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Chapter 2

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

Pulmonology • Fiberoptic bronchoscopy with bronchoalveolar lavage (BAL), endobronchial biopsy, and transbronchial biopsy. the next test for patients with a positive blood BeLPT or a strong clinical suspicion despite a negative blood BeLPT To obtain an adequate number of cells for BeLPT biopsy → granulomas present Diagnosis of berylliosis • requires all three of the following findings:

1. history of beryllium exposure,
2. positive BeLPT,
3. presence of noncaseating granulomas and/or mononuclear cell infiltrates on lung histopathology. • A clinical diagnosis can also be made based on a positive BAL BeLPT and lymphocytosis (>20 %) in bronchoalveolar lavage fluid. Complications • ↑ risk for primary lung cancer Treatment • cessation of exposure to beryllium • Acute and chronic berylliosis →Oral corticosteroid therapy (prednisone)

Coal workers' pneumoconiosis (CWP) Pathology • CWP results from inhalation and deposition of coal dust particles. • prolonged exposure to coal leads to pulmonary macrophages becoming filled with carbon, known as carbon-laden macrophages ("dust cells") • Affects upper lobes (high ventilation) Types • Simple CWP like smoking, can produce centrilobular emphysema Fine nodular opacifications (< 1 cm) in upper lung zone often asymptomatic and the diagnosis is an incidental finding on CXR. • Complicated CWP (Progressive massive fibrosis) Exposure to dust of high silicon content Fine nodular opacifications 1-2 cm with progressive massive fibrosis Chest x ray: round masses, several centimetres in diameter (˃ 1 cm), sometimes up to 10 cm. may have necrotic centres. Chest CT: Mass-like areas of lung opacification associated with radiating strands are seen; the "sausage-shaped" mass is characteristic. Mixed obstructive and restrictive lung Diagnosis • Chest x-ray → small interstitial nodules in the upper and mid zones of the lung. The presence of carbon-laden macrophages is the histologic hallmark of coal workers’ pneumoconiosis.

Complications • ↑ risk of connective-tissue disease and COPD • ↑ Risk of Caplan syndrome (coal worker's pneumoconiosis that occurs with joint manifestations of rheumatoid arthritis.) • NO association with lung cancer or TB Coughing up of black sputum (melanoptysis) is pathognomonic of coal workers pneumoconiosis. Although coal is mined from under the earth, the upper lobes of the lungs are primarily affected.

Primary ciliary dyskinesia (PCD) Definition • A rare autosomal recessive disorder characterized by absent or dysmotile cilia caused by a defect in the dynein arm of microtubules resulting in abnormal ciliary motion and impaired mucociliary clearance throughout the body. Features • Recurrent or persistent respiratory infections (which may lead to bronchiectasis) • Recurrent Sinusitis, and Otitis media • Conductive hearing loss • Male infertility (due to decreased sperm motility as a result of defective flagella) • Reduced fertility in women and ↑ risk of ectopic pregnancy due to defective movement of the cilia in the fallopian tube • In 50% of the patients, PCD is associated with situs inversus (Kartagener's syndrome): triad of situs inversus, recurrent sinusitis, and bronchiectasis Differential diagnoses • cystic fibrosis The diagnosis of CF is based on typical pulmonary and/or gastrointestinal tract manifestations and positive results on sweat test (pilocarpine iontophoresis). A negative sweat test is sufficient evidence to exclude CF. Caplan’s syndrome Coal workers pneumoconiosis associated with rheumatoid arthritis Typically bilateral, peripheral nodules 5 mm to 5 cm in size peripheral lung nodules with the histopathology of rheumatoid nodules develop on a background of pneumoconiotic opacities. In contrast to pneumoconiotic masses, they can develop rapidly, over a period of weeks, and may cavitate or calcify.

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Pulmonology Diagnosis • Nasal nitric oxide (NNO) levels the most sensitive and specific screening test for PCD Sensitivity of 97% and specificity of 90% for PCD. A low NNO (<100 parts per billion) should be followed up with confirmatory testing (nasal or bronchial brush biopsy for ciliary examination) because other conditions such as cystic fibrosis may present with low NNO. A high NNO virtually excludes PCD • Definitive diagnosis is usually based on identification of ciliary abnormalities on high speed videomicroscopy analysis (HSVA) or transmission electron microscopy (TEM). These tests require nasal or bronchial biopsy • Genetic test for dynein arm mutations is difficult due to multiple phenotypes Treatment • Reducing respiratory infections regular use of nebulized (hypertonic) saline, twice daily before airway clearance techniques; inhaled bronchodilator is administered prior to nebulized saline. Azithromycin maintenance therapy (250 mg for <40 kg or 500 mg for ≥40 kg, three times a week)

Kartagener's syndrome primary ciliary dyskinesia (PCD) + situs inversus →Kartagener's syndrome Definition • Kartagener syndrome is a subtype of primary ciliary dyskinesia characterized by the triad of situs inversus, chronic sinusitis, and bronchiectasis. • most frequently occurs in examinations due to its association with dextrocardia (e.g. 'quiet heart sounds', 'small volume complexes in lateral leads') Pathogenesis • autosomal recessive mutation. • dynein arm defect results in immotile cilia dynein is a protein found in Cilia and flagella of microtubule Features • Dextrocardia or complete situs inversus Situs inversus occurs in about half of people with

Kartagener syndrome • Bronchiectasis • Recurrent sinusitis • Male infertility and female subfertility (secondary to diminished sperm motility and defective ciliary action in the fallopian tubes) • Deafness • Hydrocephalus. H/O recurrent chest infections , situs inversus, and sperm sample shows nonmotile spermatozoa. The cause of this condition is most likely a mutation in the genes for which protein? →Dynein

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You can memorize the cause of Kartagener syndrome by thinking of Kartagener's restaurant that only has 'take-out' service because there is no dine-in (dynein). Kartagener syndrome: triad of:

1. situs inversus,
2. chronic sinusitis, and
3. bronchiectasis.

Lung cancer: General overview Epidemiology • Second most common cancer (after breast cancer in women and prostate cancer in men). • More common in males except for adenocarcinoma, which is more common in women Risk factors • Smoking increases risk of lung ca by a factor of 10 Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a 10 X 5 = 50 times increased risk Up to 15% of lung cancers in patients who do not smoke are thought to be caused by passive smoking • Occupational exposure Asbestos - increases risk of lung cancer by a factor of 5 Isocyanates occurs in chemical workers in the rubber industry → non-small-cell lung cancer , squamous-cell carcinoma Arsenic, radon, nickel • Preexisting chronic obstructive pulmonary disease (COPD), tuberculosis, and idiopathic pulmonary fibrosis (IPF). Coal dust is not a risk factor of lung cancer Types of lung cancer • Non-small cell lung cancer (NSCLC) 85% of all lung cancers Most, but not all patients will have a smoking history Less malignant than small cell lung cancer, less responsive to chemotherapy. The overall 5-year survival rate is about 15% Has main 3 subtypes: Adenocarcinoma ≈ 40% of NSCLC cases The most common form of lung cancer in non-smokers, women, and young adults Typically located on the lung periphery → normal bronchoscopy. May associate with Gynaecomastia. Histology will show: glandular mucin-producing cells

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Pulmonology Squamous ≈ 30% of NSCLC cases Typically, central (Squamous = Sentral) Associated with ↑parathyroid hormone-related protein (PTHrP) secretion → hypercalcaemia Cavitate (In 10% of cases) Histology will show: Pleomorphic cells in cluster with keratin pearls and intercellular bridges Large cell carcinoma (10%-15%). A diagnosis of exclusion. The cells belonging to this cancer will not have mucous, squamous differentiation, neuroendocrine properties, or small cell characteristics. Cells will be large with abundant amounts of cytoplasm, large nuclei, and prominent nucleoli. Originates from an epithelial cell. Most commonly grow in the periphery. Highly anaplastic and poorly differentiated. Associated ↑beta-hCG Poorly responsive to chemotherapy and often require surgical excision. Prognosis is generally poor. • Small cell lung cancer (SCLC) Also known as "oat-cell carcinoma" 15% of all lung cancers Strongly associated with smoking Usually centrally located Most aggressive cancer which

typically presents with a short history and 80–90% will have metastases at the time of presentation. Very poor prognosis. median survival is 6–12 months. Squamous cell cancer Squamous cell and Small cell lung cancer are both Sentrally (Centrally) located. Non-small cell lung cancer (NSCLC): adenocarcinoma VS squamous cell carcinoma Lung adenocarcinoma (AC) Lung squamous cell carcinoma (SCC) Location Peripheral Central Characteristics Most common type of lung cancer worldwide More common in women and nonsmokers Notes & Notes for MRCP
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 Strong association with smoking Cavitary lesions arising from a hilar bronchus

 Prognosis is usually better than in other types of lung cancer Paraneoplastic features Adenocarcinoma: HPOA → Clubbing Histology Glandular tumor Mucin-producing cells (positive mucin staining) Bronchioloalveolar carcinoma (BAC) is a pathological subtype of non-small cell lung cancer (NSCLC) • Adenocarcinoma • usually demonstrating a peripheral lesion. • grow along the alveolar walls without actually destroying them. • alveoli are often filled with mucin. • The classic massive clear frothy sputum (bronchorrhoea) can be up to one litre a day. • not resectable, poor prognosis. Features • Small tumours are often asymptomatic, so the majority of patients have either locally advanced or metastatic disease at diagnosis. • Most common presenting symptoms are cough, chest pain, haemoptysis, dyspnoea, and weight loss. • Regional adenopathy and compression of nearby structures may result in superior vena cava syndrome, hoarseness, and dysphagia. • Obstruction of a central bronchus may result in postobstructive pneumonia Referral • Consider immediate referral for patients with: signs of superior vena caval obstruction (swelling of the face/neck with fixed elevation of jugular venous pressure) stridor • Refer urgently for chest x-ray for patients with any of the following: haemoptysis unexplained or persistent (longer than 3 weeks): chest and/or shoulder pain, dyspnoea, weight loss, chest signs, hoarseness, finger clubbing, cervical or supraclavicular lymphadenopathy, cough, features suggestive of metastasis from a lung cancer (for example, secondaries in the brain, bone, liver, skin) underlying chronic respiratory problems with unexplained changes in existing symptoms • Refer urgently (for an appointment within 2 weeks) patients with: persistent haemoptysis (in smokers or ex-smokers aged 40 years and older) Notes & Notes for MRCP
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 PTHrp →Hypercalcemia Solid, epithelial tumor Intercellular bridges (desmosomes) Keratin pearls

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Pulmonology a chest X-ray suggestive of lung cancer (including pleural effusion and slowly resolving consolidation) a normal chest X-ray where there is a high suspicion of lung cancer a history of asbestos exposure and recent onset of chest pain, shortness of breath or unexplained systemic symptoms where a chest x-ray indicates pleural effusion, pleural mass or any suspicious lung pathology MRCPUK-part-1-january-2017: H/O Rapid progression (cough, lung mass and weight loss within 2 months) + paraneoplastic peripheral neuropathy. What is the most likely diagnosis? Small-cell carcinoma. (Squamous cell carcinoma and adenocarcinoma are usually very slow growing).

Lung cancer: paraneoplastic features Paraneoplastic features of lung cancer • Squamous cell: PTHrp →Hypercalcemia • Adenocarcinoma: HPOA → Clubbing • Small cell: ↑ADH → SIADH ↑ACTH → Cushing syndrome Lambert-Eaton syndrome Overview • Paraneoplastic syndromes are a result of antibody generation from or against malignant cells attacking normal tissue. • Paraneoplastic syndromes occur in 10% of patients with lung cancer • Both non-small cell and small cell lung cancers are associated with Paraneoplastic syndromes, although they are more common with the small cell due to its neuroendocrine cell origin. Paraneoplastic features associated with non-small cell lung cancer • Hypercalcemia Squamous cell carcinoma is the most common type of cancer related to hypercalcemia. Parathyroid hormone-related protein (PTH-rp) secretion causing hypercalcaemia occurs in about 15% best treated with intravenous fluids and bisphosphonates • Hypertrophic pulmonary osteoarthropathy (HPOA) More common with adenocarcinomas than squamous cell carcinomas Characterized by abnormal proliferation of the cutaneous and osseous tissues at the distal regions of the extremities. a triad of clubbed fingers, symmetric polyarthritis, and periostitis of the long tubular bones It is often painful.

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Paraneoplastic features associated with small cell lung cancers • ↑ ADH → Syndrome of inappropriate antidiuretic hormone secretion (SIADH) SIADH manifests as euvolemic hypo-osmolar hyponatremia characterized by low serum osmolality and inappropriately high urine osmolality in the absence of diuretic treatment, adrenal insufficiency, heart failure, cirrhosis, or hypothyroidism • ↑ ACTH → Hypercortisolism → Cushing syndrome not typical presentation hypertension, hyperglycaemia, hypokalaemia, alkalosis and muscle weakness are more common than buffalo hump etc. May manifest by Cushingoid facies and hyperpigmentation of the skin • Lambert-Eaton syndrome 70% occur in small cell carcinoma is a pre-synaptic disorder of auto-antibody IgG directed against the pre-synaptic voltage gated calcium channel (VGCC) leading to impaired acetylcholine release. characterised by: Proximal muscle weakness (the cranial nerves and respiratory muscles are usually spared) Depressed or absent tendon reflexes and Autonomic features (for example, dry mouth, impotence, etc). Weakness and fatiguability can be improved with guanidine hydrochloride Unlike myasthenia gravis exercise is associated with increasing muscle strength and there is a negative response to Tensilon. The presence of hyponatraemia strongly points towards a diagnosis of small cell lung cancer.

Lung cancer: stepwise investigations • Chest x-ray The best choice for an initial study. No initial examination is complete without a lateral film. Normal X-ray of the chest does not exclude bronchial carcinoma The common appearance of a tumour arising from the main central airways (70% of all cases) is enlargement of one or other hilum. An endobronchial lesion commonly leads to partial or complete atelectasis and this is the commonest sign of bronchogenic carcinoma. Consolidation and collapse distal to the tumour might have occurred Collapse of the left lower lobe is often hard to identify, as is a tumour situated behind the heart. Apically located masses or superior sulcus tumours (Pancoast tumours) can be misdiagnosed as pleural caps, and patients often have a long history of pain in the distribution of the brachial nerve roots. The mediastinum might be widened by enlarged nodes. • Contrast-enhanced CT of the lower neck, chest, and upper

abdomen Perform contrast-enhanced CT of the chest, liver adrenals and lower neck before any biopsy procedure.

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Pulmonology Shows size, location and extent of primary tumour; evaluates for hilar and/or mediastinal lymphadenopathy and distant metastases • Biopsy If the CT demonstrates a peripheral lung lesion, CT or ultrasound-guided transthoracic needle biopsy should be offered. Endobronchial ultrasound (EBUS) guided biopsy is recommended for paratracheal and peri-bronchial intra-parenchymal lung lesions. Wherever possible minimally invasive procedures should be undertaken first for mediastinal node sampling (e.g., EBUS) before embarking into more invasive procedures like VATS. • Positron-emission tomography (PET) The preferred first test after CT for intrathoracic lymph node assessment PET would determine whether there are distant metastases and is performed after the CT. For example in a patient with operable non-small-cell lung cancer, if CT has shown enlarged mediastinal nodes , he needs further assessment of his mediastinal nodes prior to surgery, because CT is not particularly good for assessing whether enlarged nodes are inflammatory or malignant. and this can be done with mediastinoscopy or a positron-emission tomography (PET) scan. Fluorodeoxyglucose is the usual tracer used for PET imaging in lung cancer PET is considered a standard staging study for patients with NSCLC; however, pathological confirmation of abnormal findings is often necessary due to false positives. For patients with known metastatic disease, PET is unnecessary.

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Performance status for patient of lung cancer and COPD • Assessing a patient's performance status is important when evaluating the most appropriate treatment options. • It is commonly used by cancer MDTs, but has a role in assessing patients with chronic illnesses including COPD. WHO (Zubrod) Scale Description

Asymptomatic

Symptomatic but ambulatory (can carry out light work)

In bed less than 50% of the day. Unable to work but can live at home with some assistance

In bed more than 50% of the day (unable to care for self)

Bedridden

Staging lung carcinoma Criteria for staging • TNM staging takes into account: The size and position of the tumour (T) Whether the cancer cells have spread into the lymph nodes (N) Whether the tumour has spread anywhere else in the body - secondary cancer or metastases (M) • CT scan is recommended as a staging procedure. • Where available, PET scanning may be

superior. Chest CT is the best method for staging squamous-cell carcinoma of the lung. The Tumor, Node, Metastasis (TNM) staging system • The International Association for the Study of Lung Cancer (IASLC) developed a eighth edition of the TNM system in 2018 replaced earlier editions: as fellow T, N, and M descriptors for the eighth edition of TNM classification for lung cancer • T: Primary tumor Tx → Primary tumor cannot be assessed or tumor proven by presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy T0 → No evidence of primary tumor Tis → Carcinoma in situ

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Pulmonology T1 →Tumor ≤3 cm in greatest dimension surrounded by lung or visceral pleura without bronchoscopic evidence of invasion more proximal than the lobar bronchus (ie, not in the main bronchus) T1a(mi) → Minimally invasive adenocarcinoma T1a →Tumor ≤1 cm in greatest dimension T1b → Tumor >1 cm but ≤2 cm in greatest dimension T1c →Tumor >2 cm but ≤3 cm in greatest dimension T2 → Tumor >3 cm but ≤5 cm or tumor with any of the following features:

1. Involves main bronchus regardless of distance from the carina but without involvement of the carina
2. Invades visceral pleura
3. Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung T2a → Tumor >3 cm but ≤4 cm in greatest dimension T2b →Tumor >4 cm but ≤5 cm in greatest dimension T3 → Tumor >5 cm but ≤7 cm in greatest dimension or associated with separate tumor nodule(s) in the same lobe as the primary tumor or directly invades any of the following structures: chest wall (including the parietal pleura and superior sulcus tumors), phrenic nerve, parietal pericardium T4 → Tumor >7 cm in greatest dimension or associated with separate tumor nodule(s) in a different ipsilateral lobe than that of the primary tumor or invades any of the following structures: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, and carina • N: Regional lymph node involvement Nx →Regional lymph nodes cannot be assessed N0 →No regional lymph node metastasis N1→ Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension N2 → Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s) N3 → Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s) • M: Distant metastasis M0 →No distant metastasis M1 →Distant metastasis present M1a →Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodule(s) or malignant pleural or pericardial effusion◊ M1b → Single extrathoracic metastasis§ M1c → Multiple extrathoracic metastases in one or more organs

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Treatment of lung cancer (NICE guidelines 2019) Non-small-cell lung cancer (NSCLC) • Surgery for early-stage NSCLC I–IIA (T1a–T2b, N0, M0) → lobectomy Advise to stop smoking, offer nicotine replacement therapy, but do not postpone surgery for that. Assessment before surgery for NSCLC assess perioperative mortality by using risk scores such as thoracoscore. Avoid surgery within 30 days of myocardial infarction. Consider revascularisation (percutaneous intervention or coronary artery bypass grafting) before surgery for people with chronic stable angina Perform spirometry and transfer factor (TLCO) • Radical radiotherapy For people with stage I–IIA (T1a–T2b, N0, M0) NSCLC who decline surgery or in whom any surgery is contraindicated, offer radical radiotherapy with stereotactic ablative radiotherapy (SABR). If SABR is contraindicated, offer either conventional or hyperfractionated radiotherapy. For eligible people with stage IIIA - IIIB NSCLC who cannot tolerate or who decline chemoradiotherapy, consider radical radiotherapy (either conventional or hyperfractionated). • Combination treatment (chemoradiotherapy) For people with stage II or III NSCLC that are not suitable for or decline surgery. For people with operable stage IIIA–N2 NSCLC: consider chemoradiotherapy with surgery. • Systemic anti-cancer therapy (SACT) for advanced NSCLC For non-squamous non-small-cell lung cancer, stages IIIB and IV If the tumour tests positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation →Afatinib If the tumour tests positive for anaplastic lymphoma kinase (ALK) gene → Crizotinib or Alectinib If the tumour tests positive for PD-L1 above 50% → Pembrolizumab

  If the tumour tests positive for PD-L1 below 50% →gemcitabine or vinorelbine and cisplatin or carboplatin If the tumour tests positive for ROS1→ Crizotinib Treatment of non-small cell lung cancer (NSCLC) NSCLC stage Treatment Stage I (cT1N0 and cT2N0) (primary tumour <5 cm) and stage II (primary tumour >5 cm, or smaller primary tumour with metastasis to a nearby lymph node) (cT1N1, cT2N1 and cT3N0) Surgery (FEV-1 should be >1.5 litres & no mets) stage III (ipsilateral lung metastases or multiple metastases to nearby lymph nodes): Sequential chemo-radiotherapy Stage IV (metastatic) chemotherapy alone • Absolute contraindications for surgery include: FEV1 < 1.5 litres is considered a general cut-off point If the tumour necessitates a pneumonectomy, the post-bronchodilator FEV should be more than 2 litres. Reduction in the gas transfer test of more than 50% is a contraindication to surgery. Metastases. stage IIIb or IV (i.e. metastases present) Tumour near hilum Vocal cord paralysis (implies extracapsular spread to mediastinal L.N) SVC obstruction Malignant pleural effusion (not just 'pleural effusion' (which may be reactive)). Most pleural effusions associated with lung carcinoma are due to the tumour (and results in classification as a T4 tumour). Spread to involve the C8, T1 and T2 nerve roots occurs by rib erosion by tumour to involve the lower roots of the brachial plexus and is known as a Pancoast tumour. Small-cell lung cancer (SCLC) • Early-stage SCLC (T1–2a, N0, M0): Consider surgery • Limited-stage disease SCLC (T1–4, N0–3, M0) → 4 to 6 cycles of cisplatin-based combination chemotherapy + thoracic radiotherapy + prophylactic cranial irradiation • Extensive-stage disease SCLC (broadly corresponding to T1–4, N0–3, M1a/b – including cerebral metastases) → platinum-based combination chemotherapy up to a maximum of 6 cycles + thoracic radiotherapy with prophylactic cranial irradiation

Treatment of small cell lung cancer (SCLC) Stage of SCLC Treatment Early stage (T1-2a,N0,M0) Surgery Early stage (T1-2a,N0,M0)- Limited disease (T1-4,N03,M0) 4-6 cycles cisplatin-based chemotherapy, carboplatin if poor renal function/poor performance status +/- radiotherapy Extensive disease (T1-4, N03, M1a/b) 6 cycles platinum-based combination chemotherapy + thoracic radiotherapy if good response The most appropriate next step in management for patients with SCLC who have a response to initial chemotherapy → Prophylactic cranial irradiation should be considered Palliative care • Impending endobronchial obstruction → external beam radiotherapy and/or endobronchial debulking or stenting • pleural effusion → pleural aspiration, talc pleurodesis for longer-term benefit. • to reduce cough → opioids, such as codeine or morphine • superior vena cava obstruction → chemotherapy and radiotherapy • for the immediate relief of severe symptoms of superior vena caval obstruction → stent insertion • for symptomatic brain metastases →dexamethasone • for bone metastasis who need palliation and for whom standard analgesic treatments are inadequate → single-fraction radiotherapy

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Lung cancer induced superior vena cava obstruction (SVCO) Overview • SVCO an oncological emergency caused by compression of the SVC. • 60 % of patients present with SVC syndrome without a preexisting diagnosis of cancer. • Most commonly associated with lung cancer. Up to 4% of patients with lung cancer will develop SVCO at some point during their disease. SVCO is much more likely to be associated with right sided lung lesion 4 times than with left sided lesions Causes • Lung cancer Non-small cell lung cancer (the most common cause ≈ 50%) Small cell lung cancer (25%) • Non-Hodgkin lymphoma (NHL) (10%) • Other malignancies (15%) metastatic seminoma, Kaposi's sarcoma, breast cancer • Aortic aneurysm • Mediastinal fibrosis • Mediastinal goitre • SVC thrombosis

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Pulmonology Features • Dyspnoea is the most common symptom • Swelling of the face, neck and arms - conjunctival and periorbital oedema may be seen • Headache • Visual disturbance • Pulseless jugular venous distension • CXR is abnormal in around 85% of cases, mediastinal widening is common. Association • Recurrent laryngeal nerve palsy (voice hoarseness): usually occurs with malignant tumour but can occur with aneurysm of aortic arch. • Horner's syndrome due to involvement of sympathetic chain. • elevated non-pulsatile jugular venous pressure (JVP) • Compression of vital structures can result in stridor and dysphagia. Diagnosis • Duplex ultrasound The initial imaging study for patients with mild symptoms • Contrast-enhanced CT The initial study for patients with clinical features suggestive of moderate SVC syndrome • Venography The first line in severe or life-threatening symptoms Catheter-based (standard) venography is preferred over CT venography because it also provide immediate treatment by thrombolysis (pharmacologic or mechanical) and SVC stenting Management • Dexamethasone Corticosteroids are most useful where the cause of compression is an underlying haematological malignancy. SVCO: immediate management →Dexamethasone IV + LMWH. • Stenting Relieves symptoms quicker than chemotherapy or radiotherapy. • Radiotherapy may be an option later. If radiotherapy is used initially then stenting becomes significantly more difficult due to local fibrosis. Mediastinal radiotherapy leads to symptomatic relief in 80% of patients

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Pancoast tumor • An apical lung carcinoma • Located in the superior sulcus of the lung (superior sulcus tumor) • Predominantly non-small cell lung cancer (NSCLC) • May lead to the development of Pancoast syndrome: a group of symptoms secondary to the mass effect of the tumor on surrounding structures Cervical sympathetic ganglion (stellate ganglion): → Horner syndrome (ipsilateral miosis, ptosis, and anhidrosis)

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 Recurrent laryngeal nerve: → hoarseness Phrenic nerve: → paralysis of the hemidiaphragm (visible as elevated hemidiaphragm on chest x-ray) Brachial plexus:→ shoulder pain, sensorimotor deficits (eg, atrophy of intrinsic muscles of the hand) Brachiocephalic vein: → unilateral edema of the arm and facial swelling • The investigation of choice → CT of chest • Treatment: usually inoperable on presentation → radiation and chemotherapy

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Lung metastases • Metastatic carcinoma is the most common malignant tumour found in the lung • Malignant metastases to the lung can present as a solitary enlarging nodule, as multiple nodules or with diffuse lymphatic involvement. • The most common causes of malignant nodules are primary lung cancer, lung metastases, and carcinoid tumors. • Breast, Colorectal, renal and lung primaries are the commonest underlying tumours. • An incidental pulmonary nodule that has clearly grown on serial imaging or is 18fluorodeoxyglucose (FDG)-avid on positron emission tomography (PET)/CT is likely to be malignant and should be evaluated with biopsy. • A diagnosis can usually be secured by percutaneous computed tomography- (CT-) guided biopsy. Lung cancer with multiple brain metastases →Hospice care is appropriate. Metastatic carcinoma Chest X-ray shows secondary tumors as multiple, wellcircumscribed, noncalcified nodules. The most common cancer to present with metastases to the hand is lung cancer. Metastatic carcinoma is the most common malignant tumour found in the lung

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Carcinoid lung tumour Carcinoid tumour as general (see gastroenterology section) • neuroendocrine tumours of predominantly enterochromaffin cell origin. • can occur in the small intestine, bronchi, rectum appendix or stomach. Overview • The vast majority of bronchial adenomas are carcinoid tumours, arising from the amine precursor uptake and decarboxylation (APUD) system, like small cell tumours. • Carcinoid tumours (so called argentafinomas as they take up silver) are neuroendocrine cells • originate from Kulchitsky (K) cells in the lung • Most often located in the main bronchi, and occur most frequency in the right middle lobe. • slow growing • smoking is NOT a risk factor Epidemiology • 1% of lung tumours • 10% of carcinoid tumours. • typical age = 40-50 years • The incidence is equal between men and women. Feature Recurrent haemoptysis with segmental collapse on x-ray is a typical presentation of bronchial carcinoid. • Often asymptomatic • long history of cough, recurrent haemoptysis • Recurrent infections: carcinoid tumours →(80-90%) develops in a bronchus → bronchial obstruction →lower respiratory

tract infection. • Carcinoid syndrome (rare) depends on associated liver metastases occurs in less than 10% of patients with carcinoid tumours, but occurs most commonly in GIT tumours. can secrete a number of vasoactive compounds (including serotonin and bradykinin), which result in bronchospasm, diarrhoea, skin flushing and rightsided valvular heart lesions. Paraneoplastic syndromes ACTH secretion and subsequent Cushing's syndrome. Ectopic growth hormone-releasing hormone [GHRH] and subsequent acromegaly Multiple endocrine neoplasia (MEN) type 1 where pancreatic neuroendocrine tumours predominate.

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Investigations The 'cherry-red' lesion is a typical finding of lung carcinoid. • Chest-X ray often centrally located and not seen on CXR. A carcinoid tumour in the left lower lobe bronchus could cause distal collapse of the left lower lobe. • Bronchoscopy: Identifies up to 80% of carcinoid tumours in the main bronchi. seen as a highly vascular 'cherry-like' tumour ('cherry red ball') Biopsy is usually followed with brisk bleeding and should be done via rigid bronchoscopy. The histological picture of granular eosinophilic staining of the cytoplasm, is highly suggestive of a carcinoid tumour. Histologically, these tumors consist of compact nests of epithelial cells surrounded by neat, delicate connective tissue capsules. histology might not be necessary prior to surgery if the clinical picture is typical. • Plasma chromograffin A is an effective screening test for carcinoid as it is very sensitive, but it is not specific. • 24-hour urinary excretion of 5-hydroxyindoleacetic acid is more specific for the diagnosis, but false positives and negatives are present. Management • Surgical resection A person with an isolated pulmonary carcinoid should be referred for tumour resection, histology might not be necessary prior to surgery if the clinical picture is typical. Prognosis • if no metastases then 90% survival at 5 years

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Lung fibrosis: Causes Acronym for causes of upper zone fibrosis: CHARTS • C- Coal worker's pneumoconiosis • H - Histiocytosis/ hypersensitivity pneumonitis • A - Ankylosing spondylitis • R - Radiation • T - Tuberculosis • S - Silicosis/sarcoidosis

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Pulmonology Fibrosis predominately affecting the upper zones • Extrinsic allergic alveolitis • Coal worker's pneumoconiosis/progressive massive fibrosis • Silicosis (Silica is found in coal dust) • Sarcoidosis • Ankylosing spondylitis (rare) • Histiocytosis: Pentalaminar X bodies (Birbeck granules) found on bronchoalveolar lavage (BAL) are diagnostic. • Tuberculosis • Allergic bronchopulmonary aspergillosis and farmers lung • Radiation Fibrosis predominately affecting the lower zones • Idiopathic pulmonary fibrosis (IPF) (previously known as Cryptogenic fibrosing alveolitis (the more common cause) • Most connective tissue disorders (except ankylosing spondylitis) • Asbestosis • Drug-induced Cardiac drugs: amiodarone, hydralazine Cytotoxic agents: busulphan, bleomycin , cyclophosphamide, leflunomide Anti-rheumatoid drugs: methotrexate, sulfasalazine, gold Antibiotics: nitrofurantoin Ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide). Opiates: e.g. heroin abuse

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Idiopathic pulmonary fibrosis (IPF) Definition • Progressive fibrosis of the interstitium of the lungs when no underlying cause exists. Epidemiology • Most common type of interstitial lung disease (ILD) • Typically seen in patients aged 50-70 years • Men are affected more than women Pathophysiology • Recurrent microinjuries to the alveolar wall → ↑growth factors secreted by the injured epithelial cells (most commonly: Transforming growth factor-beta (TGF-beta) → recruit fibroblasts → differentiate into myofibroblasts → secrete interstitial collagen, which accumulates due to imbalance between interstitial collagenases and their tissue inhibitors. Baseline pulmonary function testing is important in patients receiving bleomycin Pulmonary fibrosis can occur following pneumonia

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Risk factors • Genetic predisposition, • Cigarette smoking, environmental pollutants • Chronic microaspiration. Features • Gradual onset (over several months) of exertional dyspnoea and dry cough • Bibasal crackles on auscultation • Clubbing occurs in two-thirds of cases. Diagnosis • Chest X-ray: Bilateral lower-zone reticulonodular shadows • High resolution computed tomography (HRCT) The investigation of choice Showa radiographic pattern of usual interstitial pneumonia (UIP):

1. Peripheral (subpleural), bibasilar reticular opacities
2. Architectural distortion, including honeycomb changes and traction bronchiectasis or bronchiolectasis • Spirometry → restrictive picture (FEV1 normal/decreased, FVC decreased, FEV1/FVC increased) • Transfer factor (TLCO) reduced, most useful in determining prognosis. • Lung biopsy by video-assisted thoracoscopy (VATS) If HRCT is not diagnostic Finding → Honeycombing and collagen deposition with fibroblast foci • Exclusion of other known causes of interstitial lung disease Usual interstitial pneumonia (UIP): is a radiologic and pathologic description and can be seen in conditions other than IPF, especially connective tissue diseases, rheumatoid arthritis. Once these other conditions are reasonably excluded, a clinical diagnosis of IPF can be made. Hence UIP does not always mean IPF. But in IPF, the radiologic and pathologic pattern is UIP. Management • Supportive care (eg, supplemental oxygen, pulmonary rehabilitation, seasonal influenza and pneumococcal vaccination) • Antifibrotic agents →pirfenidone or nintedanib Action → suppresses fibroblast proliferation Indication → mild-moderate disease IPF (FVC 50-80 % predicted). Benefit → reduces disease progression by 30 % Side effects → drug-induced liver injury • Immunosuppressant therapies such as azathioprine, prednisolone and mycophenolate mofetil should not be used in IPF. • Lung transplant Prognosis • poor, average life expectancy is around 3-4 years • increased risk of developing lung cancer (by 7- to 14-fold).

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Pulmonology Chest X-ray shows sub-pleural reticular opacities that increase from the apex to the bases of the lungs CT scan showing advanced pulmonary fibrosis including 'honeycombing'

Bronchiolitis obliterans (BO) Definition • 'Bronchiolitis obliterans' is the term used to describe fibrous scarring of the small airways, characterized by fixed airway obstruction. Mechanism • submucosal and peribronchiolar inflammation and fibrosis without any intraluminal granulation tissue • BO should not be confused with bronchiolitis obliterans organising pneumonia (BOOP), a completely different disease. Causes • Inhalation of toxic fumes • Exposure to mineral dust • Respiratory infections: Viral, Mycoplasma, Legionella • post-transplantation: Bone marrow, heart-lung or lung transplantation • Connective tissue disorder: Rheumatoid arthritis or SLE • Penicillamine treatment • inflammatory bowel disease

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Feature • dry cough and dyspnoea. • wheeze might be audible. Diagnosis • Should be considered in a nonsmoker when airflow limitation is irreversible or associated with a gas transfer abnormality. • Should be considered in association with recent toxic fume exposure, symptoms of viral infection, history of organ transplantation, or concomitant rheumatic disease. • HRCT: shows expiratory air trapping (mosaic or diffuse), bronchial wall thickening, and centrilobular nodules • Spirometry →mixed obstructive/restrictive picture • Transfer factor may be low but the transfer coefficient (Kco) is often normal. • lung biopsy An open or thoracoscopic lung biopsy is required to make a definitive diagnosis will show→ a mural concentric narrowing of the lumina of the bronchioles. Transbronchial lung biopsy is often inadequate for diagnosis because the disease is patchy. Differential Diagnosis • Bronchiolitis obliterans is often misdiagnosed as asthma, chronic bronchitis, emphysema or pneumonia. Asthma → reversible airflow limitation on spirometry (unlike BO) COPD → significant cigarette smoking history and no exposure to the etiologic agents for BO. Cryptogenic organising pneumonia (COP) : differ from BO in: 'cryptogenic means unknown cause'. granulation tissue in the alveoli and bronchioles on histopathology Spirometry → restrictive pattern Responds very well to steroids Treatment • No optimal treatment. Patients rarely respond to steroids and the prognosis is poor. • This disease is irreversible and severe cases often require a lung transplant a history of inhalational exposure or hematopoietic cell or lung transplantation, the combination of airflow limitation on spirometry and HRCT showing expiratory air trapping (mosaic or diffuse), bronchial wall thickening, and centrilobular nodules are sufficient to make a diagnosis of bronchiolitis obliterans.

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Pulmonology Post-extubation stridor (PES) Prevalence • PES is a frequent complication of intubation, occurring in 2-16% of cases. Pathophysiology • pressure and ischaemia →damage to the mucosa of the larynx → inflammatory response → laryngeal oedema → acute respiratory compromise necessitating emergency reintubation. Risk factors for post-extubation stridor from laryngeal edema • prolonged duration of intubation, • traumatic intubation, (variably defined as ≥36 hours to ≥6 days) • large tube size (>8 mm in men, >7 mm in women) • Excessive cuff pressure • Aspiration • Tracheal infection • A history of asthma • Female gender

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Obstructive sleep apnoea (OSA) Sleep apnoea causes include obesity and macroglossia Definition • Cessation of breathing during sleep because of upper airway obstruction leads to apnea (respiratory arrests of ≥ 10 seconds) and hypopnea (reduction of airflow by ≥ 50% for ≥ 10 seconds). Epidemiology • More common in men : ♂ > ♀ (2:1) Causes • Obesity: the most important risk factor • macroglossia: acromegaly, hypothyroidism, amyloidosis • large tonsils • Marfan's syndrome • Small pharyngeal opening • Coexisting COPD • Sedatives such as alcohol • Collar size (Neck size) greater than (17 inches) 43 cm is strongly associated.

Features • Excessive daytime somnolence as a result of repeated arousals. • Repetitive apnoeas (cessation of airflow for more than 10 seconds) and hypopnoeas (50% reduction in airflow for greater than 10 seconds) • loud snoring, gasping, choking or interruptions in breathing while sleeping • morning headaches Complications • Pulmonary hypertension and cor pulmonale • Hypoxia-induced cardiac arrhythmia • increased risk of premature death, sudden death • myocardial infarction, stroke, • motor vehicle accidents due to microsleep • metabolic syndrome (hypertension, insulin resistance → ↑risk of type 2 diabetes.) • neurocognitive dysfunction, vascular dementia • reduced libido and erectile dysfunction • CBC may show polycythemia (↑ Hct, ↑ Hb): Hypoxia induces erythropoietin secretion by the kidneys, which stimulates the blood marrow, leading to increased RBC production Obstructive sleep apnea is one of the most common causes of secondary hypertension. Diagnosis : Sleep studies • Overnight polysomnography: first-line method The gold standard diagnostic test is. Classic findings Diagnose OSA if the Apnoea-Hypopnoea Index (AHI): ≥15 episodes/hour. ≥5 episodes/hour + additional symptoms (eg: excessive daytime sleepiness, insomnia, mood disorder, or cognitive dysfunction) or comorbidities (eg: HTN, IHD, stroke) To assess severity of obstructive sleep apnoea Apnoea-Hypopnoea Index (AHI): mild →4-14 episodes moderate →15-30 episodes severe →>30 episodes The diagnosis of obstructive sleep apnea requires sleep studies and should not be made based on clinical tools or questionnaires alone such as Epworth Sleepiness Scale (used to diagnose excessive daytime sleepiness) or Multiple Sleep Latency Test (MSLT) - measures the time to fall asleep in a dark room (using EEG criteria) In-laboratory polysomnography is the gold standard for the diagnosis of sleeprelated breathing disorders Following weight loss, CPAP is the first-line treatment for moderate/severe obstructive sleep apnoea

Pulmonology Management • Weight loss. the definitive management. But takes time • Continuous positive airways pressure ventilation (CPAP) : the treatment of choice the most appropriate initial and quickest management • Intra-oral devices (e.g. Oral appliance , mandibular advancement) if CPAP is not tolerated or for patients with mild OSA where there is no daytime sleepiness • Upper airway surgery : if CPAP or an oral appliance are declined or ineffective. • Pharmacological agents: limited evidence Modafinil is a drug that is licensed for excessive daytime sleepiness in people with OSA treated with CPAP, as well as for narcolepsy. • Avoid sedatives drugs/excess alcohol

Obesity hypoventilation syndrome (OHS) (Pickwick syndrome) Definition • a combination of obesity (body mass index [BMI] ≥30 kg/m2) and daytime hypercapnia ($PaCO_2$ ≥45 mm Hg in arterial blood gas analysis) in the absence of other causes for hypoventilation. Diagnostic criteria • BMI ≥30 kg/m2 .Commonly affects morbidly obese individuals. 90% of patients with OHS have coexistent OSA. • Arterial blood gasses showing diurnal hypercapnia ($PaCO_2$ > 45 mm Hg) serum bicarbonate ≥ 27 mEq/L • Polysomnography: hypoventilation during sleep with or without obstructive apnea events • Exclusion of other possible causes of hypoventilation (eg, neuromuscular disease). Treatment • 1st line: noninvasive positive airway pressure (PAP) together with lifestyle modifications for weight loss.

Pneumothorax Classification • primary pneumothorax : if there is no underlying lung disease. • secondary pneumothorax : if there is underlying lung disease Features • Sudden onset of chest pain, sometimes radiating to the shoulder • Dyspnoea (may not be a dominant feature) • Dry cough Obesity + feature of OSA + diurnal abnormal ABG (↑ PCO_2) (OHS)

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