014 - Pages 326-350

- 014

014

Pages 326-350

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Typical morphology of Aspergillus fumigatus. CT chest showed Aspergilloma A slightly thick-walled left upper lobe cavity contains a rounded mass. A crescent-shaped airspace, termed the air crescent sign, separates the mass from the cavity wall. An aspergilloma can often be shown to move to the dependent position within its cavity

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

Pulmonology Invasive aspergillosis • Invasive aspergillosis should be suspected in someone who is immunocompromised (neutropenia, steroids, HIV) with severe chest pain, highgrade fevers, and haemoptysis. • The treatment of choice for invasive aspergillosis is voriconazole Voriconazole → ↑risk of developing skin malignancy (malignant melanoma, squamous cell carcinoma)

Alpha-1 antitrypsin (A1AT) deficiency Alpha-1 antitrypsin deficiency - autosomal recessive / co-dominant Definition • Alpha-1 antitrypsin (A1AT) deficiency is a common inherited genetic disorder characterized by the accumulation of defective alpha-1 antitrypsin enzyme Genetics & Pathophysiology • Alpha-1 antitrypsin: a protease inhibitor that is synthesized in the liver and protects cells from breakdown by neutrophil elastase (AAT neutralises neutrophil elastase, thereby preventing lung destruction.) • The mode of inheritance: autosomal co-dominant • Mutations in SERPINA1 gene, located on the long arm of chromosome 14 → dysfunctional (or absent) AAT • A1AT deficiency is the most prevalent genetic disease in patients of finnish/scandinavian origin • Alleles classified by their electrophoretic mobility - M for normal, S for slow, and Z for very slow • 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). • Patients who manifest disease usually have PiZZ genotype • Effect on the lungs: deficient AAT → uninhibited neutrophil elastase activity → destruction of the pulmonary parenchyma → panacinar emphysema • Effect on the liver: accumulation of AAT in hepatocellular endoplasmic reticulum → hepatocyte destruction → hepatitis and liver cirrhosis

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Features • Pulmonary Panacinar emphysema, most marked in lower lobes (2% of cases of emphysema) The interplay between the environmental and genetic factors determine its onset. Patients usually present with increasing dyspnoea. • Hepatic Hepatitis Cirrhosis (15%) Increased risk of hepatocellular carcinoma (HCC) Investigations • Serum: decreased antitrypsin protein levels • Electrophoresis: decreased alpha-1 peak
• Chest x-ray Low and flat diaphragm Widened intercostal spaces Hyperinflation and increased basilar radiolucency of both lungs with rarification of peripheral pulmonary vessels • Chest CT Panacinar emphysema (in contrast to centriacinar emphysema in smokingrelated emphysema) Bronchiectasis Bullae • Liver biopsy PAS-positive, spherical inclusion bodies in periportal hepatocytes Signs of cirrhosis Management • Avoid smoking smoking is harmful to those with A1AT deficiency and can accelerate the progression of emphysema by 10 years. • Supportive Preventive vaccination (e.g., influenza vaccine, pneumococcus vaccine) Symptomatic treatment (bronchodilators) Pulmonary rehabilitation (Physiotherapy) • Intravenous alpha1-antitrypsin protein concentrates • Surgery Volume reduction surgery Lung transplantation Liver transplantation → Results in correction of AAT deficiency (Considered for end-stage liver disease Which form of lung disease develops typically in people with α1-antitrypsin deficiency? Emphysema The diagnosis of AAT deficiency should be considered in all patients with emphysema under the age of 50 years.

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

Pulmonology

Acute respiratory distress syndrome (ARDS) Definition • acute respiratory failure characterized by hypoxemia and bilateral pulmonary infiltrates that cannot be explained by heart failure or fluid overload. Causes • Sepsis (most common cause) • Trauma • Shock • Massive transfusion (TRALI) • Acute pancreatitis • Hematopoietic stem cell transplantation • Medication (e.g., salicylic acid, tricyclic antidepressants, bleomycin) • Recreational drug overdose (e.g., cocaine) • Primary damage to the lungs (Pneumonia, Aspiration, Inhaled toxins) Pathophysiology • Tissue damage (pulmonary or extrapulmonary) → release of inflammatory mediators (e.g., interleukin-1) → inflammatory reaction → migration of neutrophils into alveoli → excessive release of neutrophilic mediators (e.g., cytokines, proteases, reactive oxygen species) → injury to alveolar capillaries and endothelial cells (diffuse alveolar damage)
Phases: diffuse alveolar damage lead to: • Exudative phase: excess fluid in interstitium and on alveolar surface → pulmonary edema with normal pulmonary capillary wedge pressure (noncardiogenic pulmonary edema) → decreased lung compliance and respiratory distress • Hyaline membrane formation: exudation of neutrophils and protein-rich fluid into the alveolar space → formation of alveolar hyaline membranes → impaired gas exchange → hypoxemia Hypoxemia → compensation through hyperventilation → respiratory alkalosis Hypoxemia → chronic hypoxic pulmonary vasoconstriction → pulmonary hypertension and right-to-left pulmonary shunt (increased shunt fraction) Damage to type I and type II pneumocytes → decrease in surfactant → alveolar collapse → intrapulmonary shunting • Organizing phase (late stage): proliferation of type II pneumocytes and infiltration of fibroblasts → progressive interstitial fibrosis What would one expect to see on a histological specimen of a lung from a patient who died of

ARDS? The presence of hyaline membranes is a hallmark of ARDS.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Features • Symptoms: Acute dyspnea. Fever, cough, and chest pain may also be present. • Signs: Tachypnea, cyanosis, diffuse crackles What is the most consistent finding you would expect to see on arterial blood gases taken from patients with ARDS? increased arterial-alveolar oxygen gradient. ARDS is associated with: • Increased elastic recoil. • Low pulmonary artery wedge pressure. • Low compliance. • Restrictive lung disease Berlin criteria for ARDS • The Berlin criteria are the criteria most commonly used to define ARDS. • All four of the following conditions must be met:

1. Acute onset: respiratory failure within one week of a known predisposing factor (e.g., sepsis, pneumonia)
2. Bilateral opacities (on chest x-ray or CT) Similar appearance to pulmonary oedema Not sufficiently explained by pleural effusions, lobar or lung collapse, or nodules
3. Hypoxemia: PaO2/FiO2 ≤ 300 mm Hg (measured with a minimum of 5 cm H2O PEEP) Mild ARDS: PaO2/FiO2 = 201–300 mm Hg Moderate ARDS: PaO2/FiO2 = 101–200 mm Hg Severe ARDS: PaO2/FiO2 ≤ 100 mm Hg
4. Respiratory failure cannot be fully accounted for by heart failure or fluid overload. Patients with ARDS have normal pulmonary capillary wedge pressure (PCWP) (<18 mmHg). Management • Admit all patients with ARDS to the ICU. • Oxygenation Noninvasive ventilation: for hemodynamically stable, alert patients with mild ARDS. Endotracheal intubation: respiratory failure or rapid deterioration • Lung-protective ventilation: to decrease the risk of ventilator-induced lung injury General initial settings include: Low tidal volume (Vt 6–8 mL/kg) : prevents alveolar distention Low plateau pressure (PPlat ≤ 30 cm H2O): prevents barotrauma PEEP > 5 cm H2O: allows for alveolar recruitment PEEP and FiO2 can be adjusted to recruit collapsed alveoli and improve oxygenation. Oxygenation goal: PaO2 55–80 mm Hg or SpO2 88–95% Avoid oxygen toxicity: use lowest FiO2 possible • Identify and treat the underlying cause

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

Pulmonology • If the patient is on maximal ventilatory therapy but is still hypoxic & hypercapnic? →Extracorporeal membrane oxygenation (ECMO) (connecting a patient's circulation to an external oxygenator and pump, via a catheter placed in the right side of the heart). • Diuretics are NOT particularly effective, because the infiltrate of ARDS is primarily inflammatory. • Glucocorticoids have NOT been shown to help patients in the acute phase of ARDS. Acute respiratory distress syndrome (ARDS) diagnostic criteria: • Abnormal x-ray, • Respiratory failure < 1 week after a known or suspected trigger, • Decreased PaO2/FiO2, • Should exclude CHF or fluid overload as a potential cause of respiratory distress. ARDS patient on mechanical ventilation If the patient’s blood gases reflect hypoxaemia and a slight respiratory alkalosis, (despite high FiO2 settings and sufficient ventilation, his arterial oxygenation remains inadequate). What is the best next step? Adding positive end-expiratory pressure (PEEP) The ventilator strategy should employ a

relatively high level of PEEP. Generally, oxygenation may be improved by further increasing the FiO2 or by adding PEEP. High FiO2 is contraindicated due to the risk of pulmonary oxygen toxicity. Thus, the goal in managing mechanically ventilated patients should be to keep the FiO2 below 40% at all times. The patients FiO2 may need to be reduced soon- if more than 40% - in order to avoid pulmonary oxygen toxicity, but this should be accomplished by first increasing oxygenation by another means, such as by increasing PEEP. PEEP prevents alveolar collapse, directly counteracting the means by which ARDS causes hypoxaemia. It may also reopen some alveoli that have already collapsed. • Which therapies has been shown to most likely decrease overall mortality of ARDS? Implementing a low tidal volume ventilation protocol (6 mL/kg based upon ideal body weight) The target tidal volume is based on ideal, rather than actual body weight. Fat has no alveoli ! A target tidal volume of 6 ml/kg ideal body weight should be set maintaining plateau pressures of less than 30 cmH2O The two main ventilator methods used in the management of ARDS are: • High positive end-expiratory pressure (PEEP) • Low tidal volume ventilation (LTVV)

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Altitude related disorders Response to high altitude • The arterial partial pressure of oxygen (PaO2) decreases with altitude, resulting in progressive tissue hypoxia. The normal compensatory response to hypobaric hypoxia is termed acclimatization. Its main feature is increased ventilation. • ↓atmospheric oxygen (PiO2) → ↓PaO2 →↑ventilation → ↓Paco2 → respiratory alkalosis → altitude sickness (headaches, nausea, fatigue, lightheadedness, sleep disturbance). • Chronic ↑ in ventilation. • ↑Erythropoietin → ↑Hct and Hb (due to chronic hypoxia). • ↑ 2,3-bisphosphoglycerate (2,3-BPG) (binds to Hb → shifts the oxygen-hemoglobin dissociation curve to the right → ↑O2 release). • Cellular changes (↑mitochondria). • ↑Renal excretion of HCO_3^- to compensate for respiratory alkalosis (can augment with acetazolamide). • Chronic hypoxic pulmonary vasoconstriction → ↑pulmonary vascular resistance → pulmonary hypertension, RVH. Types • 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 (AMS) • AMS start to occur above 2,500 - 3,000m, developing gradually over 6-12 hours and potentially last a number of days. • Features Headache Nausea Fatigue • Treatment descent generally a self-limiting condition. usually resolves by day 3 with rest and gradual acclimatization to the high altitude. • Prevention 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 High altitude cerebral oedema (HACE) • Generally occur above 4,000m • HACE presents with headache, ataxia, papilloedema • Management descent dexamethasone

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

Pulmonology High altitude pulmonary oedema (HAPE) • Generally occur above 4,000m • Presents with classical pulmonary oedema features • Management (after descent) 1st line → High concentration O2 2nd line → Nifedipine, dexamethasone, acetazolamide, phosphodiesterase type V inhibitors All seem to work by reducing systolic pulmonary artery pressure Acetazolamide • Carbonic anhydrase inhibitor • Causes HCO3 – wasting (prevents HCO3 – reabsorption in the proximal tubule) metabolic acidosis, and subsequent diuresis. • Metabolic acidosis → hyperventilation (physiological response) → ↑oxygenation → prevent altitude sickness

---

Bronchiectasis Bronchiectasis should be suspected in a patient with chronic cough producing large amounts of sputum Definition • Permanent dilatation of the airways secondary to chronic infection or inflammation. Causes • Post-infective: (i.e., bacterial, viral, fungal) tuberculosis, measles, pertussis, pneumonia A history of previous whooping cough suggests bronchiectasis. • Disorders of secretion clearance, mucous plugging or bronchial obstruction Cystic fibrosis (CF) Primary ciliary dyskinesia (PCD) Allergic bronchopulmonary aspergillosis (ABPA) Kartagener syndrome α1-antitrypsin deficiency Smoking: associated with poor ciliary motility Lung cancer/foreign body • Immunodeficiency (e.g., common variable immunodeficiency, hypogammaglobulinemia, HIV) • Chronic inflammatory diseases (e.g., rheumatoid arthritis, Sjogren syndrome, Crohn disease) • Yellow nail syndrome Features The most common findings on examination are crackles (75%) and wheeze (22%). Clubbing is only found in 2%. • Chronic productive cough, with copious amounts of sputum (expectorating phlegm on most days)

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

• Dyspnea • frequent chest infections • haemoptysis • Post nasal drip - common (chronic sinusitis in around 30%) • Tiredness - many patients find this more troublesome than the productive cough • Low Ventilation perfusion ratio leading to hypercapnia →Respiratory acidosis, and the body compensate by increasing heart rate and vasodilatation. Diagnosis • Chest X-ray The best initial test can be normal in 50% of patients (Bronchiectasis cannot be ruled out with a chest x-ray) Findings: thickened and dilated bronchi, which produce tramline opacities and ring shadows “tram track” lines due to Inflammation and fibrosis of bronchial walls Retained mucus might be seen as tubular opacities, volume loss of the affected lobe. Thin-walled cysts (i.e., dilated bronchi forming sacs), possibly with air-fluid levels Late-stage bronchiectasis: honeycombing • High-resolution computed tomography scan of the lungs (HRCT) The gold standard for diagnosis of bronchiectasis. Findings tram track lines and honeycombing 'signet ring' sign increased broncho-arterial ratio (bronchus larger than neighboring pulmonary artery). The bronchus and artery should be the same size, whereas in bronchiectasis, the bronchus is markedly dilated. Differential diagnosis • Carcinoma of the lung: Lung cancer can present with non-resolving respiratory infection with productive cough due to endobronchial obstruction by tumour, but there would be a much shorter duration of symptoms. Without treatment most patients would be dead within a year of the onset of lung cancer.

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

Pulmonology Chest x-ray showing tramlines, most prominent in the left lower zone CT chest showing widespread tram-track and signet ring sign Subtypes of Bronchiectasis • Cylindrical bronchiectasis bronchi have a uniform calibre, do not taper and have parallel walls (tram track sign and signet ring sign) commonest form (47%) • varicose bronchiectasis relatively uncommon (9.9%) beaded appearances where dilated bronchi have interspersed sites of relative narrowing • cystic bronchiectasis (45.1%) severe form with cyst-like bronchi that extend to the pleural surface air-fluid levels are commonly present • multiple types: ~ 24.3% Management Symptom control in non-CF bronchiectasis →inspiratory muscle training + postural drainage The mainstay of therapy for bronchiectasis is antibiotics and chest physiotherapy. 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)

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Most common organisms isolated from patients with bronchiectasis Bronchiectasis: most common organism Haemophilus influenzae • Haemophilus influenzae (most common) • Pseudomonas aeruginosa • Klebsiella spp. • Streptococcus pneumoniae Prevention • Primary prevention: antibiotic control of bronchial and pulmonary infections in predisposed individuals • Secondary prevention: long-term low-dose macrolide treatment (e.g., azithromycin) in patients with two or more bronchiectasis exacerbations within one year.

Cystic fibrosis (CF) Genetics • Autosomal recessive; defect in CFTR gene on chromosome 7; commonly a deletion of Phe508. • The defective gene inhibits the body's ability to move salt and water in and out of cells → Deranged chloride transport → thick, viscous secretions in the lungs, pancreas, liver, intestine, and reproductive tract. Children whose parents are both heterozygous carriers of cystic fibrosis have a 25% chance of being affected by the condition. Epidemiology • Occurs in 1 in 2500 live births. • The carrier frequency in white populations is 1 in 25. • the most common genetically inherited diseases in Caucasian individuals. • Rare in patients of Afro-Caribbean and Asian origin. • 10% of people with cystic fibrosis are not diagnosed until adult life. Features • Failure to thrive and delayed puberty (100%) • Infertility Male infertility occurs in 98% due to failure of development of the vas deferens (congenital bilateral absence of the vas deferens (CBVAD); therefore, the anatomic duct through which spermatozoa pass from the testes to the urethra is absent, resulting in obstructive azoospermia) Patients may have CBVAD and cystic fibrosis transmembrane conductance regulator gene (CFTR) mutation without symptoms of CF. Female subfertility secondary to viscid cervical secretions. (only a 20% will be infertile)

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

Pulmonology • Pancreatic insufficiency The most common (85%) almost always present in adult patients Due to obstruction of the pancreatic ductules by thickened secretions. Diabetes mellitus: occurs in > 65% of patients by age 25 treatment of choice is subcutaneous insulin. Calorie intake should not be restricted in CF patients, who are prone to malnutrition due to their pancreatic insufficiency. Malabsorption (30%): steatorrhoea Fat-soluble vitamin deficiencies (including vitamins A, D, E and K) • Respiratory Recurrent chest infections (40%) Clues to a diagnosis of cystic fibrosis rather than an alternative immunodeficiency would be manifestations in other organ systems (pancreatic disease or infertility). Allergic bronchopulmonary aspergillosis (ABPA) is a recognised complication, occurring in 15% of adult CF patients Pneumothorax is seen in up to 5% of patients over 10 years of age and approximately 50% recur. • Liver disease By young adulthood, CF-associated liver disease develops in 30 % of those affected. Cholestasis due to defective CFTR protein on bile duct epithelial cells • 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. • Gastro-intestinal Distal intestinal obstruction syndrome : most common bowel complication in cystic fibrosis after Gastroesophageal reflux disease (GERD) 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. Rectal prolapse (in children) due to bulky stools Constipation is common • Renal Urinary stress incontinence Renal calculi (incidence increases with age and 1 in 20 adults are affected). Distal intestinal obstruction syndrome is the most common bowel complication in cystic fibrosis after Gastroesophageal reflux disease (GERD) Diagnosis • Sweat chloride test The most important diagnostic test Sweat chloride ≥60 mmol/L is abnormal. The patient should undergo CFTR gene mutation testing to confirm the diagnosis (false negative in 1-2% of patients). Sweat chloride ≤29 mmol/L is normal. This is sufficient to rule out CF.

 Sweat chloride 30 to 59 mmol/L is intermediate. These patients should have repeat sweat chloride testing and CFTR sequencing. sweat test is conducted using pilocarpine iontophoresis.(a direct acting muscarinic agonist) Causes of false negative sweat test nephrotic syndromes. Causes of false positive sweat test malnutrition adrenal insufficiency glycogen storage diseases nephrogenic diabetes insipidus hypothyroidism, hypoparathyroidism G6PD ectodermal dysplasia • Genetic test (DNA analysis) → CFTR gene mutation → confirm the diagnosis Should be performed for patients with intermediate or positive sweat chloride results. Management Management of pulmonary disease • Airway clearance techniques Chest physiotherapy and postural drainage, regular (at least twice daily) An airway clearance session generally begins with SABA therapy to open the airways, followed by mucolytics to thin the mucus, then airway clearance techniques. high-frequency chest wall oscillation is not recommended by NICE. • Mucoactive agents 1st line: rhDNase (dornase alfa; recombinant human deoxyribonuclease) 2nd line: rhDNase and hypertonic sodium chloride or hypertonic sodium chloride alone. 3rd line: mannitol dry powder for inhalation • Anti-inflammatory agents (e.g., macrolide antibiotics, ibuprofen, corticosteroids) are used to control inflammation in the airway • Lumacaftor-Ivacaftor Combination Used by NHS but not recommended by NICE specifically targets the most common CFTR mutation, the ΔF508 mutation. Ivacaftor potentiates the opening of the CFTR chloride ion transport channel, Lumacaftor improves the conformational stability of

ΔF508-CFTR, resulting in increased processing and trafficking of mature protein to the cell surface. Lung transplant • Indications Evidence of pulmonary hypertension FEV1 <50% predicted and rapidly declining (eg, >20% relative decline in FEV1 within 12 months) FEV1 <40% predicted and BMI <18 (while working to improve nutritional status) FEV1 <40% predicted and any of the following markers of shortened survival:

> 2 exacerbations per year requiring intravenous antibiotics

Pulmonology Massive hemoptysis (>240 mL) requiring intensive care unit admission or bronchial artery embolization. Pneumothorax FEV1 <30% predicted Any of the following, regardless of FEV1: 6-minute walk test <400 meters Hypoxemia (SpO2 <88% or PaO2 <55 mmHg, at rest or with exertion) Hypercarbia (PaCO2 >50 mmHg, confirmed on arterial blood gas) Pulmonary artery systolic pressure >50 mmHg on echocardiogram or evidence of right ventricular dysfunction in the absence of tricuspid regurgitant jet Any exacerbation requiring positive pressure ventilation • Factors that warrant earlier consideration for transplant referral Female sex, especially those who are younger Short stature (height <162 cm) Liver cirrhosis or chronic kidney disease (may require consideration of multiple organ transplantation and may affect timing or choice of transplant center) • Absolute contraindications include Sepsis multiple organ dysfunction, documented history of non-adherence to treatment, patients colonised with Burkholderia cepacia class III obesity (body mass index [BMI] 40 or above), and refractory gastro-oesophageal reflux. • Recipient criteria Age under 60 years Life expectancy of less than 18 months No underlying cancer or serious systemic disease • Donor characteristics 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. Management of extra-pulmonary disease • Nutritional interventions High calorie diet, including high fat intake CF →Weight loss → ↑ risk of exacerbations & overall mortality. For that it's important to maintain a high calorie diet the best way to manage diabetes in CF is insulin and high calorie diet to allow them to convert those calories into stored energy. Vitamin supplementation • For malabsorption First test for exocrine pancreatic insufficiency→ stool elastase (if abnormal) → pancreatic enzyme replacement. If symptoms persist → acid suppression agent (H2 receptor antagonist or a proton pump inhibitor) • For distal intestinal obstruction syndrome 1st line: diatrizoate meglumine and diatrizoate sodium solution (Gastrografin) (orally or via an enteral tube)

 2nd line: iso-osmotic polyethylene glycol and electrolyte (PEG) solution (macrogols) (orally or via an enteral tube) 3rd line: surgery Prevention by : encourage drink plenty of fluids & pancreatic enzyme replacement therapy & regular stool-softening agent such as lactulose. • Liver disease If liver function tests are abnormal → ursodeoxycholic acid Chest infections in cystic fibrosis •

Organisms Infants and young children become colonised by Staphylococcus aureus and then Haemophilus influenzae. Pseudomonas aeruginosa is the commonest colonising organism in patients with cystic fibrosis after the age of 10 years.(40 – 80%) Aspergillus colonisation is also common 19%. Burkholderia cepacia Gram-negative, aerobic, rod bacteria. Occurs in 5–10% of patients. Often multi drug resistant. Associated with the worst prognosis Infection is a relative contraindication to undergoing lung transplant due to its association with poor outcomes. In cystic fibrosis, Staphylococcus aureus infections are more common in childhood while Pseudomonas infections become more common in late adolescence and adulthood. • Antibiotics Acute exacerbations Combination of piperacillin-tazobactam, ceftazidime, meropenem plus one of the following: a fluoroquinolone, tobramycin, amikacin, or colistin. Chronic Pseudomonas aeruginosa infection the commonest colonising organism in patients with CF after the age of 10 years. Azithromycin at the time of the first positive culture test for nontuberculous mycobacteria before initiating azithromycin. Azithromycin should not be given to patients infected with nontuberculous mycobacteria, because it may induce antibiotic resistance. chronic azithromycin may reduce the efficacy of inhaled or intravenous tobramycin. 1st line → nebulised colistimethate sodium 2nd line → nebulised aztreonam, or nebulised tobramycin

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

Pulmonology Tobramycin • Aminoglycoside antibiotic • Works by binding to a site on the bacterial 30S and 50S ribosome, preventing formation of the 70S complex. As a result, mRNA cannot be translated into protein → cell death • Side effects: Nephrotoxicity ototoxicity (generally irreversible). Prognosis • The median survival is now predicted to be at least 40 years for children born in the 1990s. Occupational lung diseases • Occupational asthma • Extrinsic allergic alveolitis (EAA) • Pneumoconiosis • Asbestos and the lung • Pleural mesothelioma • Silicosis • Berylliosis • Coal workers' pneumoconiosis (CWP)

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Occupational asthma Overview • Occupational asthma is a variable airflow obstruction attributable to a particular occupational exposure and not due to stimuli outside the workplace. • Should be suspected and evaluated in every patient with adult-onset asthma. 5 to 25 % of all adult-onset asthma cases are occupationally related. • Occurs more frequently in atopic persons and smokers. Causes • Exposure to the following chemicals are associated with occupational asthma: Isocyanates - the most common cause. (e.g. occupations include spray painting and foam moulding) Metals (Platinum salts, Aluminium, Chrome, Manganese, Nickel, Zinc) Disinfectant and preservatives (glutaraldehyde, chlorhexidine , formaldehyde) Flour Proteolytic enzymes Diagnosis • Confirmation of asthma Spirometry before and after bronchodilator → reversibility of airflow limitation. • Determine occupational relationship Symptoms become better at weekends / when away from work. Serial PEFR measurement at work and at home is a useful diagnostic test to assess a workplace contribution Skin test reactivity or immunoassay for specific immunoglobulin E (IgE) can identify sensitization to known occupational sensitizers. Management • Reduction of further exposure to the allergen.
 Change the Job if possible Changing the pattern of the particular duties. An alternative is to

use industrial respirators, which filter out 98-99% of respirable dust from the ambient air. • Corticosteroid Occupational asthma should be suspected in all adult patients with asthma.

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

Pulmonology

Hypersensitivity pneumonitis (HP) (also called extrinsic allergic alveolitis) Definition • an immunologic reaction occurring within the pulmonary parenchyma caused by hypersensitivity to an inhaled agent, such as microbial, avian, animal antigens and, less commonly, organic compounds. Pathophysiology • Acute HP is predominantly mediated by antigen-antibody complex formation (type III hypersensitivity) • Subacute and chronic HP result from an interplay of T helper (Th 1), T17, and T regulatory lymphocytes leading to lymphocyte infiltration and granuloma formation (delayed hypersensitivity) (type IV). • 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). • characterised histologically by: Alveolar destruction and interstitial inflammation. Non-caseating granulomas Asteroid bodies may be found in or adjacent to the granulomas. Examples • Farmer's lung: Caused by spores of Saccharopolyspora rectivirgula (formerly Micropolyspora faeni) The commonest occupational hypersensitivity pneumonitis Contaminated hay is the most common source of Saccharopolyspora rectivirgula Serum precipitating antibodies to Saccharopolyspora rectivirgula is the most useful diagnostic test (found in 75-100% of cases during an acute episode). Disease Antigen Source Farmer's lung (The commonest occupational hypersensitivity pneumonitis) spores of Saccharopolyspora rectivirgula (commonly from Contaminated hay) Bird fanciers' lung avian proteins Malt workers' lung Aspergillus clavatus Mushroom workers' lung thermophilic actinomycetes Maple bark stripper's lung Cryptostroma corticale Cheese washer's lung Penicillium casei

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Features • Acute: occur 4-8 hrs after exposure, SOB, dry cough, fever. Symptoms subside after 12 hours to several days (in the absence of additional exposure) • Chronic (months after continuous exposure) : exertional shortness of breath and pulmonary fibrosis (typically upper-lobe). A recurrent common cold with an irritating cough and fever may indicate hypersensitivity pneumonitis. Investigation • Chest x-ray Upper/mid-zone fibrosis. Nodular shadowing or ground glass appearances. Classically show diffuse air-space consolidation • Pulmonary function test: restrictive pattern • Bronchoalveolar lavage (BAL) →lymphocytic predominance • Blood cell count → NO eosinophilia • Serology → Circulating IgG precipitins Demonstration of precipitating antibodies (precipitins) in the patient's serum to the causal antigen. Have a high false negative rate (positive results can be seen in exposed, but asymptomatic individuals). Positive serum avian precipitins are not diagnostic of HP, and only suggest the patient has had exposure to birds. • Histopathology: Noncaseating granulomas with lymphocytes and polynuclear giant cells Treatment • Removal of exposure to the antigen (change of job plan) The optimal management

Symptoms may settle within 12 hours of removal of the antigen. • Prednisolone MRCPI-part-1-january-2016: A 65-year-old farmer presents with SOB and wheeze progressively worsening over the past 6 months. He is a smoker, and has two daughters with asthma. There was obvious wheeze and coarse end-inspiratory crackles on examination of the chest. A chest X- ray shows diffuse non-specific changes consistent with lung disease. Which would be the next most appropriate investigation? Spirometry and reversibility This man either has asthma, chronic obstructive pulmonary disease or farmer's lung Spirometry and reversibility would be the investigation of choice. A restrictive defect would support a diagnosis of farmer's lung; an obstructive defect with reversibility would support a diagnosis of asthma, respiratory obstruction without reversibility would support a diagnosis of COPD.

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

Pulmonology Pneumoconiosis Definition • A group of chronic lung diseases caused by exposure to a mineral dust or a metal. Types • Asbestosis • Silicosis • Coal workers' pneumoconiosis (black lung disease), and • chronic beryllium disease. Risk factor • In silicosis and coal workers' pneumoconiosis, exposure should be (at least 10 and usually 20 or more years prior to radiographic changes) (the cumulative dose inhaled). • Beryllium is immunologically mediated with a strong genetic component, so that the typical dose response demonstrated with the other pneumoconioses is not seen (NO need for cumulative dose) Features • Asymptomatic in early stages • Dyspnoea on exertional dyspnoea , dry cough Diagnosis • Chest x-ray The presence of non-calcified, multiple (in the hundreds), rounded opacities in the upper zones is highly suggestive of silicosis or coal workers' pneumoconiosis. Asbestosis typically causes lower lobe fibrosis. • High-resolution CT (HRCT) scan chest more sensitive than CXR in identifying interstitial fibrosis. • Individuals with silicosis should be tested for TB. Treatment • Smoking cessation + removal of occupational exposure • Patients with respiratory failure → referral for lung transplant Absolute contraindications include: Associated other incurable advanced disease Addictions including tobacco, Lack of social support Documented non-adherence to medical therapy. Exposure to isocyanates most likely associated with squamous-cell carcinoma of the bronchus. Hard metal lung disease (Cobalt exposure) • 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 a bronchoalveolar lavage (BAL) of this patient? Giant cells Persons working in the hard metal industry are prone to develop a condition called hard metal lung disease. The pathological diagnosis is giant cell interstitial pneumonia (GIP).

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Asbestos and the lung Risk of asbestos exposure • Ship building, • car manufacture, • boiler making and • plumbing industries Asbestos can cause a variety of lung disease 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. • rarely cause symptoms • benign and do not undergo malignant change. • CXR may shows calcification on both hemidiaphragms which are most likely to be pleural plaques from previous asbestos exposure. • Do not require long term

follow up Asbestosis (asbestos-related pulmonary fibrosis) • Diffuse interstitial fibrosis secondary to asbestos inhalation • Slowly progressive. the latent period is typically 15-30 years. • 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. • Typically causes lower lobe fibrosis. • Pleural effusions and supradiaphragmatic pleural plaques are common findings on x-ray in patients with asbestosis. • Biopsy is not mandatory as the diagnosis can be made on clinical and radiological grounds. • On microscopic examination, asbestosis is marked by interstitial fibrosis with the presence of characteristic asbestos bodies and ferruginous bodies. • Resistant to treatment with immunosuppressive therapy. • The risk of lung cancer is raised more than 50-fold in smokers with asbestos.

Pleural mesothelioma Definition • Malignant tumor of mesothelial cells of pleura Epidemiology • More common in male than female (3:1) Risk factors • Asbestos (20- to 40-year after exposure) • Smoking, alcohol, and diet do not increase the risk. The most common malignancy associated with asbestosis is bronchogenic carcinoma, not mesothelioma

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

Pulmonology • Loss of material from chromosome 22 is commonly seen in mesothelioma cell lines Features • History of asbestos exposure in 85-90%, latent period of 20-40 years • Dyspnoea, weight loss, chest wall pain • pleural effusion Diagnosis • Chest x-ray showing either a pleural effusion or pleural thickening • CT chest with contrast → the best next step after chest x-ray Multiple nodular pleural lesions (pleural thickening) • Pleurocentesis (If a pleural effusion is present) for biochemistry and cytology exudative and hemorrhagic pleural fluid. cytology is only helpful in 20-30% of cases don’t rely on cytology alone to confirm the diagnosis • Thoracoscopy biopsy the most important investigation to confirm the diagnosis. used to investigate cytology negative exudative effusions as it has a high diagnostic yield (around 95%). Psammoma bodies are seen on histology • Positron emission tomography (PET) with CT (PET-CT) as the initial staging after histopathological confirmation of the diagnosis. Management • Radiation, with or without chemotherapy • Surgery (pleurectomy or pneumonectomy) in severe cases if operable Prognosis • Poor. The median survival after diagnosis is 1- 2 years • Bronchogenic carcinoma is the most common malignant pulmonary tumor in patients with asbestosis Bronchogenic carcinoma is more common than mesothelioma The lack of smoking history along with previous asbestos exposure and signs of a pleural effusion make malignant mesothelioma more likely than bronchial carcinoma.

Silicosis Overview • a pneumoconiosis that results from the inhalation of silica dust. • Affects upper lobes • Increases susceptibility to tuberculosis. • Risky jobs Silicosis can affect anyone involved in quarrying (رجاحملا , carving, mining (نيدعتلا), tunneling (رفحلا قافنلا), grinding (نحطلا or sand-blasting (فسنلا , if the dust generated contains quartz. manufacture of toilet bowls, sinks(لساغملا), and ceramics; hydraulic fracking while drilling for gas and oil. Pathophysiology • Macrophages activated by silica (quartz) →release fibrogenic cytokines → causes inflammation and scarring in the form of nodular lesions in the upper lobes of the lungs. Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

This patient has mesothelioma. The calcification of the pleura is a hallmark of asbestos exposure. CT scan showing mesothelioma • There is a large rind of soft tissue related to the left chest wall. • This is a malignant process as there is destruction of the associated rib.

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

Pulmonology Classifications • Acute silicosis The most severe form develops a few weeks to 5 years after exposure due to very heavy exposure. Chest X-ray shows appearances resembling pulmonary oedema. Treatment 1st line →whole lung lavage. • Accelerated silicosis Develops 5–10 years after first exposure due to ess heavy exposure • Simple nodular silicosis the most common type resulting from long-term exposure (10 -30 years) to relatively low concentrations of silica dust radiographic nodular changes similar to coal-worker's pneumoconiosis , Differential diagnosis • 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 Diagnosis • 'Egg-shell' calcification of the hilar lymph nodes is pathognomonic for silicosis; • Pulmonary function test → usually reveal mixed obstructive / restrictive picture • biopsy shows silica particles (birefringent) surrounded by collagen Complications • ↑ susceptibility to TB (silica is toxic to macrophages) • ↑ incidence of primary lung cancer • ↑ risk of connective-tissue disease, vasculitides, (COPD), and chronic renal failure.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

The chest radiograph shows "eggshell" calcification of the hilar lymph nodes, as seen with silicosis.

Berylliosis Overview • Jobs at risk: aerospace or nuclear industry workers, manufacture of electronics, manufacture of heat-resistant ceramics, dental prostheses, and metal products • Characterized by the presence of noncaseating granulomas in the lungs, nodular infiltrates, and enlarged lymph nodes (resembles sarcoidosis) • The presence of glutamic acid at position 69 of the HLA-DP1 beta chain is strongly associated with chronic beryllium disease. Diagnosis • Chest radiograph shows hilar adenopathy or reticular and nodular lung opacities. Chest x-ray →linear opacities. silicosis and coal workers' →rounded opacities • Blood beryllium lymphocyte proliferation test (BeLPT) the initial diagnostic test of choice for patients with clinical or radiographic evidence of lung disease • Beryllium lymphocyte proliferation test (BeLPT) Sensitive test that identifies individuals sensitised to beryllium. Bronchoscopic lavage fluid may be positive when the blood test is negative. The occurrence of a positive BeLPT without granulomas on histology is an indication of sensitisation to beryllium and absence of chronic beryllium disease.