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# Chapter 2

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 2

Pulmonology • Anticoagulant  First-line: apixaban or rivaroxaban  Second-line: (if apixaban or rivaroxaban are not suitable)  LMWH for at least 5 days followed by dabigatran or edoxaban OR  LMWH concurrently with a vitamin K antagonist (warfarin) for at least 5 days, or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own.  For patients with positive antiphospholipid syndrome → the 1st line is LMWH concurrently with a VKA.  Duration of anticoagulant:  For most patients →3 months  with active cancer →3 to 6 months.  For unprovoked DVT or PE→ Consider continuing anticoagulation beyond 3 months (6 months for people with active cancer) → use the HAS-BLED score for major bleeding risk → stop anticoagulation if the HAS-BLED score is 4 or more and cannot be modified.  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 patient with 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 m2) 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.  Benefit of heparin?  Heparin reduces risk of further embolism (anticoagulant) and reduces pulmonary vasoconstriction. • Thrombolysis  Indication?  Massive PE where there is haemodynamic instability demonstrated by hypotension, right ventricular strain on an ECG or signs of right heart failure.  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?

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 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 a contraindicated (eg PE following a recent haemorrhagic stroke)  if anticoagulation alone fails  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.

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Pulmonary embolism in pregnancy: diagnosis and management Diagnosis • 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]

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Pulmonology • CTPA vs V/Q scan  CTPA → ↑risk of maternal breast cancer  V/Q scanning → ↑risk of childhood cancer • D-dimer is of limited use as it 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 • 1st line: low-molecular-weight heparin (LMWH) should be employed during the remainder of the pregnancy and for at least 6 weeks postnatally and until at least 3 months of treatment has been given in total. • 2nd line: In pregnant women who are unable to tolerate heparin (LMWH or unfractionated heparin) or danaparoid and who require continuing anticoagulant therapy → use the newer anticoagulants (fondaparinux, argatroban or r-hirudin) • Unfractionated heparin (UFH)  UFH is the preferred, initial treatment in massive PE with cardiovascular compromise.

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 platelet count monitoring should be performed every 2–3 days from days 4 to 14 or until heparin is stopped. • Warfarin should not be used for antenatal VTE treatment. • Postpartum warfarin should be avoided until at least the fifth day and for longer in women at increased risk of postpartum haemorrhage. Post-thrombotic syndrome (PTS) • Develop in nearly 50% of all patients who experience a DVT. • Features: chronic leg pain, swelling, redness, and ulcers. • Prevention: prolonged use of LMWH (more than 12 weeks). References • Royal College of Obstetricians and

Fat embolism The classic triad of presentation is: • Eosinophilia • Acute renal failure and • Livedo reticularis. Definition • Entry of fat particles usually from bone marrow, in the pulmonary circulation. Causes • Traumatic (95%):  most commonly associated with long bone (especially femur) and pelvic fractures.  typically manifests 24 to 72 hours after the initial insult. • Non-traumatic (Rare): Sickle cell crisis, pancreatitis, osteomyelitis. Features • The classic triad of hypoxemia, neurologic abnormalities (eg, confusion, altered consciousness, seizure), and a petechial rash. • Less common: anemia, thrombocytopenia, fever, lipiduria, and coagulation abnormalities; • Rare: myocardial depression and shock Diagnosis • Presence of clinical triad • Exclusion of other possible causes  embolization syndromes (thrombus, amniotic fluid, tumor, foreign body, air),  acute alveolar filling diseases (eg, heart failure, pneumonia, and ARDS) and  cutaneous vasculitic disorders (eg, systemic lupus erythematosus).

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Pulmonology Treatment • Supportive  Intravenous (iv) fluids to maintain high right ventricular filling pressures.  High flow oxygen  Diuretic treatment would be strongly contraindicated in this case. This is because right ventricular output is dependent on elevated filling pressures. Reducing the preload is therefore not a good idea. • Steroids are reserved for severe or refractory cases. • Most patients fully recover spontaneously. The diagnosis of cholesterol embolism should be considered in any patient with atherosclerotic disease presenting with deteriorating renal function, multisystem disease or distal ischaemia developing after an invasive arterial procedure.

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Community-acquired pneumonia (CAP) Definition • Pneumonia acquired outside hospital or healthcare facilities. 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. Causes • Streptococcus pneumoniae  the most common cause of CAP & single lobar pneumonia (80%)  Streptococcus pneumoniae commonly causes reactivation of the herpes simplex virus resulting in 'cold sores' → herpes labialis  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 .  It's an organism often found on the skin. It is therefore commonly associated with systemic infections in intravenous drug users ,this is may hinted in questions by the presence of track marks.  It also causes a bibasal pneumonia as opposed to Streptococcus pneumoniae that is the most common cause of a single lobar pneumonia.

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 seen most frequently in the elderly and in intravenous drug users or patients with underlying disease.  It can result in a cavitating pneumonia.  Carries a 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.  the BNF advises the co-prescription of flucloxacillin.  • Atypical pneumonias due to:  Mycoplasma pneumoniae ,  Legionella pneumophila .  Coxiella burnetii (Q fever) →relation to animal sources (usually sheep).  Chlamydophila psittaci →bird contact (eg, poultry or duck workers)  Chlamydophila pneumophila • Viruses  Some studies have found that influenza virus is the most common cause of CAP in adults. • Klebsiella pneumoniae  Classically occurs in alcoholics (Friedlander's pneumonia) and immunosuppressed individuals  can cause cavitating pneumonia  usually affects the upper lobes  Chest x-ray features may include abscess formation in the middle/upper lobes and empyema.  The mortality approaches 30-50%. Features • Respiratory symptoms (e.g. cough, often with increasing sputum production, expectoration, dyspnoea, pleuritic pain, and haemoptysis) • Signs of infection (fever or chills and leukocytosis) • Non-specific symptoms such as myalgia and arthralgia. • Specific features of some causes of pneumonia:  Legionellosis can present with headache, confusion, digestive manifestations such as diarrhoea, and clinical manifestations of hyponatraemia.  Mycoplasma pneumoniae may present with extrapulmonary manifestations such as myringitis, encephalitis, uveitis, iritis, and myocarditis • Elderly patients may present atypically, often afebrile, with confusion and worsening of underlying diseases. Investigations • Chest x-ray Organism Characteristic chest x-ray Streptococcus pneumoniae lobar consolidation Legionella bibasal consolidation Staphylococcus aureus bilateral cavitating bronchopneumonia,



Pulmonology • Leukocytosis. • Biomarkers (useful for predicting inadequate host response.)  C-reactive protein (CRP) >100 mg/L makes pneumonia likely.  Procalcitonin (PCT)  Elevated PCT are correlated with bacterial pneumonia whereas lower values are correlated with viral and atypical pneumonia.  PCT is especially elevated in cases of pneumococcal pneumonia. Management Mild community acquired pneumonia (CURB 0-1) should be treated with oral penicillin therapy alone assuming no allergies and no other complicating factors • Assessed the severity of pneumonia using (CURB-65 score)  CURB-65 score criteria

1. Confusion (abbreviated mental test score ≤8/10)
2. Urea > 7 mmol/L
3. Respiratory rate ≥30 / min
4. BP: systolic ≤90 or diastolic ≤60 mmHg
5. age ≥65 years  CURB-65 score of 0 – 1 can be managed in the community.  CURB-65 score of 2 or more should be managed in hospital as this represents a severe community acquired pneumonia. • Empirical antibiotics  A summary table of empirical antibiotics as suggested by the BTS is shown below. Pneumonia Severity (based on clinical judgement and CURB score) Treatment Site First line Second line Low Severity (CURB65 = 0-1) Home Amoxicillin orally Doxycycline or clarithromycin orally Moderate severity (CURB65 = 2) Hospital Amoxicillin plus clarithromycin orally (IV if oral administration not possible) Doxycycline, Levofloxacin or moxifloxacin orally High Severity (CURB65 = 3-5) Hospital Co-amoxiclav plus clarithromycin IV Benzylpenicillin plus levofloxacin or ciprofloxacin IV OR Cefuroxime plus clarithromycin IV • BNF advice: add flucloxacillin if staphylococci suspected (e.g. In influenza) • Pneumonia possibly caused by atypical pathogens

→Clarithromycin • If Staphylococcus aureus is identified, treatment should be altered:

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 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. Panton-Valentine Leukocidin-producing Staphylococcus aureus (PVL-SA) • 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 Prognostic factors • Factors associated with a poor prognosis include:  ↑CURB-65 score  CURB-65 score of 4 → mortality rate at 30 days = 30%.  Co-morbidity such as renal disease, DM, chronic lung disease, heart failure  hypoxaemia (pO2 < 8 kPa) independent of FiO2  White cell count less than 4 ×109/L or greater than 20 ×109/L  Multi-lobar involvement on CXR  Temperature less than 35°C or more than 40°C.  Thrombocytosis is associated with increased mortality compared to thrombocytopaenia or normal platelet levels. • 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 • How quickly their symptoms should resolve?  NICE recommend that the following information is given to patients with pneumonia in terms of how quickly their symptoms should resolve: Time Progress 1 week Fever should have resolved 4 weeks Chest pain and sputum production should have substantially reduced 6 weeks Cough and breathlessness should have substantially reduced 3 months Most symptoms should have resolved but fatigue may still be present 6 months Most people will feel back to normal. Follow up • 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

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Pulmonology  Those who fail to improve after 48 h of treatment should be considered for hospital admission or chest radiography. • C-reactive protein should be re-measured, and a chest radiograph repeated in patients who are not progressing satisfactorily after 3 days of treatment. • Chest x ray in six weeks to ensure complete resolution.  What arrangements should be made for follow-up after hospital discharge?  Clinical review should be arranged for all patients at around 6 weeks.  radiological changes can take up to 6 weeks to improve.  This is to exclude any underlying cause especially malignancy.  those who have persistent shadowing on the lung need referral to a respiratory physician.

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Klebsiella Pneumonia Overview • Klebsiella is a Gram-negative rod (bacillus) encapsulated, non-motile bacterium that is part of the normal gut flora. • It can cause many infections in humans including pneumonia (typically following aspiration) and urinary tract infections. • Most frequently causes infection in hospitalized patients and in those with impaired host defenses, including patients with diabetes mellitus, alcoholism, malignancy, hepatobiliary disease, chronic obstructive pulmonary disease, and renal failure, • It is an uncommon cause of community-acquired

pneumonia. is a common cause of nosocomial pulmonary infections Pathophysiological mechanism • Colonization of the oropharynx followed by microaspiration of upper airway secretions in the setting of decreased consciousness (due to heavy alcohol drinking). Features • more common in alcoholic and diabetics • may occur following aspiration • 'red-currant jelly' sputum  One stark difference between Streptococcus pneumonia and Klebsiella pneumonia is the type of sputum produced. The sputum produced by S. pneumoniae is described as “blood-tinged” or “rust-colored,” however, the sputum blood-tinged by those infected by K. pneumoniae is described as “currant jelly.” • Cavitating lesions, often affects upper lobes. • Typically causes a lobar infiltrate that is in the posterior aspect of the right upper lung. • Another non-specific sign of K. pneumoniae on a chest radiograph is the bulging fissure sign. This is related to the large amount of infection and inflammation that the organism can cause. • commonly causes empyema and less commonly lung abscess Treatment • Community-acquired K. pneumoniae pneumonia → third-generation cephalosporins or quinolones • Extended-spectrum beta-lactamase (ESBL) K. pneumoniae → carbapenem therapy



Prognosis • mortality is 30-50% History of alcoholism and cavitations are suggestive of Klebsiella as the etiology.

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Legionella pneumonia (Legionnaires' disease) Legionella pneumophilia is best diagnosed by the urinary antigen test Aetiology • Legionella bacteria are aerobic, gram-negative rod, intracellular pathogens that are commonly found in water and soil. Human infection is typically acquired through inhalation of aerosols from these substances. • L. pneumophila serotype 1 is the most common cause of human Legionella infections. Epidemiology • Cause 2-5% of community-acquired pneumonia admitted to hospital. • Incubation period 2-10 days • More common in males and age of > 50 years. • Can cause outbreaks in large facilities such as hospitals, hotels, or apartment buildings due to contaminated communal water supplies Source infections • It is typically colonizes hot water tanks and hence questions may hint at airconditioning systems or foreign holidays. • Factors that encourage colonisation and multiplication are temperature (20-45 °C) and stagnation. Transmission • By inhalation of contaminated water droplets (aerosol) • Person-to-person transmission is not seen Features • Flu-like symptoms (present in > 95% of patients), dry cough • Gastrointestinal symptoms such as nausea, vomiting, and diarrhea • Elevated hepatic transaminases • Relative bradycardia • Lymphopaenia  A marked neutrophil leukocytosis may be associated with concomitant lymphopenia. • Hyponatraemia  Secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH) The classic features of Legionnaires' disease are: • Recent foreign travel • Relative bradycardia • prominent headache • Hyponatraemia



Pulmonology Diagnosis • Urinary antigen  the most useful diagnostic test  Sensitivity 80%; specificity >99%.  Rapid test  Only detects L. pneumophila serotype 1, so a negative result does not exclude the diagnosis of Legionella infection.  results are positive during early infection and

remain positive for several weeks or months and it is, therefore, not a test for cure. • Polymerase chain reaction (PCR) using sputum or bronchoalveolar lavage specimen  has high diagnostic accuracy (if available) and detects all Legionella species and serogroups • The organism does not show up on Gram-staining. • Cultures  on buffered charcoal yeast extract (BCYE) agar.  Sensitivity 20% to 95%; specificity 100% • Chest x-ray: Diffuse reticular opacities are commonly seen Management • First line: fluoroquinolones or macrolides  Fluoroquinolones: levofloxacin (preferred), ciprofloxacin, or moxifloxacin,  Macrolides: Azithromycin (preferred), clarithromycin or erythromycin. • Second line  Tetracyclines: doxycycline Pontiac fever • Non-pneumonic Legionella infection • causes a mild, self-limiting course of legionellosis without pneumonia. • flu-like symptoms (e.g. fever, headache, and muscle ache) • Not require antibiotic.

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Mycoplasma pneumoniae Pathogen • Mycoplasma pneumoniae is a cause of atypical pneumonia, more closely related to gram positive bacteria. • Because it lacks a cell wall, it is not visible on Gram stain and is not susceptible to antibiotics that inhibit cell wall synthesis, such as penicillins. Epidemiology • Most commonly affects younger patients (15-30 years). • Accounts for 7% of all community-acquired pneumonias. • Can occurs epidemic outbreaks, most commonly among persons living in close quarters, such as households, schools, and military facilities

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Features • URI and acute bronchitis are the most common (flu-like symptoms classically precede a dry cough) • Systemic upset (arthralgia, haemolytic anaemia, erythema multiforme, Neurological, pericarditis/myocarditis, GIT, renal) • Bilateral consolidation on x-ray Complications → (Extra-pulmonary manifestations occur in ~10% of cases) • Rash → Erythema multiforme, erythema nodosum • Neurological : meningoencephalitis, Guillain-Barré syndrome, transverse myelitis • Cardiac: Myocarditis, Pericarditis • Renal failure: acute glomerulonephritis • Hepatitis • Haemolytic anaemia (found in up to 50% of cases)  the most common extra-pulmonary manifestations and is typically mild and selflimited.  Presence of IgM antibodies (cold agglutinins) directed against the I antigen of the erythrocyte membrane → Spherocytes → Haemolysis → Features of haemolysis (direct Coombs' test, ↑reticulocyte counts, ↑unconjugated bilirubin, ↑LDH, ↓haptoglobins, fragmented red blood cells) Mycoplasma pneumoniae → Serology is diagnostic Diagnosis • Mycoplasma serology  the "gold standard" diagnostic test  92% sensitivity and 95% specificity  more sensitive than culture for detecting acute infection • Positive cold agglutination test  occur in only half of patients • Chest X-ray  might not correlate with the patient's condition →much worse than would be suggested by the clinical examination  the commonest chest x-ray abnormality is bilateral interstitial infiltrate (90%) • Nucleic acid amplification test (NAAT), such as polymerase chain reaction (PCR)  Sensitivity is very high  Faster than serology  Cannot distinguish between active infection and asymptomatic carriage  Causes of Positive PCR but negative serology tests  Asymptomatic carriage of M. pneumoniae (after disease, or during incubation period)  Immunocompromised patients,→no diagnostic antibody response.  Early successful antibiotics therapy. • Culture  rarely used for routine diagnosis  sensitivity may be no more than 60% , but when positive, its specificity is 100%, • WBC can be normal

Pulmonology Mycoplasma pneumonia if allergic/intolerant to macrolides →doxycycline High titer of cold agglutinins (IgM), which can agglutinate RBCs. Mycoplasma gets cold without a coat (no cell wall). Management • First line →macrolides (eg, azithromycin), tetracyclines (eg, doxycycline), and respiratory fluoroquinolones (eg, levofloxacin or moxifloxacin). • Second-line →Tetracyclines such as doxycycline. Prognosis • Most cases resolve spontaneously within a few weeks. Indolent onset, concurrent URI symptoms (eg, rhinorrhea, pharyngitis, ear ache), and the presence of non-respiratory tract manifestations (eg, hemolysis) are suggestive Mycoplasma pneumoniae

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Aspiration pneumonia Definition • a type of pneumonia that occurs as a result of oropharyngeal secretions and/or gastric contents aspiration • also known as Mendelson syndrome Risk factors • ↓level of consciousness (e.g. seizure, Alcohol use, stroke, post-anaesthesia) → impaired gag or swallowing reflex →aspiration occurred several weeks earlier. • Gastroesophageal reflux disease, esophageal motility disorders, dysphagia. • poor oral hygiene Features • Immediate symptoms: bronchospasms , crackles on auscultation, hypoxemia with cyanosis • Late symptoms: fever, shortness of breath, cough with foul-smelling sputum Site of aspiration • which lung?  Due to the angle of the bronchi, the right lung is more commonly affected by aspiration than the left lung.  The right mainstem is more vertical and wider than the left mainstem bronchus. • Which lobe?  Depends on patient's position during aspiration:  in a patient who aspirates while recumbent (lying down):



 superior segment of the right lower lobe (most common site of aspiration)  in a patient who aspirates while sitting upright:  posterior basal segment of the right lower lobe Organisms • Anaerobes and Gram-negative organisms are the usual organisms in abscesses following aspiration. • Sputum or tracheal Gram stain reveals mixed flora. Complications • lung abscess and empyema  air-fluid level is characteristic of a lung abscess. Treatment • Combination of antibiotics → Cefuroxime + Metronidazole • If the patient is allergic to penicillin or cephalosporin→Vancomycin + Metronidazole The slide shows an abscess in the right mid-zone.

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Psittacosis (Chlamydia psittaci pneumonia) (Atypical pneumonia) Exposure to an ill bird and a rash (Horder’s spots) are pathognomonic Definition • Psittacosis is a disease caused by Chlamydia psittaci, an obligate intracellular organism, transmitted to humans from birds., induces prominent systemic manifestations and some respiratory.



Pulmonology Pathogenesis • Humans are usually infected by inhalation of organisms in dried feces or in bird feather dust. • Pet owners, vets and zoo keepers are most at risk. • The incubation period is usually 5 to 14 days. Diagnosis • typical clinical features (fever, headache, myalgias, dry cough)

in a patient with a history of bird contact • In a patient presenting with pneumonia, severe headache, splenomegaly, and failure to respond to beta-lactam antibiotics may be other clues to the diagnosis. • Serology: (e.g. microimmunofluorescent antibody testing, or complement fixation assay) the most useful diagnostic test • Abnormal LFTs in up to 50%. • Chest X-ray: segmental or diffuse multi-lobar consolidation. • Culture is discouraged since C. psittaci is highly infectious when cultured and is only performed in specialized laboratories. Complications • Respiratory failure, hepatitis, endocarditis, and encephalitis. Treatment • 1st line : tetracyclines e.g. doxycycline • 2nd line: macrolides e.g. erythromycin or azithromycin

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Pseudomonas pneumonia Overview • P. aeruginosa is a common cause of gram-negative hospital-acquired pneumonia • Community-acquired P. aeruginosa pneumonia occurs mainly in  immunocompromised patients (eg, HIV, post-transplant, or neutropenic hosts)  structural lung abnormalities (e.g. cystic fibrosis, bronchiectasis, COPD) • 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 • Antibiotics used for the treatment of Pseudomonas aeruginosa infections Class Agent Penicillin-beta-lactamase combinations Piperacillin-tazobactam Cephalosporins Ceftazidime or Cefepime Fluoroquinolones Ciprofloxacin or Levofloxacin Carbapenems Meropenem, Imipenem • Fluoroquinolones are the only class of antibiotics with antipseudomonal activity that have an oral formulation. • The only antipseudomonal penicillin is piperacillin.

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Hospital-acquired pneumonia (HAP) Definition • Hospital-acquired pneumonia (HAP): nosocomial pneumonia, with onset > 48 hours after admission Prevalence • The third most common hospital-acquired infection after urinary tract infections and wound infections. Causes • Gram-negative organisms are the most common causes, especially aerobic gramnegative bacilli, such as:  Pseudomonas aeruginosa,  Escherichia coli,  Klebsiella pneumoniae, and  Acinetobacter species. Diagnosis • A new and/or persistent alveolar shadowing on chest x-ray or CT scan confirms the diagnosis. Treatment • most commonly as combination therapy. A third generation cephalosporin with an aminoglycoside is the current British Thoracic Society (BTS) recommendation. Choice of antibiotic Antibiotics for adults aged 18 years and over (NICE guidelines, September 2019) Treatment Antibiotic First-choice oral antibiotic if non-severe symptoms or signs, and not at higher risk of resistance (guided by microbiological results when available) Alternative oral antibiotics if non-severe symptoms or signs, and not at higher risk of resistance, for penicillin allergy or if co-amoxiclav unsuitable. Doxycycline Cefalexin (caution in penicillin allergy) Levofloxacin First-choice if severe symptoms or signs (e.g. sepsis) or ↑risk of resistance. Piperacillin with tazobactam Ceftazidime Ceftriaxone Cefuroxime Meropenem Ceftazidime with avibactam Levofloxacin If suspected or confirmed methicillin resistant Staphylococcus aureus infection (dual therapy with a firstchoice intravenous antibiotic) Notes & Notes for MRCP
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Co-amoxiclav Vancomycin Teicoplanin Linezolid (if vancomycin cannot be used)

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Pneumocystis Jirovecii pneumonia (PCP) Pneumocystis jiroveci pneumonia - pneumothorax is a common complication Pathogen • Pneumocystis jiroveci is an ubiquitous, yeast-like fungus unicellular eukaryote. Association • PCP is the most common opportunistic infection in AIDS  Pneumocystis jirovecii pneumonia is unlikely in a patient who has had a CD4 count above 200 cells/mm3 in the preceding 2 months in the absence of other HIV-associated symptoms. • Immunosuppressed patients, particularly after organ transplantation 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 • Exercise-induced desaturation • Very few chest signs: The lungs are commonly clear on auscultation • Pneumothorax is a common complication of PCP. Investigation • Lymphopenia is very suggestive of PCP with AIDS (and therefore low CD4 lymphocyte count). • Lactate dehydrogenase raised in 90% of patients with PCP (but this can occur with other pulmonary diseases). • Chest x-ray  Typically shows bilateral interstitial pulmonary infiltrates (diffuse ground-glass opacities)  30% have non-specific or inconclusive findings.  10-15% of patients with PCP have normal chest radiographs • Bronchoalveolar lavage (BAL)  often needed to demonstrate PCP  silver stain shows characteristic cyst phase of the organism  Spontaneously expectorated sputum should not be used for diagnostic studies because it has poor sensitivity for PCP. Use induced sputum instead Pneumocystis jiroveci pneumonia → Definitive diagnosis is by bronchial alveolar lavage with silver staining

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Management • 1ST line : Co-trimoxazole  should be given for 21 days in HIV, but can be shorter in other causes of immunosuppression.  the preferred initial therapy during pregnancy  Glucose 6-phosphate dehydrogenase deficiency (G6PD) levels should be checked prior to TMP-SMX, dapsone or primaquine use • 2nd line: in severe cases or in patients who are intolerant of co-trimoxazole → IV pentamidine • Steroids  Reduces mortality and prevent lung damage in people with moderate-to-severe PCP.  a 21-day tapering course has been shown to be safe and effective.  The severity is determined on the basis of 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). Any patient with PaO2 <70 and A-a gradient >35 should be started on steroid therapy. Prophylaxis • All patients with a CD4 count < 200/mm should receive PCP prophylaxis (Cotrimoxazole is the preferred agent. Dapsone and inhaled pentamidine are also used.) • Primary Pneumocystis prophylaxis should be discontinued if the patient responded to ART with an increase in CD4 counts ≥200 cells/mm3 for ≥3 months. MRCPUK-part-1-January 2016 exam HIV positive but poorly compliant with his antiretroviral therapy (ART). CD4 : 180 cells/ml. oxygen saturations 97% on room air with a temperature of 38.1ºC. He has coarse crackles on the right side of his chest. A chest x-ray shows consolidation of the right mid zone. What is the most likely causative organism?  Streptococcus pneumoniae  (Whilst Pneumocystis jirovecii is of course

associated with HIV, patients who are immunocompromised are more likely to develop infections due to the common pathogens which affect immunocompetent individuals. Streptococcus pneumoniae is therefore the most likely cause of community-acquired pneumonia in this patient. Pneumocystis jirovecii tends to present with very few chest signs and bilateral interstitial pulmonary infiltrates on chest x-ray)

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Pulmonology Coronavirus disease 2019 (COVID-19) Overview • Caused by coronaviruses, SARS-CoV-2 • The transmission occurs mainly through respiratory droplets (particles are greater than 5-10 micrometers in diameter) from coughing and sneezing. • The incubation period is 2-14 days. • Host cell entry occurs by attachment of viral spike protein to angiotensin-converting enzyme 2 receptor on cell membranes. Features • Most common: Fever, Fatigue, Dry cough • Common: Shortness of breath, Loss of smell and/or taste • Less common: Thromboembolic events (e.g., pulmonary embolisms) • Complications include respiratory failure, hypercoagulability, shock, organ failure. Cytokine storm: • an excessive release of proinflammatory cytokines that causes hyperactivation of immune system and exaggerated immune response leading to multiorgan dysfunction. • Initial treatment with tocilizumab plus a glucocorticoid Risk factors for severe illness • Increasing age, • Obesity, • Diabetes, hypertension, chronic kidney disease, and severe cardiopulmonary illness. Pathogenesis • In the normal lung, type II pneumocytes secrete pulmonary surfactant; this phospholipid coats the alveoli and keeps them open and available for gas exchange. The initial lung injury in COVID-19 infection may occur via loss of surfactant and alveolar collapse. • A cytokine storm occurs when white blood cells (WBCs) release large numbers of inflammatory cytokines (eg, interleukin [IL]-1, IL-6) in response to the virus, leading to further WBC activation Diagnosis • RT-PCR (most common)  The nucleic acid amplification test (NAAT) is the diagnostic test of choice for COVID19. NAAT is performed using RT-PCR. • Antigen and antibody tests are available (less accurate) • Chest x-ray may be normal in early or mild COVID-19. Findings in COVID-19 pneumonia include bilateral or peripheral consolidation or opacities • CT scan findings may include ground glass opacities and consolidations, especially in the lung periphery Management • Cough  Avoid lying on the back  Use simple measures first, e.g. honey.  If it is distressing→ Consider short-term use of codeine linctus, codeine phosphate tablets or morphine sulfate oral solution in people 18 years and over to suppress coughing

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• Breathlessness  Identify and treat reversible causes of breathlessness, for example, pulmonary oedema, pulmonary embolism, chronic obstructive pulmonary disorder and asthma.  encouraging relaxation and breathing techniques, and changing body positioning  If hypoxia is the likely cause of breathlessness: consider a trial of oxygen therapy  Consider continuous positive airway pressure (CPAP) when:  hypoxaemia not responding to supplemental oxygen with a fraction of inspired oxygen of 0.4 (40%) or more, and escalation to invasive mechanical ventilation would be an option but it is not immediately needed, or it is agreed that respiratory support should not be escalated beyond CPAP.  Consider using high-flow nasal oxygen for people having continuous positive airway pressure (CPAP) when they need:  a break from CPAP, such as at mealtimes 

humidified oxygen  weaning from CPAP. • Corticosteroids  Indication: people with COVID-19 who need supplemental oxygen.  1st choice : dexamethasone. Hydrocortisone or prednisolone when dexamethasone cannot be used or is unavailable. • Combination of casirivimab and imdevimab  to people aged 12 and over hospitalised because of COVID-19 who have no detectable SARS-CoV-2 antibodies (seronegative).  Not recommended for patients who have detectable SARS-CoV-2 antibodies (seropositive) • Remdesivir  Indication: hospitalised patient who are ˃ 12 year old and weight ≥ 40 kg and need low-flow supplemental oxygen.  Not recommended for patient who need NIV or invasive mechanical ventilation. • Tocilizumab: (Single dose)  Indications  hospitalised with severe COVID-19 (need O2 and CRP ≥75 mg/litre)  no evidence of a bacterial or viral infection (other than SARS-CoV-2) that might be worsened by tocilizumab.  Consider sarilumab if tocilizumab is unavailable or cannot be used • Medication not recommended to treat COVID-19.  Azithromycin, budesonide, colchicine, doxycycline • Venous thromboembolism (VTE) prophylaxis  only for in hospital patients, consider a prophylaxis dose of low molecular weight heparin (LMWH) if the risk of VTE outweighs the risk of bleeding.  Do not base prophylactic dosing of heparin on levels of D-dimer. • Antibiotics: Should not be used unless there is clinical suspicion of additional bacterial coinfection.  Procalcitonin tests could be useful in identifying whether there is a bacterial infection.  High C-reactive protein levels do not necessarily indicate whether pneumonia is due to bacteria or SARS-COV-2.  Low C-reactive protein level indicates that a secondary bacterial infection is less likely.  Do not use C-reactive protein to assess whether a person has a secondary bacterial infection if they have been having immunosuppressant treatment.

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Pulmonology • Medicines for end-of-life care: opioid and benzodiazepine combination. Remdesivir • Remdesivir is a nucleotide prodrug of an adenosine analog. • It binds to the viral RNA-dependent RNA polymerase • It inhibits viral replication by terminating RNA transcription prematurely. • Adverse Effects: ↑ transaminase levels & prothrombin time (Liver function tests and prothrombin time tests should be performed for all patients before they receive remdesivir). COVID-19 enters the lungs via type II pneumocytes. Tocilizumab • Mode of action  Antagonizes the IL-6 receptor, which leads to a reduction in cytokine and acute phase reactant production. • Common adverse effects (>10%)  Neutropenia  ↑ liver enzyme  ↑ serum cholesterol  Constipation Treatment of COVID-19 in pregnant patients Initial management

1. Oxygen – titrate supplemental oxygen to keep sats >94%
2. Thromboprophylaxis – prophylactic LMWH dose according to weight
3. Corticosteroids – if oxygen dependent give for a total of 10 days a. Oral prednisolone 40mg OD; or b. IV hydrocortisone 80mg BD
4. If steroids used for fetal lung maturation use Dexamethasone 12mg IM 24 hourly (2 doses) followed by either (a) or (b) above for 10 days Clinical deterioration

• Increased O2 requirements : O2 sat<93 , RR > 22  Give tociluzimab (or sarilumab if unavailable) if needing escalation of care and/or if CRP>75  Check COVID-19 antibodies, if negative consider 2.4g Ronapreve IV once (RONAPREVE contains the active ingredients casirivimab and imdevimab.) Discharge • Thromboprophylaxis for at least 10 days • Encourage COVID19 vaccination: can be given 28 days following recovery • Advise: if given tocilizumab/sarilumab, be aware of an increased

risk of infection without typical signs for several months.

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Aspergillosis: Types Overview • Aspergillosis is the collective term for diseases caused by mold species in the genus Aspergillus. • Most common: Aspergillus fumigatus and Aspergillus flavus • Transmission: airborne exposure to mold spores ABPA Chronic pulmonary aspergillosis (e.g. Aspergilloma) Main features Asthmatic symptoms Dry cough, septic shock, multisystem involvement Laboratory tests • ↑ IgE levels • Eosinophilia • ↑ ESR • Positive Aspergillus antigen skin test • Positive galactomannan antigen test: (galactomannan is a protein found in Aspergillus cell wall). • Positive 1,3-β-D glucan test • Septate hyphae on tissue biopsy Chest x-ray and CT • Bronchiectasis • Pulmonary infiltrates Notes & Notes for MRCP
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Invasive aspergillosis Hemoptysis, shortness of breath Positive Aspergillus IgG serology • Mobile fungus ball (demonstrated by moving the patient from a supine position to a prone or lateral recumbent position) • Monod sign: a peripheral air crescent around a fungus ball in a preexisting lung cavity • The upper lobe is mostly • Multiple nodules • Halo sign: hemorrhagic ground glass opacities around nodules

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Pulmonology affected Treatment • Oral prednisone if severe • Itraconazole if recurrent The most important diagnostics for the different aspergillosis types are: • ABPA: increased IgE and eosinophil count. • Aspergilloma: positive culture or serology and fungus ball seen on chest imaging. • Invasive aspergillosis: positive culture or biopsy showing septate hyphae.

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Allergic bronchopulmonary aspergillosis (ABPA) In the exam questions often give a history of bronchiectasis and eosinophilia. Definition • ABPA results from an allergy to Aspergillus spores (Type I hypersensitivity to Aspergillus fumigatus). • a hypersensitivity reaction caused by exposure to Aspergillus that mostly occurs in patients with cystic fibrosis or asthma • Aspergillus fumigatus is the most common airborne fungus causative organism for ABPA. Risk factors • Preexisting bronchopulmonary conditions (e.g., asthma, cystic fibrosis) Features • Bronchoconstriction: wheeze, cough, dyspnoea (clinical deterioration in asthma symptoms) • Bronchiectasis (proximal) Investigations • Serum eosinophilia • Raised IgE: helpful test, but not specific enough to establish the diagnosis. • Aspergillus skin-prick test (the most specific investigation)  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 to (ABPA). specific  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 in up to 10% of patients with asthma. • Pulmonary infiltrates on CXR. Lobar collapse can also occur, due to mucus plugging. Notes & Notes for MRCP
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• Surgical resection (e.g., lobectomy) IV voriconazole • Itraconazole OR voriconazole (should be used preoperatively and postoperatively) most

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Allergic bronchopulmonary aspergillus: both of the following must be present to confirm the diagnosis:  Aspergillus skin test positivity or detectable IgE levels against aspergillus fumigatus and  Elevated total serum IgE concentration. Management • First line →steroids (prednisone) • Second line → add itraconazole or voriconazole  Itraconazole leads to significant reductions in corticosteroid dose, decreases IgE levels, greater resolution of pulmonary infiltrates, and improves exercise tolerance.

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Aspergilloma The clue can be a lack of improvement with broad spectrum intravenous antibiotics, haemoptysis and chest X-Ray findings. Definition • An aspergilloma is a mycetoma (mass-like fungus ball) which often colonises an existing lung cavity (e.g. secondary to tuberculosis, lung cancer, cystic fibrosis or emphysema) Feature • often asymptomatic • cough • haemoptysis in up to three quarters of patients (may be severe and fatal ) • Systemic symptoms of weight loss, lethargy and fever are less common. Investigations • chest x-ray containing a rounded opacity within a cavity often associated with a rim of air. These features are seen more clearly on CT. • High titres Aspergillus precipitins (IgG antibodies) present in 95% of cases. Treatment • 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 Aspergilloma should be considered in patients with chronic lung disease and radiographs showing intracavitary mass lesions.

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Pulmonology Images

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Invasive aspergillosis (IA) Definition • a severe form of Aspergillus infection with severe pneumonia and septicemia, most commonly occurs in immunocompromised individuals. Risk factors • immunosuppression (e.g., due to HIV/chemotherapy, after organ transplantation) or neutropenia (e.g., due to chronic granulomatous infection). Features • Symptoms of active infection & haemoptysis. Investigations • the classical signs on CT scanning the 'halo sign' air crescent sign • galactomannan test:  Galactomannan is a component of the cell wall of the Aspergillus and is released during growth.  Detection of galactomannan in blood by ELISA is used to diagnose invasive aspergillosis • Silver staining shows →hyphae.  Haematoxylin and eosin (H&E) stain does not stain most of the fungi, except the Aspergillus species. Treatment • 1st line voriconazole: start iv before oral (as oral 10 days to get therapeutic levels). • 2nd line (If voriconazole is not tolerated): amphotericin B Prognosis • Mortality vary from 40-90%