which will most likely receive information regarding these changes?
Solitary nucleus (in the medulla oblongata)

Bohr Effect

Increasing acidity (or pCO2) means O2 binds less to Hb.

Haldane effect

Increasing pO2 means CO2 binds less well to Hb

Chloride shift

CO_2 diffuses into RBCs
$CO_2 + H_2O$ (carbonic anhydrase) → $HCO3^- + H^+$
H^+ combines with Hb
$HCO3^-$ diffuses out of the cell, Cl^- replaces it
Therefore, during exercise, there is increased formation of CO_2 in the peripheral tissues that need to be transported to the lungs. Since exercise increases, CO_2 production which will enter the venous blood the values of HHb, $HbCO_2$, RBC Cl^- content and plasma $HCO3^-$ will all increase.

Lung compliance is defined as the change in lung volume per unit change in airway pressure.

Oxygen Dissociation Curve

Oxygen Dissociation Curve describes the relationship between the percentage of saturated haemoglobin and partial pressure of oxygen in the blood.
It is not affected by Hb concentration but affected by its quality (HbF, MetHb).

Shifts to right = ↓ affinity/ saturation of Hb towards O_2 i.e. Enhanced O_2 delivery to tissues
Shifts to left = ↑ affinity/ saturation of Hb with O_2 i.e. ↓oxygen delivery to tissues

Shifts to Right = Raised oxygen delivery	Shifts to Left = Lower oxygen delivery
Raised [H+] (acidity) **Raised PCO2** **Raised 2,3-DPG** **Raised temperature**	**Low [H+] (alkali)** **Low PCO2** **Low 2,3-DPG** **Low temperature** **HbF, methaemoglobin, carboxyhaemoglobin**

Carbon monoxide (CO) has a much higher affinity for haemoglobin than oxygen does. In CO poisoning, oxygen cannot be transported and released to body tissues thus resulting in hypoxia.
With Fetal haemoglobin, the shift facilitates diffusion of oxygen across the placenta.
The oxygen dissociation curve for myoglobin exists even further to the left.

A fall in the partial pressure of oxygen (pO2) in the blood leads to vasoconstriction of the pulmonary arteries. This allows blood to be delivered to better-aerated areas of the lung and improves the efficiency of gaseous exchange.

The P_{50} is the oxygen tension at which haemoglobin is 50% saturated.
The normal P_{50} is 26.7 mm Hg.

Pulmonary function tests

Tidal Volume (TV) : 500ml in ♂s, 350ml in ♀s

(Volume inspired or expired with each breath at rest)

Inspiratory Reserve Volume (IRV) = 2-3 L

Maximum volume of air that can be inspired after normal tidal inspiration

Expiratory Reserve Volume (ERV) = 750ml

Maximum volume of air that can be expired after a normal tidal expiration

Residual volume (RV) = 1.2L

The volume of air remaining after maximal expiration

(↑ with age, ↑Increased in obstructive lung disease due to air trapping)

RV = FRC – ERV (Functional Residual Capacity - Expiratory Reserve Volume)

Inspiratory capacity = TV + IRV

Vital Capacity (VC) = 5L

VC = IC + ERV

Total lung capacity (TLC) is the sum of the vital capacity + residual volume

Minute ventilation : Tidal volume (volume of air moved in normal breathing) multiplied by the respiratory rate.

Forced vital capacity (FVC)

Respiratory muscle function is best monitored by frequent assessment of the forced vital Capacity (FVC).
Diseases such as GBS& Myasthenia Gravis require frequent FVC Measurement to asses Respiratory muscle functioning.
ITU admission is recommended when FVC is <20 mL/kg.
Intubation is recommended in most cases when FVC is <15 mL/kg.

“All our dreams can come true, if we have the courage to pursue them.” – Walt Disney

Obstructive vs. Restrictive lung diseases

	Obstructive	Restrictive
Spirometry	**FEV1/FVC < 80%** **(FEV1/FVC <0.7)**	**FEV1/FVC > 80%** **(FEV1/FVC >0.7)**
	FEV1 - significantly reduced (<80% predicted)	**FEV1** - reduced (<80% predicted)
	FVC - reduced or normal FEV1% (FEV1/FVC) - reduced	**FVC** - significantly reduced (<80% predicted) FEV1% (FEV1/FVC) - normal (>0.7) or increased
Examples	COPD Asthma chronic bronchitis emphysema Bronchiectasis	Intrapulmonary idiopathic pulmonary fibrosis extrinsic allergic alveolitis coal worker's pneumoconiosis/progressive massive fibrosis silicosis sarcoidosis histiocytosis drug-induced fibrosis: amiodarone,bleomycin, methotrexate asbestosis Extrapulmonary neuromuscular disease: polio, myastheniagravis obesity scoliosis

Explanation of high FEV-1/FVC ratio in lung fibrosis:

In lung fibrosis both (FEV-1) and (FVC) are reduced below predicted values, but because of high elastic recoil most forced expiratory volume will be expelled in the first second - this leads to a relatively high FEV-1/FVC ratio.

Pulmonary function in obesity

Obesity could show a significant restrictive defect.
It is associated with hypoventilation and thus can cause hypercapnia.
would not affect the transfer coefficient (KCO) (ie after correcting for alveolar volumes).
the gas exchange after correcting for the alveolar volume would in fact be high.
FVC falls when measured in the supine position due to increased abdominal fat, leading to a functional reduction in FVC.

Peak expiratory flow rate (PEFR)

PEFR readings are an objective measure of airway obstruction and are advised for regular assessment of lung function.
Serial PEFR readings Diary is maintained for diagnosing Occupational Asthma.

A mid-expiratory flow rate (between 25% and 75% of the expired vital capacity) is a good measure of airways obstruction.
It is more sensitive than the forced expiratory volume in 1 second (FEV-1) for identifying early airway obstruction. It is effort-independent.

Transfer factor

DLCO or TLCO (diffusing capacity or transfer factor of the lung for Carbon Monoxide.

Raised: asthma, haemorrhage, left-to-right shunts, polycythaemia
Low: everything else

The transfer factor describes the rate at which a gas will diffuse from alveoli into the blood, measured using CO. The diffusion capacity of CO depends on the thickness of the alveolar wall.
Results may be given as the total gas transfer (TLCO) or Corrected for lung volume (transfer coefficient, KCO).
Where alveolar haemorrhage occurs, the TLCO tends to increase due to the enhanced uptake of CO by intra-alveolar haemoglobin.

Causes of a raised TLCO	Causes of lowered TLCO
• Asthma • **pulmonary haemorrhage** (Wegener's, Goodpasture's) • left-to-right cardiac shunts • **polycythaemia** • hyperkinetic states • early left heart failure • male gender, exercise	• pulmonary fibrosis • pneumonia • pulmonary emboli • pulmonary oedema • emphysema • anaemia • low cardiac output

Asthma is most likely associated with normal TLCO, but sometimes increased during an attack, and the cause of this change is not known.

Pulmonary AV malformations cause right-to-left shunts, so reducing TLCO values and provoking hypoxaemia (↓ Pao2), with a normal lung volume (eg FEV1 & FVC).

Transfer coefficient (KCO)

It is useful to understand the relationship between TLCO and transfer co-efficient of carbon monoxide (KCO), to know why they are affected differently in different diseases
KCO is a measure of the efficiency of gas exchange in the bloodstream.
It is reduced if the lungs are damaged and increased if there is additional blood in the lungs to remove carbon monoxide.
TLCO = KCO x Alveolar volume (Va)
The transfer coefficient (KCO) represents the uptake of carbon monoxide per litre of effective alveolar volume (va):
The KCO tends to be normal after lung resection when both TLCO and Va are reduced to roughly the same degree

Causes of an increased KCO
usually as results from an increase in red blood cells in the lungs due to greater blood flow, haemorrhage, or polycythaemia.
KCO also tends to increase with age.

Causes of an increased KCO with a normal or reduced TLCO

(Low TLCO but normal/high KCO (ie the same cardiac output is going through a smaller alveolar volume) is characteristic of extra-thoracic restriction:
pneumonectomy/lobectomy
scoliosis/kyphosis
neuromuscular weakness
ankylosis of costovertebral joints e.g. ankylosing spondylitis
Severe thoracic skin thickening,
pleural involvement

In intrapulmonary restriction, both (TLCO & KCO) usually decreased.

Causes/Diagnosis of Pulled/Pushed Trachea

Trachea pulled toward the white-out	**Trachea central**	**Trachea pushed away from the white-out**
Pneumonectomy	Consolidation	**Pleural effusion**
Complete lung collapse (Atelectasis) e.g.	Pulmonary oedema	**Diaphragmatic hernia**
endobronchial intubation	(usually bilateral)	**Large thoracic mass**
Pulmonary hypoplasia	**Mesothelioma**	

Alveolar-arterial (A-a) oxygen gradient

is a measure of the difference between the alveolar concentration (**A**) of oxygen and the arterial (**a**) concentration of oxygen.
It is used in diagnosing the source of hypoxemia. For example,
in high altitude, the arterial oxygen PaO_2 is low but only because the alveolar oxygen (PAO_2) is also low.
in states of **ventilation-perfusion mismatches,** such as pulmonary embolism or right-to-left shunt, oxygen is not effectively transferred from the alveoli to the blood which results in an elevated A-a gradient
the normal approximately 0.5-2.0 kPa (< 15 mmHg).
Causes of widening A-a gradient
Ventilation/perfusion (V/Q) mismatch,
diffusion abnormalities and
right-to-left shunting
Hypoventilation causes hypoxaemia with a normal A-a gradient.
This means that changes in the alveolar-arterial gradient occur with ventilatory disorders such as pneumonia and disorders of the vasculature such as a pulmonary embolus.
The alveolar-arterial (a-a) gradient is calculated using the following equation (where PAO2 = alveolar oxygen and the Pao2 and PaCO2 are the arterial O2 and CO2 levels respectively):
A–a gradient = **P**A**O**2 **–** PaO2
A-a gradient is approximated: **$(150 - 5/4(pCO_2)) - Pa_{O2}$**

Flow volume loop ↓ Assessing compression of the upper airway

Flow volume loop is the investigation of choice for upper airway compression.
A normal flow-volume loop is often described as a 'triangle on top of a semi-circle'

Cough

An acute cough is defined as one lasting less than 3 weeks
Chronic cough is defined as one lasting more than 8 weeks.
There is a grey area between 3 to 8 weeks and this includes post-viral coughs.
GORD is also a common cause for cough (mostly Nocturnal).
Proton pump inhibitors and alginates should be taken for a minimum of 3 months.

Respiratory failure

Type 1 → hypoxaemia (P_aO_2 < 8.0 kPa) without hypercapnoea (P_aCO_2 normal or decreased (<6.0 kPa)

Causes:

Low ambient oxygen (e.g. at high altitude)
Ventilation-perfusion mismatch (parts of the lung receive oxygen but not enough blood to absorb it, e.g. pulmonary embolism)
Alveolar hypoventilation (decreased minute volume due to reduced respiratory muscle activity,
e.g. in acute neuromuscular disease); this form can also cause type 2 respiratory failure if severe
Diffusion problem (oxygen cannot enter the capillaries due to parenchymal disease, e.g. in pneumonia or ARDS)
Shunt (oxygenated blood mixes with non-oxygenated blood from the venous system, e.g. right-to-left shunt)

Type 2 → Hypoxemia (PaO2 <8kPa) with Hypercapnia (PaCO2 >6.0kPa).

Causes:

Increased airways resistance (COPD, asthma, suffocation)
The commonest cause is chronic obstructive airway disease,
Reduced breathing effort ↓ hypoventilation:
acutely due to drug overdose and brain stem lesion
chronically due to gross obesity, kyphoscoliosis (and similar musculoskeletal disorders)
Hypoventilation, where inadequate alveolar ventilation results in low alveolar PO_2, is the only cause of hypoxia that inevitably causes raised $PaCO_2$.
A decrease in the area of the lung available for gas exchange (such as in chronic bronchitis)
Neuromuscular problems (**respiratory muscle weakness**) (Guillain-Barre syndrome, motor neuron disease)
Deformed (kyphoscoliosis), rigid (ankylosing spondylitis), or flail chest.

Bronchial Asthma

Be ready to be tested vastly on the various treatment guidelines, especially provided by BTS, updated regularly, for Asthma. One of the most extensively tested topics of MRCP(UK) Exams.

Basics

There are two phases, Immediate & Late Phase Reaction.
Inhalation of allergens by individuals with atopic asthma initiates Immediate response:

Type 1 hypersensitivity: Immunomodulators involved:	
Mast cells	**prostaglandin D2**
Histamine	**Leukotriene C4 (LTC4) & D4**

The result is an immediate bronchoconstriction reaction. Usually subsides within two hours. Reversible with bronchodilators.

Late phase:
Type IV hypersensitivity response.
Immunomodulators involved:

- Eosinophil cationic protein (ECP)
- Major basic protein (MBP)
- Platelet activating factor (PAF)
- T_{H2} lymphocytes

Results in bronchoconstriction, airways inflammation, hyper-responsiveness and oedema. Less susceptible to bronchodilators.
This typically occurs three to 12 hours after the immediate response. That's why you always get patients with an acute attack complaining of Detterioration in symptoms after you've already treated them acutely.

Pathogenesis of Asthma:

Asthma occurs due to a combination of airway hyper-responsiveness, airflow limitation and airway inflammation. The alveolar functional structure is preserved in asthma.

Classification of Asthma severity

Mild, intermittent asthma - symptoms occur less than weekly, with normal or near-normal lung function between episodes
Mild persistent asthma - symptoms occur more than weekly but less than daily, with normal or near-normal lung function between episodes
Moderate persistent asthma - symptoms occur daily, with mild to moderate variable airflow limitation
Severe persistent asthma - symptoms occur daily and interfere with normal activities; there is frequent nocturnal waking and moderate to severe variable airflow limitation
Severe asthma - severe distressing symptoms prevent sleep; severe airflow limitation responds poorly to inhaled bronchodilators and can be life-threatening.

Near-fatal asthma

The British Thoracic Society defines near-fatal asthma as an attack with raised $PaCO_2$ and/or requiring mechanical ventilation with raised inflation pressures.
A raised $PaCO_2$ is an important sign that intubation may be required if the patient is not responding to maximum medical management.

Diagnosis of asthma in adults

Asthma – intermediate probability – do spirometry first-line
Asthma diagnosis – if the high probability of asthma – start treatment.

If the FEV1/FVC < 0.7 then a trial of treatment is appropriate. Otherwise further investigations should be performed.
If a patient has typical symptoms of asthma, a trial of treatment is recommended.
we should classify patients as having either a high, intermediate or low probability of asthma based on the presence or absence of certain symptoms.
For adults, it is recommended that they have a **clinical assessment including spirometry** (or
Peak Expiratory Flow measurement if spirometry is not available).

The BTS produced a list of features, which are helpful when deciding this:

Features that make a diagnosis of asthma more likely	Features that make a diagnosis of asthma less likely
More than one of the following symptoms: wheeze, breathlessness, chest tightness and cough, particularly if: **symptoms worse at night and in the early morning** **symptoms in response to exercise, allergen exposure and cold air** **symptoms after taking aspirin or beta-blockers** **History of atopic disorder** **Family history of asthma and/or atopic disorder** **Widespread wheeze heard on auscultation of the chest** **Otherwise unexplained low FEV1 or PEF (historical or serial readings)** **Otherwise unexplained peripheral blood eosinophilia**	**Prominent dizziness, light-headedness, peripheral tingling** **Chronic productive cough in the absence of wheeze or breathlessness** **Repeatedly normal physical examination of chest when symptomatic** **Voice disturbance Symptoms with colds only** **Significant smoking history (ie > 20 pack-years)** **Cardiac disease** **Normal PEF or spirometry when symptomatic**

Spirometry is the preferred initial test
Treatment should be partly guided by the FEV_1/FVC ratio:
a ratio of < 0.7 is suggestive of asthma ↓ trial of treatment
a ratio of < 0.7 ↓ further investigation/consider referral

Spirometer vs peak flow meter

A spirometer measures the total volume of air that can be exhaled or inhaled. It can also measure the rate at which a certain volume of air is expelled from the lungs.
Spirometry is the most accurate breathing test for asthma.
spirometry may be normal in asymptomatic patients so it may be necessary to repeat spirometry or peak flow readings on a number of occasions in patients where the diagnosis is not clear.
In adults with obstructive spirometry, an improvement in FEV1 of 12% or more in response to either β2 agonists or corticosteroid treatment trials, together with an increase in the volume of 200 ml or more, is regarded as a positive test. (British

guideline on the management of asthma 2016) (this fact was tested in MRCP part 1 Sep 2017)
The peak flow meter, on the other hand, only measures the rate at which air is forced out of the
lungs. This is known as the peak expiratory flow.
It is now advised to interpret peak flow variability with caution due to the poor sensitivity of the test
diurnal variation % = [(Highest-Lowest PEFR) / Highest PEFR] x 100
assessment should be made over 2 weeks
greater than 20% diurnal variation is considered significant
A variation of > 25% on a peak flow chart (pre-and post-bronchodilator) would support a diagnosis of asthma.

Management of asthma

Stepwise management of asthma in adults
The British Thoracic Society recommend adding a long-acting B2 agonist if there is an inadequate response to the addition of inhaled steroid.
The inhaled steroid dose should be increased if there is an inadequate response to the long-acting B2 agonist.

The management of stable asthma is now well established with a step-wise approach: (Table on next page)

"I've missed more than 9,000 shots in my career. I've lost almost 300 games. 26 times I've been trusted to take the game winning shot and missed. I've failed over and over and over again in my life and that is why I succeed." – Michael Jordan

Step	Management - As Per BTS Guidelines*
Step 1	**Inhaled short-acting B2 agonist as required**
Step 2	**Add inhaled steroid at 200-800 mcg/day* 400 mcg is an appropriate starting dose for many patients. Start at a dose of inhaled steroid appropriate to the severity of the disease**
Step 3	**1. Add inhaled long-acting B2 agonist (LABA)** **2. Assess control of asthma:** • **good response to LABA - continue LABA** • **benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose)** • **no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline**
Step 4	**Consider trials of:** • **increasing inhaled steroid up to 2000 mcg/day (beclometasone dipropionate or equivalent)** • **addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet** • **the BTS say there is little evidence to separate the different options available. They do however suggest that leukotriene receptor antagonists are least likely to cause side effects. Monitoring of serum concentrations may also be required for theophyllines**
Step 5	**Use daily steroid tablets in the lowest dose providing adequate control. Consider other treatments to minimize the use of steroid tablets Maintain high dose inhaled steroid at 2000 mcg/day* Refer patient for specialist care.**

B-blockers, including eye drops, are contraindicated in patients with asthma

Steroid inhalation

Inhaled steroids (step 2) should be considered for patients who are:
Have had exacerbations of asthma in the last 2 years
Using inhaled B2-agonists three times a week or more
Symptomatic three times a week or more, or waking one night a week
Fluticasone is more lipophilic and has a longer duration of action than Beclometasone(This is an example of Basic Sciences Mcq)

Long-acting B2-agonists

Acts as bronchodilators but also inhibit mediator release from mast cells.
A recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose.
Salmeterol → may cause paradoxical bronchospasm
Salmeterol has been reported to produce an acute exacerbation of asthma, possibly through an acute hypersensitivity reaction.
The duration of action of salmeterol is around 12 hours and has gone completely by 36 hours.

Leukotriene receptor antagonists

e.g. Montelukast, zafirlukast
Zileuton → blocks leukotriene synthesis by inhibiting 5-lipoxygenase,
have both anti-inflammatory and bronchodilatory properties
should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
particularly useful in aspirin-induced asthma
associated with the development of Churg-Strauss syndrome

Asthma drugs: leukotriene inhibitor action:
Zafirlukast → Antagonist of lipoxygenase
Zilueton → Inhibitor of LT receptor

NON-PHARMACOLOGICAL MANAGEMENT (British guideline on the management of asthma 2016)

Stop smoking.
Weight-loss interventions (including dietary and exercise-based programmes) can be considered for overweight and obese with asthma to improve asthma control.
A Breathing exercise programme (including physiotherapist-taught methods) can be offered to people with asthma as an adjuvant to pharmacological treatment to improvequality of life and reduce symptoms.

Teaching diaphragmatic breathing, (as opposed to thoracic breathing which is practised by many asthmatics), may significantly impact symptoms. Reducing the likelihood of future attendance in the Emergency department.

Acute severe asthma

Patients with acute severe asthma are stratified into moderate, severe or life-threatening.

Moderate	Severe	Life-threatening
• PEFR 50-75% best or predicted • Speech normal • RR < 25 / min • Pulse < 110 bpm	• PEFR 33 - 50% best or predicted • Can't complete sentences • RR > 25/min • Pulse > 110 bpm	• PEFR < 33% best or predicted • Oxygen saturation < 92% • PaO_2 <8 kPa • Normal $PaCO_2$ (4.6-6.0 kPa) • Silent chest, cyanosis or feeble (Poor) respiratory effort • Bradycardia, dysrhythmia or hypotension • Exhaustion, confusion or coma

Note that a patient having any one of the life-threatening features should be treated as having a life-threatening attack.
A pH less than 7.35 likely represents carbon dioxide retention in a tiring patient and is an
ominous sign in acute asthma.
A normal or elevated pCO2 in an asthmatic indicates failing respiratory effort, and although oxygen saturation maybe not be severely depressed, the patient is in danger of decompensation and - aside from high flow oxygen, nebulised salbutamol and ipratropium, and steroids - it would be prudent to inform the ICU. Therefore, even though it is in the normal range, this is the most worrying result for life-threatening.
A normal PaCO2 in an asthmatic is a warning of impending respiratory failure as the patient becomes too tired to ventilate adequately.
If PCO2 is just outside the upper limit of normal, the patient will require urgent admission
to the Intensive Therapy Unit.

Lung function in an acute asthma attack
The classic abnormalities are **reduced** (FEV-1) & (FVC) & FEV-1/FVC ratio.
Because of gas trapping there is an **increase in residual volume** and an increase in total lung capacity, but the ratio of residual volume (RV) to total lung capacity (TLC) is increased (TLC = vital capacity [VC] + RV).
Airway conductance (the reciprocal of airway resistance) is decreased in acute asthma.
The gas transfer would be difficult to measure in acute asthma but can be elevated in stable asthma where there might be chronic hyperinflation giving rise to a greater surface area for blood/gas interfacing.
asthma is most likely associated with an obstructive spirometry and normal Tlco (transfer factor for carbon monoxide)

Management

In acute severe asthma, β2-agonists should be administered as soon as possible, preferably nebulised driven with high flow oxygen.
salbutamol administration can rapidly worsen the V/Q mismatch which is the cause of hypoxia in asthma. They can therefore cause reduction in arterial oxygen tension unless supplemental oxygen is given

Physiologic changes following a nebuliser in acute asthma :

initially , poor ventilation → hypoperfusion to certain lung areas .
Following a nebuliser and subsequent improved ventilation, there is then a ventilation/perfusion mismatch which may lead to **a transient drop in oxygen saturation**.

Nebulised ipratropium bromide should be added for patients with acute severe or life threatening asthma, or those with a poor initial response. It's addition produces significantly greater bronchodilation than a β2-agonist alone.

Oxygen

Targeted oxygen in asthma => SpO2 level of 94–98%.
Patients with saturations less than 92% on air should have an ABG to exclude hypercapnia. However, starting treatment should not be delayed to do the ABG.
Initially high-flow oxygen is used, and then weaned to maintain adequate saturations.
Unless you suspect COPD there is no need to be cautious with oxygen therapy.

Steroids:

steroids reduce mortality, relapses, subsequent hospital admission and requirement for β2-agonists1.
The earlier they are given in the attack, the better the outcome.
A dose of 40-50 mg should be given once oxygen and nebuliser therapy has been established. This should be continued for five days, and can then be stopped abruptly.

Nice 2013 People aged 5 years or older presenting to a healthcare professional with a severe or life-threatening acute exacerbation of asthma receive oral **or** intravenous steroids **within 1 hour** of presentation.

Magnesium sulphate recommended as next step for patients who are not responding (2g IV over 20 mins) .
Mechanism: not fully understood, but it is thought that low magnesium levels in bronchial smooth muscle favour bronchoconstriction.
reduce rates of admission to intensive therapy units
little evidence to support use of IV aminophylline (although still mentioned in management plans)
if no response consider IV salbutamol
Intensive care is indicated for patients with severe acute or life threatening asthma who are failing to respond to therapy.
Strongest indicator of a need for intubation and ventilation? PH 7.31

Asthma in pregnancy

In general, the medicines used for asthma are safe during pregnancy.
The British Thoracic Society (BTS) guidelines make it clear that short-acting /long-acting beta 2-agonists, inhaled and oral corticosteroids should all be used as normal during pregnancy.
The BNF advises that 'inhaled drugs, theophylline and prednisolone can be taken as normal during pregnancy and breast-feeding'.
Asthma during labour:
Women receiving steroid tablets at a dose exceeding prednisolone 7.5 mg per day for more than two weeks prior to delivery should receive parenteral hydrocortisone 100 mg 6–8 hourly during labour.:
prostaglandin F2α ↓ inducing bronchoconstriction

Pulsus paradoxus:

The right heart responds directly to changes in intrathoracic pressure, while the filling of the left heart depends on the pulmonary vascular volume.
At high respiratory rates, with severe air flow limitation (for example, acute asthma) there is an increased and sudden negative intrathoracic pressure on inspiration and this will enhance the normal fall in blood pressure.

Exercise-induced asthma:

The most likely diagnosis would be with **spirometry before and after exercise**, (NOT before and after administration of bronchodilators) where a typical obstructive pattern may be displayed following exercise.

Cough-variant asthma

airway inflammation but minimal bronchoconstriction.
Response to steroids is helpful when making the diagnosis of asthma.
Bronchodilators often have little effect.
No typical asthma history; the cough is typically worse in the mornings, in the cold air and after exercise.
Treatment is with high-dose inhaled steroids for at least 2 months, or a short course of oral steroids.

Difficult asthma ↓ persisting asthma, despite prescription of high-dose asthma therapy.
Always consider poor adherence to maintenance therapy.
Consider monitoring induced sputum eosinophil counts to guide steroid treatment.
Dysfunctional breathing should be considered as part of a difficult asthma assessment.
allergen testing to moulds should be performed.
Commonly associated with co-existent psychological

Chronic Obstructive Pulmonary Disease (COPD)

COPD is a Chronic Respiratory condition characterised by Partially Reversible Airflow Obstruction. Similar to Asthma in only the amount of questions asked by RCP.

Pathophysiology

In **emphysema**, which is a subtype of COPD, the final outcome of the inflammatory responses is **elastin breakdown** and subsequent loss of alveolar integrity.
In **chronic bronchitis**, another phenotype of COPD, these inflammatory changes lead to ciliary dysfunction and **increased goblet cell size and number**, which leads to the excessive mucus secretion. These changes are responsible for decreased airflow, hypersecretion, and chronic cough.
In both conditions, changes are progressive and usually not reversible.
Hypoxic induced pulmonary vasoconstriction: Mechanism most likely responsible for the increased mean arterial pulmonary pressure in COPD.

Causes

Smoking
Alpha-1 antitrypsin deficiency
patients from the developing world present with a COPD-like history from using open fires in their homes for cooking or heating (accounting for up to 1 million deaths worldwide as a result of COPD without smoking history)
Other causes (particularly **occupational exposures**, such as harmful dust and chemicals)
cadmium (used in smelting) (recognised cause of emphysema specifically)
coal, cotton, cement, grain

Types

Emphysema and chronic Bronchitis are the two main subtypes of COPD
Emphysema refers to the damged adjacent alveolar walls, creating larger air spaces with reduced surface area. Eventually being capable of less elastic recoil, leading to air-trapping during expiration!
Chronic bronchitis is defined as chronic cough and sputum production for at least three months of two consecutive years in the absence of other disease which could explain these symptoms.

Emphysema

Emphysema is an irreversible degenerative condition;
Characterised by focal destruction limited to the air spaces distal to terminal bronchioles.
Although airflow limitation is virtually irreversible, the small inflammatory component can respond to high-dose inhaled corticosteroids.
Hyper-expanded lung fields on CXR, reduced transfer factor and an FEV1/FVC < 70 %.
MacLeod syndrome is unilateral emphysema following childhood bronchiolitis.
CO transfer factor is reduced.

↑ Residual Volume (RV)
↑ Total Lung Capacity (TLC)
Giving typical obstructive pathology
Flattening of diaphragms: ↑ lung volumes
Enlarged left pulmonary artery
Attenuation of vessels
Diffuse hyperlucency

Types of emphysema

Type	Centriacinar (centrilobula)	Panacinar
Prevalence	the most common type	**Less common**
Destruction	focal destruction mainly localized to the proximal respiratory bronchioles	**destroys the entire alveolus uniformly**
Location	upper lung zones.	**the lower half of the lungs.**
causes	**smoking & dust**	**alpha 1-antitrypsin (AAT) deficiency**

Symptoms

Shortness of breath
Chronic cough
Chronic Sputum Production

Risk factors

Host factors
Tobacco
Occupational
Indoor/outdoor pollution
Spirometry is required to establish the diagnosis.
NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are smokers or ex-smokers and have symptoms such as exertional breathlessness, chronic cough or regular sputum production.
The following investigations are recommended in patients with suspected COPD:
Post-bronchodilator spirometry to demonstrate airflow obstruction: FEV1/FVC ratio less than 70%
Chest x-ray: hyperinflation, bullae, flat hemidiaphragm. Also important to exclude lung cancer
Full blood count: exclude secondary polycythaemia
Body mass index (BMI) calculation
Measuring peak expiratory flow is of limited value in COPD, as it may underestimate the degree of airflow obstruction.
A methacholine challenge is useful in differentiating between asthma and chronic obstructive pulmonary disease (COPD).
methacholine utilizes the M3 receptor for bronchoconstriction.
In long-standing COPD, the bicarbonate is likely to be normal or raised if the patient has chronic hypercapnia. (a low pH, low pO_2, high pCO_2 and a high HCO_3)
Peripheral oedema may be present as a dependent oedema, as patients with COPD may have limited mobility due to dyspnoea, and therefore does not necessarily indicate heart failure.

The severity of COPD is categorised using the FEV1*: GOLD Staging

Post-bronchodilator FEV1/FVC	FEV1 (of predicted)	Severity
< 0.7	> 80%	Stage 1 - Mild**
< 0.7	50-79%	Stage 2 - Moderate
< 0.7	30-49%	Stage 3 - Severe
< 0.7	< 30%	Stage 4 - Very severe

Acute exacerbation

The most common bacterial organisms that cause infective exacerbations of COPD are:
Haemophilus influenzae (most common cause)
The patient should be treated with a course of amoxicillin or a tetracycline together with prednisolone.
Streptococcus pneumoniae
Moraxella catarrhalis
If the patient had pneumonia then *Streptococcus pneumoniae* would be the most likely causative organism. But if the chest x-ray shows no evidence of consolidation this will make a diagnosis of pneumonia unlikely.
Respiratory viruses account for around 30% of exacerbations, with the human rhinovirus being the most important pathogen.
COPD: management of acute exacerbations: NICE guidelines from 2010 recommend the following:
increase the frequency of bronchodilator use and consider giving via a nebuliser
Give prednisolone 30 mg daily for 7-14 days. Prolonged courses offer no additional benefit
It is common practice for all patients with an exacerbation of COPD to receive antibiotics. NICE do not support this approach. They recommend giving oral antibiotics 'if sputum is purulent or there are clinical signs of pneumonia'

If pt is not improving after pharmacological management, consider NIV.

COPD: stable management

COPD - the reason for using inhaled corticosteroids - reduced exacerbations
COPD - still breathless despite using inhalers as required? • FEV1 > 50%: LABA or LAMA • FEV1 < 50%: LABA + ICS or LAMA COPD - LTOT if 2 measurements of pO2 < 7.3 kPa
NICE guidance (2021)
smoking cessation advice
annual influenza vaccination
one-off pneumococcal vaccination
Bronchodilator therapy
a short-acting beta2-agonist (SABA) or short-acting muscarinic antagonist (SAMA) is a first-line treatment
for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1
FEV1 > 50%
long-acting beta2-agonist (LABA), for example, salmeterol, or:
long-acting muscarinic antagonist (LAMA), for example, tiotropium

FEV1 < 50%
LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
LAMA

For patients with persistent exacerbations or breathlessness
if taking a LABA then switch to a LABA + ICS combination inhaler
otherwise, give a LAMA and a LABA + ICS combination inhaler

Oral theophylline
NICE only recommends theophylline after trials of short and long-acting bronchodilators or to people who cannot use inhaled therapy
the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed. **Usually Theophylline is never the answer of any COPD question, unless being asked what not to be given!**
Mucolytics
should be 'considered in patients with a chronic productive cough and continued if symptoms improve
Cor pulmonale
features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
use a loop diuretic for oedema, consider long-term oxygen therapy
ACE-inhibitors, calcium channel blockers and alpha-blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD

smoking cessation - the single most important intervention in patients who are still smoking
long term oxygen therapy in patients who fit criteria
LTOT should be offered to patients with a pO2 of < 7.3 kPa
(or) those with a pO2 of 7.3 - 8 kPa and one of the following:
secondary polycythaemia
nocturnal hypoxaemia
peripheral oedema
pulmonary hypertension
LTOT give mortality benefit only when used for >15hrs per day.

lung volume reduction surgery in selected patients

Inhaled steroids have been shown to improve quality of life and reduce hospitalisation rates by reducing the number of exacerbations, but they do not slow the rate of decline of FEV_1 (hence do not affect prognosis).
Inhaled steroids are only added in COPD pts who show steroid responsiveness.
Management of side effects of steroid inhaler: (oropharyngeal and oesophageal candidiasis)
The patient should be taught adequate inhaler techniques. Advise him to rinse his mouth each time he uses his inhaler and use a spacer device and review him in a month.Resistant symptoms can be managed with oral nystatin or a course of fluconazole.

Oxygen therapy

When managing patients with COPD, once the pCO2 is known to be normal the target oxygen saturations should be 94-98%.
Patients with (COPD) should not in general receive more than 24-28% oxygen without arterial blood gas monitoring.

Oxygen saturation targets

acutely ill patients: 94-98%
patients at risk of hypercapnia (e.g. COPD patients): 88-92%
oxygen should be reduced in stable patients with satisfactory oxygen saturation.
Before the availability of blood gases, use a 28% Venturi mask at 4 l/min and aim for an oxygen saturation of 88-92% for patients with risk factors for hypercapnia but no prior history of respiratory acidosis
adjust target range to 94-98% if the pCO2 is normal
Consider reducing O_2 Flow to 28% if COPD pt shows signs of hypercapnia after being brought in by Ambulance Crew who would have put him on Uncontrolled O_2 therapy.

Situations where oxygen therapy should not be used routinely if there is no evidence of hypoxia:
myocardial infarction and acute coronary syndromes
stroke
obstetric emergencies
anxiety-related hyperventilation

There are three forms of domiciliary supplemental oxygen therapy:

1. Long-term controlled oxygen therapy for at least 15 hours per day in patients with chronic respiratory failure
2. Portable oxygen therapy for exercise-related hypoxaemia
3. Short-burst oxygen therapy, as a palliative treatment for the temporary relief of symptoms.

“Don’t limit yourself. Many people limit themselves to what they think they can do. You can go as far as your mind lets you. What you believe, remember, you can achieve.” – Swami Vivekananda

Non-invasive ventilation (NIV)

It is appropriate for conscious patients with a pH < 7.35 who have not improved on controlled oxygen and standard medical therapy.
(NIV) is the treatment of choice for persistent hypercapnic ventilation failure despite optimal medical therapy.
According to the guidelines, 'maximal medical therapy is defined as:
Controlled oxygen to maintain SaO2 88-92%
Nebulised salbutamol 2.5-5 mg
Nebulised ipratropium 500 µg
Prednisolone 30 mg
Antibiotic agent (when indicated).
The evidence surrounding the use of NIV in COPD shows that patients with a pH in the range of 7.25-7.35 achieve the most benefit.
If the pH is < 7.25 then invasive ventilation should be considered if appropriate.
Non-invasive ventilation - key indications
COPD with respiratory acidosis pH 7.25-7.35
pCO_2 >6.0 (fits the criterion for respiratory acidosis)
type II respiratory failure secondary to chest wall deformity, neuromuscular disease or obstructive sleep apnoea
cardiogenic pulmonary oedema unresponsive to CPAP
weaning from tracheal intubation

Recommended initial settings for bi-level pressure support in COPD

The 2008 Royal College of Physicians guidelines recommend an initial IPAP of 10 cm H20. The 2002 British Thoracic Society guidelines had previously advocated starting at 12-15 cm H20

Expiratory Positive Airway Pressure (EPAP): 4-5 cm H2O
Inspiratory Positive Airway Pressure (IPAP): RCP advocate 10 cm H20 whilst BTS suggest 12-15 cm H2O.
back up rate: 15 breaths/min
back up inspiration: expiration ratio: 1:3
ABGs should be repeated after 1 hour of NIV therapy, and 1 hour after subsequent change in settings or 4 hours in stable patients.

If gas exchange is not significantly improved the IPAP can be gradually increased at a rate of approximately 5 cms (2-5cm) H2O every 10 minutes with a usual target of 20cm H2O or until a response has been achieved or patient tolerability has been reached. Increases in EPAP are not recommended without specialist advice.

Important complication of NIV
ventilation associated pneumothorax is (most important complication of NIV ==> present acutely)
Ventilator associated pneumonia ==> present in patients who have been ventilated for long period of time and would not present so acutely).

Contraindications to NIV include:

facial burns/trauma/recent facial or upper airway surgery
vomiting
fixed upper airway obstruction
undrained pneumothorax
upper gastrointestinal surgery
inability to protect the airway
copious respiratory secretions
life threatening hypoxaemia
haemodynamically unstable requiring inotropes/pressors (unless in a critical care unit)
severe co-morbidity
confusion/agitation
bowel obstruction
patient declines treatment

Non-invasive, positive-pressure ventilation (NIPPV) has been shown to reduce intubation rates, lower hospital mortality rates and lead to shorter hospital stays.

Invasive ventilation

Patients with a pH <7.26 should be managed with a low threshold for intubation.
Mechanical ventilation might be necessary if the patient is unconscious or if the pH is below 7.25.
give NIV whilst awaiting for intensive care.
in Guillain Barre syndrome with respiratory involvement => the parameter used to assess whether a patient needs ventilator support is an FVC <15-20ml/kg.
Decision to ventilate in COPD
If the patient had a written advanced directive, properly witnessed, **while he was well**, then it would not be possible to consider intervention if he wished for it not to happen.
On the other hand, if he has significant hypoxia, he might not be able to give a rational decision with respect to his further treatment.
The family should not have the final decision with respect to intubation - the decision on.
so if significantly hypoxic patient refused intubation during acute exacerbation => Intubate and act on the best interests of the patient, while informing the relatives

Intermittent positive-pressure ventilation (IPPV)
Effects of increased lung volume
Volumes are significantly increased when compared with spontaneous ventilation
↑↑tidal volume ↓ pulmonary vascular resistance, which may lead to ↓ pulmonary hypertension ↓ right ventricular compromise.
over-inflated alveoli ↓ compression of the alveolar blood vessels ↓ ↑↑ right ventricle volume ↓↓↓ left ventricle (LV) filling (ventricular interdependence)
Hyperinflation also leads to prostaglandin release which may be a protective mechanism against lung injury

Effects of increased intrathoracic pressure
Intrathoracic pressure is increased at all points in the respiratory cycle
Inspiration during IPPV ↓ ↑↑ intrathoracic pressure ↓ ↑↑ right atrial pressure ↓ ↓↓ venous return ↓ ↓↓ cardiac output
The increased intrathoracic pressure also decreases the gradient across the LV that it has to work against, which results in a decreased afterload. Both these effects reduce intrathoracic blood volume.

Long-term oxygen therapy (LTOT)

COPD - LTOT if 2 measurements of pO2 < 7.3 kPa

Assessment is done by measuring arterial blood gases on 2 occasions at least 3 weeks apart in patients with stable COPD on optimal management.

Blood gases should be performed in a stable state, which should be at least four weeks after an exacerbation of the disease.

Offer LTOT to patients with a pO2 of < 7.3 kPa or to those with a pO2 of 7.3 - 8 kPa and one of the following:
secondary polycythaemia
nocturnal hypoxaemia
peripheral oedema
pulmonary hypertension
Borderline results should be repeated in three months (eg PO2 = 7.3 or slightly above, without additional factors).

LTOT is usually prescribed indefinitely and to be of benefit has to be used for a minimum of 15 hours a day including at night time.

At least 15 hours of oxygen therapy per day is required to reduce the pulmonary hypertension associated with (COPD) and to treat the underlying pathology of incipient right heart failure.

Assess patients if any of the following:
Very severe airflow obstruction (FEV1 < 30% predicted).

Assessment should be 'considered' for patients with severe airflow obstruction (FEV1 30-49% predicted)
cyanosis
polycythaemia
peripheral oedema
raised jugular venous pressure
oxygen saturations less than or equal to 92% on room air

The indications for LTOT are well established. The British Thoracic Society (BTS) advises that LTOT may be of benefit in patients with the following conditions:

Chronic obstructive pulmonary disease
Severe chronic asthma
Interstitial lung disease
Cystic fibrosis
Bronchiectasis
Pulmonary vascular disease
Primary pulmonary hypertension
Pulmonary malignancy
Chronic heart failure

Patients with any of the above conditions can be assessed to see if they would benefit from LTOT. BTS guidelines currently state that patients should have a P_aO_2 consistently at or below 7.3kPa on air at a time when they are clinically stable (absence of exacerbation in previous five weeks).

Continued cigarette smoking should be a relative contraindication to long-term oxygen therapy.

Effects of supplementary oxygen therapy:

Improvement in survival
Improvement in exercise endurance, associated with a reduction in ventilation at a given submaximal work rate, and an improvement in walking distance and in the ability to perform daily activities.
After 6 months of oxygen therapy, 42% of patients showed evidence of an improvement in cognitive function, but little change in mood or quality of life.
Affect the polycythaemia that occurs in patients with chronic hypoxaemia, by reducing both the haematocrit and the red cell mass.

"The best time to plant a tree was 20 years ago. The second best time is now." – Chinese Proverb

COPD Prognosis:

Once respiratory failure criteria have been met, the 5-year survival rate is only around 25%.

Prognostic indicators in COPD

The strongest predictors of survival in patients with (COPD) are:
FEV1.
Age
Fewer than 50% of patients whose FEV-1 has fallen to 30% of predicted are alive 5 years later.
There is a stronger relationship between survival and the post-bronchodilator FEV-1, rather than the pre-bronchodilator FEV-1.
Other unfavourable prognostic factors which become apparent in patients with the severe disease include:
Severe hypoxaemia
Raised pulmonary arterial pressure
Low carbon monoxide transfer
Factors favouring improved survival are:
stopping smoking
marked bronchodilator response.
A reduced FEV-1 is also an important additional risk factor for lung cancer, independent of age or cigarette smoking.

MRC dyspnoea scale:

One of the main symptoms of chronic obstructive pulmonary disease (COPD) is breathlessness and the MRC dyspnoea scale should be used to quantify this.

Grade	Degree of breathlessness related to activities
1	**Not troubled by breathlessness except on strenuous exercise**
2	**Short of breath when hurrying or walking up a slight hill**
3	**Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at his own pace**
4	**Stops for breath after walking about 100 metres or after a few minutes on level ground**
5	**Too breathless to leave the house, or breathless when dressing or undressing**

BODE index, an index of mortality in COPD developed by the Medical Research Council (**MRC**). This index also incorporates the body mass index, dyspnoea and exercise capacity (as evidenced by a 6-minute walk test). The BODE index can also be used to estimate the risk of hospitalisation.

Air flight in COPD
Assessment of severity of (COPD) and O2 sat at sea level should be performed. A summary is present in the table below:

Assessment	Advice
Sea level SpO2 > 95%	**Oxygen not required**
Sea level SpO2 92-95% and NO additional risk factor	**Oxygen not required**
Sea level SpO2 92-95% and additional risk factor	**Perform hypoxic challenge test with arterial or capillary measurements**
Sea level SpO2 < 92%	**In-flight oxygen**
Receiving supplemental oxygen at sea level	**Increase the flow while at cruising altitude.**

The additional risk factors
1. hypercapnia
2. FEV1 <50% predicted, lung cancer
3. restrictive lung disease involving the parenchyma [fibrosis], chest wall [kyphoscoliosis] or respiratory muscles
4. ventilator support
5. within six weeks of discharge for an exacerbation of chronic lung or cardiac disease
6. cerebrovascular or cardiac disease

Hypoxic challenge test: (to assess flight fitness if SpO2= 92 – 95% **+** additional risk factor in COPD)
Give the patient FiO2 15% for 15 minutes and measure PaO2.
PaO2 > 7.4 kPa (> 55 mmHg) - Oxygen not required.
PaO2 6.6-7.4 kPa (50-55 mmHg) - Borderline. A walk test may be helpful.
PaO2 < 6.6 kPa (< 50 mmHg) - In-flight oxygen (2L/min).

Pulmonary rehabilitation

This is a programme of aerobic lower-extremity training combined with education.
It leads to improvements in exercise capacity (walking distance should improve after the rehabilitation programme) but little change in lung function testing.
Patients who have completed pulmonary rehabilitation experience no fewer hospital admissions because of chest problems, but their hospital stays are likely to be shorter.
A decline in exercise tolerance and heath status tends to occur 6-12 months after the completion of a course.

Pulmonary embolism

PE can cause ventilation- perfusion mismatches. When blood flow to the lung is decreased to embolism, the perfusion (Q) is diminished, but ventilation remains unchanged. This results in increasing physiologic dead space.
Decreased perfusion + normal ventilation

Risk factors

Accordingly, to the latest British Thoracic Society (BTS) guidelines, for pulmonary embolism, the factors predisposing to the development of VTE are classed as major & minor risk factors.

major risk factors (relative risk 5-20) in the development of VTE	minor risk factors with a relative risk of (2-4)
• **lower limb problems including a fracture or varicose veins** • **postoperative intensive care** • **hospitalisation** • **abdominal/pelvic or advanced malignancy** • **previous VTE, and** • **pregnancy.**	• **occult malignancy** • **long-distance travel** • **hypertension** • **congestive cardiac failure, and** • **thrombotic disorder.** • **use of the oral contraceptive pill**

Features of PE

Sudden shortness of breath, pleuritic chest pain with haemoptysis and tachypnoea are the commonest features. (triad of pleuritic chest pain, dyspnoea and haemoptysis)
Chest pain worse on deep breathing
Pulmonary embolism can present with virtually any cardiorespiratory symptom/sign depending on its location and size.
If a patient presents with signs or symptoms of pulmonary embolism (PE) performed chest x-ray to exclude other pathology.
estimate the clinical probability of PE by two-level PE Wells score

Clinical feature	Points
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	**3**
An alternative diagnosis is less likely than PE	**3**
Heart rate > 100 beats per minute	**1.5**
Immobilisation for more than 3 days or surgery in the previous 4 weeks	**1.5**
Previous DVT/PE	**1.5**
Haemoptysis	**1**
Malignancy (on treatment, treated in the last 6 months, or palliative)	**1**

Clinical probability simplified scores	
PE likely	**More than 4 points**
PE unlikely	**4 points or less**

PE likely (> 4 points):
arrange an immediate computed tomography pulmonary angiogram (CTPA).
If there is a delay in getting the CTPA then give low-molecular-weight heparin until the scan is performed.
If the patient has an allergy to contrast media or renal impairment a V/Q scan should be used instead of a CTPA.
ventilation/perfusion single-photon emission computed tomography (V/Q SPECT) scan
if a V/Q SPECT scan is not available ↓ V/Q planar
PE unlikely (≤ 4 points):
arranged a D-dimer test:
If this is positive arrange an immediate (CTPA).
If there is a delay in getting the CTPA then give low-molecular-weight heparin until the scan is performed.

It is interesting to note that the Well's criteria for diagnosing a PE use tachycardia rather than tachypnoea.

Investigations of PE
Pulmonary embolism – CTPA is the first-line investigation.
Pulmonary embolism - normal CXR
Chest x-ray
Should be performed in all patients with symptoms or signs suggestive of PE
to exclude other pathology
usually normal in PE
Computed tomographic pulmonary angiography (CTPA)
the first-line investigation
Advantages compared to V/Q scans?
speed, easier to perform out-of-hours,
reduced need for further imaging
if the CTPA is negative then patients do not need further investigations or treatment for PE
the possibility of providing an alternative diagnosis if PE is excluded
Disadvantages of CTPA
peripheral emboli affecting subsegmental arteries may be missed.
↓ Low sensitivity for detecting pulmonary emboli in sub-segmental pulmonary arteries

Ventilation-perfusion (V/Q) scans

Indication?
If CTPA is contra-indicated
renal impairment (as the contrast media used during CPAs is nephrotoxic).
allergy to contrast media
the high risk from irradiation
which type of (V/Q SPECT) scan?
If CTPA is contra-indicated ↓ ventilation/perfusion single-photon emission computed tomography (**V/Q SPECT**) scan
if a V/Q SPECT scan is not available ↓ **V/Q planar**
Sensitivity & specificity?
sensitivity = 98%; specificity = 40%
predictive value of (V/Q) scans?
high negative predictive value, i.e. if normal virtually excludes PE
other causes of a mismatch in V/Q?
old pulmonary embolisms,

AV malformations,
vasculitis,
previous radiotherapy
COPD
Asthma
Increased pulmonary venous pressure, especially secondary to mitral valve disease, causes the increased flow to the upper lobes.
(V/Q) scan in pregnancy
Ventilation quotient (VQ) scan is not contraindicated in pregnant women, although the perfusion only scan is adequate.
Radiation to the fetus is small.
Which materials are used in (V/Q) imaging?
Xenon is used for imaging **ventilation**, whilst technetium labelled macroaggregated human serum albumin (**MAA**) is used to image **perfusion**.
D-dimers:
Measurement of D-dimer should only be performed when the probability of PE is low when a normal value would be taken as reassuring and further investigation would not be pursued.
Sensitivity & specificity?
high sensitivity (95-98%), but poor specificity
A negative d-dimer is useful for excluding PE in patients who are clinically thought to be at low risk, but a 'positive' result does not establish the diagnosis.
The predictive value of d-dimer?
the negative predictive value is greater than the positive predictive value
only 30% of patients with positive d-Dimer have a confirmatory diagnosis of PE
d-dimers can be positive in:
hospitalised patients
obstetric patients
patients with peripheral vascular disease, cancer and inflammatory conditions
increasing age
D-Dimer measurements should not be performed if:
an alternative diagnosis is likely,
the clinical probability is high or
there is a probable massive PE.

ECG

sinus tachycardia
the most common abnormality; seen in 44% of patients.
the classic ECG changes ↓ S1Q3T3 (seen in no more than 20% of patients)
large S wave in lead I
large Q wave in lead III
inverted T wave in lead III
Right bundle branch block
seen in 18% of patients.
associated with increased mortality;
Right axis deviation (seen in 16% of patients).
Pulmonary angiography
the gold standard
significant complication rate compared to other investigations
Elevated cardiac troponin levels also occur in patients with pulmonary embolism because of right ventricular dilation and myocardial injury

Management of PE

Start low molecular weight heparin and request CT pulmonary angiography if the symptoms and findings point towards pulmonary embolism (PE).
Fluid resuscitation is the most appropriate immediate measure before further investigations confirm the presence of a pulmonary embolism (PE).
Massive PE + hypotension – thrombolyse
anticoagulant
Heparin
When should be started?
For patients with a high or intermediate probability of a non-massive PE ↓ **low molecular weight heparin should be given before imaging**
For patients with a low probability of non-massive PE ↓ immediately after diagnosis.
Which type?
For **non-massive PE** ↓Low molecular weight heparin (LMWH) or fondaparinux.
For patients with severe renal impairment
([eGFR] <30 ml/min/1.73 m^2) offer either:
unfractionated heparin (UFH) with dose adjustments based on the APTT **or**
LMWH with dose adjustments based on an anti-Xa assay.
For patients with an **increased risk of bleeding** consider UFH.
for **massive PE** where **thrombolysis** is being considered, ↓
unfractionated heparin should be used
For how long?
the LMWH or fondaparinux should be continued for at least 5 days or until the international normalised ratio (INR) is 2.0 or above for at least 24 hours, whichever is longer, i.e. LMWH or fondaparinux is given at the same time as warfarin until the INR is in the therapeutic range
for patients with active cancer, NICE recommend using LMWH for 6 months
The benefit of heparin?
Heparin reduces the risk of further embolism (anticoagulant) and reduces pulmonary vasoconstriction.
Warfarin
a vitamin K antagonist (i.e. warfarin) should be given within 24 hours of the diagnosis
for how long?
warfarin should be continued for at least 3 months.
NICE advise extending warfarin beyond 3 months for patients with *unprovoked* PE.
This essentially means that if there was no obvious cause or provoking factor (surgery, trauma, significant immobility)
Thrombolysis
Indication?
Thrombolysis is now recommended as the first-line treatment for **massive PE** where there is a circulatory failure (e.g. hypotension).
Haemodynamic instability may be demonstrated by hypotension, the right ventricular strain on an ECG or signs of right heart failure.
Thrombolysis is indicated in the cardiac arrest situation for suspected PEs. However, it can take 90 minutes to be effective and therefore must only be used if it is appropriate to continue CPR for this duration.

Cardiac arrest for suspected PEs ↓ Intravenous thrombolysis followed by CPR for 90 minutes
Which drug? by which root?

"Only the paranoid survive"
– Andy Grove

Give alteplase 100 mg over 1.5 hours peripherally.
Thrombolysis administered through a peripheral vein is as effective as through a pulmonary artery catheter
percutaneous insertion of Inferior vena cava (IVC) filter
Indication?
If anticoagulation is contraindicated (eg PE following a recent haemorrhagic stroke)
if anticoagulation alone fails
The benefit of IVC filter?
May be as effective as anticoagulation.

Recurrent pulmonary emboli

Recurrent pulmonary emboli should always be considered in cases of progressive shortness of breath with no obvious cause.
Predisposing factors for recurrent pulmonary embolism include:
Antithrombin III deficiency
Protein C deficiency
Factor V Leiden mutation
Possible clues include pulmonary hypertension, right ventricular enlargement, hypoxia with a low PaCO2 and a low transfer factor.
Widening of the alveolar-arterial (A-a) gradient on exercise is likely to be found.
Mismatched defects are classic features of pulmonary embolus.
Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as:
increasing target INR to 3–4 for long- term high-intensity oral anticoagulant therapy **or** switching treatment to LMWH.

DVT/PE in pregnancy

Investigations

In suspected pulmonary embolism in pregnant patients the Royal College of Obstetricians and Gynaecologists recommend the following (updated in 2015):
Chest x-ray and ECG to look for an alternative diagnosis such as pneumonia and pneumothorax.
If the chest x-ray is normal:
In women with suspected PE who also have **symptoms and signs of DVT** ↓
consider a compression duplex doppler of both legs to exclude a DVT.
this may provide indirect evidence of a pulmonary embolism and negate the need for further radiation exposure
If this is positive, the patient is treated with full-dose low molecular weight heparin (LMWH) (warfarin is of course teratogenic).
In women with suspected PE **without symptoms and signs of DVT** ↓
ventilation/perfusion (V/Q) lung scan **or** a computerised tomography pulmonary angiogram (CTPA) should be performed.
When the **chest X-ray is abnormal** and there is a **clinical suspicion of PE**, **CTPA** should be performed in preference to a **V/Q** scan. [New 2015]
Current guidance however favours a perfusion scan as it has lower lung radiation doses than a CTPA.
Half dose VQ involves a lower dose of radiation and is therefore preferred.
If V/Q scan or CTPA is normal but the clinical suspicion of PE remains:
Alternative or repeat testing should be carried out
Anticoagulant treatment should be continued until PE is definitively excluded.
Comparing CTPA to V/Q scanning in pregnancy

CTPA	V/Q scanning
CTPA slightly increases the lifetime risk of maternal breast cancer (increased by up to 13.6%, background risk of 1/200 for study population). Pregnancy makes breast tissue particularly sensitive to the effects of radiation	**V/Q scanning carries a slightly increased risk of childhood cancer compared with CTPA (1/280,000 versus less than 1/1,000,000)**

D-dimer is of limited use in the investigation of thromboembolism as it is often raised in pregnancy.

Treatment of PE in pregnancy

In clinically suspected DVT or PE, treatment with low-molecular-weight heparin (LMWH) should be commenced immediately until the diagnosis is excluded by objective testing
Obstetric patients who are postoperative and receiving unfractionated heparin should have platelet count monitoring performed every 2–3 days from days 4 to 14 or until heparin is stopped. [New 2015]
Postpartum warfarin should be avoided until at least the fifth day and for longer in women at increased risk of postpartum haemorrhage. [New 2015]
Intravenous unfractionated heparin is the preferred, initial treatment in massive PE with cardiovascular compromise.

Post-thrombotic syndrome (PTS)

can develop in nearly half of all patients who experience a DVT
symptoms include chronic leg pain, swelling, redness, and ulcers
prevention of the post-thrombotic syndrome
prolonged use of LMWH (more than 12 weeks) is associated with a significantly lower chance of developing post-thrombotic syndrome. [New 2015]
Following a DVT, elastic compression stockings should be worn on the affected leg to reduce pain and swelling.
the role of compression stockings in the prevention of post-thrombotic syndrome is **unclear**. [New 2015]

Fat embolism

Overview

Unlike emboli that arise from a thrombus, fat emboli are small and multiple producing widespread effects.
They may occur one to three days following a fracture
more common in closed fractures on the long bones or pelvis.
mechanism:
release of lipid globules from damaged bone marrow fat cells. (eg fracture femur).
increased mobilisation of fatty acids peripherally.

Features:

Pulmonary symptoms (shortness of breath, hypoxia) are caused by the ventilation-perfusion mismatch.
may progress to respiratory failure and ARDS requiring mechanical ventilation.
Neurological (confusion and agitation)
Cerebral emboli produce neurological signs in up to 86% of cases.
often occur after the onset of respiratory symptoms
Usually, there is an acute confusional state with or without focal signs.
Most neurological deficits are transient and reversible.
Haematological (thrombocytopenia, anaemia).
Dermatological: Petechial rash caused by capillary damage in the skin.
Multiple petechiae in the distribution of the axilla or upper body are characteristic of a fat embolism.
The petechial rash is pathognomonic of this syndrome but occurs in only 30-50% of cases
A rash is seen in the conjunctiva, mucous membranes, skin folds of the upper body particularly neck and axilla, appearing within the first 36 hours.
Other features:
pyrexia
tachycardia
ECG changes (ST-segment depression and right heart strain)
fluffy retinal exudates
coagulopathy, and
renal changes (oliguria, lipiduria, proteinuria or haematuria).

Treatment

Initial resuscitation should involve
high flow oxygen
intravenous (iv) fluids to maintain high right ventricular filling pressures.
Continuous positive airways pressure ventilation would help in the management of pulmonary oedema and is the next consideration after IV fluids.
Steroid therapy is normally introduced later in ARDS, used at an early stage can worsen pulmonary oedema, and evidence is equivocal as to benefit.
It should be noted that diuretic treatment would be strongly contraindicated in this case. This is because the right ventricular output is dependent on elevated filling pressures. Reducing the preload is therefore not a good idea.

Pneumonia

Community-acquired pneumonia (CAP)

Streptococcus pneumoniae is associated with cold sores.
Preceding influenza predisposes to Staphylococcus aureus pneumonia.

Both Klebsiella and Staphylococcus are associated with empyema formation and cavitating lung lesions.
Community-acquired pneumonia (CAP) may be caused by the following infectious agents:

Streptococcus pneumoniae

(accounts for around 80% of cases) is the most common cause of CAP & single lobar pneumonia.
Streptococcus pneumoniae commonly causes reactivation of the herpes simplex virus resulting in 'cold sores'
S. pneumoniae is the most important cause of fulminant sepsis in patients with hyposplenism.

Haemophilus influenzae

more likely to be associated with exacerbations of COPD

Staphylococcus aureus:

commonly after the 'flu.
the BNF advises the co-prescription of flucloxacillin.
It's an organism often found on the skin. It is therefore commonly associated with systemic infections in intravenous drug users, this is maybe hinted in questions by the presence of track marks.
It also causes bibasal pneumonia as opposed to *Streptococcus pneumoniae* that is the most common cause of single lobar pneumonia.
seen most frequently in the elderly and intravenous drug users or patients with underlying disease.
It can result in cavitating pneumonia.
Carries high mortality, and therefore if suspected treatment should initially be for a severe CAP.
Capable of production of Panton-Valentine-Leucocidin toxin, associated with severe illness and high mortality.
Pneumothorax, pleural effusion and empyema are common in staphylococcal pneumonia.

Atypical pneumonia (e.g. Due to *Mycoplasma pneumoniae*)

Coxiella burnetii (Q fever) ==> relation to animal sources (usually sheep).
Chlamydophila psittaci ==> bird contact (eg, poultry or duck workers)

Viruses

Klebsiella pneumoniae is classically in alcoholics.
Klebsiella pneumonia (Friedlander's pneumonia) typically occurs in middle-aged alcoholic men.
Chest x-ray features may include abscess formation in the middle/upper lobes and empyema.
The mortality approaches 30-50%.

Characteristic features of pneumococcal pneumonia

rapid onset
high fever
pleuritic chest pain
herpes labialis

Management

Mild community-acquired pneumonia (CURB 0-1) should be treated with oral penicillin therapy alone assuming no allergies and no other complicating factors

CURB-65 criteria of severe pneumonia
Confusion (abbreviated mental test score <= 8/10)
Urea > 7 mmol/L
Respiratory rate >= 30 / min
BP: systolic <= 90 or diastolic <= 60 mmHg
age >= 65 years
Patients with 3 or more (out of 5) of the above criteria are regarded as having a severe pneumonia

The British Thoracic Society published guidelines in 2009:
low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to the hospital. There is a high incidence of *Staphylococcus aureus* pneumonia in patients the following influenza. As a result, the BNF advises the co-prescription of flucloxacillin in this situation.
high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin
the current BNF has slightly different recommendations for high severity CAP: intravenous benzylpenicillin + clarithromycin OR benzylpenicillin + doxycycline. For 'life-threatening' infections the BNF recommends the same as the BTS guidelines for high-severity CAP

Intravenous clarithromycin is an extremely irritant drug and it should be avoided wherever possible if a patient can take it orally. Where patients require intravenous administration this should be via a wide bore cannula and the site checked regularly for signs of thrombophlebitis.

Follow up

NICE have guided what advice patients should be given in terms of response to treatment and recovery, by:
week 1: fever should resolve
week 4: chest pain and sputum should have been significantly reduced
week 6: cough and shortness of breath should have been significantly reduced
month 3: most symptoms should have resolved, except for tiredness

month 6: should be returned to normal

A repeat chest X-ray may be indicated to ensure resolution and that there is no underlying pathology, but **radiological changes can take up to 6 weeks to improve**.

A summary table of empirical antibiotics as suggested by the BTS is shown below.

Adding a fluoroquinolone is an option for those with high severity pneumonia not responding to a b-lactam/ macrolide combination antibiotic regimen (BTS 2009).
The chance of cross-reactivity of penicillin allergy with beta-lactams is only 10%. A rash is not a contraindication for this.

Panton-Valentine Leukocidin-producing Staphylococcus aureus (PVL-SA)
is a rare cause of high severity pneumonia, associated with rapid lung cavitation (necrotising pneumonia) and multiorgan failure.
empirical antibiotic combination of IV linezolid 600 mg twice daily, IV clindamycin 1.2 g four times a day and IV rifampicin 600 mg twice daily
For those patients referred to the hospital with suspected life-threatening CAP, general practitioners should administer I.V Penicillin G 1.2 g or amoxicillin 1 g orally. (BTS 2009).
For high severity the BNF suggest benzylpenicillin with either clarithromycin or doxycycline as the first line, however, if the patient has a life-threatening infection, gram-negative organisms are suspected, co-morbidities are present or the patient is a nursing or residential home resident (probably the vast majority of hospital inpatients) then co-amoxiclav and clarithromycin should be used.

If *Staphylococcus aureus* is identified, treatment should be altered:
Non-MRSA organisms should be treated with flucloxacillin and/or rifampicin; an alternative for penicillin-allergic patients is teicoplanin and rifampicin.
MRSA should be treated with vancomycin.

BNF antibiotic guidelines

The following is based on current BNF guidelines:

Respiratory system

Condition	Recommended treatment
Exacerbations of chronic bronchitis	**Amoxicillin or tetracycline or clarithromycin**
Uncomplicated community-acquired pneumonia	**Amoxicillin (Doxycycline or clarithromycin in penicillin-allergic, add flucloxacillin if staphylococci suspected e.g. In influenza)**
Pneumonia possibly caused by atypical pathogens	**Clarithromycin**
Hospital-acquired pneumonia	**Within 5 days of admission: co-amoxiclav or cefuroxime** **More than 5 days after admission: piperacillin with tazobactam OR a broad-spectrum cephalosporin (e.g. ceftazidime) OR a quinolone (e.g. ciprofloxacin)**

Pneumonia: prognostic factors

The British Thoracic Society recommends that patients should be assessed for the severity of their pneumonia using several core prognostic features (CURB-65 score).

The CURB-65 score is as follows:

Criterion	Marker
C	Confusion (abbreviated mental test score <= 8/10)
U	Urea >7 mmol/L
R	Respiration rate >= 30/min
B	Blood pressure: systolic <= 90 mmHg and/or diastolic <= 60 mmHg
65	Aged >= 65 years

Patients with a CURB-65 score of 0 should be managed in the community.
Patients with a CURB-65 score of 1 should have their SaO_2 assessed which should be >92% to be safely managed in the community and a CXR performed. If the CXR shows bilateral/multilobar shadowing hospital admission is advised.
Patients with a CURB-65 score of **2 or more** should be managed in hospital as this represents severe community-acquired pneumonia.
The CURB-65 score also correlates with an increased risk of mortality at 30 days with patients with a CURB-65 score of 4 approaching a 30% mortality rate at 30 days.
Other factors associated with a poor prognosis include:
presence of coexisting disease
hypoxaemia (pO2 < 8 kPa) independent of FiO2

How to define mental confusion in the CURB65 severity score?
The Abbreviated Mental Test (each question scores 1 mark, total 10 marks)

1. Age
2. Date of birth
3. Time (to the nearest hour)
4. Year
5. Hospital name
6. Recognition of two persons (eg, doctor, nurse)
7. Recall address (eg, 42 West Street)
8. Date of First World War
9. Name of monarchs
10. Count backwards 20 R 1

A score of 8 or less has been used to define mental confusion in the CURB65 severity score.

"If people are doubting how far you can go, go so far that you can't hear them anymore." – Michele Ruiz

The risk of death at 30 days increases as the score increases:

Score	Risk of death at 30 days
0	0.7%
1	3.2%
2	13.0%
3	17.0%
4	41.5%
5	57.0%

Similarly, with any infection, the risk of mortality increases as the CURB score increases

Score	Risk of death at 30 days
0 to 1	<5% mortality
2 to 3	< 10% mortality
4 to 5	15-30% mortality

Pneumonia Severity (based on clinical judgement and CURB score)	Treatment Site	First-line	Second line
Low Severity (CURB 65 = 0-1)	Home	Amoxicillin orally	Doxycycline or clarithromycin orally
Moderate severity (CURB 65 = 2)	Hospital	Amoxicillin plus clarithromycin orally (IV if oral administration not possible)	Doxycycline, Levofloxacin or moxifloxacin orally
High Severity (CURB 65 = 3-5)	Hospital (High Dependency Unit/ITU)	Co-amoxiclav plus clarithromycin IV	Benzylpenicillin plus levofloxacin or ciprofloxacin IV OR Cefuroxime plus clarithromycin IV

Follow up:

Chest x-ray in six weeks to ensure complete resolution. This is to exclude any underlying cause especially malignancy. those who have persistent shadowing on the lung need a referral to a respiratory physician**.**

What review policy should be adopted in patients managed in the community?
Review is recommended after 48 h or earlier if clinically indicated for disease severity assessment
Those who fail to improve after 48 h of treatment should be considered for hospital admission or chest radiography.
C-reactive protein should be remeasured and a chest radiograph repeated in patients who are not progressing satisfactorily after 3 days of treatment.
What arrangements should be made for follow-up after hospital discharge?
The clinical review should be arranged for all patients at around 6 weeks.

Complications of pneumonia
Acute complications: might be obvious at presentation or might appear after an interval (empyema, abscess, fistula and organising pneumonia).
Chronic complication: bronchiectasis only diagnosed after the illness because temporary or reversible bronchial dilatation is sometimes seen during the acute illness.
Prevention and vaccination
All patients aged 65 years or at risk of invasive pneumococcal disease who are admitted with CAP and who have not previously received pneumococcal vaccine should receive 23- valent pneumococcal polysaccharide vaccine (23-PPV)

Klebsiella

Pneumonia in an alcoholic – Klebsiella
Klebsiella is a Gram-negative rod that is part of the normal gut flora.
It can cause a number of infections in humans including pneumonia (typically following aspiration) and urinary tract infections.
The pathophysiological mechanism is colonization of the oropharynx followed by microaspiration of upper airway secretions in the setting of decreased consciousness (due to heavy drinking).

Features of *Klebsiella* pneumonia

more common in alcoholic and diabetics
may occur following aspiration
'red-currant jelly' sputum
Cavitating lesions, often affects upper lobes.

Treatment

Third-generation cephalosporins or quinolones are used as standard therapy

Prognosis

commonly causes lung abscess formation and empyema
mortality is 30-50%

Legionella

Legionella pneumophilia is best diagnosed by the urinary antigen test. Questions will most likely provide a history of recent travel, cruise, conference etc .

Features which strongly suggest Legionella:

recent foreign travel
flu-like symptoms
hyponatraemia
pleural effusion

Etiology

Legionnaire's disease is caused by the intracellular bacterium *Legionella pneumophilia*.
It is typically colonizes water tanks.
The most common sources in buildings in which Legionella organisms have been found are:
Hot-water calorifiers/ Air Conditioning Systems
Storage tanks
Piped water, especially hot water from the calorifiers in large buildings and industrial complexes with long runs of pipework

Other well-recognised sources include:
Recirculating water in air-conditioning and cooling systems
Whirlpool spas and other warm-water baths
Decorative fountains
Nebulisers and humidifier reservoirs of hospital ventilation machines if topped up with contaminated tap water
Dissemination of infection is by contaminated water droplets (aerosol), which are inhaled. To cause infection the droplets must be of a size that can reach the alveoli of the lungs (less than 5 mm in diameter). Taps and shower-heads produce very localised aerosols, whereas the water droplets (drift) contained in the airstream released from a cooling tower can be carried a considerable distance and expose a greater number of people to risk.

Features

flu-like symptoms including fever (present in > 95% of patients)
dry cough
relative bradycardia
confusion (think hyponatremia as a cause)
lymphopaenia
hyponatraemia
deranged liver function tests
pleural effusion: seen in around 30% of ptients
Typically, starts with high fever, shivers, severe headache and muscle pains.
dyspnoea is common
Amnesia on recovery is common.

Diagnosis

urinary antigen (the most useful diagnostic test**)**
It is important to remember that the organism does not show up on Gram-staining.

Management

Legionnaires' disease is treated with antibiotics that achieve high intracellular concentration, particularly macrolides or **fluoroquinolones (such as levofloxacin). The latter is favoured when the illness is severe enough to warrant admission.**
treat with erythromycin or clarithromycin .(500-1000 mg every 6 hours for erythromycin and 500 mg twice daily for clarithromycin)
if patient allergic or intolerant to macrolides => ciprofloxacin
Ciprofloxacin is also a useful drug in combination with clarithromycin for severe infections .
Both doxycycline and ciprofloxacin are reasonable second line choices for the treatment of *Legionella*. Clinicians should be alert to the potential small risk of cardiac electrophysiological abnormalities with quinolone-macrolide combinations.
Rifampicin is often recommended as additional therapy to erythromycin, in a dose of 600 mg once or twice daily in patients with severe infection or who are deteriorating.
Legionella resistance to rifampicin is noted, therefore this is not a first line option.
A small recent study also noted increased liver function abnormalities in patients with legionnaire's exposed to rifampicin.

Prevention

The most important principle to follow is to avoid holding water at temperatures between 20 °C and 45 °C, which is the range in which Legionella multiplication occurs.

“Write it. Shoot it. Publish it. Crochet it, sauté it, whatever. MAKE.”
– Joss Whedon

Mycoplasma pneumoniae

Mycoplasma pneumoniae is a cause of atypical pneumonia which often affects younger patients
most commonly causes disease in individuals aged 15-30 years.
accounts for about 7% of all community-acquired pneumonias.
It is associated with a number of characteristic complications such as erythema multiforme and cold autoimmune haemolytic anaemia.
it occurs in epidemics every 4 years , more commonly among close-knit populations like those in schools and colleges.
It is important to recognise atypical pneumonias as they may not respond to penicillins or cephalosporins due to it lacking a peptidoglycan cell wall.,

Features

> The longer duration of symptoms and unusual features of abdominal pain, dry cough and hyponatraemia should alert you to an atypical organism of which *Mycoplasma pneumoniae* is one of the commonest.

the disease typically has a prolonged and gradual onset
flu-like symptoms classically precede a dry cough
It is characterised by Headaches, malaise and cough.
bilateral consolidation on x-ray
complications may occur as below

Extrapulmonary manifestations occur in ~10% of cases:

Rash
erythema multiforme
erythema nodosum
urticarial
Neurological syndromes
aseptic meningitis
encephalitis,
neuropathies
Guillain-Barré syndrome
transverse myelitis
cardiac:
Myocarditis
Pericarditis
Renal failure
Hepatitis
Pancreatitis (rarely).
Arthritis
Cold agglutinins
Haemolytic anaemia.
found in up to 50% of cases**.**
Presence of spherocytes or fragmented red blood cells on the film is suggestive of haemolytic anaemia.
In mycoplasma infection spherocytes are a result of cold agglutinin damage to the red cell membrane.
Nucleated red cells may also be seen.
Haemolysis is associated with the presence of IgM antibodies (cold agglutinins) directed against the I antigen of the erythrocyte membrane.
Haemolysis would be confirmed on a blood film and a direct Coombs' test.

Reticulocyte counts are increased
bilirubin is predominantly unconjugated.
Lactate dehydrogenase (LDH) is increased and haptoglobins are reduced.
Urinary urobilinogen is increased and haemosiderinuria may be seen.

Complications

cold agglutins (IgM) may cause an haemolytic anaemia, thrombocytopenia
erythema multiforme, erythema nodosum
meningoencephalitis, Guillain-Barre syndrome
bullous myringitis: painful vesicles on the tympanic membrane
pericarditis/myocarditis
gastrointestinal: hepatitis, pancreatitis , Vomiting , Diarrhoea
renal: acute glomerulonephritis

Investigations

Mycoplasma? - Serology is diagnostic

diagnosis is generally by Mycoplasma serology
positive cold agglutination test (cold agglutinins occur in only half of patients)
The chest X-ray findings might not correlate with the patient's condition.theX-ray appearances are usually much worse than would be suggested by the clinical examination of the respiratory system.
The white blood count can be normal

Management

Mycoplasma pneumonia if allergic/intolerant to macrolides – doxycycline

erythromycin/clarithromycin
tetracyclines such as doxycycline are an alternative
Most cases resolve **spontaneously** within a few weeks.
The pathogen does not have a cell wall and so is not susceptible to penicillin, cephalosporins or other antibiotics that are active against the bacterial cell wall.

Aspiration pneumonia

The typical patient with aspiration pneumonia has gingival crevice disease combined with a predisposition for aspiration that is usually due to a suppressed level of consciousness or dysphagia.
Chest X-rays usually show infection in a dependent segment (usually the superior segments of the lower lobes or posterior segments of the upper lobes as these are dependent in the recumbent position),
Aspiration pneumonia → typically affects **right lower lobe** in persons with impaired swallowing.

Psittacosis (Chlamydia psittaci pneumonia)

Chlamydia psittaci infection (psittacosis) is characterised by malaise, fever, myalgia and pneumonia.
Exposure to an ill bird and a rash (Horder's spots) are pathognomonic.
Pet owners, vets and zoo keepers are most at risk. It is rare in children.
Person to person transmission occurs especially in a hospital environment.
Sputum Gram stain reveals a few leucocytes and no predominant bacteria. There are few signs and few laboratory/x ray findings.
The chest X-ray can show segmental or diffuse consolidation.
Relative bradycardia with non-specific chest signs, coupled with diffuse chest x ray changes, a low white count and abnormal LFTs are consistent with the disease.
Abnormal LFTs in up to 50%.
Positive serology is with complement-fixing antibodies.
Diagnosis is confirmed by enzyme immunoassay
Erythromycin or tetracyclines are the drugs of choice.

Pseudomonas pneumonia

Pseudomonas is a common pathogen in patients with bronchiectasis and cystic fibrosis.
It also causes hospital-acquired infections, particularly in intensive care units or after surgery. Nosocomial or **hospital-acquired infections**
should be suspected in patients with an onset of symptoms at least 48 hours after admission to the hospital.
Treatment is with anti-pseudomonal penicillin, ceftazidime, meropenem or ciprofloxacin.

Hospital-acquired pneumonia

The third most common hospital-acquired infection after urinary tract infections and wound infections.

Gram-negative organisms are far more common, owing to:
Colonisation of the oropharynx by Gram-negative bacilli, which is very common in hospitalised patients, who have often been on broad-spectrum antibiotics already
Increased risk of micro-aspiration of nasopharyngeal secretions
Increased likelihood of immunodepression
Treatment: most commonly as combination therapy. A third generation cephalosporin with an aminoglycoside is the current British Thoracic Society (BTS) recommendation

Mendelson syndrome

Is an acute pneumonia caused by regurgitation of stomach contents and aspiration of chemical material, usually gastric juices.
Often follows anaesthesia, when the gag reflex is depressed.
Symptoms develops rapidly, and within hours the patient can become tachypnoeic, hypoxic and febrile. **It can cause severe bronchospasm**. There is minimal sputum.

Chest auscultation signs

Whispering pectoriloquy is a sign of consolidation. It can occur because of the tumour and the locally trapped secretions.
Polyphonic wheeze can indicate obstructive lung disease,
inspiratory crackles can be associated with pulmonary fibrosis or heart failure as well as with consolidation.

Lung abscess

Predisposing factors include →
dental disease,
impaired consciousness, for example, alcohol, post-anaesthesia,
bronchial carcinoma
and immunosuppression

Radiation pneumonitis

Occur in 10-30% of patients following radiotherapy for lung cancer.
Symptoms: cough (which can be severe and can produce thick sputum), breathlessness and fever.
On examination there might be tachypnoea, cyanosis in severe disease, and local crepitations. Telangiectases, the result of cutaneous radiation damage, are often observed in the overlying skin.
Radiographic changes: The most characteristic X-ray feature is an area of hazy consolidation demarcated by a sharp margin (crossing anatomical pulmonary planes) that corresponds to the limits of the irradiation field, though additional effects are usually detectable beyond these boundaries.
Computed tomography (CT) provides the best means of early identification, ground-glass attenuation and interalveolar septal thickening being the early characteristic features.
Dense local fibrosis can develop up to 1-2 years after radiation, and magnetic resonance Imaging (MRI) might be required to differentiate this from tumour recurrence.

Management

If symptoms are slight, no specific treatment is needed.
In more severe diseases, corticosteroids produce symptomatic relief
Response to corticosteroids occurs within 3-4 days, with clinical and radiographic improvement, and treatment should be continued for 3-4 weeks before tapering and stopping.
Corticosteroids do not, however, influence the extent of subsequent pulmonary fibrosis.
Symptomatic relief of cough and hypoxaemia by an opioid antitussive and oxygen supplementation may also be needed.

HIV: Pneumocystis jiroveci pneumonia

Pneumocystis jiroveci pneumonia - pneumothorax is a common complication
Whilst the organism *Pneumocystis carinii* is now referred to as *Pneumocystis jiroveci*, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use.
Pneumocystis jiroveci is a unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoan.
PCP is the most common opportunistic infection in AIDS

Pathophysiology

The organism is confined to the alveolar space of the lung and produces debris and cysts in the alveolar space with interstitial infiltration of lymphocytes and plasma cells. As a result, it can cause profound disturbance of oxygen exchange and fatal hypoxaemia if left untreated.
The morphological appearance of *Pneumocystis jirovecii* infection in the lung => An interstitial pneumonitis with foamy intra-alveolar exudate

Features

dyspnoea
dry cough
fever
very few chest signs

Pneumothorax is a common complication of PCP.

Extrapulmonary manifestations are rare (1-2% of cases), may cause
hepatosplenomegaly
lymphadenopathy
choroid lesions can result in
pancytopenia, retinal cotton wool spots and thyroid masses.

The lungs are commonly clear on auscultation

Investigation

Pneumocystis carinii pneumonia=> Definitive diagnosis is by bronchial alveolar lavage with silver staining.

CXR: typically shows bilateral interstitial pulmonary infiltrates (usually diffuse ground-glass opacities) but can present with other x-ray findings e.g. lobar consolidation. May be normal
exercise-induced desaturation
sputum often fails to show PCP, bronchoalveolar lavage (BAL) is often needed to demonstrate PCP (**silver stain shows characteristic cysts**).
The organism may be identified on microscopy after:
methenamine silver staining for the cyst phase of the organism
Giemsa staining that demonstrates the small, punctate nuclei of the trophozoites and intracystic sporozoites, or
fluorescence-tagged monoclonal antibody.
Lactate dehydrogenase - raised in 90% of patients with PCP (but this can occur with other pulmonary diseases).

Management

co-trimoxazole (120 mg/kg daily in divided doses) for 3 weeks (should be given for 21 days in HIV, but can be shorter in other causes of immunosuppression)
IV pentamidine in severe cases (or In patients who are intolerant of co-trimoxazole)
allergic to co-trimoxazole alternative therapy would be IV pentamidine or clindamycin with primaquine.
Steroids have been shown to reduce mortality and prevent lung damage in people with moderate-to-severe PCP. (The severity is determined based on arterial blood gas results).
severe PCP is defined by a room air arterial oxygen pressure (pO2) of less than 9 kPa (70 mmHg) or an arterial-alveolar O2 gradient that exceeds 4.5 kPa (35 mmHg).
if pO2 < 9.3kPa then steroids reduce the risk of respiratory failure by 50% and death by a third
While it is true that long term steroid use is immunosuppressive a **21-day** tapering course is safe and effective.
co-trimoxazole is the preferred initial therapy during pregnancy according to consensus guidelines. The BNF states that there is a teratogenic risk in the first trimester (as trimethoprim is a folate antagonist), and neonatal haemolysis and methaemoglobinaemia in the third trimester. However, there is also a considerable risk of harm to the foetus if the mother is unwell. The benefits in this situation, therefore, outweigh the risks, and it should be used.
Glucose 6-phosphate dehydrogenase deficiency (G6PD) levels should be checked before TMP-SMX, dapsone or primaquine use
If allergic to co-trimoxazole, IV pentamidine or clindamycin are appropriate.

For the treatment of infections that are resistant to TMP-SMX, the combination of clindamycin and primaquine is likely to be more effective than intravenous pentamidine.
Prophylaxis
all patients with a CD4 count < 200/mm should receive PCP prophylaxis (Co-trimoxazole is the preferred agent. Dapsone and inhaled pentamidine are also used.)
Discontinuing Primary Prophylaxis
Primary Pneumocystis prophylaxis should be discontinued if the patient responded to ART with an increase in CD4 counts >= 200 cells/ mm3 for >= 3 months.

“Fairy tales are more than true: not because they tell us that dragons exist, but because they tell us that dragons can be beaten.”
— Neil Gaiman

Allergic bronchopulmonary aspergillosis (ABPA)

Allergic bronchopulmonary aspergillosis results from an allergy to Aspergillus spores (Type I hypersensitivity to Aspergillus fumigatus).
It predominantly affects patients with asthma, cystic fibrosis and bronchiectasis.
In the exam questions often give a history of bronchiectasis and eosinophilia.
It is defined by several criteria, including:
Clinical deterioration in asthma symptoms
Raised IgE levels
Positive Aspergillus serology

Pulmonary infiltrates on chest X-ray

Features

bronchoconstriction: wheeze, cough, dyspnoea
bronchiectasis (proximal)

Investigations

serum eosinophilia
Pulmonary infiltrates on CXR. Lobar collapse can also occur, due to mucus plugging.
Positive radioallergosorbent (RAST) test to Aspergillus.
Immediate (type I) reactions occur in virtually all patients with ABPA following intradermal injections of Aspergillus fumigatus extracts, with only 16% developing delayed (type IV) reactions. An early positive skin-prick test for Aspergillus fumigatus is the most specific to (ABPA). Positive skin-prick tests reflect antigen-specific IgE.
Positive IgG precipitins (not as positive as in aspergilloma) in 70% of patients.
Precipitins (IgG) are more usual with an aspergilloma but may be positive in ABPA or up to 10% of patients with asthma.
raised IgE
Management
steroids
itraconazole is sometimes introduced as a second-line agent

Aspergilloma

An aspergilloma is a mycetoma (mass-like fungus ball) that often colonises an existing lung cavity (e.g. secondary to tuberculosis, lung cancer or cystic fibrosis)
Feature: Usually asymptomatic but features may include
cough
haemoptysis (may be severe)

Investigations

chest x-ray containing a rounded opacity
high titres Aspergillus precipitins (IgG antibodies)
aspergilloma can develop in an emphysematous cavity, the clue can be a lack of improvement with broad-spectrum intravenous antibiotics, haemoptysis and chest X-Ray findings.

Treatment:

Up to 10% of aspergillomas resolve spontaneously but, if treatment is required, possibilities are surgical excision or long-term treatment with oral itraconazole.

Surgery should be considered as a first-line option where erosion into a major vessel and massive haemoptysis is a possibility
In case of massive haemoptysis the next appropriate management – after transfusion and resuscitation- is => Angiography and embolisation, after that => lobar resection as the intervention of next resort

Invasive aspergillosis

Risk factors of fungal infections:
patients undergoing chemotherapy,
stem cell transplant,
patients on immunosuppressive medications for autoimmune conditions
HIV positive.

Features:

Symptoms of active infection & haemoptysis.

Investigations:

the classical signs on CT scanning the 'halo sign'
Silver staining shows => hyphae.

Treatment:

The first line treatment is voriconazole which should be started intravenously before oral dosing is considered. This is due to oral voriconazole taking at least 10 days to get to therapeutic levels.
If voriconazole is not tolerated, then lipsomal amphotericin should be used.
Prognosis
Mortality for invasive aspergillosis vary from 40-90% in the literature. As such it is important to identify it and treat quickly.

Alpha-1 antitrypsin deficiency

Alpha-1 antitrypsin deficiency - autosomal recessive / co-dominant

Alpha-1 antitrypsin (A1AT) deficiency is a common inherited condition
Caused by a lack of a protease inhibitor (Pi) normally produced by the liver.
the main role of alpha-1 antitrypsin in the body Protease inhibitor
The role of A1AT is to protect cells from enzymes such as neutrophil elastase.

Genetics

located on the long arm of chromosome 14
inherited in an autosomal recessive / co-dominant fashion*
alleles classified by their electrophoretic mobility - M for normal, S for slow, and Z for very slow
normal = PiMM
homozygous PiSS (50% normal A1AT levels)
Heterozygote patients such as those with the PiMZ genotype have alpha-1 antitrypsin levels approximately 35% of normal. They therefore have a low risk of developing clinically evident lung disease.
homozygous PiZZ (10% normal A1AT levels)

The serum levels of some of the common genotypes are:
PiMM: 100% (normal)
PiMS: 80% of normal serum level of A1AT
PiSS: 60% of normal serum level of A1AT
PiMZ: 60% of normal serum level of A1AT
PiSZ: 40% of normal serum level of A1AT

PiZZ: 10-15% (severe alpha 1-antitrypsin deficiency).
Cigarette smoking is especially harmful to those with A1AT deficiency and can accelerate the progression of emphysema by 10 years.

Features

patients who manifest disease usually have PiZZ genotype
lungs: panacinar emphysema, most marked in lower lobes (2% of cases of emphysema)
75% of patients develop chest pathology
liver: cirrhosis and hepatocellular carcinoma in adults, cholestasis in children .(15% of patients have associated cirrhosis)

Investigations

A1AT concentrations

Management

Strictly no smoking
supportive: bronchodilators, physiotherapy
intravenous alpha1-antitrypsin protein concentrates
surgery: volume reduction surgery, lung transplantation
*trusted sources are split on which is a more accurate description

Associated conditions:
A1AT deficiency is associated with a number of malignancies including hepatocellular cancer, lung cancer, bladder cancer and lymphoma.
Other associated conditions include

- Cirrhosis
- Pancreatitis
- Gall stones
- COPD
- Bronchiectasis
- Primary sclerosing cholangitis
- Wegener's granulomatosis and
- Pelvic prolapse.

Acute respiratory distress syndrome (ARDS)

Basics

ARDS caused by increased permeability of alveolar capillaries leading to fluid accumulation in alveoli i.e. non-cardiogenic pulmonary oedema
in pathophysiology there is ALSO a deficiency in surfactant which reduces lung compliance
and predisposes to collapse (especially in dependent zones)
there tends to be a type 1 respiratory failure, rather than type 2.

Diagnostic Criteria (American-European Consensus Conference)
Acute onset
Bilateral infiltrates (on chest x ray or CT scan)

PaO2:FiO2 ratio < 26.7 kPa (200 mmHg)
Lack of evidence of left atrial hypertension
(pulmonary artery wedge pressure (PAWP) <18 mmHg if available).

Causes

infection: sepsis, pneumonia
the most common CAUSE is systemic inflammation.
massive blood transfusion
trauma, Burs
smoke inhalation
pancreatitis
cardio-pulmonary bypass
Direct and indirect causes:
Direct pulmonary causes include:
Inhalation of gastric contents (pH <2)
Infective (pneumonia, tuberculosis)
Pulmonary trauma
Near drowning
Toxic gas inhalation and
Oxygen toxicity.
Indirect causes include:
Sepsis
Non-thoracic trauma
Uraemia
Bowel infraction
Anaphylaxis

Treatment:

Which therapies has been shown to most likely decrease overall mortality of ARDS?
Implementing a low tidal volume ventilation protocol
mechanical ventilation itself can injure the damaged lungs causing ventilation-induced lung injury.
The main goal of treatment is to minimise any additional damage while maintaining adequate gas exchange. This has been effectively done by maintaining low tidal volume ventilation.
low tidal volume ventilation reduces the absolute mortality by about 7-9% as compared to using higher tidal volumes.
Extracorporeal membrane oxygenation (ECMO):
If the patient is on maximal ventilatory therapy but is still hypoxic & hypercapnic? □ (ECMO)
trial demonstrated a significant increase in survival without significant disability

ECMO involves connecting a patient's circulation to an external oxygenator and pump, via a catheter placed in the right side of the heart.
It requires the continuous infusion of anticoagulant, and as such bleeding is the most commonly associated complication.
Infection and haemolysis are also a risk.
Since the infiltrate of ARDS is primarily inflammatory, diuretics are NOT particularly effective. Over-diuresis also runs the risk of hemodynamic compromise, further decreasing the patient's already insufficient oxygen delivery to tissues.
glucocorticoids have NOT been shown to help patients in the acute phase of ARDS.
There is some evidence that they may help in the fibroproliferative stage but not acutely.
The ventilator strategy should employ a relatively high level of positive end- expiratory pressure (PEEP)

Acute Respiratory Distress Syndrome (ARDS) & Acute Lung Injury (ALI):
ARDS is a severe form of Acute Lung Injury (ALI)
ARDS has the same definition except that the PaO2/FiO2 ratio is less than 200.
ALI has a specific definition:
PaO2/FiO2 ratio of less than 300
Bilateral infiltrates on a chest radiograph
Pulmonary capillary wedge pressure of less than 18 mmHg

Prognosis:

ARDS mortality is generally high (40%), but is determined by the cause with aspiration pneumonia having a mortality rate of almost 80% when associated with ARDS.

Altitude related disorders
There are three main types of altitude related disorders:
1. acute mountain sickness (AMS), which may progress to
2. high altitude pulmonary edema (HAPE) or
3. high altitude cerebral edema (HACE).

All three conditions are due to the chronic hypobaric hypoxia which develops at high altitudes
Acute mountain sickness
Acute mountain sickness is generally a self-limiting condition.

Features of AMS start to occur above 2,500 - 3,000m, developing gradually over 6-12 hours and potentially last a number of days:
headache
nausea
fatigue
Prevention and treatment of AMS
the risk of AMS may actually be positively correlated to physical fitness

gain altitude at no more than 500 m per day
acetazolamide (a carbonic anhydrase inhibitor) is widely used to prevent AMS and has a supporting evidence base
treatment: descent

A minority of people above 4,000m go onto develop high altitude pulmonary oedema (HAPE) or high altitude cerebral oedema (HACE), potentially fatal conditions
HAPE presents with classical pulmonary oedema features
•HACE presents with headache, ataxia, papilloedema
Management of HACE
descent
dexamethasone
Management of HAPE
descent
High concentration O2
oxygen should be initiated first
Is the next most appropriate intervention
nifedipine, dexamethasone, acetazolamide, phosphodiesterase type V inhibitors*
If high-flow oxygen is not available, then nifedipine can be used as second line.
*All seem to work by reducing systolic pulmonary artery pressure

Bronchiectasis

Definition: permanent dilatation of the airways secondary to chronic infection or inflammation.

Causes

post-infective: tuberculosis, measles, pertussis, pneumonia
A history of previous whooping cough suggests bronchiectasis.
cystic fibrosis
bronchial obstruction e.g. lung cancer/foreign body
immune deficiency: selective IgA, hypogammaglobulinaemia
allergic bronchopulmonary aspergillosis (ABPA)
ciliary dyskinetic syndromes:
Kartagener's syndrome (situs inversus and sinusitis associated with non-motile cilia),
Young's syndrome (a combination of bronchiectasis, rhinosinusitis and infertility)
Inflammatory bowel disease (including Crohn's disease)
yellow nail syndrome
Rheumatoid arthritis (3-4% of RA developed bronchiectasis).
Features: The most common findings on examination are crackles (75%) and wheeze (22%). Clubbing is only found in 2%.
expectorating phlegm on most days
frequent chest infections
haemoptysis
Post nasal drip - common (chronic sinusitis in around 30%)
tiredness - many patients find this more troublesome than the productive cough

Diagnosis

A high-resolution computed tomography scan of the lungs (HRCT) is the gold standard for the diagnosis of bronchiectasis.

The diagnostic criteria for bronchiectasis on HRCT depend on finding both dilatation and thickening of the affected bronchi,
Dilatation being present if the internal diameter of the bronchus is greater than the diameter of its accompanying pulmonary artery.
The classic appearance of a cross-section of a thick-walled dilated bronchus next to the accompanying pulmonary artery is the 'signet ring' sign.
Bronchial dilatation is also recognised when airways are seen in longitudinal section on CT and there is a failure of tapering as the bronchus courses towards the periphery.

Chest X-ray
can be normal in at least 50% of patients
If it is abnormal, the findings reflect thickened and dilated bronchi, which produce tramline opacities and ring shadows.
Retained mucus might be seen as tubular opacities,
There can be associated volume loss of the affected lobe.

Bronchiectasis: management
Bronchiectasis: most common organism = Haemophilus influenzae

Bronchiectasis describes a permanent dilatation of the airways secondary to chronic infection or inflammation. After assessing for treatable causes (e.g. immune deficiency) management is as follows:

physical training (e.g. inspiratory muscle training) - has a good evidence base for patients with non-cystic fibrosis bronchiectasis
postural drainage
antibiotics for exacerbations + long-term rotating antibiotics in severe cases
bronchodilators in selected cases
Immunisations: Influenza and pneumococcal vaccinations are strongly recommended.
surgery in selected cases (e.g. Localised disease that fails to resolve after I.V antibiotic)
Most common organisms isolated from patients with bronchiectasis:
Haemophilus influenzae (most common)
Pseudomonas aeruginosa
Klebsiella spp.
Streptococcus pneumoniae

Cystic fibrosis

It'd be a cardinal Sin to enter the exam without thorough knowledge of this quintessential topic for exam, which happens to be the the most common genetically inherited diseases in Caucasian individuals. Rare in patients of Afro-Caribbean and Asian origin.

Autosomal Recessive transmission
Due to mutation of CFTR gene on chromosome 7. Precisely 7q31. The most common mutation is delta- F508.
Occurs in 1 in 2500 live births.
The carrier frequency in white populations is 1 in 25.

If both parents are carriers of the CF gene: (Basic Sciences is back again):
The chance of another child being affected (homozygote) is 1 in 4 (25%).
The chance of their child being free from the CF gene is also 1 in 4 (25%)
And the chance of a child being a carrier (heterozygote) is 1 in 2 (50%).
The sibling of an affected person has a 3 in 4 chance of being a CF carrier or having the disease. if one sibling is not affected , the chance of being a carrier for the CF gene is 2 in 3.
10% of people with cystic fibrosis are not diagnosed until adult life, so beware of questions depicting young adults (17-25yr old) presenting with disease featuresfor the first time.

The most common features:
failure to thrive and delayed puberty (100%)
infertility
male infertility occurs in 98% due to failure of development of the vas deferens
Female subfertility secondary to viscid cervical secretions. (only 20% will be infertile)
Pancreatic insufficiency (very common, 85%)
diabetes mellitus: occurs in > 65% of patients by age 25
main manifestations => weight loss repeated respiratory infections and decline in lung function.
(Nb. Questions talking of a wheezy & chesty child may point towards CF, Ig deficiency or Asthma)
Calorie intake should not be restricted in CF patients, who are prone to malnutrition due to their pancreatic insufficiency.
Recurrent chest infections (40%)
malabsorption (30%): steatorrhoea, It is associated with pancreatic insufficiency, which is almost always present in adult patients
Constipation is common
hepatobiliary dysfunction (cholestasis)
due to Defective cystic fibrosis transmembrane regulator (CFTR) protein on bile duct epithelial cells
neonatal period (around 20%): meconium ileus, less commonly prolonged jaundice
other features (10%): liver disease

Other features of cystic fibrosis
short stature
rectal prolapse (due to bulky stools)
nasal polyps

While nasal polyps occur in adults secondary to recurrent episodes of rhinitis, nasal polyps in children should always raise the suspicion for cystic fibrosis.
Depletion of sodium, chloride and potassium due to excessive sweating, and secondary renal chloride retention, can result in presentation with dehydration and heat exhaustion in an otherwise apparently completely fit adult.

Pneumothorax is seen in up to 5% of patients over 10 years of age and approximately 50% recur.
Allergic bronchopulmonary aspergillosis (ABPA) in 1 in 6 adult CF patients. About 20%
Manifestations=> asthma symptoms, flitting opacities on chest X-ray, ↑↑eosinophil count, hyper-reactivity to skinprick test and ↑↑ plasma IgE.
Main treatment => high-dose corticosteroids initially, with a smaller maintenance dose.
Heart-lung transplantation
Moderately reduced body mass index (BMI) is an indication for transplantation. A severe reduction in BMI is a relative contraindication to transplantation because it is associated with reduced survival but it is not an absolute contraindication.
Distal intestinal obstruction syndrome :
Occurs in 10-20% of patients with cystic fibrosis and incidence increases with age.
About 80% of cases present for the first time in adults.
The pathogenesis is partially due to loss of CFTR function in the intestine which results in deregulation of chloride secretion from the crypts, bicarbonate secretion from Brunner's glands and sodium transport. This leads to the accumulation of viscous mucus and faecal material in the terminal ileum, caecum and ascending colon.

Diagnosis

Sweat test
patient's with CF have abnormally high sweat chloride
normal value < 40 mEq/l, CF indicated by > 60 mEq/l
99% of children with CF have sweat chloride > 70 and sodium levels > 60.
In normal children, sweat sodium is higher than chloride. The reversed ratio is another pointer to CF.
A negative sweat test is a sufficient evidence to exclude cystic fibrosis.
More than 60 mmol/L of chloride is diagnostic of CF when one or more other criteria are present.

Management

Management of cystic fibrosis involves a multidisciplinary approach
the most appropriate advice regarding his diet : High calorie and high fat with pancreatic enzyme supplementation for every meal (Previous texts have mentioned something else, but this seems to be the latest consensus.)

Key points

regular (at least twice daily) chest physiotherapy and postural drainage. Parents are usually taught to do this. Deep breathing exercises are also useful
high-calorie diet, including high fat intake*
vitamin supplementation
pancreatic enzyme supplements taken with meals
heart and lung transplant

*This is now the standard recommendation - previously high calorie, low-fat diets have been recommended to reduce the amount of steatorrhoea

Chest infections in cystic fibrosis:

bronchiectasis associated with CF frequently results in recurrent infections with Pseudomonas.

In cystic fibrosis, the airways become obstructed by thick mucus due to defective chloride secretion and increased sodium resorption. This leads to bacterial colonisation early in life.
The bacteria present depend on the age of the patient:

infants and young children become colonised by Staphylococcus aureus and then Haemophilus influenzae.
In teenagers, Pseudomonas aeruginosa colonisation occurs.
Other organisms which can cause infection include Streptococcus pneumoniae, Burkholderia cepacia (which confers a worse prognosis), Mycobacterium tuberculosis, other mycobacteria, Aspergillus fumigatus and viruses.
In the UK, antibiotics are usually given when:
the sputum becomes purulent,
pulmonary function deteriorates,
or the patient is unwell (e.g. weight loss).
In teenagers groups, Pseudomonal cover is needed and a combination of intravenous antibiotics is used to reduce the risk of resistance developing. The usual combination is ceftazidime and tobramycin, for two weeks.

Pseudomonas aeruginosa is the commonest colonising organism in patients with cystic fibrosis after the age of 10 years, with a reported prevalence of 40-80%.
Most colonising types of P. aeruginosa are sensitive to antibiotics at first, but over the years and in association with antibiotic treatment, multiple resistance to most antibiotics (except colistin) develops.

Burkholderia cepacia is seen in severe lung disease and is often associated with rapid deterioration.

The combination of piperacillin and tazobactam (Tazocin®) is indicated for the treatment of cystic fibrosis exacerbations.
The usual dose of Tazocin® for adults is 4.5 g every 8 hours, usually continued for 7-10 days.
Rash and fever are seen in association with this drug combination more often in patients with cystic fibrosis than in patients without cystic fibrosis.

Nebulised tobramycin for Pseudomonas colonisation of the lower respiratory tract*
*Nebulised tobramycin or gentamicin may be given when airway pathogens are resistant to oral antibiotics, or where the infection is difficult to control at home.
*Gentamicin can be used in place of tobramycin, but has a poorer pseudomonal cover and is associated with significant side effects (nephrotoxicity and ototoxicity).
Lung transplantation in cystic fibrosis
Indications for the treatment
Age under 60 years
The life expectancy of fewer than 18 months
No underlying cancer or serious systemic disease

Donor characteristics

The donor is matched for ABO grouping.
Rhesus blood group compatibility is not essential.
The donor should have had good cardiac and lung function
The donor should have been under the age of 40.
The chest of the donor should be slightly smaller than that of the recipient.
A double lung transplant is usually performed because of the risk of chronic infection in the remaining lung.

Prognosis: The median survival is now predicted to be at least 40 years for children born in the 1990s.
Median survival has increased significantly over the past 10 years and is now around 37 years.

"We need to accept that we won't always make the right decisions, that we'll screw up royally sometimes – understanding that failure is not the opposite of success, it's part of success."
– Arianna Huffington

Occupational lung diseases

Occupational asthma

Isocyanates are the most common cause of occupational asthma.

Serial peak flow measurements at work and home are used to detect occupational asthma.
Occupational asthma occurs more frequently in atopic persons and smokers.
Causes: Exposure to the following chemicals is associated with occupational asthma:
Isocyanates - the most common cause. Example occupations include spray painting and foam moulding using adhesives (used in the manufacture of foams/plastics)
platinum salts
other metals: Aluminium, Chrome, Manganese, Nickel, Zinc
soldering flux resin
glutaraldehyde (and other disinfectant and preservatives: Chlorhexidine, Formaldehyde)
flour
epoxy resins
proteolytic enzymes

Diagnosis

Patients may either present with concerns that chemicals at work are worsening their asthma or you may notice in the history that symptoms seem better at weekends / when away from work.
Serial measurements of peak expiratory flow are recommended at work and away from work. Recordings should be performed two hourly for four weeks or if this is not possible methacholine/histamine challenges can be undertaken after days at work and away from work.

Management

Referral should be made to a respiratory specialist for patients with suspected occupational asthma.
Reduction of further exposure to the allergen.
Affected individuals who continue to work in the occupation responsible for their disease can often reduce their exposure substantially by changing the pattern of their particular duties. An alternative is to use industrial respirators, which filter out 98-99% of respirable dust from the ambient air.
Corticosteroid

Extrinsic allergic alveolitis (EAA)

Saccharopolyspora rectivirgula causes farmer's lung, a type of EAA.
Aspergillus clavatus causes malt workers' lungs, a type of EAA.
Extrinsic allergic alveolitis (EAA, also known as hypersensitivity pneumonitis) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles.
It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase.
Despite its name, EAA is not allergic and therefore features associated with allergy and type I reactions do not tend to occur in EAA (ie wheeze, immediate symptoms, raised IgE, positive skin-prick test, eosinophilia of blood or sputum).
Examples
bird fanciers' lung: avian proteins
farmer's lung: spores of Saccharopolyspora rectivirgula (formerly Micropolyspora faeni) the commonest occupational hypersensitivity pneumonitis
Contaminated hay is the most common source of Saccharopolyspora rectivirgula caused by dust from mouldy hay contaminated with thermophilic Actinomyces bacteria
Basal crackles are the typical feature.
Serum precipitating antibodies to Saccharopolyspora rectivirgula is the most useful diagnostic test
precipitins to Saccharopolyspora rectivirgula or Thermoactinomyces Vulgaris are found in 75-100% of cases during an acute episode.
malt workers' lung: Aspergillus clavatus
mushroom workers' lung: thermophilic actinomycetes
maple bark stripper's lung: caused by Cryptostroma corticale
Penicillium species are responsible for respiratory disease in cheese and cork workers and are due to fungal contaminants of materials.

Presentation

acute: occur 4-8 hrs after exposure, SOB, dry cough, fever

chronic: exertional shortness of breath and pulmonary fibrosis (typically upper-lobe).
Investigation
Chest x-ray: upper/mid-zone fibrosis. nodular shadowing or ground glass appearances. Classically show diffuse air-space consolidation
Broncho alveolar lavage: lymphocytosis , eosinophilia
Blood: Circulating IgG precipitins. NO eosinophilia
confirmed by demonstration of precipitating antibodies (precipitins) in the patient's serum to the causal antigen.

Treatment:

Prednisolone
Symptoms may settle within 12 hours of removal of the antigen.
Optimal management is removal of exposure to the antigen, change of job plan

Byssinosis

Rare in UK, occurs in areas of cotton production, such as India.
Characteristic symptoms: shortness of breath, cough and chest tightness that begin on the first day of the working week and ease during the remainder of the working week.
It is thought to be due to endotoxin released by bacteria that are found in cotton dust.
Usually no chest X-ray changes.
The more severe changes noted in some patients might be related to associated asthma or cigarette smoking.

Pneumoconiosis

Due to deposition of coal dust in parenchyma and reaction to its presence.
Is an x ray diagnosis.
The types - simple/complicated - are diagnosed on x ray appearance.
Simple coal worker's pneumoconiosis causes no symptoms or physical signs, but it predisposes to progressive massive fibrosis
Coal-worker's pneumoconiosis is not associated with an increased risk of tuberculosis or lung cancer.

Categories: depends on chest x-ray appearance
Category 1 disease is the least severe, with fewer opacities and normal lung markings visible.
Category 2 pneumoconiosis is less severe, with several opacities but normal lung markings still visible;
Category 3 pneumoconiosis: chest X-ray reveals a large number of small round opacities within the lung fields, with almost complete obscuration of normal lung markings.

The relevance of the categories is the associated percentage progression to progressive massive fibrosis (category 1 virtually never, category 2 around 7%, category 3 around 30%).

Caplan's syndrome

Is the combination of rheumatoid arthritis with pneumoconiosis related to coal dust.
There is a rapid development of basal peripheral nodules, which can progress to severe pulmonary fibrosis.

Asbestos and the lung

Ship building, car manufacture, boiler making and plumbing industries are all associated with a risk of asbestos exposure.
Asbestos can cause a variety of lung diseases from benign pleural plaques to mesothelioma.
Pleural plaques
the most common form of asbestos-related lung disease
occur after a latent period of 20-40 years.
benign and do not undergo malignant change.
Pleural thickening
Asbestos exposure may cause diffuse pleural thickening in a similar pattern to that seen following an empyema or haemothorax.
The underlying pathophysiology is not fully understood.

Asbestosis (asbestos-related pulmonary fibrosis)
The latent period is typically 15-30 years.
The condition is slowly progressive
The severity of asbestosis is related to the length of exposure. This is in contrast to mesothelioma where even very limited exposure can cause disease.
Asbestosis typically causes lower lobe fibrosis.
As with other forms of lung fibrosis the most common symptoms are shortness of breath and reduced exercise tolerance.
Clubbing occurs in 43% of people with asbestosis.
A biopsy is not mandatory as the diagnosis can be made on clinical and radiological grounds.
The only management advice is to avoid further asbestos exposure and to stop smoking.
resistant to treatment with immunosuppressive therapy.
The risk of lung cancer is raised more than 50-fold in smokers with asbestos.

Mesothelioma

Mesothelioma is a malignant disease of the pleura. Crocidolite (blue) asbestos is the most dangerous form.
features
progressive shortness-of-breath
chest pain
pleural effusion
treatment
palliative chemotherapy
there is also a limited role for surgery and radiotherapy.
prognosis is very poor, with a median survival from diagnosis of 8-14 months.
Lung cancer

Asbestos exposure is a risk factor for lung cancer and also has a synergistic effect with cigarette smoke.

hard metal lung disease (Cobalt exposure)
Persons working in the hard metal industry are prone to develop a condition called hard metal lung disease.
A worker in the hard metal industry comes with progressive dyspnea. Chest X-ray shows diffuse interstitial fibrosis bilaterally. what is the typical cellular component found in the bronchoalveolar lavage (BAL) of this patient?
Giant cells
Pathological findings in lung biopsy include bronchiolitis and bizarre multinucleated giant cells in the alveoli. The pathological diagnosis is giant cell interstitial pneumonia (GIP).

Silicosis

Is a form of occupational lung disease caused by inhalation of crystalline silica dust, usually in the form of quartz.
It causes inflammation and scarring in the form of nodular lesions in the upper lobes of the lungs.
It is a type of pneumoconiosis
Risky jobs: Silicosis can affect anyone involved in quarrying, carving, mining, tunnelling, grinding or sand-blasting, if the dust generated contains quartz.

The history of significant exposure to stone dust, coupled with the relatively modest reduction in PEFR and changes on chest X-Ray, are pointers towards a diagnosis of silicosis. Pulmonary function testing normally reveals a mixed obstructive/restrictive picture. Smoking is likely to accelerate deterioration in his shortness of breath, and he should therefore be given every assistance to stop.

Classifications:

Acute silicosis:
The most severe form
develops a few weeks to 5 years after exposure
acquired after very heavy exposure over just a few months, patients become intensely breathless and die within months.
The X-ray shows appearances resembling pulmonary oedema.
Accelerated silicosis:
develops 5–10 years after first exposure
Less heavy exposure causes progressively less dramatic symptoms, progressive upper lobe fibrosis with slowly increasing exertional dyspnoea over several years
Simple nodular silicosis:
the most common type
resulting from long-term exposure (10 years or more) to relatively low concentrations of silica dust
Usually appearing 10–30 years after first exposure
radiographic nodular changes similar to coal worker's pneumoconiosis,

usually associated with exposure to dust containing 10-30% silica over a prolonged period.
In early disease, no signs or symptoms, but abnormalities may be detected by x-ray.
Chronic cough and exertional dyspnoea are common findings
Radiographically, chronic simple silicosis reveals a profusion of small (<10 mm in diameter) opacities, typically rounded, and predominating in the upper lung zones.

Simple nodular silicosis differs from coal worker's pneumoconiosis in that :
the lesions tend to be larger (3-5 mm)
and it is progressive even after dust exposure ceases
Silicosis is a risk factor for developing TB (silica is toxic to macrophages) Features fibrosing lung disease
'eggshell calcification of the hilar lymph nodes

Other occupational risks and cancer

Exposure to isocyanates is most likely associated with squamous-cell carcinoma of the bronchus.

Aromatic amines are associated with bladder carcinoma,
exposure to vinyl chloride is associated with angiosarcoma of the liver.

Churg-Strauss syndrome

Churg-Strauss syndrome is an ANCA associated small-medium vessel vasculitis.

Features

asthma
blood eosinophilia (e.g. > 10%)
paranasal sinusitis
mononeuritis multiplex
pANCA positive in 60%
Commonly associated with antimyeloperoxidase antibodies.
Rarely, it can cause ischaemic optic neuropathy, which presents with visual loss.
Leukotriene receptor antagonists may precipitate the disease

A diagnosis of Churg-Strauss syndrome requires four of the following features:
Asthma
Eosinophilia greater than 10%
Mononeuropathy or polyneuropathy
Paranasal sinus abnormality
Non-fixed pulmonary infiltrates visible on chest radiographs and
Blood vessels with extravascular eosinophils on biopsy.
It is diagnosed clinically, although a biopsy should be sought for pathological confirmation.

Skin biopsy reveals small-vessel arteriopathy with granuloma formation and is the diagnostic investigation of choice.

Treatment:

High-dose methylprednisolone, with or without cyclophosphamide is the treatment of choice
Prognosis:
Without treatment, the 5-year survival rate for Churg-Strauss syndrome is around 25%; with appropriate therapy this rises to over 60%.

Kartagener's syndrome

Kartagener's syndrome (also known as primary ciliary dyskinesia)
most frequently occurs in examinations due to its association with dextrocardia (e.g. 'quiet heart sounds', 'small volume complexes in lateral leads')

Pathogenesis

autosomal recessive mutation.
dynein arm defect results in immotile cilia
dynein is a protein found in Cilia and flagella of microtubule

Features

Dextrocardia or complete situs inversus
Situs inversus occurs in about half of people with Kartagener syndrome
bronchiectasis
recurrent sinusitis
male infertility and female subfertility (secondary to diminished sperm motility and defective ciliary action in the fallopian tubes)
Deafness
Hydrocephalus.

H/O recurrent chest infections, situs inversus, and sperm sample shows nonmotile spermatozoa. The cause of this condition is most likely a mutation in the genes for which protein? ↓ Dynein

Lung cancer: risk factors

Smoking
increases risk of lung ca by a factor of 10
Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a 10 * 5 = 50 times increased risk
Whilst many chemicals have been implicated in the development of lung cancer passive
smoking is the most likely cause.
Up to 15% of lung cancers in patients who do not smoke are thought to be caused by passive smoking

Other factors: (coal dust is not a risk factor

Lung cancer (types)

The most common types of lung cancer:
In the UK: squamous cell cancer (In the USA: Adenocarcinoma)
squamous: c. 35%
adenocarcinoma: c. 30%
small (oat) cell: c. 15%
large cell: c. 10%
other c. 5%
Other tumours
alveolar cell carcinoma: not related to smoking, ++sputum
bronchial adenoma: mostly carcinoid

Lung cancer: non-small cell

There are three main subtypes of non-small cell lung cancer:
1. Squamous cell cancer:
2. Adenocarcinoma:
3. Large cell lung carcinoma:

Squamous cell cancer

Typically central (Squamous= Sentral)
associated with:
parathyroid hormone-related protein (PTHrP) secretion → hypercalcaemia
strongly associated with finger clubbing
hypertrophic pulmonary osteoarthropathy (HPOA)
The presence of clubbing and tender wrists without synovitis makes pulmonary osteoarthropathy the most likely diagnosis.
It is usually associated with underlying carcinoma of the lung.
The most sensitive diagnostic investigation is isotope bone scan: increase in the uptake in long bones, around periarticular surfaces, and also mandible and scapulae.
Regression of the pain has been reported with successful resection of the tumour and after vagotomy.
Hyperthyroidism due to ectopic TSH
Cavitate (In 10% of cases)
Most squamous-cell carcinomas present as obstructive lesions, which can manifest as infection.
Life threatening haemoptysis is a medical emergency that requires prompt action.
Pulmonary angiography will identify the blood supply to the tumour and embolisation of this vessel(s) will immediately stem the bleeding.

Histology will show clusters of lightly stained cells, often associated with groups of partially keratinized, acidophilic cell clusters.
Pleomorphic cells in cluster with keratin pearls and intercellular bridges

Adenocarcinoma

Lung adenocarcinoma
Most common type in non-smokers
Peripheral lesion.
most common type of lung cancer in non-smokers, although the majority of patients who develop lung adenocarcinoma are smokers
Typically located on the lung periphery ↓ Normal bronchoscopy.
May associate with Gynaecomastia.
PET/CT scan offers the best imaging modality to determine **LN** involvement in bronchial adenocarcinoma
Histology will show: malignant cells more often arranged in small clusters with an **obvious lumen and duct-like structures.**
Mucin-containing tumor cells with glandular differentiation
Management of non-small cell lung cancer
Contraindications to lung cancer surgery include SVC obstruction, FEV < 1.5, Malignant pleural effusion, vocal cord paralysis.

Surgery

only 20% suitable for surgery
Stage I (cT1N0 and cT2N0) and stage II (cT1N1, cT2N1 and cT3N0) tumours should be considered operable.
Stage IIIA (cT3N1 and cT1-3N2) tumours have a low chance of being cured by surgery alone, but it can be used in combination with chemotherapy.
Stage IIIB and IV tumours considered inoperable.
mediastinoscopy performed prior to surgery as CT does not always show mediastinal lymph node involvement
The functional criteria for pneumonectomy are:
Forced expiratory volume in 1 second (FEV-1) of >1.5 litres
FEV-1 > 50% of the observed forced vital capacity, and
Normal partial pressure of arterial CO2 (Paco2) with the patient at rest
Prognosis after surgery is about 50-67% at 5 years with stage 1disease
Absolute contraindications for surgery include:
Patient refusal
FEV1 < 1.5 litres is considered a general cut-off point*
If the tumour necessitates a pneumonectomy, the post-bronchodilator FEV should be more than 2 litres.
However, if FEV1 < 1.5 for lobectomy or < 2.0 for pneumonectomy then some authorities advocate further lung function tests as operations may still go ahead based on the results
Metastases.
stage IIIb or IV (i.e. metastases present)
tumour near hilum
vocal cord paralysis (implies extracapsular spread to mediastinal L.N)
SVC obstruction
malignant pleural effusion (not just 'pleural effusion' (which may be reactive))
Most pleural effusions associated with lung carcinoma are due to the tumour (and results in classification as a T4 tumour).
Relative contraindications include:
Cell type: small cell carcinoma are usually inoperable

Poor respiratory reserve - FEV1 > 1.2l is necessary for lobectomy, and > 1.8l for pneumonectomy
Raised PaCO2 is a contraindication for surgery
Other disease - especially myocardial
surgery should be delayed until 6 weeks following myocardial infarct if possible.
Mediastinal involvement
Age - in patients over 70, surgery is usually inadvisable because the benefits are outweighed by operative morbidity and mortality.
Age over 80 alone is not a contraindication to lobectomy or wedge resection for stage I disease, but may be a contraindication to pneumonectomy.
Radiotherapy ↓ Curative or palliative
Radical radiotherapy is indicated for patients with stage I, II or III NSCLC who have good performance status (WHO 0, 1)
Sequential chemo-radiotherapy should be offered to patients with stage III NSCLC who are not suitable for surgery but are eligible for radical radiotherapy.
Chemotherapy and radical radiotherapy is the first choice treatment in eligible patients with stage IIIa non-small cell lung cancer (NSCLC).

Radical radiotherapy

Definition =>That is, radiotherapy with intention to cure using doses of at least 60 Gy.
Indication =>Patients with potentially operable tumours that are either too unfit for surgery or refuse surgery may be suitable for radical radiotherapy,
Benefit => using continuous hyperfractionated accelerated radiotherapy (CHART) can improve two year survival significantly from 20% to 29% compared with conventional radiotherapy1.
Contraindications =>
tumours larger than 4 cm
and poor pulmonary function (generally taken as FEV1 less than 50% predicted).
Malignant pleural effusion
Chemotherapy ↓ poor response Prognosis

Overall lung cancer survival is less than 15% at five years

Performance status

Assessing a patient's performance status is important when evaluating the most appropriate treatment options.
It is commonly used by cancer MDTs, but has a role in assessing patients with chronic illnesses including COPD.

WHO (Zubrod) Scale	Description
0	**Asymptomatic**
1	**Symptomatic but ambulatory (can carry out light work)**
2	**In bed less than 50% of the day. Unable to work but can live athome with some assistance**
3	**In bed more than 50% of the day (unable to care for self)**
4	**Bedridden**

Staging lung carcinoma

It is important to remember the criteria for staging carcinoma of the lung. TNM staging takes into account;
The size and position of the tumour (T)
Whether the cancer cells have spread into the lymph nodes (N)
Whether the tumour has spread anywhere else in the body - secondary cancer or metastases (M)
Computed tomographic (CT) scanning is recommended as a staging procedure. Where available, PET scanning may be superior, but there are a limited number of scanners in the UK.
CT can be performed with or without contrast enhancement, but Contrast enhancement makes it easier for inexperienced observers to interpret the CT.
Overall, preoperative CT staging has been shown to overstage or understage when compared with operative findings in 40% of patients. So biopsy is also needed.

SEVENTH EDITION OF THE TNM SYSTEM

The International Association for the Study of Lung Cancer (IASLC) developed a **SEVENTH EDITION OF THE TNM SYSTEM** in 2010 replaced earlier editions: as fellow

Primary tumor — (T)

T0 – No evidence of primary tumor.
Tis – Carcinoma in situ.
T1 – Tumor that is ≤3 cm
T1a: Tumor is ≤2 cm
T1b: Tumor is >2 cm, but ≤3 cm
T2 – Tumor that is >3 cm but ≤7 cm
T2a: Tumor is >3 cm, but ≤5 cm
T2b: Tumor is >5 cm, but ≤7 cm
T3 – Tumor that is >7 cm ; invades the chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium
T4 – Tumor of any size that invades the mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, or carina; or separate tumor nodule(s) located in a different lobe of the ipsilateral lung.

Regional lymph nodes — (N)

N0 – No regional lymph node involvement.
N1 – Involvement of ipsilateral intrapulmonary, peribronchial, or hilar lymph nodes.
N2 – Involvement of ipsilateral mediastinal or subcarinal lymph nodes.
N3 – Involvement of contralateral mediastinal or hilar lymph nodes.

Metastasis — (M)

M0 – No distant metastasis
M1a – Malignant pleural effusion, pericardial effusion, pleural nodules, or metastatic nodules in the contralateral lung
M1b – Distant (extrathoracic) metastasis

Carcinoid lung

Overview

Carcinoid tumours (so called argentafinomas as they take up silver) are
neuroendocrine cells
originate from Kulchitsky (K) cells in the lung
slow growing
smoking is **NOT** a risk factor

Incidence: Lung carcinoid accounts
1% of lung tumours
10% of carcinoid tumours.
typical age = 40-50 years
The incidence is equal between men and women.

Feature

Recurrent haemoptysis with segmental collapse on x-ray is a typical presentation of bronchial carcinoid.

Often asymptomatic
long history of cough,
Recurrent haemoptysis
Recurrent infections
carcinoid tumours ↓ (80-90%) develops in a bronchus ↓ bronchial obstruction ↓ lower respiratory tract infection.
Carcinoid syndrome (rare)
Associated conditions with carcinoid tumour in the lung
carcinoid syndrome (**rare**)
depends on associated liver metastases
occurs in less than 10% of patients with carcinoid tumours, but occurs most commonly in GIT tumours.
can secrete a number of vasoactive compounds (including serotonin and bradykinin), which result in:
bronchospasm
diarrhoea,
skin flushing and
right-sided valvular heart lesions.
ACTH secretion and subsequent Cushing's syndrome.
ectopic growth hormone-releasing hormone [GHRH] and subsequent acromegaly
multiple endocrine neoplasia (MEN) type 1 where pancreatic neuroendocrine tumours predominate.

Investigations:

The 'cherry-red' lesion is a typical finding of lung carcinoid.

CXR
often **centrally** located and not seen on CXR.
Usually occur in the major bronchi, 85% can be seen bronchoscopically.
most often located in the main bronchi, and occur most frequency in the right middle lobe.
A carcinoid tumour in the left lower lobe bronchus could cause distal collapse of the left lower lobe.

Bronchoscopy:

identifies up to 80% of carcinoid tumours in the main bronchi.
seen as a highly vascular 'cherry-like' tumour ('cherry red ball')
Biopsy is usually followed with brisk bleeding and should be done via rigid bronchoscopy.
The histological picture of granular eosinophilic staining of the cytoplasm, is highly suggestive of a carcinoid tumour.
Histologically, these tumors consist of compact nests of epithelial cells surrounded by neat, delicate connective tissue capsules.
histology might not be necessary prior to surgery if the clinical picture is typical.
Plasma chromograffin A is an effective screening test for carcinoid as it is very sensitive, but it is not specific.
24 hour urinary excretion of 5-hydroxyindoleacetic acid is more specific for the diagnosis, but false positives and negatives are present.
Scintigraphic imaging with labelled somatostatin increases the ability to diagnose a carcinoid tumour, but biopsy is required to confirm.

Management

surgical resection
A person with an isolated pulmonary carcinoid should be referred for
tumour resection,
histology might not be necessary prior to surgery if the clinical picture is typical.

Prognosis

if no metastases then 90% survival at 5 years

Small cell lung cancer

The presence of hyponatraemia strongly points towards a diagnosis of small cell lungcancer.

Also known as "oat-cell carcinoma"
Usually, central
arise from APUD* cells
*An acronym for
Amine - high amine content
Precursor **U**ptake - high uptake of amine precursors
Decarboxylase - high content of the enzyme decarboxylase

Features

ectopic ADH → hyponatraemia
ectopic ACTH → Cushing's syndrome
(not typical, hypertension, hyperglycaemia, hypokalaemia, alkalosis, hirsutism and muscle weakness are more common than buffalo hump etc.)
ACTH secretion can cause bilateral adrenal hyperplasia,
the high levels of cortisol can lead to hypokalaemic alkalosis
in case of chronic heavy smoker with chest infection + hyperglycaemia + ↓ K + ↑ HCO3**?**
Suspect SCLC with ectopic ACTH secretion.
But if with ↓Na and ↑K ↓ think of Adrenal metastasis ↓ MRI adrenals
Lambert-Eaton syndrome: antibodies to voltage gated calcium channels causing myasthenic like syndrome
Histologically, Small cell carcinoma has clusters of small, **basophilic cells** and surrounding areas of tissue necrosis.

Management

Surgery

patients with very early stage disease (T1-2a, N0, M0) are now considered for surgery.
usually metastatic disease by time of diagnosis. Surgery is therefore not recommended as first-line treatment in the UK.

Chemotherapy and radiotherapy

most patients with limited disease receive a combination of chemotherapy and radiotherapy. they are very sensitive to combination chemo-radiation. It is the **standard treatment in the UK.**
Because of the frequent presence of occult metastatic disease, chemotherapy is the cornerstone of treatment for patients with limited-stage small cell lung cancer.
The chemotherapy should be initiated immediately, whilst the radiotherapy is being planned,
radiotherapy should be started during either the first or second cycle of chemotherapy.
Current programmes yield overall objective response rates of 65% to 90% and complete response rates of 45% to 75%.
Patients who are not fit enough for concurrent chemoradiotherapy should be offered sequential chemo-radiation: 4 to 6 cycles of platinum-etoposide chemotherapy with consolidative radiotherapy for those who respond to chemotherapy.
patients with more extensive disease are offered palliative chemotherapy

Prognosis

Very poor and survival beyond two 2 years is exceptional

Adverse prognostic factors in small cell lung cancer:

Serum Na < 132 mmol/l
Weight loss > 10%
WHO performance status > 2
Alkaline phosphatase > 1.5 times upper limit of normal
LDH > 1.5 times upper limit of normal
Extensive disease (occurring outside one hemi-thorax and ipsilateral supraclavicular fossa nodes).

Bronchial Carcinoma

This also appears more commonly in the Exam paper than in patients.
20-30% of cases with bronchial carcinoma are of small (oat) cell type from endocrine K-cells (Kulchitsky) cells.
Primary bronchial cancer ↓ the tumour edge may have a fluffy or spiked appearance.
Paraneoplastic manifestations:
SIADH (5 - 10%)
ACTH (5 %)
ANP
The most appropriate tool to confirm the diagnosis of bronchial carcinoma is ↓
Bronchoscopy ± Trans bronchial biopsy (NOT CT-guided FNA biopsy).

Bronchoalveolar cell carcinoma

1% of all bronchial carcinomas.
classically presents with progressive breathlessness and the production of large amounts of sputum (bronchorrhoea).
The tumour spreads using the alveolar walls as a frame and the alveoli are often filled with mucin.

Superior vena cava obstruction (SVCO)

(SVCO) an oncological emergency caused by compression of the SVC.
most commonly associated with lung cancer.
Up to 4% of patients with lung cancer will develop SVCO at some point during their disease.
Both Non-small cell cancer and small cell malignancy may cause SVCO.
Up to 10% of SCLC will present with SVCO.
SVCO is much more likely to be associated with right sided lung lesion 4 times than with left sided lesions

Features

dyspnoea is the most common symptom
swelling of the face, neck and arms - conjunctival and periorbital oedema may be seen
headache
visual disturbance
pulseless jugular venous distension
may be associated with voice hoarseness
CXR is abnormal in around 85% of cases, mediastinal widening is common.

Causes

the most common cause ↓ Non-small cell lung cancer
common malignancies: small cell lung cancer, lymphoma
other malignancies: metastatic seminoma, Kaposi's sarcoma, breast cancer
aortic aneurysm
mediastinal fibrosis
Mediastinal goitre
SVC thrombosis

Below are the rates of SVC obstruction with different malignancies (UpToDate,2016)

Malignancy	Percent
Non-small cell lung cancer	50%
Small cell lung cancer	25%
Non-Hodgkin lymphoma	10%
Other malignancies	15%

Association:

Recurrent laryngeal nerve palsy (voice hoarseness): usually occurs with malignant tumour but can occur with aneurysm of aortic arch.
Horner's syndrome due to involvement of sympathetic chain.
elevated non-pulsatile jugular venous pressure (JVP)
Compression of vital structures can result in stridor and dysphagia.

Management

general: dexamethasone, balloon venoplasty, stenting
Corticosteroids are most useful where the cause of compression is an underlying haematological malignancy.
➢ SVCO: immediate management ↓ Dexamethasone IV + LMWH.
In 2004 NICE recommended considering **stenting** in the majority of cases of SVCO.
This is a minimally invasive procedure which **relieves symptoms quicker than chemotherapy or radiotherapy.**
Stenting is better than radiotherapy in terms of relief of symptoms.
Radiotherapy may be an option **later**. If radiotherapy is used initially then stenting becomes significantly more difficult due to local fibrosis.
Mediastinal radiotherapy leads to symptomatic relief in 80% of patients,

small cell: chemotherapy + radiotherapy
non-small cell: radiotherapy

Prognosis:

Median survival of lung cancer presenting with SVCO, even with treatment is five months.
Lymphoma has a better prognosis and will require specific chemotherapy ± radiotherapy.

Lung cancer: paraneoplastic features

Paraneoplastic features of lung cancer

Squamous cell: PTHrp, TSH, Clubbing, HPOA
Adenocarcinoma: Gynaecomastia
Small cell: ADH, ACTH, Lambert-Eaton syndrome
Bronchial carcinoma: SIADH, ACTH, ANP

Paraneoplastic syndromes are a result of antibody generation from or against malignant cells attacking normal tissue.
Both non-small cell and small cell lung cancers are associated with Paraneoplastic

syndromes, although they are more common with the small cell due to its neuroendocrine cell origin.

Squamous cell

Parathyroid hormone-related protein **(PTH-rp)** secretion causing hypercalcaemia occurs in about 15%
best treated with intravenous fluids and bisphosphonates
clubbing
hypertrophic pulmonary osteoarthropathy **(HPOA)**
(HPOA) is a proliferative peri-ostisis typically involves the long bones.
It is often painful.
hyperthyroidism due to ectopic **TSH**

Adenocarcinoma

Gynaecomastia
Bronchial carcinoma can presents with ataxia and bilateral Gynaecomastia .
It can be painful and may be associated with testicular atrophy.
Ataxia can occur as a result of a paraneoplastic cerebellar degeneration associated with the malignancy.

Small cell

ADH
Symptomatic hyponatraemia due to SIADH is treated with demeclocycline which induces nephrogenic diabetes insipidus leading to excretion of excess water.
ACTH
not typical, hypertension, hyperglycaemia, hypokalaemia, alkalosis and muscle weakness are more common than buffalo hump etc.
May manifest by Cushingoid facies and hyperpigmentation of the skin

Lambert-Eaton syndrome

70% occur in small cell carcinoma

is a pre-synaptic disorder of auto-antibody IgG directed against the pre-synaptic voltage gated calcium channel (VGCC) leading to impaired acetylcholine release.
characterised by:
Proximal muscle weakness (the cranial nerves and respiratory muscles are usually spared)
Depressed or absent tendon reflexes and
Autonomic features (for example, dry mouth, impotence, etc).
Weakness and fatiguability can be improved with guanidine hydrochloride
Unlike myasthenia gravis exercise is associated with increasing muscle strength and there is a negative response to Tensilon.
Electromyography is useful in confirming the diagnosis where repeated nerve stimulations cause a progressive increase in the size of the muscle action potential.

Cerebellar ataxia:

Paraneoplastic syndromes are a result of antibody generation from or against malignant cells attacking normal tissue.
Examples include antineuronal antibodies (anti-Hu, anti-Yo, anti-Ri) directed against the Purkinje cells of the cerebellum leading to the cerebellar syndrome (truncal ataxia).

To diagnose this ↓ Anti-Purkinje cell antibody levels.

Lung cancer: When to Refer?

Consider immediate referral for patients with:
signs of superior vena caval obstruction (swelling of the face/neck with fixed elevation of jugular venous pressure)
stridor
Refer urgently (for an appointment within 2 weeks) patients with:
persistent haemoptysis (in smokers or ex-smokers aged 40 years and older)
a chest X-ray suggestive of lung cancer (including pleural effusion and slowly resolving consolidation)
a normal chest X-ray where there is a high suspicion of lung cancer
a history of asbestos exposure and recent onset of chest pain, shortness of breath or unexplained systemic symptoms where a chest x-ray indicates pleural effusion, pleural mass or any suspicious lung pathology
Refer urgently for chest x-ray for patients with any of the following:
haemoptysis
unexplained or persistent (longer than 3 weeks): chest and/or shoulder pain, dyspnoea, weight loss, chest signs, hoarseness, finger clubbing, cervical or supraclavicular lymphadenopathy, cough, features suggestive of metastasis from a lung cancer (for example, secondaries in the brain, bone, liver, skin)
underlying chronic respiratory problems with unexplained changes in existing symptoms

Under NICE guidelines a hoarse voice for three weeks or more is an indication for investigation to exclude malignancy.

Lung cancer: stepwise investigations

X-ray :NICE guidelines recommend urgent chest radiograph in patients with haemoptysis or unexplained, persistent (>3 weeks) cough, chest or shoulder pain, dyspnoea, weight loss, chest signs, hoarseness, finger clubbing, cervical or supraclavicular lymphadenopathy. If this suggests lung carcinoma, patients should be referred urgently to the lung cancer multidisciplinary team (MDT).
CT: Patients should then be offered a contrast-enhanced CT chest (including the liver and adrenals). before bronchoscopy or any other biopsy procedure.
Biopsy: If the CT demonstrates a peripheral lung lesion, CT or ultrasound-guided transthoracic needle biopsy should be offered.
Endobronchial ultrasound guided biopsy is recommended for paratracheal and peri-bronchial intra-parenchymal lung lesions.
Enlarged mediastinal lymph nodes (>10 mm maximum short axis on CT) or other lesions should be biopsied in preference to the primary lesion if determination of stage affects treatment.
Sputum cytology is rarely indicated and should be reserved for the investigation of patients who have centrally placed masses and are unable to tolerate, or unwilling to undergo, bronchoscopy or other invasive tests.

Radiographical features of pulmonary tumours

No initial examination is complete without a **lateral film**.
normal X-ray of the chest does not exclude bronchial carcinoma as patients presenting with haemoptysis and a normal chest X-ray are sometimes found to have a central tumour on bronchoscopy.
The common appearance of a tumour arising from the main central airways (70% of all cases) is **enlargement of one or other hilum**.
Consolidation and collapse distal to the tumour might have occurred.
Collapse of the left lower lobe is often hard to identify, as is a tumour situated behind the heart.
Apically located masses or superior sulcus tumours (Pancoast tumours) can be misdiagnosed as pleural caps, and patients often have a long history of pain in the distribution of the brachial nerve roots.
Loss of the head of the first, second or third rib is not unusual.
The mediastinum might be widened by enlarged nodes.
Involvement of the phrenic nerve can lead to paralysis and elevation of the hemidiaphragm, which then moves paradoxically on sniffing.
Spread of tumour from mediastinal nodes peripherally along the lymphatics gives the characteristic appearance of lymphangitis carcinomatosa - bilateral hilar enlargement with streaky shadows fanning out into the lung fields on either side.
Pleural effusion: either by Tumour spread to the pleura **or** secondary to infection beyond obstruction caused by a central tumour.
Rarely, localised obstructive emphysema is observed.
PET in lung cancer assessment
Positron-emission tomography (PET) would determine whether there are distant metastases and is performed after the CT.
Routine imaging to screen for distant metastases is not required for every case of suspected NSCLC. Imaging for metastatic disease should be symptom-focused or CT-directed
For example in a patient with operable non-small-cell lung cancer, if CT has shown enlarged mediastinal nodes , he needs further assessment of his mediastinal nodes prior to surgery, because CT is not particularly good for assessing whether enlarged

nodes are inflammatory or malignant. and this can be done with mediastinoscopy or a positron-emission tomography (PET) scan.
In a PET scan radiolabeled glucose is injected peripherally and is taken up by metabolically active tissues, such as the brain and any cancer. It would show metastases from the primary cancer.

Radiological signs:

An endobronchial lesion commonly leads to partial or complete **atelectasis** and this is the commonest sign of bronchogenic carcinoma.
Bronchial stenosis and post-stenotic changes are commonly seen because most non-small-cell carcinomas demonstrate intraluminal growth. Narrowing of the main bronchi or a complete cut-off can be identified on chest Xrays.
Complete endobronchial obstruction can sometimes produce distal mucoid impaction, which can be visible on plain chest X-rays as a tubular or branching opacity. The opacity can contain air bronchograms and air alveolograms. This presentation is often seen with adenocarcinoma and bronchoalveolar carcinoma.

Mediastinal masses

Anterior/superior mediastinum may relate to the thymus, thyroid.
Inferior or middle mediastinal masses relate to the aorta, lungs, hilar lymph nodes, oesophagus and heart.
Posterior mediastinal masses may relate to the nerves and vertebrae.

Lung metastases

Metastatic carcinoma is the most common malignant tumour found in the lung
Malignant metastases to the lung can present as a solitary enlarging nodule, as multiple nodules or with diffuse lymphatic involvement.

Solitary metastases

represents some 10% of round lesions in general, but some 70% of round lesions in patients with a known malignancy.
Colorectal cancer is reported to be the commonest tumour of origin.
A diagnosis can usually be secured by percutaneous computed tomography- (CT-) guided biopsy.
In general, the longer the interval between resection of the primary tumour and the appearance of the metastases, the better the prognosis.

Multiple metastases

Range in size and number, from cannon balls to miliary shadowing, and can be accompanied by hilar lymphadenopathy or pleural effusion.
Breast, colon, renal and lung primaries are the commonest underlying tumours.
A diagnosis might be made on the basis of cytology or histology (from pleura, lung or sputum).
Solitary or multiple Kaposi's sarcoma:
Is a feature of AIDS, and can involve the bronchi and pleura as well as lung tissue.

Lymphangitis carcinomatosa:

Most commonly due to breast and primary lung tumours (usually adenocarcinomas).
Patients can be asymptomatic when the disease is first suspected on the basis of an X-ray showing diffusely increased interstitial markings accompanied by Kerley B lines, hilar lymphadenopathy or pleural effusion.
Although the diagnosis can be established by cytology from sputum or pleural fluid, it often requires a bronchoscopic or transbronchial lung biopsy.

Later, progressive and severe breathlessness with hypoxaemia often develops, and patients require vigorous palliative relief with opiates and oxygen.

Bronchial metastases

Not visible on a plain chest X-ray - diagnosis requires bronchoscopy.
Present with haemoptysis, effectively controlled by radiotherapy.
Renal carcinoma and malignant melanoma are recorded cause

Pancoast tumour:

a neoplasm of the apex of the lung that typically invades the chest wall and brachial plexus and is causing Horner's syndrome (ptosis and constriction of the pupil).
The tumour causes pain in the C8 and T1 distribution and Horner's syndrome.
It may cause small muscle wasting of the hands and erosion of the first rib.

Lung fibrosis

Fibrosis predominately affects the upper zones
extrinsic allergic alveolitis
coal worker's pneumoconiosis/progressive massive fibrosis
silicosis (Silica is found in coal dust)
sarcoidosis
ankylosing spondylitis (rare)
histiocytosis:
(Pentalaminar X bodies (Birbeck granules) found on bronchoalveolar lavage (BAL) are diagnostic)
tuberculosis
Allergic bronchopulmonary aspergillosis and farmers lung
Radiation
Fibrosis predominately affects the lower zones
cryptogenic fibrosing alveolitis (the more common cause)
most connective tissue disorders (except ankylosing spondylitis)
drug-induced: amiodarone, bleomycin, methotrexate
asbestosis

Idiopathic pulmonary fibrosis

Idiopathic pulmonary fibrosis (IPF, previously termed cryptogenic fibrosing alveolitis) is a chronic lung condition characterised by progressive fibrosis of the interstitium of the lungs.
Whilst there are many causes of lung fibrosis (e.g. medications, connective tissue disease,
asbestos) the term IPF is reserved when no underlying cause exists.
IPF is typically seen in patients aged 50-70 years and is twice as common in men.

Features

progressive exertional dyspnoea :
bibasal crackles on auscultation
dry cough
Clubbing occurs in two-thirds of cases.

Diagnosis

spirometry: classically a restrictive picture (FEV1 normal/decreased, FVC decreased, FEV1/FVC increased)
impaired gas exchange: reduced transfer factor (TLCO)
imaging: bilateral interstitial shadowing (typically small, irregular, peripheral opacities - 'ground-glass' - later progressing to 'honeycombing') may be seen on a chest x-ray but **high-resolution CT scanning is the investigation of choice** and required to make a diagnosis of IPF.
The first chest x-ray findings develops → small, peripheral opacities in the lower zones (The classic finding =>reticular opacities predominantly in the bases)
The late chest x-ray findings develops → Honeycombing
ANA positive in 30%, rheumatoid factor positive in 10% but this does not necessarily mean that the fibrosis is secondary to a connective tissue disease. Titres are usually low.
Arterial oxygen desaturation on exercise is an early feature and this is reflected in widening of the alveolar-arterial (a-a) gradient on exercise.
IPF lungs are stiff, ie poorly compliant, and therefore if compliance is low then **elastic recoil will be high** as the two are inversely related.

Management

pulmonary rehabilitation
pirfenidone (an antifibrotic agent) may be useful in selected patients . Pirfenidone reduces the risk of disease progression by 30 % and has been approved by NICE for use in mild-moderate disease (FVC 50-80 % predicted). The precise mechanism of action of Pirfenidone is unknown but includes antifibrotic, anti-inflammatory and antioxidant effects.
many patients will require supplementary oxygen and eventually a lung transplant
Treatment of idiopathic pulmonary fibrosis with immunosuppression has been shown by meta-analysis to have no benefit. N-acetyl cysteine, Nintedanib and Co-trimoxazole have all shown possible benefit in preliminary trials with the further investigation ongoing.
only 20% of patients may be steroid responsive (1 in 5)

Prognosis

poor, average life expectancy is around 3-4 years
People with idiopathic pulmonary fibrosis have a 7- to 14-fold increased risk of developing lung cancer.

Idiopathic interstitial pneumonitis (IIP).

IIP is further subdivided into:
Usual interstitial pneumonia and
Non-usual interstitial pneumonitis.

Usual interstitial pneumonia (UIP)

((previously known as idiopathic pulmonary fibrosis, or cryptogenic fibrosing alveolitis)
causes 70% of IIP
typically found in an older population
characterised by gradual onset with acute exacerbations.
It is worse in smokers.
Diagnosis: typical HRCT findings =>Reticular abnormalities, honeycombing and traction bronchiectasis.
Treatment: UIP has a poor response to steroids and immunosuppressants.
Prognosis: the median survival is 2 - 3 years post-diagnosis.
Non-usual interstitial pneumonitis (non-UIP):
Contains :
Non-specific interstitial pneumonia (NSIP): is the most common non-UIP
Cryptogenic organising pneumonia (COP): is subacute and tends to cause patchy consolidation and/or nodules on CT scans.
Desquamative interstitial pneumonia (DIP); is a form of severe RB-ILD.
Respiratory bronchiolitis - interstitial lung disease (RB-ILD
On CT there is typically ground glass appearance and there is better steroid responsiveness when compared to UIP, with improved survival.

Progressive massive fibrosis PMF:

It is due to exposure to dust of high silicon content and hence PMF is more likely with higher silicon exposure than in simple coal worker's lung.
Is diagnosed by chest x-ray as round masses, several centimetres in diameter, sometimesup to 10 cm usually in the upper lobes. They may have necrotic centres. In silicosis a more
accurate term is 'conglomerate nodules'
There are also emphysematous changes. There is a mixed obstructive and restrictive lung defect with a reduced transfer factor. Rheumatoid factors and antinuclear antibodies areoften positive.
There is usually a history of dust inhalation (eg coal dust), and. PMF can progress rapidly, even in the absence of further dust exposure, leading to respiratory failure and eventually death.
An unusual, but the **pathognomonic symptom** is melanopsin -the expectoration of theblack contents of a cavitated lesion.
Category 2 pneumoconiosis progresses to PMF in around 7% of cases. The rate of progression of category 3 pneumoconiosis is much higher, at around 30%.

Respiratory manifestations of rheumatoid arthritis

Methotrexate-induced pneumonitis usually occurs within 4 months of starting the drug. A CT scan would show pulmonary infiltrates.
A variety of respiratory problems may be seen in patients with rheumatoid arthritis:
pulmonary fibrosis
found in up to 60% of patients with rheumatoid arthritis, but chest X-ray changes are seen in only 5%.
Interstitial fibrosis - occurs in up to 20% of patients with rheumatoid arthritis
pleural effusion
pulmonary nodules

bronchiolitis obliterans ↓ (spirometry reveals an obstructive picture)
complications of drug therapy e.g. methotrexate pneumonitis (Acute interstitial pneumonitis is associated with methotrexate).
Methotrexate is a recognised cause of pulmonary fibrosis. However, it is sometimes used in the treatment of idiopathic pulmonary fibrosis as a steroid-sparing agent.
pleurisy
Caplan's syndrome - massive fibrotic nodules with occupational coal dust exposure infection (possibly atypical) secondary to immunosuppression
Organising pneumonia: can occur in rheumatoid arthritis, with fever, dyspnoea and multifocal consolidation. This response dramatically to steroids.
Rheumatoid respiratory nodules:
Commonly associated with the disease.
Associated with increased risk of respiratory tract infection.
CXR - Nodular changes
If the appearance on chest X-ray has not changed over long times **(from previousCXR)**, no intervention is required, only observation.
They are typically benign but can lead to pleural effusion, pneumothorax, haemoptysis, secondary infection, and bronchopulmonary fistula.

Bronchiolitis obliterans (BO)

'Bronchiolitis obliterans' is the term used to describe fibrous scarring of the small airways, characterized by fixed airway obstruction.
the mechanism involves inflammation that results in scar tissue formation.
submucosal and peribronchiolar inflammation and fibrosis **without any intraluminal granulation tissue**
OB should not be confused with bronchiolitis obliterans organising pneumonia (BOOP),a completely different disease.

Causes

Inhalation of toxic fumes
Exposure to mineral dust
Respiratory infections: Viral, Mycoplasma, Legionella
post-transplantation: Bone marrow, heart-lung or lung transplantation
BO is seen as early as 3 months post-transplant and is responsible for over 50% of deaths after the first year.
Connective tissue disorder: **Rheumatoid arthritis** or SLE
rheumatoid arthritis is considered the commonest connective tissue disease to be associated with obliterative bronchiolitis
Penicillamine treatment
inflammatory bowel disease
Idiopathic obliterative bronchiolitis disorder is **rare**

Feature

dry cough and dyspnoea.
wheeze might be audible.

Investigations

HRCT: there are often sharply defined, areas of decreased lung attenuation associated withvessels of decreased calibre. These changes represent a combination of air trappingand oligaemia. This combination can give a mosaic attenuation pattern.
air trapping
thickening in the airway and haziness in the lungs.

spirometry
a mixed obstructive/restrictive picture would be seen.
Inflammation in the small distal airways leads to obstructive spirometry .
Air trapping can occur, which leads to increased lung volumes.
Rheumatoid serology often worsens with the onset of bronchiolitis obliterans.
The chest X-ray findings can vary from normal to a reticular or reticulonodular pattern.
lung biopsy
The diagnosis can be confirmed by lung biopsy.
Histologically there is a mural concentric narrowing of the lumina of the bronchioles.
Transthoracic lung biopsies are preferable for diagnosis of constrictive BO comparedto transbronchial biopsies

Differential Diagnosis

Bronchiolitis obliterans is often misdiagnosed as asthma, chronic bronchitis, emphysema or pneumonia.

Treatment

Patients rarely respond to steroids and the prognosis is poor.
This disease is irreversible and severe cases often require a lung transplant

Drugs causing lung fibrosis

Causes

Cardiac drugs: amiodarone, hydralazine, tocainide
cytotoxic agents: busulphan, bleomycin cyclophosphamide, carmustine , leflunomide
anti-rheumatoid drugs: methotrexate, sulfasalazine, gold
antibiotics: nitrofurantoin
ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide).
Opiates: e.g. heroin abuse

Sulphasalazine pulmonary toxicity

Is rare, but is increasingly recognised.
Typically presents with new-onset dyspnoea and pulmonary infiltrates visible on chest radiograph.
There may be peripheral blood eosinophilia.
Histology most commonly demonstrates an eosinophilic pneumonia with interstitial inflammation and fibrosis.
Drug withdrawal is standard treatment, with or without the addition of corticosteroids.

Penicillamine

is associated with pulmonary toxicity in the form of diffuse alveolar damage, hypersensitivity pneumonitis and obliterative bronchitis.
It does not cause pulmonary fibrosis however, and D-penicillamine has actually beenshown to stabilse pulmonary fibrosis in the setting of systemic sclerosis.

Cyclophosphamide-induced lung fibrosis:

is rare
most likely occur in patients who have had concomitant pulmonary radiation therapy orhave taken other drugs associated with pulmonary toxicity.
The disorder usually occurs in patients who have been taking low doses for relatively prolonged periods (over six months) and presents several years after cessation of the drug and
hence the deterioration of symptoms with time.

The diagnosis is clinical. Chest X-ray reveals reticulonodular shadowing of the **upper zones**. Lung function tests demonstrate a restrictive lung defect. Lung biopsy is not helpful.
Cyclophosphamide *per se* is not toxic to the lungs; however, it is metabolized in the liverto toxic metabolites such as hydroxycyclophosphamide, acrolein and phosphoramide mustard, which are responsible for pulmonary damage.
Genetic factors may play a role in determining which individuals develop pulmonary fibrosis after exposure to the drug.
Cyclophosphamide therapy can also result in an acute pneumonitis during treatment withthe drug that causes cough, dyspnoea, hypoxia and bilateral nodular opacities **in the upper zones** of the lung.
Acute cyclophosphamideinduced pneumonitis responds to cessation of the drug and corticosteroid therapy.

Pulmonary disorder associated with inflammatory bowel disease

Alveolitis**:**

Restrictive defect.
A clinical picture similar to cryptogenic fibrosing alveolitis,
responsive to steroids,
Seen more often in patients with Crohn's, rather than ulcerative colitis.
Bronchiectasis: lower zone signs would be more prevalent.
Bronchiolitis obliterans: mixed obstructive/restrictive picture would be seen.

Lung disease in systemic sclerosis => Fibrosing alveolitis

History

Lung disease is sometimes the first manifestation of systemic sclerosis,
dyspnoea occurs in around 55% of patients.
Cough is a less frequently reported symptom, but when it occurs it is dry and non-productive.
There is often a history of Raynaud’s phenomenon..
Clinical findings
Digital clubbing is rare because of the poor vasculature of the digits.
Fine crackles are heard at the bases and are of a 'Velcro' character.
Lung fibrosis occurs more commonly in patients with the Scl 70, anti-DNA topoisomeraseautoantibody.
Chest X-ray series have identified diffuse lung disease in up to 67% of patients.
Oesophageal dilatation may be seen on chest X-ray and is almost universally present onhigh-resolution computed tomography.

Cricoarytenoid arthritis and stridor

This is seen in up to 75% of patients with rheumatoid arthritis.
It can cause sore throat, hoarse voice and stridor, but is often asymptomatic.
symptoms can rapidly worsen in the postoperative period.

The flow-volume loop can be abnormal, as can direct laryngoscopy and high-resolution CT of the larynx.
Patients can need urgent tracheostomy and steroids, both orally and via joint injection.

Post-extubation stridor (PES)

PES is a frequent complication of intubation, occurring in 2-16% of cases.
It is caused by laryngeal oedema that results from damage to the mucosa of the larynx.
Mucosal damage is caused by pressure and ischaemia resulting in an inflammatory response.
Laryngeal oedema, in severe cases, can lead to acute respiratory compromise necessitating emergency re-intubation.

Risk factors for PES include:

Female gender: may be due to the female mucous membrane being less resistant to trauma and thinner than that in men.
Intubation >36 hours.
Excessive cuff pressure.
Large tube size.
Tracheal infection.

Obstructive sleep apnoea/hypopnoea syndrome

Sleep apnoea is characterised by cessation of breathing during sleep.
This causes extreme restlessness with frequent respiratory pauses during night sleep.
Consequently, patients report daytime drowsiness and irritability. Affects 1-2% of the population.

Pathophysiology

Respiratory muscle activity is reduced during sleep, especially during rapid eye movement (REM) sleep, when the diaphragm is the only active muscle. Apnoea occurs when the sucked-back tongue closes the airway at the back of the throat.
When awake, this tendency is overcome by the action of the opening muscles of the higher airway, but these become hypotonic during sleep. Partial narrowing causes snoring, while critical narrowing leads to sleep apnoea results in hypoxia and an increased respiratory-effort stimulus to overcome the obstruction.
The combination of the hypoxia and increased effort awakens the patient, but these awakenings are so brief that the patient remains unaware of them. Ultimately, the conditionresults in sleep deprivation, especially REM sleep, with consequent daytime sleepiness andimpaired intellectual performance.

Sleep apnoea, causes include obesity and macroglossia.

The Sleep Heart Health Study showed that when these two conditions do coexist, this is the resultof chance alone.

Associations and Predisposing factors

obesity
macroglossia: acromegaly, hypothyroidism, amyloidosis

large tonsils
Marfan's syndrome
Small pharyngeal opening
Coexisting chronic obstructive pulmonary disease
Myxedema
micrognathia/retrognathia.
Sedatives such as alcohol.
small or set-back mandible
Collar size greater than (17 inches) 43 cm is strongly associated. **Neck size is the best predictor of obstructive sleep apnoea (OSA)**.
Consequence:
The dominant symptom is hypersomnolence (sleepiness).Other more common symptoms include:
Apparent personality changes
Witnessed apneas, and
True nocturnal polyuria.
Reduced libido and erectile dysfunction is less common.
daytime somnolence
hypertension
Sleep apnoea is an independent risk factor for stroke, Sudden death (and death from allcauses), and is associated with hypertension, impaired glucose tolerance (IGT) and insulin resistance.

Problems linked to sleep apnoea include hypertension and hyperglycaemia.

These patients are insulin-resistant and have an increased long-term risk of developing type 2diabetes due to obesity.
SIGN guidelines for the diagnosis and management of patients with OSAHS were published in2003

Assessment of sleepiness

Epworth Sleepiness Scale - questionnaire completed by patient +/- partner
Multiple Sleep Latency Test (MSLT) - measures the time to fall asleep in a dark room (usingEEG criteria)

Diagnostic tests

Sleep studies - ranging from monitoring of pulse oximetry at night to full polysomnography where a wide variety of physiological factors are measured including EEG, respiratory airflow, thoraco-abdominal movement, snoring and pulse oximetry
The diagnosis is established by polygraphic recording of sleep which shows periods (at least 30 of 10 or more seconds' duration in seven hours of sleep) of apnoea associated witha fall in arterial oxygen saturation.
full polysomnographic studies are the most conclusive. The diagnosis is confirmed if there are more than 15 apnoea or hypopnoea episodes in any 1 hour of sleep.
The severity of obstructive sleep apnoea/hypopnoea syndrome is dependent on the patients symptoms but generally an apnoea/ hypopnoea index (AHI) of 4-14 is consideredmild, 15-30 moderate and >30 severe.

Management

Weight loss. first-line ,the definitive management
CPAP is first line for moderate or severe OSAHS

CPAP (continuous positive pressure airways ventilation), is the most appropriate initial andquickest management which acts as a splint to keep the airway open, leading to a normal night's sleep.
Intra-oral devices (e.g. mandibular advancement) may be used if CPAP is not tolerated orfor patients with mild OSAHS where there is no daytime sleepiness.
limited evidence to support use of pharmacological agents
Modafinil is a drug that is licensed for excessive daytime sleepiness in people with OSA treated with CPAP, as well as for narcolepsy.

BiPAP (bilevel positive airways pressure ventilation) is used if people are in respiratory failure: although this is rare with OSA alone, it can occur if they have an associated problem, such as obesity hypoventilation or COPD.

Pneumothorax (British Thoracic Society (BTS) guidelines 2010)

A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is.

Clinical features include:

Sudden onset of chest pain, sometimes radiating to the shoulder
Dyspnoea (may not be a dominant feature)
Dry cough.
Left-sided pneumothoraces may be associated with a clicking sound synchronouswith the heart-beat and may occasionally be audible to the patient.
Young adult males, often tall and slim, are frequently affected by spontaneous pneumothorax.

Investigations

If the history and examination are suggestive of a pneumothorax and the patient being relativelystable, not in extremis (tension pneumothorax not suggested), the most appropriate first step would be → confirmation with chest x ray.

Questions sometimes discuss the size of the pneumothorax in percentage terms rather than giving the interpleural distance.
A 50% pneumothorax is likely to have a rim of > 3cm.
A pneumothorax of 20% is therefore within the 2 cm limit
As a very general rule of thumb:

Average interpleural distance	Approximate size of pneumothorax
0.5 cm	**10%**
1 cm	**15 %**
2 cm	**30%**
3 cm	**45%**
4 cm	**60%**

The next investigation to investigate the underlying cause of recurrent pneumothorax:

A CT scan is non-invasive and would therefore be a logical next step in elucidating any abnormality which may predispose to pneumothorax.
If CT not help in pointing to a structural abnormality, and a further episode was to occur, then video assisted thoracoscopy would be considered.
Ultrasound scanning is mainly used in the diagnosis and management of pneumothorax in the trauma setting.

Primary pneumothorax

Definition**:** Spontaneous primary pneumothorax is defined as:
age less than 50-years-old
no significant smoking history, and
no evidence of underlying lung disease.
Caused by the rupture of apical pleural blebs.

Management

if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
otherwise aspiration should be attempted
if this fails (defined as > 2 cm or still short of breath) then a chest drain should be inserted
patients should be advised to avoid smoking to reduce the risk of further episodes - the lifetime risk of developing a pneumothorax in healthy smoking men is around 10% compared with around 0.1% in non-smoking men
if **following aspiration** the rim of air is < 2cm and the breathing has improved then discharge should be considered with outpatient review.
Asthmatics should be treated as a secondary

Secondary pneumothorax**:** Recommendations include:
if the patient is > 50 years old and the rim of air is > 2cm and/or the patient is short of breath then a chest drain should be inserted.
Insert a small bore chest drain (8-14 FG) and attach to an underwater seal drain
otherwise aspiration should be attempted if the rim of air is between 1-2cm. If aspiration fails (i.e. pneumothorax is still greater than 1cm a chest drain should be inserted.
All patients should be admitted for at least 24 hours
if the pneumothorax is less the 1cm then the BTS guidelines suggest giving oxygen and admitting for 24 hours. Supplemental oxygen accelerates reabsorption of air by a factor of four
if the patient is very dyspneoic a drain should be inserted.even though the pneumothorax is small (< 2cm).
All patients should be advised to avoid smoking to reduce the risk of further episodes - the lifetime risk of developing a pneumothorax in healthy smoking men is around 10% compared with around 0.1% in non-smoking men.

Iatrogenic pneumothorax:

less likelihood of recurrence than spontaneous pneumothorax
majority will resolve with observation, if treatment is required then aspiration should be used
ventilated patients need chest drains, as may some patients with COPD

Tension pneumothorax

should be suspected in people on mechanical ventilators or nasal non-invasive ventilation who suddenly deteriorate or develop EMD arrest, and is frequently missed in the intensive care unit setting.
Treatment:
needle thoracocentesis
Advanced Trauma Life Support (ATLS) guidelines recommend the use of a 3- 6-cm-long cannula to perform needle thoracocentesis.
However, in 57% of patients with tension pneumothorax the thickness of the chest wall has been found to be greater than 3 cm.
It is therefore recommended that a cannula length of at least 4.5 cm should be used.
The cannula should be left in place until bubbling is confirmed in the underwater-seal system to confirm proper function of the intercostal tube.

Chest drains for pneumothorax

Insertion of a small bore chest drain using a Seldinger technique in the mid-axillary line
The most appropriate point for chest drain insertion is in the 'safe triangle', in the mid-axillary line.
Scarring from insertion is less obvious than in the second intercostal space and mid-clavicular line, particularly important in women.
insert 14F drain immediately above a rib margin
When the patient coughs, nothing happens. When he breathes in and out, the fluid in the tube moves up and down that means ↓ Air is no longer draining from the pleural space, but the drain is still working.
(The fluid level rising and falling in the drain (swinging) shows that it is still in contact with the pleural space and the fluid level is moving with respiration).
Air is not bubbling out of the drain when the patient coughs because the air has stopped draining from the pleural space and the lung has re-inflated.
If a drain does not bubble or swing, then it is blocked or kinked and is not working.
With a simple pneumothorax, there would be minimal fluid drainage from the chest.
Suction is necessary if the drain is still bubbling but the lung has not fully re-inflated on the chest X-ray.

After chest drain if pneumothorax fails to re-expand or if there is a persistent air leak (bubbling present) after 48 hours, then you should ↓ refer the patient to a respiratory specialist because negative suction might be required.
The normal intrapleural pressure is -3.4 cm H2O during expiration, rising to -8 cmH2O during inspiration**. Negative suction should be started at -10 to -20 cmH2O (-1 to -2 kPa**
= -7.5 to -15 mmHg) using a high-volume/low-pressure suction system.
If high-volume/high-pressure suction is used, then high-airflow suction might be generated, which can lead to air stealing, hypoxaemia and/or the persistence of air leaks.
If appropriate suction fails to result in adequate re-expansion by 5-7 days in patients without pre-existing lung disease (earlier if there is lung disease), then **↓ referral to a thoracic surgeon is indicated.**
If a repeat chest X-ray reveals a persistent pneumothorax despite low-pressure, large-volume suction. You confirm on examination that the chest drain appears to have remained in position and is bubbling ↓ **Cardiothoracic surgical referral**

This patient appears to have developed a **bronchopleural fistula**, as evidenced by failure of the lung to re-inflate despite the drain remaining in place for 48 h and low-pressure suction being deployed.

Video assisted thoracoscopic surgery is indicated in:
Second ipsilateral pneumothorax
Bilateral spontaneous pneumothorax
Spontaneous haemothorax
Persistent air leak (more than five to seven days of drainage)
Certain occupations, for example, pilots or divers.
Chemical pleurodesis through the chest drain: is used in older patients with recurrent pneumothorax, where surgery would be high risk. Failure rates can be 10-20%.

Fitness to fly

Air travel is acceptable once the pneumothorax has fully resolved.
CAA suggest patients may travel 2 weeks after successful drainage if there is no residual air.
The British Thoracic Society now recommend **1 week post check x-ray**.
However, the British Thoracic Society emphasises that the recurrence risk only significantly falls after 1 year, and therefore in the absence of a definitive surgical procedure patients might wish to defer travel until then.

Diving

The British Thoracic Society (BTS) guidelines state: 'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'

Pleural effusion (British Thoracic Society (BTS) produced guidelines in 2010)

Exudate (> 30g/L protein)	Transudate (< 30g/L protein)
• **infection: pneumonia, TB, sub-phrenic abscess** • **connective tissue disease: RA, SLE** • **neoplasia: lung cancer, mesothelioma, metastases** • **pancreatitis** • **pulmonary embolism** • **Dressler's syndrome** • **yellow nail syndrome**	• **heart failure** • **hypoalbuminaemia** ➢ **liver disease,** ➢ **nephrotic syndrome,** ➢ **malabsorption** • **hypothyroidism** • **Meigs' syndrome**

Investigation

Imaging
Posterior-anterior (PA) chest x-rays should be performed in all patients
ultrasound is recommended: it increases the likelihood of successful pleural aspiration and is sensitive for detecting pleural fluid septations
Patients with cytology negative exudative effusions
Local anaesthetic thoracoscopy has a high yield and is now the investigation of choice in patients with cytology negative exudative effusions.
Pleural aspiration

as above, ultrasound is recommended to reduce the complication rate
a 21G needle and 50ml syringe should be used
fluid should be sent for pH, protein, lactate dehydrogenase (LDH), cytology and microbiology

Light's criteria
developed to distinguish between a transudate and an exudate.
The BTS recommend using the criteria for borderline cases:
exudates have a protein level of >30 g/L, transudates have a protein level of <30 g/L
if the protein level is between 25-35 g/L, Light's criteria should be applied.
An exudate is likely if at least one of the following criteria are met:
pleural fluid **protein** divided by serum protein >0.5
pleural fluid **LDH** divided by serum LDH >0.6
pleural fluid **LDH** more than two-thirds the upper limits of normal serum LDH
Pleural infection
all patients with a pleural effusion in association with sepsis or a pneumonic illness require diagnostic pleural fluid sampling
if the fluid is purulent or turbid/cloudy a chest tube should be placed to allow drainage
if the fluid is clear but the pH is less than 7.2 in patients with suspected pleural infection a test tube should be placed

Other characteristic pleural fluid findings:
Low glucose: rheumatoid arthritis, tuberculosis, empyema and malignancy.
raised amylase: pancreatitis, oesophageal perforation
Heavy blood-staining: mesothelioma, pulmonary embolism, tuberculosis, or malignancy.
A rheumatoid effusion is unlikely when peripheral joint disease is so well controlled.
Pleural fluid eosinophilia (> 10%) makes malignancy and TB less likely, and suggests air in the pleural cavity.
The presence of antinuclear factor is virtually diagnostic of systemic lupus erythematosus (SLE).

Video-assisted thoracoscopic surgery (VATS) :
An underlying pleural pathology should be strongly suspected in the case of thickened pleura, restrictive lung function and non-specific constitutional symptoms.
VATS is appropriate to differentiate pleural thickening between organised empyema or mesothelioma, and also to obtain tissue to differentiate mesothelioma from other primary or metastatic cancers.
VATS is optimally performed with a small amount of pleural fluid in situ.
Indications
It should be considered after other non-invasive tests have proven negative.
Advantages of **VATS**
Ensure adequate pleural biopsies are obtained
Drain pleural fluid
Allow pleurodesis to prevent recurrence.
pleural procedures **should not take place out-of-hours** except in an emergency due to increased risk

Indications for chest tube insertion in patients with an infected pleural effusion are:
Presence of organisms on a Gram stain of the pleural fluid
Frankly purulent pleural fluid
Pleural pH < 7.2 in the setting of an infected pleural effusion
Loculated pleural effusions

Poor clinical progress despite antibiotic treatment

Meigs syndrome

Characterised by the presence of a benign ovarian fibroma, associated with ascites and a right-sided pleural effusion.
The average age at presentation is 48 years.
Meigs syndrome is associated in 0.004% of ovarian tumours.
The aetiology of the pleural effusion is thought to be related to the size of fibroma, leading to accumulated peritoneal ascites that flows into the pleural cavity via the lymphatics or via abdominal-pleural communications (via the foramen of Bochdalek).
Removal of the ovarian mass is associated with resolution of the ascites and pleural effusion and patients have an excellent prognosis.

Pleural effusion in rheumatoid arthritis

Around 5% of patients with rheumatoid arthritis develop pleural effusions. These mainly occur in older male patients
who have subcutaneous nodules. About a quarter of patients experience bilateral effusions.
These effusions are characterised by some or all of the following:
Low glucose (< 1.6 mmol/l)
High lactate dehydrogenase (> 700 IU/l)
Low pH (< 7.2)
A high rheumatoid factor titre (> 1:320)
High cholesterol levels
The majority of these effusions resolve spontaneously within 3 months. Occasionally they persist and massive pleural
thickening develops. These patients might need decortication if they are symptomatic.

Contraindications for Thoracentesis

Absolute contraindications:
uncooperative patient
coagulation disorders that can not be corrected
Relative contraindications:
cases in which the site of insertion has known bullous disease (e.g. emphysema),
use of positive end-expiratory pressure (PEEP, in mechanical ventilation)
only one functioning lung (due to diminished reserve).
The aspiration should not exceed 1L as there is a risk of development of pulmonary edema.

Chylothorax

A chylothorax occurs when lymph fluid from the thoracic duct or its tributaries accumulates in the pleural space. Chylous ascitic fluid can also flow into the pleural space.
The etiologies of chylothorax can be categorized as nontraumatic or traumatic .Malignancy is the leading cause of nontraumatic chylothorax.

Chyle (lymphatic fluid of intestinal origin) has a high content of triglycerides in the form of chylomicrons, which produce the milky, opalescent appearance of lymphatic fluid.
The diagnosis of chylothorax is based on the pleural fluid triglyceride level .A triglyceride concentration greater than 110 mg/dL (1.24 mmol/L) strongly supports the diagnosis.
lymphatic imaging typically performed when the diagnosis of thoracic duct tear is uncertain after pleural fluid analysis and chest computed tomography, when a chylothorax recurs after thoracic duct ligation, or when anomalous thoracic duct anatomy is suspected.
It is differentiated from **empyema** because the latter yields a clear supernatant on centrifugation.
Pseudochyle is differentiated from chylothorax by :
high cholesterol pleural effusion, **(** cholesterol greater than
200 mg/dL (5.18 mmol/L) and a triglyceride below 110 mg/dL (1.24 mmol/L).
Cholesterol crystals are diagnostic if present. chylomicrons, which are associated with chylothoraces, are absent.
and is typically seen in patients with tuberculosis.

Causes of chylothorax

Common causes
Trauma (eg surgery)
Malignancy, usually a lymphoma (metastatic lung deposits can cause chylothorax, but less commonly)
Less common causes:
congenital :absence of thoracic ducts , Down syndrome, Noonan syndrome)
filariasis
tuberculous mediastinal lymphadenitis
lymphangioleiomyomatosis (occurring much more commonly in
females of child bearing age)
yellow nail syndrome
CVD :left subclavian venous thrombosis , thoracic aortic aneurysm, , venous thrombosis, mitral stenosis, heart failure,
others : pleuritis, cirrhosis , lupus, tuberculosis, sarcoidosis, amyloidosis, nephrosis, thyroid goiter, tuberous sclerosis,

Haemothorax

A bleeding into the pleural space,
Diagnosed on the basis of having a haematocrit that is more than half that of peripheral blood. This distinguishes it from a blood-stained effusion.
Management
The treatment of choice is to insert a large intercostal drain (28-32 F)
If this reveals continued bleeding, a thoracotomy might be required.
Surgery is not indicated simply to remove any residual blood clots because there is spontaneous lysis with no residual damage in the majority of patients.

Atelectasis

Atelectasis is when part or all of one lung collapses, preventing normal oxygen absorption. Breath sounds are quietened over areas of atelectasis. During expiration normal breath sounds rapidly fade out, probably due to the decreasing airflow rate.

Causes of atelectasis
Obstruction of an air passage by a thick mucus plug from an infection or other disease, such as cystic fibrosis
Tumours in the air passages
Tumours or blood vessels outside the air passages, causing pressure on the airways
Inhaled objects, such as peanuts or small toys
Prologoned chest or abdomincal surgery under general anaesthetic
Chest injury or fractured ribs
Penetrating wounds

Mesothelioma

Basics

Malignancy of mesothelial cells of pleura
Metastases to contralateral lung and peritoneum
Right lung affected more often than left
Risk factors and pathophysiology
Exposure to asbestos is the primary risk factor
The role of cigarette smoking has not been proved
Loss of material from chromosome 22 is an abnormality commonly seen in mesothelioma, and may contain code for tumour suppressor genes

Features

Dyspnoea, weight loss, chest wall pain
Clubbing
30% present as painless pleural effusion
Only 20% have pre-existing asbestosis
History of asbestos exposure in 85-90%, latent period of 30-40 years

Investigation/diagnosis

Suspicion is normally raised by a chest x-ray showing either a pleural effusion or pleural thickening (Be aware that only 20% of mesothelioma patients present with radiographic changes consistent with asbestosis, although the majority present with pleural abnormalities).
the next step is normally a pleural CT.
If a pleural effusion is present fluid should be sent for MC&S, biochemistry and cytology (but cytology is only helpful in 20-30% of cases)
local anaesthetic thoracoscopy is increasingly used to investigate cytology negative exudative effusions as it has a high diagnostic yield (around 95%). Tissue can be obtained from **thoracoscopy with biopsy** from abnormal looking areas => **the most appropriate investigation to deliver the diagnosis.**
if an area of pleural nodularity is seen on CT then an image-guided pleural biopsy may be used
In cases of mesothelioma, CT might show pleural thickening and nodularity, which would be amenable to either CT-guided biopsy or thoracoscopy. CT pleural biopsy has been shown to have a diagnostic advantage over a blind Abrams' biopsy in cytologically negative malignant pleural effusions with pleural thickening, with a sensitivity of 87% vs 47%

Management

Symptomatic
Industrial compensation

Chemotherapy, Surgery if operable
Prognosis poor, median survival 12 months

Radiotherapy to the thoracoscopy tract site is effective for preventing tumour seeding and growth and is recommended after pleural procedures. This is routine practice, along with providing symptomatic treatment.

Patients with good performance status could be considered for palliative chemotherapy, which can result in tumour shrinkage.
Palliative radiotherapy can be useful to reduce chest pain, shortness of breath and to relieve superior vena cava obstruction. There is no evidence of benefit for radiology at the surgical port sites and surgical resection remains controversial.
Chest drains are usually reserved for recurrent pleural effusions and those that fail talc pleurodesis.
Prognosis**:** The median survival after diagnosis is 2 years

Pulmonary eosinophilia

The defining characteristics of pulmonary eosinophilia include:
peripheral blood eosinophilia
radiographic evidence of pulmonary parenchymal disease;
histopathologic evidence of lung tissue eosinophilia in a transbronchial or open lung biopsy specimen;
increased eosinophils in bronchoalveolar lavage fluid (eg, >10 %). As peripheral blood eosinophils are not always increased in eosinophilic lung diseases, the other methods (bronchoalveolar lavage [BAL], biopsy) are sometimes needed to document lung eosinophilia.

Causes of pulmonary eosinophilia

Churg-Strauss syndrome
allergic bronchopulmonary aspergillosis (ABPA)
Loffler's syndrome
eosinophilic pneumonia
hypereosinophilic syndrome
tropical pulmonary eosinophilia
drugs: nitrofurantoin, sulphonamides
less common: Wegener's granulomatosis

Loffler's syndrome

transient CXR shadowing and blood eosinophilia
thought to be due to parasites such as *Ascaris lumbricoides* causing an alveolar reaction
presents with a fever, cough and night sweats which often last for less than 2 weeks.
generally a self-limiting disease

Cryptogenic pulmonary eosinophilia
In this condition pulmonary eosinophilia occurs with **no identifiable cause**
patients usually non-atopic (but 10% have had previous asthma)
When the disease is self-limiting and lasts less than 1 month it is known as Loeffler syndrome.

Feature

Systemic features: Malaise, fever, weight loss
asthma (in around 50%) Investigations
widespread, mainly peripheral pulmonary infiltrates
blood eosinophilia
Raised ESR Treatment
The disease responds to steroid treatment, which needs to be continued for about 1 year.
Tropical pulmonary eosinophilia
associated with ***Wuchereria bancrofti*** infection (a condition associated with microfilaria).
seen in the Asian subcontinent
Presents with cough, wheeze, fever, lassitude and weight loss.
The treatment of choice is a 10-14-day course of **diethylcarbamazine** to eradicate the infection.

Chronic eosinophilic pneumonia (CEP)

Definition

CEP is an idiopathic disorder characterized by an abnormal accumulation of eosinophils in the interstitial and alveolar spaces

Feature

dyspnea, cough, fever, and wheezing over three weeks to several months.

Diagnosis

Chest imaging
showing predominantly peripheral or pleural-based opacities described as the "photographic negative" of pulmonary edema, are virtually pathognomonic for CEP
Peripheral alveolar filling infiltrate **predominantly in the upper lobes** on a chest radiograph is typical of chronic eosinophilic pneumonia.

Bronchoalveolar lavage (BAL):
To look for eosinophilia ↓ cell count showing eosinophilia (≥25 %).
To exclude infection.
Treatment: prednisolone

Organising pneumonia

Organising pneumonia (formerly called bronchiolitis obliterans organizing pneumonia or BOOP), classified in to :
Cryptogenic organizing pneumonia (COP):idiopathic
secondary organizing pneumonia: can be seen in association with connective tissue diseases, a variety of drugs, malignancy, and other interstitial pneumonias

is a type of diffuse interstitial lung disease that affects the distal bronchioles, respiratory bronchioles, alveolar ducts, and alveolar walls.
The primary area of injury is within the alveolar wall.

Onset is typically in the fifth or sixth decades of life, with men and women affected equally

Causes of organizing pneumonia

Cryptogenic organizing pneumonia (previously called bronchiolitis obliterans organizing pneumonia)
Organizing diffuse alveolar damage
Diffuse alveolar hemorrhage
Drugs
Amiodarone
Cocaine
Infections (organizing)
Mycoplasma
Viral
Pneumocystis jirovecii (carinii)
Bacterial
Connective tissue diseases
Hypersensitivity pneumonitis
Idiopathic pulmonary fibrosis (minor scattered foci)
Aspiration

Features

Persistent nonproductive cough (72%)
Dyspnea (66 %)
Fever (51 %)
Malaise (48 %)
Weight loss of greater than 10 pounds (57%)
Hemoptysis is rarely reported as a presenting manifestation of COP

Cryptogenic organising pneumonia (COP)

is a non-specific inflammatory pulmonary process, with buds of granulation tissue forming in the distal air spaces.
Organising pneumonia can have a number of causes, including connective tissue disease, infection and drugs, but **if there is no obvious cause it is called 'cryptogenic'.**

Features

dry cough
non-specific symptoms of fever, malaise, anorexia and weight loss.

Investigations

↑WBC and C-reactive protein (CRP) levels.
chest X-ray
can show consolidation, nodules or thickened septal lines.
The consolidation typically occurs in different places at different times.
The most common chest imaging features are multiple ground-glass or consolidative opacities.
Pulmonary function tests usually show a restrictive pattern with an associated gas transfer defect.
CT findings are characteristic, with multiple patchy alveolar opacities, which often spontaneously migrate.
Reversed halo sign, better known as an atoll sign.
a region of ground-glass opacity surrounded by crescentic or annular denser tissue .
Cryptogenic organising pneumonia is the most common condition described in immunocompetent patients with this sign (found in 20% of the cases of COP)

Diagnosis

The diagnosis might be made on the basis of CT alone, or on transbronchial or open lung biopsy.
Histopathologic characteristic lesions include excessive proliferation or “plugs” of granulation tissue within alveolar ducts and alveoli, associated with chronic inflammation in the surrounding alveoli.
The diagnosis requires histopathologic identification of a predominant pattern of organizing pneumonia and the exclusion of any possible cause

Differential diagnosis

Recurrent lobar bacterial infection is unusual in an immunocompetent adult.
Eosinophilic pneumonia leads to flitting peripheral chest X-ray shadows.
Lymphangioleiomyomatosis is a rare disease affecting women of childbearing age, who have abnormal proliferation of atypical smooth muscle cells throughout their lungs and airways - CT shows multiple small cysts.
Pulmonary alveolar proteinosis is a rare defect in which the alveoli become filled with proteinaceous material that cannot be cleared. CT shows air-space shadowing.

Treatment

Mild stable disease: monitor without therapy & reassessed at 8 to 12 week intervals
For symptomatic patients with moderate or severe disease: oral prednisolone
COP usually responds to corticosteroid.
Initial doses of 0.75–1 mg/kg, weaning over 6–12 months, are reasonable.
Persistent or gradually worsening disease methylprednisolone 500 to 1000 mg intravenously each day for three to five days rather than a lower oral dose
Failure to respond to systemic glucocorticoids: cyclophosphamide or azathioprine

Prognosis

- Relapse is common

Bronchiolitis obliterans organizing pneumonia (BOOP)

Definition

BOOP is differentiated from organizing pneumonia, which is defined by the presence of granulation tissue in the distal air spaces; but when **associated with granulation tissue in the bronchiolar lumen**, organizing pneumonia is qualified by the term bronchiolitis obliterans (BO). Hence the term ‘bronchiolitis obliterans organizing pneumonia’ is used.
BOOP is characterized by the presence of **granulation tissue** in the **bronchiolar** lumen, **alveolar ducts** and some **alveoli**, associated with a variable degree of interstitial and airspace infiltration by mononuclear cells and foamy macrophages.

Feature

Approximately 50% of patients present with influenza-like illness followed by a short illness of few months' duration characterized by a persistent nonproductive cough, effort dyspnea, low-grade pyrexia, malaise and weight loss.
Less common symptoms include pleuritic chest pain and hemoptysis.
fine, dry lung crepitations is common.

Causes

most cases are idiopathic.
Association

Associated collagen vascular disorder is found in 16%
inhalation exposure to toxins in 17%
organ transplantation, especially with bone marrow transplant
post infection: bacterial , viral, CMV pneumonia
Radiotherapy
Drugs: phenytoin , carbamazepine

Investigations

chest radiographs revealed that bilateral patchy infiltrates and reticulonodular opacities
HRCT
Patchy ground-glass opacities in a subpleural and/or peribronchovascular distribution (80%).
Bilateral basal airspace consolidation (70%)
Bronchial wall thickening and cylindrical bronchial dilatation in areas of air bronchogram (70%)
the consolidation in BOOP commonly involves the lower zones
Cytological profile of bronchoalveolar lavage
reveals a mixed cell pattern with an increase in lymphocytes (20-40%),
↑lymphocytes differentiate the condition from parenchymal pulmonary disease.
Neutrophils (10%), eosinophils (5%), mast cells, foamy macrophages and occasional plasma cells increase in patients with **Idiopathic pulmonary fibrosis (IPF)**

Lung biopsy is the preferred method for establishing the diagnosis.
Most patients with BOOP require open-lung biopsy for diagnosis.
ESR is usually elevated,
pulmonary function tests show a restrictive pattern.

Treatment

BOOP responds well to corticosteroid therapy, while **Usual interstitial pneumonia** (**UIP**) and **IPF** usually does not.
The dosage is generally 0.75 mg/kg/day for 1 to 3 months, then 0.50 mg/kg mg/day for 3 months, then 10 to 20 mg/day or every other day **for a total of 1 year.**
Approximately 30% of the patients experience relapse upon withdrawal of treatment.

Pulmonary arterial hypertension: features and management

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean **pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise**. pulmonary artery wedge pressure <= 15 mmHg and pulmonary vascular resistance > 3 Wood units.

Features

exertional dyspnoea is the most frequent symptom
chest pain and syncope may also occur
loud P2
left parasternal heave (due to right ventricular hypertrophy)

Mechanisms and causes:

Pulmonary venous hypertension

Increased left atrial pressure: most commonly caused by left ventricular dysfunction as in congestive cardiac failure, which causes an elevation in PA pressure by increased back-pressure through the lungs.
mitral stenosis or insufficient,
fibrosing mediastinitis
veno-occulsive disease.
mechanical obstruction of the pulmonary arteries
Acute or chronic thromboembolism.
hypoxia leads to constriction of the pulmonary arteries
Interstitial lung disease (ILD)
Chronic obstructive airways disease (COAD)
Acute respiratory distress syndrome (ARDS)

Familial primary pulmonary hypertension (PPH): account for 15-20% of cases of PPH and is due to an inherited mutation in the BMPR2 gene which codes for a receptor in the TGF beta family.

Pulmonary hypertension in pregnancy:

Pregnant with pulmonary hypertension have a high mortality of at least 30% - some authors put it at 50% - seemingly highest immediately after delivery.
Gold standard for diagnosis is right-heart catheterisation, but echocardiogram can also give useful information.
The mainstay of treatment is with pulmonary vasodilators, but use in pregnancy needs to be discussed with the cardiology and obstetric team, and a decision made regarding early delivery of the baby.
Drugs:
anorectic (fenfluramine, dexfenfluramine),
amphetamine
Cocaine (but not heroin).

Investigations

Ventilation/perfusion lung scans typically show one or more mismatched segmental or larger perfusion defects, with most patients having several bilateral mismatched perfusion defects.

Pulmonary angiography is the definitive diagnostic test. It shows narrowed segmental pulmonary arteries, sometimes accompanied by post-stenotic dilatation, irregularity of the intima, luminal narrowing of the central arteries and oddly shaped vessels.
Pulmonary fibreoptic angioscopy is useful to define surgical accessibility.

Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy.
Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide
If there is a positive response to acute vasodilator testing

oral calcium channel blockers
If there is a negative response to acute vasodilator testing

prostacyclin analogues: treprostinil, iloprost
endothelin receptor antagonists: bosentan
phosphodiesterase inhibitors: sildenafil
Sequence of treatment:
10-15% of patients benefit from calcium channel antagonists.
If symptoms going on the ideal next step would be an endothelin A receptor antagonist, such as Bosentan.
following Bosentan, another oral therapy such as Sildenafil could be a logical next step, followed by Prostacyclin.
Prostacyclin is currently delivered by infusion, oral prostaglandin receptor agonists are currently under development.

Prognosis:

Several studies report a mean survival of only 2.5 years from diagnosis,
Patients with mean pulmonary artery pressures over 30 mmHg have a 5-year survival rate of 30%, but this rate falls to 10% if the mean pulmonary artery pressure is over 50 mmHg.

Respiratory acidosis

Respiratory acidosis may be caused by a number of conditions
COPD
decompensation in other respiratory conditions e.g. life-threatening asthma / pulmonary oedema
sedative drugs: benzodiazepines, opiate overdose

Signs and symptoms of respiratory acidosis		
Central nervous system	Respiratory system	**Cardiovascular system**
Cerebral vasodilation	Breathlessness	**Flushing, bounding pulse**
Increased intracranial pressure	Cyanosis	**Cor pulmonale**
Headache, confusion, agitation	Pulmonary hypertension	**Systemic hypotension**
Hallucinations, transient pyschosis		**Arrhythmias**
Myolonic jerks, flapping tremor, extensor plantars, depressed reflexes		**Initially good cardiac output, then decreases**
Papilloedema, constricted pupils		
Seizures, coma		

Pathophysiological changes in case of acute acidosis:

Occurred too quickly for metabolic compensation to occur via renal bicarbonate reabsorption, which takes 3-5 days to occur. **(bicarbonate will be normal in acute respiratory acidosis)**
The oxygen dissociation curve is shifted to the right in acute acidosis, i.e. haemoglobin has a decreased affinity for oxygen.
High pulmonary pressures would be expected after this arrest scenario, as the pulmonary arterioles constrict in response to hypoxia.
Compensated respiratory acidosis ==> normal PH, high CO_2, low O_2 .The fact that the pH is normal means that there must be bicarbonate retention to compensate.
In **bronchopulmonary dysplasia**, there is usually long-term CO_2 retention with compensatory increase in bicarbonate leading to a positive base excess and normal pH.

Respiratory alkalosis

Anxiety leading to hyperventilation (Hyperventilation will result in carbon dioxide being 'blown off', causing an alkalosis.) **=>** high PH , low PCO2 , normal PO2. not associated with hypoxia.
pulmonary embolism
Acute severe asthma : associated with hypoxia and normal or rising CO_2
salicylate poisoning*
CNS disorders: stroke, subarachnoid haemorrhage, encephalitis
altitude
pregnancy
pain
Excessive mechanical ventilation.

*salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis.

Differential diagnosis of respiratory alkalosis with type 1 respiratory failure (low pO_2 and low pCO_2.):
Chronic venous thromboembolism (most likely).
Pulmonary fibrosis (but basal crackles may be expected).

Respiratory tract infections: NICE guidelines

NICE issued guidance in 2008 on the management of respiratory tract infection, focusing on the prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care.

A no antibiotic prescribing or delayed antibiotic prescribing approach is generally recommended for patients with acute otitis media, acute sore throat/acute pharyngitis/acute tonsillitis, common cold, acute rhinosinusitis or acute cough/acute bronchitis.

However, an immediate antibiotic prescribing approach may be considered for:

children younger than 2 years with bilateral acute otitis media
children with otorrhoea who have acute otitis media
patients with acute sore throat/acute pharyngitis/acute tonsillitis when 3 or more Centor criteria are present

The Centor criteria* are as follows:

presence of tonsillar exudate
tender anterior cervical lymphadenopathy or lymphadenitis
history of fever
absence of cough

If the patient is deemed at risk of developing complications, an immediate antibiotic prescribing policy is recommended

are systemically very unwell
have symptoms and signs suggestive of serious illness and/or complications (particularly pneumonia, mastoiditis, peritonsillar abscess, peritonsillar cellulitis, intraorbital or intracranial complications)
are at high risk of serious complications because of pre-existing comorbidity. This includes patients with significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis, and young children who were born prematurely
are older than 65 years with acute cough and two or more of the following, or older than 80 years with acute cough and one or more of the following:
- hospitalisation in previous year
- type 1 or type 2 diabetes
- history of congestive heart failure
- current use of oral glucocorticoids

The guidelines also suggest that patients should be advised how long respiratory tract infections may last:

acute otitis media: 4 days
acute sore throat/acute pharyngitis/acute tonsillitis: 1 week
common cold: 1 1/2 weeks
acute rhinosinusitis: 2 1/2 weeks
acute cough/acute bronchitis: 3 weeks

*if 3 or more of the criteria are present there is a 40-60% chance the sore throat is caused by Group A beta-haemolytic *Streptococcus*

Sarcoidosis

Sarcoidosis CXR

Sarcoidosis Staging of CXR
1 = BHL (Bilateral Hilar Lymphadenopathy)
2 = BHL + Infiltrates
3 = Infiltrates only
4 = Fibrosis

Definition

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas.

Epidemiology

More common in black people (African descent) and subjects of Caribbean origin in Europe, sarcoid is commonest amongst Caucasians and has a significantly higher incidence in the **Irish**.
most common in black women
More common in young adults.
Has a bimodal age distribution with 2 peaks in the third and fifth decades.

Pathology

noncaseating granulomas in the organ involved.
This non-caseating granulomas may occur anywhere
The central area of the granuloma will occasionally contain a Schaumann body, formed of crystallised material (calcium phosphate).
These granulomas have the capacity to produce 1,25 vitamin D explaining the associated hypercalcaemia.

Presentation

initially presents with one or more of the following **Abnormalities:**
Bilateral hilar lymphadenopathy
Pulmonary reticular opacities
Lungs and lymph nodes affected in >90% of patients.
Skin, joint and/or eye lesions

Features:

Dry cough
Dyspnoea (Pulmonary fibrosis)
Arthralgia
Inflammatory arthritis in sarcoidosis typically targets the **ankle joint**.
Uveitis (25% of cases)
Skin lesions:
Erythema nodosum (10% of cases)
lupus pernio
Systemic symptoms:
Fever
weight loss

Investigations :

There is no one diagnostic test for sarcoidosis and hence diagnosis is still largely clinical.

Chest x ray
Chest x ray is abnormal in 85% of lung sarcoid, but 30-60% are asymptomatic (that is, incidental chest x ray finding).
All patients should have a chest x-ray, which may show bilateral hilar lymphadenopathy.
The differential of bilateral hilar lymphadenopathy includes:
Sarcoidosis. A positive tuberculin test in a patient with chronic sarcoidosis is suggestive of active tuberculosis
Tuberculosis
Malignancy including lymphoma
Cystic fibrosis
Churg Strauss disease
HIV
Extrinsic allergic alveolitis
Phenytoin
Pneumoconioses, especially berylliosis. (Exposure to beryllium is seen in the nuclear power, telecommunications, semi-conductor and electronics industries).

Stage	Finding	Likehood of spontaneous resolution
0	Normal chest radiograph	**>90%**
I	Bilateral hilar lymphadenopathy (BHL)	**60-90%**
II	BHL plus pulmonary infiltrates	**40-60%**
III	Pulmonary infiltrates (no BHL)	**10-20%**
IV	**Pulmonary fibrosis (+/- bullae)**	**<20%**

Other investigations

CT scan:
It can demonstrate the degree of fibrosis, micronodules in a subpleural or bronchoalveolar distribution, fissural nodularity and bronchial distortion.
Irregular linear opacities and ground-glass shadowing may also be seen.
If the CT scan is diagnostic, then mediastinoscopy, bronchoscopy or biopsies can often be avoided.
Tissue biopsy: non-caseating granulomas
If the history and radiology is typical, the diagnosis of sarcoidosis can be confidently made and there may not be a need to proceed to tissue biopsy.
The presentation of erythema nodosum, arthropathy, bilateral hilar lymphadenopathy is so characteristic that histological diagnosis is not necessary.
If there were atypical features and tissue biopsy was required, either transbronchial or open lung biopsy is preferable.
With less characteristic presentations, positive biopsies are needed. Mediastinoscopy is the method of choice for anterior mediastinal nodes.
If you are asked to specify the investigation most likely to confirm the diagnosis, only transbronchial biopsy will determine whether non-caseating granulomas are present or not.
Skin biopsy
ACE levels

It is elevated in about 70% of patients with active sarcoidosis.
have a sensitivity of 60% and specificity of 70% and are therefore not reliable in the diagnosis of sarcoidosis although they may have a role in monitoring disease activity.
hypercalcaemia (seen in 10% if patients)
Hypercalcaemia, a potentially important complication of sarcoidosis, occurs in fewer than 10% of patients and is thought to be owing to elevated levels of 1,25-dihydroxyvitamin D (calcitriol), which is produced by macrophages within the granulomas.
hypercalciuria (up to 50%) are well recognised in sarcoidosis.
The pattern resembles hypervitaminosis D, with:
Elevated serum calcium
Normal serum phosphate and
Normal/slightly raised alkaline phosphotase.
Raised ESR.
Hypergammaglobulinaemia (↑ Immunoglobulins) in 30-80%.
Leukopenia in 5-10% of patients
Spirometry usually shows a restrictive defect (Decreased gas-transfer factor (Tlco) with decreased gas-transfer coefficient (Kco)
Broncho-alveolar lavage typically shows a lymphocytosis
TB should be excluded by sending sputum or BAL washings for AFB
tuberculin test is negative in approximately 80-90 % of sarcoidosis cases
gallium-67 scan - not used routinely
the Kveim test (where part of the spleen from a patient with known sarcoidosis is injected under the skin) is no longer performed due to concerns about cross-infection

Chest x-ray and CT scan showing stage 2 sarcoidosis with both bilateral hilar lymphadenopathy + interstitial infiltrates. The reticulonodular opacities are particularly noted in the upper zones. Remember that pulmonary fibrosis (which this case has not yet progressed to) may be divided into conditions which predominately affect the upper zones and those which predominately affect the lower zones - sarcoidosis is one of the former. The CT of the chest demonstrates diffuse areas of nodularity predominantly in a peribronchial distribution with patchy areas of consolidation particularly in the
upper lobes. There is some surrounding ground glass opacities. No gross reticular changes to suggest fibrosis.

Management

The majority of patients with sarcoidosis get better without treatment.
the fate of acute sarcoidosis
Spontaneous remission ↓ occurs in two-thirds of patients
progress to chronic course ↓ in 10-30%.
Spontaneous remissions occur in 55% to 90% of patients with stage I, 40% to 70% of patients with stage II, and about 20% of patients with stage III disease, but no remissions are expected in stage IV.
Duration of remission
Remissions often occur within the **first 6 months** after diagnosis.
50% of patients with **stage 2 sarcoidosis** (ie hilar lymphadenopathy and parenchymal infiltrate) recover spontaneously in **2 years**.
Treated with topical corticosteroids for mild local cutaneous disease. Systemic corticosteroids are the mainstay of treatment for severe disease.

Prednisolone is the mainstay of initial treatment for sarcoidosis, continued for 12 months or more in those patients who respond, but tapered to the minimal effective dose to stop within 2 years maximum.
Methotrexate and hydroxychloroquine may be added as steroid sparing agents.

Indications for steroids

- patients with chest x-ray stage 2 or 3 disease who have moderate to severe or progressive symptoms. Patients with asymptomatic and stable stage 2 or 3 disease who have only mildly abnormal lung function do not require treatment
- hypercalcaemia (10% of cases)
- eye, heart or neuro involvement

Prognosis

Erythema nodosum is associated with a good prognosis in sarcoidosis.

Sarcoidosis remits without treatment in approximately two-thirds of people
The prognosis is excellent with less than 10% having persistent disease.
Mortality in the UK from sarcoidosis is less than 5%.

Factors associated with a good prognosis

HLA B8
Lofgren's syndrome (bilateral hilar lymphadenopathy, erythema nodosum, polyarthritis and fever).

Factors associated with poor prognosis

insidious onset, symptoms > 6 months (chronic pulmonary involvement)
absence of erythema nodosum
extrapulmonary manifestations: e.g.
lupus pernio
Lupus pernio: is a chronic raised indurated (hardened) lesion of the skin, often purplish in colour, and is associated with sarcoid.
splenomegaly
Cardiac involvement
Cardiac sarcoidosis is rare but can manifest as a prolonged PR interval.
Chronic hypercalcaemia
Nasal mucosal involvement
Neurosarcoidosis
CXR: stage III-IV features
black people (Afro-Caribbean or Afro-American race)
Age of onset >40 years

Lofgren's syndrome

Lofgren's syndrome is an acute form sarcoidosis characterised by:
bilateral hilar lymphadenopathy (BHL)
erythema nodosum,
fever
and polyarthralgia.
it typically occurs in young females and carries an excellent prognosis.
It is typically more common in Scandanavian patients and less common in Afro-Caribbean patients and typically has amuch better prognosis.

- Treatment:

For less symptomatic patients then supportive measures and NSAIDs for arthralgia are the preferred treatment options.
For patients who are not responsive to steroids or steroid intolerant then immunosuppressant agents such as methotreaxtae can be tried.

Loffler's syndrome is a cause of pulmonary eosinophilia thought to be caused by parasites suchas Ascaris lumbricoides

Mikulicz syndrome:

- It is a chronic condition associated with sarcoidosis
- characterized by the abnormal enlargement of parotids, lacrimal, salivary glands, tonsilsand other glands in the soft tissue of the face and neck.

Heerfordt's syndrome
is an acute presentation of sarcoidosis, which presents with fever, uveitis (red, painful eyes), bilateral swelling of the parotid and other salivary and lacrimal glands. Facial nervepalsy (LMNL) may be a feature, and other features of sarcoidosis may co-exist (e.g. skin lesions, pulmonary involvement).
As it represents a form of neuro-sarcoidosis, other neurological features may be present(e.g. meningism, ophthalmoplegia and pupillary reflex dysfunction).

Pulmonary side effects of drugs

Cardiac drugs
Aspirin ↓ nasal polyps, asthma
Atenolol ↓ bronchoconstriction
Lisinopril ↓ cough
Amiodarone ↓ pulmonary fibrosis
Furosemide ↓ bronchoconstriction (very rarely)

Pulmonary complications of cytotoxic and immunosuppressive drugs
Methotrexate(disease-modifying anti-rheumatoid drug (DMARD → may cause
Pulmonary pneumonitis (inflammation of the lung).
Penicillamine (DMARD) → may cause bronchiolitis obliterans.

Other drugs:
Non-steroidal anti-inflammatory drugs can cause asthma or pulmonary eosinophilia.
Phenytoin characteristically causes pulmonary eosinophilia.
Idiopathic pulmonary haemosiderosis
Idiopathic pulmonary haemosiderosis tends to occur in younger people and is characterised by pallor, weakness,
lethargy, dry cough and occasional haemoptysis
There are no extrapulmonary features. There are no abnormal immunological features, which differentiates it from Goodpasture syndrome
Gas transfer is elevated as blood is already in the alveolar space.
There are no signs of sinusitis or renal disease, making Wegener's less likely
Finger clubbing
Loss of the natural angle between the nail and the nail bed is seen in clubbing. An increased
curvature of the nail
develops later. Causes include:
Suppurative diseases:
long-standing bronchiectasis
acute lung abscesses
empyema
Malignant disease - especially carcinoma of the bronchus and pleural malignancy
Fibrosing alveolitis
Asbestosis
Finger clubbing is not seen in uncomplicated bronchitis. Finger clubbing may also be associated with hypertrophic
pulmonary osteoarthropathy, a painful osteitis of the distal ends of the long bones of the lower arms and legs.
Malignancy is associated in 95% of these cases.

Hypereosinophilic syndrome:

characterised by a peripheral blood eosinophil count of >1.5 for more than 6 months.
Generalised symptoms are fatigue, myalgia, fever, night sweats, diarrhoea and pruritus.
Other symptoms depend on the organ involved: cardiac disease causes chest pain and dyspnoea, respiratory disease presents with a dry cough.

Investigations:

Desaturation on SaO_2 (using an oximeter) in spite of normal PaO_2:
This is a typical description of Methaemoglobinaemia , which is the accumulation of reversibly oxidised methaemoglobin causing reduced oxygen affinity of the Hb molecule with consequent cyanosis. It can occur due to an inherited condition or as a consequence of drugs such as nitrites.

Cyanosis

Persistent cyanosis without hypoxia (a normal Pao2) suggests a diagnosis of methaemoglobinaemia or sulfhaemoglobinaemia.
In a cyanosed patient the amount of reduced haemoglobin in the blood is at least 5 g/dl
The blue colour of the skin and mucous membranes is due to hypoxia and not hypercapnia. Hypoxia should be corrected by oxygen therapy

Yellow nail syndrome

It is an abnormality of lymphatic drainage.
Slowing of the nail growth leads to the characteristic thickened and discoloured nails seen in yellow nail syndrome.
the nails are yellow, thickened, curved, stop growing and may become detached from the nail bed.

Associations

congenital lymphoedema
pleural effusions
bronchiectasis (40%)
chronic sinus infections
Yellow discolouration of the nails.

Hepatopulmonary syndrome:

This is characterised by an oxygenation defect induced by pulmonary vascular dilatation in patients with liver cirrhosis or portal hypertension.
This oxygenation defect consists of a wide alveolar-arterial gradient (>15mmHg). The vascular dilatation is thought to be induced by increased pulmonary levels of nitric oxide. It is seen in 15- 30% of patients with cirrhosis and is a poor prognostic indicator.

Features:

Most patients are asymptomatic or have dyspnoea with an insidious onset.
Dyspnoea whilst standing (platypnoea) and hypoxaemia exacerbated by being upright (orthodeoxia) are characteristic, and are thought to be due to the predominance of vascular dilatation in the lung bases. Blood flow to these areas is increased in the upright position.
Desaturation during sleep
Clubbing, cyanosis.

Investigations:

Contrast-enhanced transthoracic echocardiography is the best test to demonstrate intrapulmonary vascular dilatation. It can also exclude intracardiac shunting which may result in similar signs and symptoms to hepatopulmonary syndrome.
This is performed by injecting agitated saline intravenously during transthoracic echocardiography. In a normal subject microbubbles are visualised in the right ventricle within seconds, which are then absorbed in the alveoli. Immediate visualisation in the left ventricle (within three cardiac
cycles) indicates intracardiac shunting. Delayed visualisation in the left ventricle (3-6 cardiac cycles) is diagnostic of intrapulmonary shunting.
Radionuclide lung perfusion scanning can also be used. Chest radiographs can be normal or show non-specific interstitial changes. ABGs should be taken in the sitting position to grade the severity of the condition based on the degree of hypoxaemia.

Treatment:

Liver transplantation is the only proven beneficial available treatment, with 85% of patients showing resolution or significant improvement in gas exchange postoperatively.
Smoke inhalation
Inhalation of hot smoke can burn the upper airways and contributes significantly to deaths due to fires.
Upper airway obstruction due to heat injury and mucosal swelling usually develops within 24 hours of exposure, but stenosis due to scarring can develop later.
A hoarse voice, stridor, severe conjunctivitis, burnt nasal hairs and falling peak flow values
all suggest significant upper airway damage.
Bronchoscopy is then the best tool to establish whether there is significant oedema or mucosal ulceration obstructing the airways.
Pulmonary alveolar microlithiasis (PAM)

Definition

rare autosomal recessive disease in which calcalcium phosphate accumulate in the alveoli causes widespread damage to the alveoli and surrounding lung tissue

Pathophysiology

SLC34A2 gene mutations ↓ activity of the type IIb sodium-phosphate cotransporter (which located mainly in alveolar type II cells) ↓ accumulation of phosphate in the alveoli
↓ formation of microliths
SLC34A2 gene is responsible for the uptake of phosphate released from phospholipids in outdated surfactant.

Feature

usually diagnosed before age 40.
Commonly asymptomatic, Often the disorder is discovered before symptoms develop, when medical imaging is done for other reasons. The condition typically worsens slowly over many years.
Often patients may have no symptoms despite striking radiological abnormalities.
persistent cough
dyspnea, especially during physical exertion.
PFT shows restrictive pattern
chest pain that worsens when coughing, sneezing, or taking deep breaths.

People with pulmonary alveolar microlithiasis can also develop calcium phosphate deposits in kidneys, gallbladder, testes, and aortic valve.

Diagnosis

the best diagnostic schedule for PAM is the association of **BAL** and chest **HRCT**,
as the BAL can document the diagnosis while the HRCT provides further information about the degree of inflammation and/or fibrosis or calcification of the interstitium.
A 'sandstorm-appearing' chest radiograph is a typical diagnostic finding.
In the initial stages, the radiological finding may mimic miliary tuberculosis.
Calcified nodules are found in later stages.
An interesting radiological sign in PAM is a **black pleura sign**. Here, the calcification of alveoli and the adjacent rib make the pleura resemble a black line in between two white signals.
BAL and biopsy show the characteristic calciospherocitis (microliths) in the alveoli (deposition of calcium and phosphate crystals).
Biopsy also shows variable degrees of fibrosis in the lung interstitium

Treatment

lung transplantation is the only effective therapy.
No medical intervention has proved successful
Bronchial lavage is not useful, unlike in pulmonary alveolar proteinosis.

Pulmonary Alveolar Proteinosis (PAP)

Definition

It is a rare diffuse lung disease in which the alveolar sacs become filled with proteins that characteristically stain for periodic acid-Schiff (PAS) , a protein derived from surfactant .

Epidemiology

Incidence of PAP is increased in patients with hematologic malignancies and AIDS, suggesting a relationship with immune dysfunction.
prevalence of 1 case per 100,000
Incidence for males is 4 times higher than for females
It usually affects people aged between 20-60 years who have no previous lung disease,

Causes

- It can be primarily or secondary, the latter being related to infections with, for example, pneumocystitis Jirovecii or atypical mycobacteria, or to immunosuppressants, organic dusts and haematological malignancy .

Feature

Pulmonary symptoms: Persistent dry cough, progressive dyspnea and leuritic chest pain
General symptoms: Fatigue, malaise, weight loss and low-grade fever
Clubbing (25%)

Diagnosis

Diagnosis based on bronchial lavage or biopsy with PAS-positive stains and increased presence of surfactant proteins A and D .
Flexible bronchoscopy with broncho-alveolar lavage (BAL) remains the criterion standard.

HRCT chest shows a classical picture of dense infiltrates, often referred to as crazy paving .
Spirometry shows a restrictive pattern with reduced lung capacity and reduced CO diffusion .
↑ autoantibody against GM-CSF (immunoglobulin G [IgG] isotype) in serum and BAL fluid

Treatment

Most patients do not require treatment unless their SOB is disabling .
washing the alveoli out with salt solution.
This can be done with bronchoscopy or under general anaesthesia through the trachea.
If both lungs need washing then they are done about 5 days apart.
The number of washing depends on symptoms .
Prognosis is good.

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