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Chapter 1

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 1

Endocrinolog & Metabolism

Tip to remember Testosterone and LH levels can help distinguish between different causes of abnormal sexual development: 1- High testosterone and high LH: defective androgen receptor (androgen insensitivity syndrome) 2- High testosterone and low LH: testosterone-secreting tumor 3- Low testosterone and high LH: primary hypogonadism 4- Low testosterone and low LH: hypogonadotrophic hypogonadism

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Delayed puberty
The first visible sign of puberty in males is testicular enlargement, while in females it is breast development.

Definition
• Absent or incomplete development of secondary sex characteristics by the age of 14 years in boys or 13 years in girls

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Causes • Constitutional delay of growth and puberty (normal variants of growth): the most common cause of delayed puberty • Primary/ hypergonadotrophic hypogonadism: e.g. Klinefelter's and Turner's syndromes. • Secondary/ hypogonadotrophic hypogonadism: causes
 Genetic defects: (e.g., Kallmann syndrome, Prader-Willi syndrome, Gaucher disease) Malnutrition (e.g., anorexia nervosa)
 Chronic diseases (e.g., inflammatory bowel disease, hypothyroidism, cystic fibrosis)

Delayed puberty with short stature Delayed puberty with normal stature Turner's syndrome Prader-Willi syndrome Noonan's syndrome

polycystic ovarian syndrome androgen insensitivity Kallman's syndrome Klinefelter's syndrome

Features • Signs of delayed puberty in girls include: Absence of breast development by age 14 years Pubic hair absent by age 14 More than five years between the start and completion of

breast growth Menarche has not occurred by age 16. • Signs of delayed puberty in boys include: No testicular enlargement by age 14 years Pubic hair absent by age 15 More than five years between the start and completion of growth of the genitalia. Diagnosis • Primary hypogonadism → ↓gonadal hormones (testosterone in boys and estradiol in girls)

- ↑ luteinizing hormone (LH) and follicle-stimulating hormone (FSH).
  • Secondary hypogonadism → ↓hypothalamic gonadotropin-releasing hormone (GnRH) → low to normal LH and FSH → ↓gonadal hormones
  • Constitutional delay is usually assessed using a bone age assessment (radiography of the hand and wrist) and measuring the patterns of ossification at the epiphyses of the bones of the hands → delayed bone age.

Management • Constitutional delay: Observation
• Organic delay: Sex-steroid therapy to induce puberty + lifelong hormone replacement therapy after puberty

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Endocrinolog & Metabolism Multiple endocrine neoplasia Genetic inheritance
• Autosomal dominant disorder, high penetrance • The table below summarises the three main types of multiple endocrine neoplasia (MEN)

Type 1 multiple endocrine neoplasia (MEN 1)

• a defect in the gene MEN1, a tumor-suppressor gene found on chromosome 11 that codes for menin protein.
• For MEN1, remember the triad of three Ps, which includes pituitary, parathyroid, and pancreatic tumors.
 Pituitary tumors →↑prolactin → galactorrhea, decreased libido, or infertility. Hyperparathyroidism is the most common manifestation in MEN 1 (occurs in 90% of cases) → hypercalcemia → constipation, kidney stones, polyuria, and polydipsia. The pancreas is the second most commonly involved organ in MEN 1.
 60% of pancreatic endocrine tumours are gastrinomas (most common) →↑gastrin (Zollinger-Ellison syndrome) → recurrent peptic ulcers.
 insulinoma → recurrent episodes of hypoglycemia, leading to confusion, dizziness, or loss of consciousness.
 endoscopic ultrasound of the pancreas is the most sensitive modality for the detection of an insulinoma.

• The single most useful investigation to monitor patients with MEN 1 → Serum calcium • Diagnosis → genetic testing • Management Genetic screening for first-degree relatives Pituitary prolactinomas → cabergoline, a dopamine agonist Hyperparathyroidism → partial or total surgical parathyroidectomy Gastrinomas with peptic ulcer disease → proton pump inhibitor drugs.

MEN1 = three Ps Pituitary, Parathyroid, Pancreas

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Type 2 multiple endocrine neoplasia (MEN 2)

• MEN2A and MEN2B are both due to mutations in the gene RET. This is a protooncogene found on chromosome 10 that codes for a receptor tyrosine kinase. • A gain-of-function mutation in the RET proto-oncogene makes it an oncogene, which causes the uncontrolled cell division seen in cancer. • MEN-2 is strongly associated with a family history of unexplained death in childbirth

• Subtypes
 MEN Type 2a MEN type 2A includes two Ps and one M—parathyroid tumors and pheochromocytoma, combined with medullary thyroid carcinoma. pheochromocytoma →↑catecholamines such as epinephrine →hypertension and often intermittent episodes of headaches, palpitation, pallor caused by vasoconstriction, and heavy sweating. Medullary thyroid cancer often metastasized at presentation →hoarseness
 Serum calcitonin levels should be obtained in the workup for medullary thyroid cancer. young-onset hypertension with feature of hyperparathyroidism (↑ Ca & ↓ P) → MEN Type 2a

 MEN-2b
 MEN-2b present earlier than 2a
 MEN type 2B is associated with a single P and two Ms—pheochromocytoma, medullary thyroid carcinoma, and mucosal neuromas. Mucosal neuromas (benign tumors) develop in the mouth, eyes, and submucosa of almost all organs in the first decade of life and appear in 100% of patients with MEN2B (yellowish-white painless nodules on the lips or tongue, sclera, or eyelids).
 Marfanoid habitus → long limbs, wide arm span, and hyperlaxity of joints.

MEN2A = two Ps and one M Parathyroid, Pheochromocytoma, Medullary thyroid carcinoma

MEN2B = one P and two Ms Pheochromocytoma, Medullary thyroid carcinoma, Mucosal neuromas

• Diagnosis → genetic testing • Management Genetic screening for first-degree relatives All first-degree relatives who screen positive for the RET mutation should undergo prophylactic thyroidectomy given the very high risk of medullary thyroid cancer. For underlying phaeochromocytoma. full alpha blockade with an agent such as phenoxybenzamine is essential the most appropriate additional medication to control blood pressure is phenoxybenzamine Beta blockade without first alpha blocking raises the possibility of rebound hypertension due to unopposed action of the alpha vasoconstrictors; as such it is inadvisable to consider bisoprolol or atenolol. The pheochromocytoma puts the patient at greatest risk, and therefore should be removed before other surgical procedures are performed.

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 Annual testing of calcium and PTH from the age of 10 is recommended for child with family history of MEN-2

Which of the manifestations of MEN-2 has the most malignant potential? C cell hyperplasia

Which finding in a blood test will be the most characteristic in (MEN 2B) patient? • Elevated metanephrines → phaeochromocytoma • Elevated Calcitonin → Medullary thyroid cancer (used for screening, prognosis and monitoring)

Multiple endocrine neoplasia type II is due to mutation in which sort of receptor? Membrane-bound tyrosine kinase receptor

What is the single most useful investigation to monitor patients with MEN 1?
Serum calcium

Multiple endocrine neoplasia MEN 1 3 "P"s = Parathyroid, Pancreas, Pituitary gland MEN 2A 1 "M", 2 "P"s = Medullary thyroid carcinoma, Pheochromocytoma, MEN 2B 2 "M"s, 1 "P" = Medullary thyroid carcinoma, Marfanoid habitus/Multiple neuromas, Pheochromocytoma

Autoimmune polyendocrinopathy syndrome (APS) (Polyglandular syndrome)

Type Polyglandular syndrome type 1 Polyglandular syndrome type 2 Also called (Schmidt's disease) inheritance autosomal recessive caused by mutation of AIRE1 gene on chromosome 21 Prevalence Rare More common
Age of presentation

Usually begins in childhood. Feature Most common
• Mucocutaneous candidiasis (100%) (typically first feature as young child) • Hypoparathyroidism (90%) • Adrenal insufficiency (60%)

Less common
• Other autoimmune diseases • gonadal failure • Primary hypothyroidism

Patients have Addison's disease plus either: type 1 diabetes mellitus or
autoimmune thyroid disease.

No Hypoparathyroidism

Diagnosis 2 out of 3 needed: • chronic mucocutaneous candidiasis (100%) • primary hypoparathyroidism (90%), • Addison's disease (60%) • Tryptophan hydroxylase autoantibodies may be found in autoimmune polyendocrine syndrome associated with an autoimmune malabsorption. Notes & Notes for MRCP
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polygenic inheritance linked to HLA DR3/DR4.
Usually begins in adult (most cases occurring between age 20 and 40 years) Most common
• Adrenal insufficiency (100%) (the initial manifestation) • Hypothyroidism • Type-1 diabetes

Less common
• Other autoimmune diseases
• Gonadal failure • Diabetes insipidus (rare)

Third edition Notes & Notes By Dr. Yousif Abdallah Hamad Pulmonology Updated

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Pulmonology Lung anatomy Lung lobes • Right lung has 3 lobes; Left has less lobes (2) and lingula (homolog of right middle lobe). Instead of a middle lobe, left lung has a space occupied by the heart • The left lung have a part that the right lung does not have: the lingula, which is the homolog of the middle lobe of the right lung Lung fissures • The oblique fissure divides the superior and inferior lobes in the posterior aspect of both the right and left lungs • Horizontal fissure is found only in the right lung Lung bronchi • Right lung is a more common site for inhaled foreign bodies because right main stem bronchus is wider, more vertical, and shorter than the left. If you aspirate a peanut: While supine — usually enters superior segment of right lower lobe. While lying on right side — usually enters right upper lobe. While upright — usually enters right lower lobe. • Airway resistance highest in the large-to medium-sized bronchi and least in the terminal bronchioles Cell types in respiratory zone • Pseudostratified ciliated columnar cells are found in bronchi/early terminal bronchioles. • Cuboidal cells are found in terminal bronchioles onward • Simple squamous is the primary type of epithelium present in the alveoli

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Anatomical land marks • Cartilage and goblet cells extend to the end of bronchi. • 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 main stem bronchi (carina). • Structures perforating diaphragm: At T 8: IVC, right phrenic nerve At T 10: oesophagus, Vagus (CN10; 2 trunks) At T 12: aorta, thoracic duct, azygos vein. • The trachea bifurcates at the level of T4 ("bi-four-cates at 4") • Diaphragm is innervated by C3, 4, and 5 (phrenic nerve). Pain from diaphragm irritation (eg, air, blood, or pus in peritoneal cavity) can be referred to shoulder (C5) and trapezius ridge (C3, 4). Azygous lobe of the lung • An azygos lobe is a normal variant that develops when a laterally displaced azygos vein creates a deep pleural fissure into the apical segment of the right upper lobe during embryological development. • azygous lobe is seen in about 0.5% of routine chest X-rays and is a normal variant. • The azygous lobe is formed when the posterior cardinal vein fails to migrate over the apex. • It is seen as a 'reverse comma sign' behind the medial end of the right clavicle. Top Tips A patient aspirates vomit. Is the right or left lung a more common site for inhaled foreign bodies and why? Right lung, because the right mainstem bronchus is wider, more vertical, and shorter than the left A patient chokes on a peanut while upright. Where exactly in the lungs do you expect to find the peanut? Right lower lobe

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Pulmonology Diaphragmatic paralysis (Phrenic nerve palsy) Innervation • The diaphragm is innervated by the phrenic nerve (C3,4,5). Causes • Unilateral diaphragmatic paralysis (more common than bilateral) Trauma e.g. Thoracic surgery, Compression: cervical spondylosis, cervical compressive tumors viral infections (eg, Herpes zoster, poliomyelitis) • Bilateral: Guillain-Barré Infection Features • Unilateral paralysis: usually asymptomatic • Bilateral : dyspnoea may progress to ventilatory failure
Diagnosis of unilateral paralysis: • suggested by asymmetric elevation of the affected hemidiaphragm on X-ray • Spirometry (in the supine and sitting positions) The forced vital capacity (FVC) is ↓to 70 - 80 % of predicted and typically ↓↓ decreases further by 15 to 25 % in the supine position. • Confirmed by fluoroscopy 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 pushing the paralysed hemidiaphragm cephalad (paradoxical motion) Fluoroscopy is inaccurate for the diagnosis of bilateral paralysis. Treatment • Unilateral diaphragmatic paralysis: do not require treatment. • Bilateral : may require noninvasive positive pressure ventilation (NPPV) , usually a bilevel positive airway pressure device (BPAP).

Lung physiology Pulmonary surfactant • Surfactant is a mixture of phospholipids, carbohydrates and proteins • first detectable around 28 weeks of gestation • Released by type 2 pneumocytes • The main functioning component in surfactant is dipalmitoyl phosphatidylcholine (DPPC) or lecithin. which reduces alveolar surface tension. • as alveoli decrease in size, surfactant concentration is increased, helping prevent the alveoli from collapsing • reduces the muscular force needed to expand the lungs (i.e. decreases the work of breathing)

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• 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 cmH2O. Pulmonary circulation • The normal pulmonary circulation is characterised by:

1. low pressures,
2. low flow rates,
3. high compliance vessels. • Chronic hypoxic vasoconstriction may lead to pulmonary hypertension +/– cor pulmonale. • A fall in the partial pressure of oxygen (pO2) in the blood causes a hypoxic vasoconstriction that shifts blood away from poorly ventilated regions of lung to wellventilated regions of lung and improves the efficiency of gaseous exchange. Pulmonary arteries vasoconstrict in the presence of hypoxia Chloride shift • Cells metabolism → ↑CO2 → diffuses into RBCs → CO2 + H2O → carbonic anhydrase → carbonic acid (H2CO3) → HCO3- + H+ • H+ combines with Hb • HCO3- diffuses out of cell, - Cl- replaces it • CO2 produced in the periphery is converted into bicarbonate inside RBCs and then shifted out with chloride replacement Bohr Effect • Increasing acidity (or pCO2) means O2 binds less well to Hb • High CO2 and H+ concentrations (from tissue metabolism) cause decreased affinity for O2 → O2 that is bound to Hb is released to tissue

(the O2-Hb dissociation curve is shifted to the right).

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Pulmonology Haldane effect • ↑ pO2 means CO2 binds less well to Hb • When Hb is oxygenated (in high pO2, for example, in the lungs): • Oxygenated Hb has a decreased affinity for CO2 → CO2 that is bound to Hb is released in the pulmonary arteries to diffuse into the alveoli (the O2-Hb dissociation curve is shifted to the left). Acclimatisation to life at high altitudes • Acclimatisation results in increased Hb with erythrocytosis. • Pulmonary artery pressure increases to oxygenate more blood. • 2,3-DPG increases. • Respiration is normal when subjects are acclimatised to altitude as is cardiac output. (Periodic respiration is a feature of non-acclimatisation). Lung compliance is defined as change in lung volume per unit change in airway pressure Causes of ↓ compliance • Pulmonary edema • Pulmonary fibrosis • Pneumonectomy • Kyphosis Causes of ↑ compliance • Age • Emphysema • Which part of the conducting zone of the respiratory tree has the least airway resistance? □ Terminal bronchioles The cough center of the brain, located in the nucleus tractus solitarius of the medulla of the brainstem

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Oxygen Dissociation Curve Definition • Oxygen Dissociation Curve describes the relationship between the percentage of saturated hemoglobin and partial pressure of oxygen in the blood. • Each hemoglobin molecule has the capacity to carry four oxygen molecules. Meaning of shifting the curve to the right or left • Shifts to right = for given oxygen tension there is ↓ saturation of Hb with oxygen i.e. Enhanced oxygen delivery to tissues • Shifts to left = for given oxygen tension there is ↑ saturation of Hb with oxygen i.e. ↓ oxygen delivery to tissues

Causes of shifting the curve to the right or left Shifts to Right = Raised oxygen delivery (The R rule) Shifts to Left = Lower oxygen delivery (The L rule) • Raised [H+] (acidity) • Raised PCO2 • Raised 2,3-DPG • Raised temperature The curve and Affinity • Left shift of the curve is a sign of hemoglobin's ↑ affinity for oxygen (e.g. at the lungs). • Similarly, right shift shows ↓ affinity, as would appear with an ↑ in body temperature, hydrogen ion, 2,3- diphosphoglycerate (2,3-DPG) or carbon dioxide concentration (the Bohr effect) • Carbon monoxide has a much higher affinity for hemoglobin than oxygen does. In carbon monoxide poisoning, oxygen cannot be transported and released to body tissues thus resulting in hypoxia. Notes & Notes for MRCP
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• Low [H+] (alkali) • Low PCO2 • Low 2,3-DPG • Low temperature • HbF, methemoglobin, carboxyhaemoglobin
Diagram of Oxygen Dissociation Curve: □ Red line demonstrating shifting to the right. □ The green line demonstrating shifting to the left

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Pulmonology Top tips Blood in the skeletal muscle is exposed to high temperatures, lower pH, and higher CO2. The oxygen-hemoglobin dissociation curve shifts to the right, facilitating oxygen delivery to the tissue. In the pulmonary vein, blood is exposed to a higher pH and lower CO2. The

oxygenhemoglobin dissociation curve shifts to the left, facilitating oxygen binding to hemoglobin. 2,3-Diphosphoglycerate (2,3-DPG) 2,3-DPG is an important molecule made by tissue in response to a low pH and low oxygen environment. It may be helpful to think of 2,3-DPG as a help flag made by tissues in response to stress. When hemoglobin comes across higher 2,3-DPG, it “knows” that the tissue is in trouble and drops off extra oxygen. Therefore, as 2,3-DPG increases, the binding affinity of oxygen for hemoglobin decreases, which results in a rightward shift of the dissociation curve. Question A 24-year-old woman is evaluated before and after practice to assess oxygen delivery to her muscles. The hemoglobinoxygen dissociation curve is shown. Curve B is taken before practice. Which characteristics will most probably describe curve A? Answer: If curve B is taken before practice, it will be used as reference point. Curve A shows shifts to the left. Increased pH with decreased 2,3diphosphoglycerate concentration

Pulmonary function tests Pulmonary function tests can be used to determine whether a respiratory disease is obstructive or restrictive. Normal lung volumes Definition Normal range Total lung capacity (TLC) Volume of air in the lungs after maximal inhalation [= vital capacity + residual volume]. Vital capacity (VC) Maximum volume of air that can be expired after a maximal inspiration. [↓ with age] Residual volume (RV) Volume of air that remains in the lungs after maximal exhalation.[↑ with age & obstructive lung disease] Tidal volume (TV) Volume of air that is inhaled and exhaled in a normal breath at rest ~500 mL or 7 mL/kg Inspiratory reserve volume Maximum volume of air that can still be forcibly inhaled following the inhalation of a normal TV Inspiratory capacity (IC) Maximum volume of air that can be inhaled after the exhalation of a normal TV. [IC = TV + IRV] Expiratory reserve volume (ERV) Maximum volume of air that can still be forcibly exhaled after the exhalation of a normal TV Expiratory capacity (EC) Maximum volume of air that can be exhaled after the inspiration of a normal TV Functional residual capacity (FRC) Volume of air that remains in the lungs after the exhalation of a normal TV Dead space areas of the lung not involved in gas exchange. Anatomic dead space includes the nonrespiratory airways and exists in all healthy lungs. Physiologic dead space includes the anatomic dead space plus any alveoli that are not perfused and thus cannot participate in gas exchange

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Obstructive vs. Restrictive lung diseases Obstructive Restrictive FEV1/FVC <0.7 (˂70%) FEV1/FVC >0.7 (> 70%) FEV1 - significantly reduced (<80% predicted normal) Spirometry FVC - reduced or normal FEV1% (FEV1/FVC) - reduced Notes & Notes for MRCP
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6–6.5 L 4.5–5 L 1–1.5 L 3–3.5 L 3.5–4 L 1.5 L 2 L 2.5–3 L 150 ml FEV1 - reduced (<80% predicted normal) FVC - significantly reduced (<70% predicted normal) FEV1% (FEV1/FVC) - normal (>0.7) or increased

Chapter 2

Pulmonology Obstructive Restrictive Examples Chronic obstructive pulmonary disease • chronic bronchitis • emphysema Asthma Bronchiectasis Forced vital capacity (FVC) • A measure of the force, volume, and speed with which air can be maximally expelled from the lungs. • The maneuver would be to take a deep breath, and then blow it out as hard as you can for as long as you can to maximally expel air from the lungs. • Indications commonly done to assess patients

with asthma and chronic obstructive pulmonary disease. the best way to monitor respiratory function in any neurological disorders that can affect the respiratory muscles (e.g. GBS, myasthenia gravis). ITU admission is recommended when FVC is less than 20 mL/kg and intubation is recommended in most cases when FVC is less than 15 mL/kg. Peak expiratory flow rate (PEFR) • Definition : The maximum airflow rate attained during forced expiration. • Normal values PEF values are usually expressed as L/min; when measured as part of spirometry, values are expressed in L/sec. To convert, multiply L/sec x 60 sec/min = L/min. Peak flow meters are handheld devices used to measure PEFR in the ambulatory setting Normally : ≥ 80% of the predicted average value Dependent upon factors such as gender, age and height. The most accurate correlation of the peak expiratory flow rate (PEFR) is with height. PEFR is typically higher in males than females and higher in taller patients. • Advantages It is effort-independent. In patients with asthma, the PEFR % predicted correlates reasonably well with the FEV1 and provides an objective measure of airflow limitation when spirometry is not available Notes & Notes for MRCP
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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, myasthenia gravis • obesity • scoliosis

• Disadvantages predominantly assesses large airway caliber and can underestimate the effects of asthma in the small airways. Restrictive processes that limit full inspiration, such as chest wall disease, obesity, and muscle weakness, can lead to a reduced PEF in the absence of airflow limitation. Thus, values for PEF that are less than 80 percent of predicted should be further evaluated with spirometry before assuming that the abnormality is due to asthma. • The differences between Peak Flow Meters and Spirometry Peak Flow Meter Spirometry Measures ability to exhale Will vary with lung capacity Use with charts to detect OBSTRUCTIVE disease Can be used by patients to monitor lung ‘function’ Flow-volume loop • provides additional information about the location of airway constriction • Best test for upper way obstruction. the upper airway is defined as that portion of the airway extending from the mouth to the mainstem bronchi Explanation of high FEV-1/FVC ratio in lung fibrosis • Lung fibrosis → ↑↑high elastic recoil → most forced expiratory volume (FEV1) will be expelled in the first second compared to full forced expiration → a relatively high FEV-1/FVC ratio. Obesity → extra-thoracic restriction • Obesity could show a significant restrictive defect. Patients with respiratory muscle weakness show spirometric findings of restrictive lung disease. • What is the best pre-operative screen of pulmonary function for a smoker patient evaluated for a coronary artery bypass graft (CABG).? Ratio of the forced expiratory volume in 1 second to the forced vital capacity Notes & Notes for MRCP
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 Simultaneous measurement of flow and capacity Can be used to diagnose both OBSTRUCTIVE and RESTRICTIVE disease (gold standard) Costs more than peak flow meters

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Pulmonology

Transfer factor (DLCO or TLCO (diffusing capacity or transfer factor of the lung for carbon monoxide (CO)) • The transfer factor describes the rate at which a gas will diffuse from alveoli into blood. • Carbon monoxide is used to test the rate of diffusion. • Results may be given as the total gas transfer (DLCO, TLCO) or that corrected for lung volume (transfer coefficient, KCO). • Diffusion capacity of carbon monoxide depends on the thickness of the alveolar wall. diffusion will be increased in healthy compared with unhealthy lungs, where the thickness is likely to increase and the surface area available for gas exchange to decrease. Diffusing capacity of the lungs for carbon monoxide (DLCO) (also known as transfer factor for carbon monoxide or TLCO) • DLCO measures the ability of the lungs to transfer gas from inhaled air in the alveoli to the red blood cells in pulmonary capillaries. • Used to identify the cause of dyspnea or hypoxemia, Factors interfere with interpretation of the Diffusing capacity (DLCO) test • Smoking patients should avoid cigarette smoking on the day of the test Carbon monoxide in cigarette smoke → ↑ carboxyhaemoglobin (COHb) (to as high as 10-15% (normal value 1-2%) →↓ DLCO. Increasing COHb reduces DLCO • Supplemental oxygen discontinue any supplemental oxygen for at least 15 minutes prior to testing. • Significant amount of Alcohol in the morning of the test (not small amount) • Severe kyphosis (not mild) • Sever scoliosis (not mild) Causes of raised and lower DLCO • Where alveolar haemorrhage occurs, the DLCO tends to increase due to the enhanced uptake of carbon monoxide by intra-alveolar haemoglobin. Causes of a raised DLCO Causes of a lower DLCO • Asthma • Pulmonary haemorrhage (Wegener's, Goodpasture's) • Left-to-right cardiac shunts • Polycythaemia • Hyperkinetic states • Early left heart failure • Male gender • Exercise • Obesity • Pulmonary fibrosis • Pneumonia • Pulmonary emboli • Pulmonary oedema • Emphysema • bronchiolitis obliterans • Anaemia • Low cardiac output • Pulmonary AV malformations • carboxyhemoglobinemia. • hepatopulmonary syndrome • lymphangioleiomyomatosis • Transfer factor (DLCO) and transfer co-efficient (KCO) can be normal or elevated in patients with asthma but are always reduced in emphysema.

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• Pulmonary AV malformations cause right-to-left shunts, so reducing Tlco values and provoking hypoxaemia (↓Pao2), with a normal lung volumes (eg FEV1 & FVC). • Low DLCO combined with reduced lung volumes suggests interstitial lung disease. • Normal DLCO associated with low lung volumes suggests → an extrapulmonary cause of the restriction, such as pleural effusion, pleural thickening, neuromuscular weakness, or kyphoscoliosis. Top Tips

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Transfer coefficient of carbon monoxide (KCO) Overview • The transfer coefficient (Kco) represents the uptake of carbon monoxide per litre of effective alveolar volume (Va) • KCO is a measure of the efficiency of gas exchange into the blood stream. Causes of reduced Kco: (It is reduced if the lungs are damaged) • Restrictive lung disease e.g. Interstitial lung disease the best test - after CT- to confirm restrictive lung disease due to a parenchymal disorder Normal KCO may rule out significant restrictive lung disease • Sarcoidosis would reduce the transfer coefficient as there is damage to the alveolar cells themselves Causes of an increased Kco • Increased if there is additional blood in the lungs to remove carbon monoxide (e.g. ↑blood flow, haemorrhage, or polycythaemia). • Extrapulmonary volume restriction density of pulmonary capillaries is

unusually high in relation to the (restricted) lung volume at which the measurement is made. • 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 disease, extensive bilateral pleural thickening Obesity • In intrapulmonary restriction, both (Tlco & Kco) are usually decreased.

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Pulmonology • Isolated decreases in gas transfer are typical of pulmonary vascular diseases such as vasculitis and recurrent pulmonary embolism. Relation between DLco, VA (alveolar volume) & KCO (transfer coefficient) • Dlco is simply the product of Va and Kco • TLCO = KCO x Alveolar volume (VA)

Arterial Blood Gas (ABG) Arterial blood gases should be used for assessing respiratory failure in Critically ill Patients or those with Shock or Hypotension (Systolic blood pressure < 90mmHg) (British Thoracic Society, 2017) Reference ranges • PaCO2: 35–45 mm Hg • SaO2: ≥ 95% • pH: 7.35–7.45 • HCO3-: 21 to 27 mEq/L • Resting PaO2 > 80 mm Hg is considered normal. Procedure • A modified Allen test must be performed before the radial artery is punctured to assess collateral circulation in the hand. Contra-Indications of ABG sampling • Absent ulnar circulation – as demonstrated by Modified Allen's Test. • Impaired circulation e.g. Raynaud's Disease • History of arterial spasms • Distorted anatomy/ arteriovenous fistula trauma/burns to the limb - at or proximal to the attempted arterial puncture site • Medium or high dose anticoagulation therapy, or history of clotting disorder • Severe coagulopathy • Abnormal or infectious skin processes at/or near puncture site Modified Allen's test • modified Allen test measures arterial competency, and should be performed before taking an arterial sample. Ask the patient to clench his fist; if the patient is unable to do this, close the person's hand tightly. Using your fingers, apply occlusive pressure to both the ulnar and radial arteries, to obstruct blood flow to the hand. While applying occlusive pressure to both arteries, have the patient relax his hand, and check whether the palm and fingers have blanched. If this is not the case, you have not completely occluded the arteries with your fingers. Release the occlusive pressure on the ulnar artery only to determine whether the modified Allen test is positive or negative. If the hand flushes within 5-15 seconds it indicates that the ulnar artery has good blood flow →positive test.

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 If the hand does not flush within 5-15 seconds, it indicates that ulnar circulation is inadequate or nonexistent; in this situation, the radial artery supplying arterial blood to that hand should not be punctured. Interpretation of ABG • Hypoxemic respiratory failure (type 1 respiratory failure): ↓ PaO2 • Hypercapnic respiratory failure (type 2 respiratory failure): ↑ PaCO2 and ↓ PaO2 • Mixed metabolic and respiratory acidosis pH →below 7.35 PCO2 →elevated (> 6 kPa) indicating a respiratory cause for acidosis Bicarbonate →reduced (< 20 mmol/L) which is contributing to the

acidosis. the most likely biochemical imbalance seen in fluid inhalation is →Mixed metabolic and respiratory acidosis inhalation of fluid →disordered gas exchange →respiratory acidosis.

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Pulmonology Metabolic acid results from intravascular volume depletion, hypotension and consequent tissue hypoxia. • Compensated respiratory acidosis →normal PH, high CO2, low O2 . The fact that the pH is normal means that there must be bicarbonate retention to compensate. In bronchopulmonary dysplasia, there is usually long-term CO2 retention with compensatory increase in bicarbonate leading to a positive base excess and normal pH. • 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 arrest scenario, as the pulmonary arterioles constrict in response to hypoxia.

Chest x-ray Differential diagnosis of cavitating lung lesion • abscess (Staph aureus, Klebsiella and Pseudomonas) • squamous cell lung cancer • tuberculosis • Wegener's granulomatosis • Progressive massive fibrosis: is a complicated coal worker's pneumoconiosis where pulmonary nodules coalesce and cavitate. • pulmonary embolism • Systemic embolisation: occurs in 20-50% of cases of infective endocarditis, and can involve the lungs, central nervous system, coronary arteries, spleen, bowel and extremities. • rheumatoid arthritis • aspergillosis, histoplasmosis, coccidioidomycosis • Actinomycosis: is a chronic granulomatous disorder caused by a Gram-positive anaerobe. Differential diagnosis of diffuse opacities on chest X-ray • Pulmonary oedema • Interstitial lung disease • Vasculitic lung disease • Pulmonary haemorrhage Coin lesions on chest x-ray • Coin lesions (solitary pulmonary nodule) malignant tumour: lung cancer or metastases benign tumour: hamartoma infection: pneumonia, abscess, TB, hydatid cyst AV malformation

White lung lesions on chest x-ray • causes of white shadowing in the lungs including: • consolidation • pleural effusion • collapse • If there is a 'white-out' of a hemithorax it is useful to assess the position of the trachea - is it central, pulled or pushed from the side of opacification. Trachea pulled toward the white-out Trachea central Trachea pushed away from the whiteout Pneumonectomy Complete lung collapse (Atelectasis) e.g. endobronchial intubation Pulmonary hypoplasia Consolidation Pulmonary oedema (usually bilateral) Mesothelioma • In the context of an acute aspiration, the most likely process is atelectasis secondary to bronchial obstruction. • Obstruction of the mainstem bronchus will prevent gas from entering the affected lung and will lead to the collapse of that lung. • The collapsed lung will cause complete whiteout of the hemithorax on chest X-ray and will cause ipsilateral tension on the mediastinum leading to shifting of the trachea toward the affected lung. Characteristics of consolidation on chest x-ray • Consolidation in the left lower lobe → obliterates the diaphragm. • Lingular consolidation → obliterate the left heart border. • Consolidation of the right middle lobe → obscures the right heart border (right atrial edge). More extensive consolidation also involves the right and left peri-hilar regions. The superior extent is well demarcated, due to the horizontal fissure. Notes & Notes for MRCP

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• pneumonectomy • specific lesions e.g. tumours • fluid e.g. pulmonary oedema Pleural effusion Diaphragmatic hernia Large thoracic mass Lung collapse

- note how the trachea is pulled towards the side of the white-out

Chapter 2

Pulmonology • Right upper lobe collapse results in → displacement of the horizontal fissure upwards. The right hilum can also appear enlarged. The classical signs of right upper lobe consolidation → abnormal opacity within the right upper lobe abutting the horizontal fissure. The loss of the left heart border is a classic sign of left lingual consolidation. Lobar collapse on chest x-ray (Atelectasis) • Signs of lobar collapse on a chest x-ray tracheal deviation towards the side of the collapse mediastinal shift towards the side of the collapse elevation of the hemidiaphragm • Causes lung cancer (the most common cause in older adults) foreign body mucous plugging (e.g. in cystic fibrosis, post-operative complication , asthma) Treatment adequate hydration and chest physiotherapy. Bronchoscopy with lavage may be required if this is unsuccessful. Notes & Notes for MRCP
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This patient has a left upper lobe collapse. The following can be seen on the film to support this: • hazy opacity projected over the left upper zone • deviation of the trachea to the left • elevation of the left hemidiaphragm • loss of lung volume in the left hemithorax