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ХАРКІВСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ

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ДЛЯ СТУДЕНТІВ
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Навчальна дисципліна	Основи внутрішньої медицини
Модуль №	1
Змістовний модуль № 3	Основи діагностики, лікування та профілактики хвороб органів дихання
Тема заняття	Основні симптоми пульмонологічної патології та методи дослідження в пульмонології
Курс	4
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Module 3. "The basic foundations of diagnostics, treatment and prophylaxis of common pulmonary diseases".

Practical lesson N 20

"**Common symptoms of pulmonary diseases and methods of investigations in pulmonology**"

Topicality

The main role of the respiratory system is to extract oxygen from the external environment and dispose of waste gases, principally carbon dioxide. This requires the lungs to function as an efficient bellows, expelling used air, bringing fresh air in and mixing it efficiently with the air remaining in the lungs. The lungs have to provide a large surface area for gas exchange and the alveoli walls have to present minimal resistance to gas diffusion. For maximum efficiency, ventilation must be matched accurately to blood flow through the pulmonary capillary bed. Altogether, this means the lungs have to present a large area to the environment and this can be damaged by dusts, gases and infective agents. Host defence is therefore a key priority for the lung and is achieved by a combination of structural and immunological defenses.

Patients with disease of the respiratory system generally present because of symptoms, an abnormality on a chest radiograph, or both. These findings often lead to a set of diagnostic possibilities; the differential diagnosis is then refined on the basis of additional information gleaned from the history and physical examination, pulmonary function testing, additional imaging studies, and bronchoscopic examination.

Educational goals:

- To know common complains of patients with pulmonary diseases;
- To understand the pathophysiological mechanisms of common pulmonary symptoms;
- To differentiate common and specific symptoms of pulmonary diseases;
- To learn methods of physical investigations of pulmonary diseases;
- To learn how to interpret data of plain X-ray, computed tomography, bronchoscopy;
- To analyze results of spirometry and pickflowmetry.

What student should know?

- The basic anatomy and physiology of pulmonary system;
- The basic clinical syndroms of pulmonary diseases;
- The main complaints of patients with pulmonary diseases;
- The methods of physical examination of patients with pulmonary pathology;

- The diagnostic value of laboratory blood and sputum analysis;
- The diagnostic meaning of plain X-ray, computed tomography, bronchoscopy, bronchography, spirometry, pulmoangiography.
- The diagnostic and curative significance of pleural puncture.

What student should know how to do?

- the identification of main clinical syndromes of pulmonary diseases;
- the physical examination of patients with pulmonary diseases;
- the interpretation of laboratory findings in pulmonary diseases;
- the interpretation of results of instrumental investigations in pulmonary diseases;

Practical skills:

- Inspection of chest (shape, symmetry, type of constitution);
- Assessment of respiratory rate;
- Palpation of chest (elasticity, resistance, vocal fremitus);
- Topographic percussion of lungs;
- Assessment of low lung edge excursion;
- Comparative percussion of lungs;
- Auscultation of lungs;
- Assessment of bronchophony;

ANATOMY AND PHYSIOLOGY

The function of the nose is to facilitate smell and respiration. The nose also filters, moistens and warms inspired air and in doing so assists the normal process of respiration.

The major functions of nasal breathing are:

- to heat and moisten the air
- to remove particulate matter.

About 10 000 L of air are inhaled daily. The relatively low flow rates and turbulence of inspired air are ideal for particle deposition, and few particles greater than 10 microns pass through the nose. Deposited particles are removed from the nasal mucosa within 15 minutes, compared with 60-120 days from the alveolus. Nasal secretion contains many protective proteins in the form of IgA antibodies, lysozyme and interferon. In addition, the cilia of the nasal epithelium move the mucous gel layer rapidly back to the oropharynx where it is swallowed. Bacteria have little chance of settling in the nose. Mucociliary protection against viral infections is more difficult because viruses bind to receptors on epithelial cells. The majority of rhinoviruses bind to an adhesion molecule, intercellular adhesion molecule 1 (ICAM-1), shared by neutrophils and eosinophils. Many noxious gases, such as SO_2, are almost completely removed by nasal breathing.

The throat can be considered as the oral cavity, the pharynx and the larynx. The oral cavity extends from the lips to the tonsils. The pharynx can be divided into three areas:

- nasopharynx - extending from the nasal openings to the soft palate
- orpharynx - extending from the soft palate to the tip of the epiglottis
- hypopharynx - extending from the tip of the epiglottis to just below the level of the cricoid cartilage where it is continuous with the oesophagus.

Lying within the hypopharynx is the larynx. This consists of cartilaginous, ligamentous and muscular tissue with the primary function of protecting the distal airway. The pharynx is innervated from the pharyngeal plexus. There are two vocal cords which abduct (open) during inspiration and adduct (close) to protect the airway and for voice production (phonation). The main nerve supply of the vocal cords comes from the recurrent laryngeal nerves (branches of the vagus nerve) which arise in the neck, but on the left side passes down around the aortic arch and then ascends in the tracheo-oesophageal groove to the larynx.

Normal vocal cords vibrate between 90 (male) and 180 (female) times per second, giving the voice its pitch or frequency. A healthy voice requires full closure of the vocal cords with a smooth, regular pattern of vibration, and any pathology that prevents full closure will result in air escaping between the vocal cords during phonation and a 'breathy' voice.

The trachea is 10-12 cm in length. It lies slightly to the right of the midline and divides at the carina into right and left main bronchi. The carina lies under the junction of the manubrium sternum and the second right costal cartilage. The right main bronchus is more vertical than the left and, hence, inhaled material is more likely to end up in the right lung.

The right main bronchus divides into the upper lobe bronchus and the intermediate bronchus, which further subdivides into the middle and lower lobe bronchi. On the left the main bronchus divides into upper and lower lobe bronchi only. Each lobar bronchus further divides into segmental and subsegmental bronchi. There are about 25 divisions in all between the trachea and the alveoli.

The ciliated epithelium is a key defence mechanism. Each cell bears approximately 200 cilia beating at 1000 beats per minute in organized waves of contraction. Each cilium consists of nine peripheral parts and two inner longitudinal fibrils in a cytoplasmic matrix.Mucus, which contains macrophages, cell debris, inhaled particles and bacteria, is moved by the cilia towards the larynx at about 1.5 cm/min (the 'mucociliary escalator').

The bronchioles finally divide within the acinus into smaller respiratory bronchioles that have alveoli arising from the surface. Each respiratory bronchiole supplies approximately 200 alveoli via alveolar ducts. The term 'small airways' refers to bronchioles of less than 2 mm; there are 30 000 of these in the average lung.

There are approximately 300 million alveoli in each lung. Their total surface area is 40-80 m^2. The epithelial lining consists largely of *type I pneumocytes*. These cells have an extremely attenuated cytoplasm, and thus provide only a thin barrier to gas exchange. They are derived from type II pneumocytes. *Type I cells* are connected to each other by tight junctions that limit the fluid movements in and out of the alveoli. *Type II pneumocytes* are slightly more numerous than type I cells but cover less of the epithelial lining. They are found generally in the borders of the alveolus and contain distinctive lamellar vacuoles, which are the source of surfactant. Macrophages are also present in the alveoli and are involved in the defense mechanisms of the lung. The pores of Kohn are holes in the alveolar wall allowing communication between alveoli of adjoining lobules.

The lungs are separated into lobes by invaginations of the pleura, which are often incomplete. The right lung has three lobes, whereas the left lung has two. The upper lobe lies mainly in front of the lower lobe and therefore physical signs on the right side in the front of the chest are due to lesions of the upper lobe or the middle lobe. Because of the contrast in density between healthy and diseased lung, plain radiography enables accurate localization of disease processes, especially if postero-anterior (PA) and lateral views are taken.

Each lobe is further subdivided into bronchopulmonary segments by fibrous septa that extend inwards from the pleural surface. Each segment receives its own segmental bronchus.

The bronchopulmonary segment is further divided into individual lobules approximately 1 cm in diameter and generally pyramidal in shape, the apex lying towards the bronchioles supplying them. Within each lobule a terminal bronchus supplies an acinus, and within this structure further divisions of the bronchioles eventually give rise to the alveoli.

The pleura is a layer of connective tissue covered by a simple squamous epithelium. The visceral pleura covers the surface of the lung, lines the interlobar fissures, and is continuous at the hilum with the parietal pleura, which lines the inside of the hemithorax. At the hilum the visceral pleura continues alongside the branching bronchial tree for some distance before reflecting back to join the parietal pleura. In health, the pleurae are in apposition apart from a small quantity of lubricating fluid.

The diaphragm is covered by parietal pleura above and peritoneum below. Its muscle fibres arise from the lower ribs and insert into the central tendon. Motor and sensory nerve fibres go separately to each half of the diaphragm via the phrenic nerves. Fifty per cent of the muscle fibres are of the slow-twitch type with a low glycolytic capacity; they are relatively resistant to fatigue.

The lung is unusual in having a dual blood supply. It receives deoxygenated blood from the right ventricle via the pulmonary artery and also has a systemic supply via the bronchial circulation.

The pulmonary artery divides to accompany the bronchi. The arterioles accompanying the respiratory bronchioles are thin-walled and contain little smooth muscle. The pulmonary venules drain laterally to the periphery of the lobules, pass centrally in the interlobular and intersegmental septa, and eventually join to form the four main pulmonary veins.

The bronchial circulation arises from the descending aorta. These bronchial arteries supply tissues down to the level of the respiratory bronchiole. The bronchial veins drain into the pulmonary vein, forming part of the physiological shunt observed in normal individuals.

Lymphatic channels lie in the interstitial space between the alveolar cells and the capillary endothelium of the pulmonary arterioles.

The tracheobronchial lymph nodes are arranged in five main groups: pulmonary, bronchopulmonary, subcarinal, superior tracheobronchial and paratracheal. In practical terms these form a continuous network of nodes from the lung substance up to the trachea.

The innervation of the lung remains incompletely understood. Parasympathetic (from the vagus) and sympathetic (from the adjacent sympathetic chain) nerve supplies entwine in a plexus at the nerve root and branches accompany the pulmonary arteries and the airways. Airway smooth muscle is innervated by vagal afferents, postganglionic muscarinic vagal efferents and vagally derived non-adrenergic non-cholinergic (NANC) fibres. Neurotransmitters (peptides and purines) may be involved. Three muscarinic receptor subtypes have been identified: M_1 receptors on parasympathetic ganglia, a smaller number of M_2 receptors on muscarinic nerve terminals, and M_3 receptors on airway smooth muscle. The parietal pleura is innervated from intercostal and phrenic nerves but the visceral pleura has no innervation.

Lung ventilation can be considered in two parts:

- the mechanical process of inspiration and expiration
- the control of respiration to a level appropriate for the metabolic needs.

Inspiration is an active process and results from the descent of the diaphragm and movement of the ribs upwards and outwards under the influence of the intercostal muscles. In

healthy individuals at rest, inspiration is almost entirely due to contraction of the diaphragm. Respiratory muscles are similar to other skeletal muscles but are less prone to fatigue. However, muscle fatigue contributes to respiratory failure in patients with severe chronic airflow limitation. Muscle weakness can also result from primary neurological and muscle disorders.

Expiration follows passively as a result of gradual relaxation of the intercostal muscles, allowing the lungs to collapse under the influence of their own elastic forces.

Inspiration against increased resistance may require the use of the accessory muscles of ventilation, such as the sternomastoid and scalene muscles. Forced expiration is also accomplished with the aid of accessory muscles, chiefly those of the abdominal wall, which help to push up the diaphragm.

The lungs have an inherent elastic property that causes them to tend to collapse away from the thoracic wall, generating a negative pressure within the pleural space. The strength of this retractive force relates to the volume of the lung; thus, at higher lung volumes the lung is stretched more, and a greater negative intrapleural pressure is generated.

Coordinated respiratory movements result from rhythmical discharges arising in an anatomically ill-defined group of interconnected neurones in the reticular substance of the brainstem, known as the respiratory centre. Motor discharges from the respiratory centre travel via the phrenic and intercostal nerves to the respiratory musculature.

The pressures of oxygen and carbon dioxide in arterial blood are closely controlled. In a typical normal adult at rest:

- The pulmonary blood flow of 5 L/min carries 11 mmol/min (250 mL/min) of oxygen from the lungs to the tissues.
- Ventilation at about 6 L/min carries 9 mmol/min (200 mL/min) of carbon dioxide out of the body.
- The normal pressure of oxygen in arterial blood (P_aO_2) is between 11 and 13 kPa (83 and 98 mmHg).
- The normal pressure of carbon dioxide in arterial blood (P_aCO_2) is 4.8-6.0 kPa (36-45 mmHg).

SYMPTOMS AND SIGNS

Cough

Cough is an explosive expiration that clears and protects the airways. It is one of the most common presenting complaints encountered in an outpatient practice. A cough is under both voluntary and involuntary control. The latter is the cough reflex, which has five components: cough receptors, afferent nerves, cough center (medulla), efferent nerves, and effector organs. The afferent limb of the cough reflex includes the sensory branches of the trigeminal, glossopharyngeal, and vagus nerves. Inflammatory, mechanical, chemical, or thermal stimulation of the receptors and sensory pathways can trigger cough. The efferent limb includes the recurrent laryngeal and spinal nerves that innervate the expiratory and laryngotracheobronchial musculature. Lesions in the nose, ears, pharynx, larynx, bronchi, lungs, pleura, or abdominal viscera can cause cough.

Chronic cough is cough that lasts 3 weeks or more without an obvious cause such as cigarette smoking. The most common causes of chronic cough are postinfectious (viral, *Mycoplasma*, *Chlamydia pneumoniae* TWAR, or *Bordetella pertussis*), postnasal drip, asthma, gastroesophageal reflux, and chronic obstructive pulmonary disease (COPD). Connective tissue

diseases such as giant cell arteritis, rheumatoid bronchiolitis, and Sjögren syndrome may also present with cough. Cough can be the presenting manifestation or the only manifestation of asthma. Cough is a complication in up to 10% of patients who take angiotensin-converting enzyme inhibitors (ACEIs).

Angiotensin-converting enzyme receptor blockers (ARBs) are much less likely to produce cough. About one-half of the patients with persistent cough may have more than one cause for the cough. Initial diagnostic testing may include computed tomography (CT) of the sinuses and ear-nose-throat consultation, sputum analysis, methacholine inhalation challenge, 24-hour esophageal pH monitoring, or esophagography. If no chest radiographic (CXR) abnormalities are detected, bronchoscopy has a low (4%) diagnostic yield. In cough syncope, a hard cough produces increased intrathoracic pressure, which decreases cardiac output and cerebral perfusion. Other complications include rib fracture and pneumothorax.

Sputum

Purulent sputum is found in bronchiectasis and lung abscess. The sputum is frothy pink in pulmonary edema. Expectoration of bronchial casts, mucous plugs, or thin strings occurs in asthma, bronchopulmonary aspergillosis, and mucoid impaction syndrome. Plastic bronchitis is the formation of thick bronchial casts in asthma, bronchopulmonary aspergillosis, and other conditions. Bronchorrhea (expectoration of thin serous fluid >100 mL daily) occurs in 20% of patients with diffuse alveolar cell carcinoma. Sputum analysis may identify eosinophils, Charcot-Leyden crystals, and Curschmann spirals, which are seen with asthma. The most important cause of broncholithiasis is histoplasmosis.

Hemoptysis

Hemoptysis is the expectoration of blood or blood-streaked sputum that originates below the level of the larynx. *Pseudohemoptysis* is expectoration of blood previously aspirated into the airways from the gastrointestinal tract, nose, or supraglottic areas. History, examination, and CXR findings are important in the diagnosis of hemoptysis.

Bronchial arterial bleeding occurs in chronic bronchitis, bronchiectasis, malignancies, and broncholithiasis and with the presence of foreign bodies. Pulmonary arterial bleeding occurs in pulmonary arteriovenous malformations, fungus ball, tumors, vasculitis, pulmonary hypertension, and lung abscess. Pulmonary capillary bleeding occurs in mitral stenosis, left ventricular failure, pulmonary infarction, vasculitis, Goodpasture syndrome, and idiopathic pulmonary hemosiderosis. A common cause of streaky hemoptysis is acute exacerbation of chronic bronchitis. Airway-vessel fistula (e.g., tracheoinnominate) can cause massive hemoptysis (>200 mL/24 h).

The cause of death in massive hemoptysis is asphyxiation, not exsanguination.

Dyspnea

Dyspnea is the subjective awareness of breathlessness. It usually is the result of increased work of breathing. Other mechanisms include abnormal activation of respiratory centers, voluntary hyperventilation, and Cheyne-Stokes respiration. Dyspnea may be due to cardiopulmonary disease or to disorders of the skeletal (e.g., kyphoscoliosis), endocrine, metabolic, neurologic, or hematologic systems.Other causes are physiologic dyspnea of pregnancy, drugs, psychogenic, deconditioning, and obesity. The grades of severity are based on the New York Heart Association classification: grade 0, no dyspnea except with strenuous

exercise; grade 1, slight dyspnea on hurrying on a level surface or walking up a hill; grade 2, dyspnea while walking on a level surface and being unable to keep up with peers and having to stop to catch breath; grade 3, dyspnea on walking 100 yards or after a few minutes and the need to stop for breath; grade 4, dyspnea on dressing or undressing or minimal exertion; and grade 5, dyspnea at rest. Recent studies have suggested that an increased serum level of brain natriuretic peptide (>100 pg/mL) differentiates dyspnea due to congestive heart failure from that due to pulmonary dysfunction.

A medical history, physical examination, CXR, electrocardiography (ECG), complete blood count, and pulmonary function tests (PFTs) are required for most patients. Arterial blood gases and cardiopulmonary physiologic testing may also be required.

Tachypnea is breathing more than 20 breaths/min, and *bradypnea* is fewer than 10 breaths/min.

Orthopnea is dyspnea in the supine posture, as in congestive heart failure, bilateral diaphragmatic paralysis, severe COPD, asthma, sleep apnea, or severe gastroesophageal reflux disease.

Trepopnea is dyspnea in the lateral decubitus position, as occurs with tumors of the main bronchi, unilateral pleural effusion, or after pneumonectomy.

Platypnea is dyspnea in the upright posture and is due to an increased right-to-left shunt in lung bases; it is seen in liver disease, severe lung fibrosis, or after pneumonectomy.

Paroxysmal nocturnal dyspnea is nocturnal episodes of dyspnea, resulting in frequent waking up (associated with pulmonary edema and asthma).

Chest Pain

Pulmonary causes of chest pain are often difficult to distinguish from cardiac and other causes. Tightness of the chest and dyspnea are also described as “chest pain” by patients. Pleuritic pain is encountered in pleuritis, pleuropericarditis, pericarditis, pneumothorax, pleural effusion, mediastinitis, pulmonary embolism, pulmonary infarction, esophageal disease, aortic dissection, and chest wall trauma.

Subdiaphragmatic diseases that produce chest pain include pancreatitis, cholecystitis, and colonic distention.

Cyanosis

Cyanosis, the bluish discoloration of the skin and mucous membranes that appears when the capillary content of reduced hemoglobin is greater than 5 g/dL, may be difficult to detect clinically.

The causes of central cyanosis are severe hypoxia (arterial oxygen tension [PaO2] is usually <55 mm Hg), anatomical right-to-left shunt, mild hypoxia with polycythemia (“red cyanosis”), shock, and abnormal hemoglobin level. Methemoglobinemia and sulfhemoglobinemia cause cyanosis in the setting of normal PaO2.

Certain systemic diseases, such as argyria (silver deposition) can cause blue-gray discoloration of the nails which is not cyanosis. Cherry-red flush (not cyanosis) is caused by carboxyhemoglobinemia. Anemia does not cause cyanosis. Peripheral cyanosis results from decreased peripheral perfusion with increased oxygen extraction.

Clubbing

Clubbing is the bulbous enlargement of the distal segment of a digit (fingers or toes) caused by increased soft tissue mass. Its mechanisms are neurogenic, humoral/hormonal, hereditary, and idiopathic. The mnemonic *CLUBBING* is a reminder of common causes for clubbing including the following: **C**yanotic heart diseases and cystic fibrosis; **L**ung cancer and lung abscess; **U**lcerative colitis; **B**ronchiectasis; **B**enign mesothelioma; **I**nfective endocarditis, idiopathic pulmonary fibrosis, idiopathic, and inherited; **N**eurogenic tumors; and **G**astrointestinal diseases (e.g., cirrhosis and regional enteritis).

Clubbing can be the presenting manifestation of any of the above entities, and it may precede other clinical features of lung cancer.

Hypertrophic Pulmonary Osteoarthropathy

Hypertrophic pulmonary osteoarthropathy (HPO) is characterized by clubbing, painful periosteal hypertrophy of long bones, and symmetrical arthralgias of large joints (usually knees, elbows, and wrists).

Other features include gynecomastia, fever, and an increased erythrocyte sedimentation rate (ESR). The mechanisms of HPO are neurogenic (vagal afferents), hormonal, and idiopathic. The most common cause is bronchogenic carcinoma, usually adenocarcinoma or large cell carcinoma. HPO is an early sign of pulmonary metastasis from nasopharyngeal carcinoma. Clubbing is present in 30% of patients with non–small cell lung cancer; it is more common in women than in men (40% vs. 19%). Radiographs of long bones show thickened and raised periosteum. Bone scans show increased uptake of radionuclide by the affected periosteum. If HPO does not resolve after tumor resection, treatment options include the administration of a somatostatin analogue or ipsilateral vagotomy.

Horner Syndrome

Horner syndrome consists of ipsilateral miosis, anhidrosis, and ptosis on the side of the lesion. It is a complication of a superior sulcus tumor (Pancoast tumor) of the lung.

Other Signs and Symptoms of Pulmonary Disease

Conjunctival suffusion is seen in severe hypercarbia, superior vena cava syndrome, and conjunctival sarcoidosis. Mental obtundation is seen with hypercarbia. Asterixis is seen in severe acute or subacute hypercarbia. Telangiectasia of the skin and mucous membranes occurs in patients with pulmonary arteriovenous malformation. Skin lesions of various types occur in patients with pulmonary involvement of Langerhans cell granulomatosis (eosinophilic granuloma or histiocytosis X), tuberous sclerosis, sarcoidosis, or lung cancer.

History and Examination

Information about risk factors for lung disease should be explicitly explored to ensure a complete basis of historic data. A history of current and past smoking, especially of cigarettes, should be sought from all patients. The smoking history should include the number of years of smoking, the intensity (i.e., number of packs per day), and, if the patient no longer smokes, the interval since smoking cessation. The risk of lung cancer falls progressively in the decade following discontinuation of smoking, and loss of lung function above the expected age-related decline ceases with the discontinuation of smoking. Even though chronic obstructive lung disease and neoplasia are the two most important respiratory complications of smoking, other

respiratory disorders (e.g., spontaneous pneumothorax, respiratory bronchiolitis–interstitial lung disease, pulmonary Langerhans cell histiocytosis, and pulmonary hemorrhage with Goodpasture's syndrome) are also associated with smoking. A history of significant secondhand (passive) exposure to smoke, whether in the home or at the workplace, should also be sought as it may be a risk factor for neoplasia or an exacerbating factor for airways disease.

The patient may have been exposed to other inhaled agents associated with lung disease, which act either via direct toxicity or through immune mechanisms. Such exposures can be either occupational or avocational, indicating the importance of detailed occupational and personal histories, the latter stressing exposures related to hobbies or the home environment. Important agents include the inorganic dusts associated with pneumoconiosis (especially asbestos and silica dusts) and organic antigens associated with hypersensitivity pneumonitis (especially antigens from molds and animal proteins). Asthma, which is more common in women than men, is often exacerbated by exposure to environmental allergens (dust mites, pet dander, or cockroach allergens in the home or allergens in the outdoor environment such as pollen and ragweed) or may be caused by occupational exposures (diisocyanates). Exposure to particular infectious agents can be suggested by contacts with individuals with known respiratory infections (especially tuberculosis) or by residence in an area with endemic pathogens (histoplasmosis, coccidioidomycosis, blastomycosis).

A history of coexisting nonrespiratory disease or of risk factors for or previous treatment of such diseases should be sought, as they may predispose a patient to both infectious and noninfectious respiratory system complications. Common examples include systemic rheumatic diseases that are associated with pleural or parenchymal lung disease, metastatic neoplastic disease in the lung, or impaired host defense mechanisms and secondary infection, which occur in the case of immunoglobulin deficiency or with hematologic and lymph node malignancies. Risk factors for AIDS should be sought, as the lungs are not only the most common site of AIDS-defining infection but can also be involved by noninfectious complications of AIDS. Treatment of nonrespiratory disease can be associated with respiratory complications, either because of effects on host defense mechanisms (immunosuppressive agents, cancer chemotherapy) with resulting infection or because of direct effects on the pulmonary parenchyma (cancer chemotherapy, radiation therapy, or treatment with other agents, such as amiodarone) or on the airways (beta-blocking agents causing airflow obstruction, angiotensin-converting enzyme inhibitors causing cough).

Family history is important for evaluating diseases that have a genetic component. These include disorders such as cystic fibrosis, α_1-antitrypsin deficiency, pulmonary hypertension, pulmonary fibrosis, and asthma.

The general principles of inspection, palpation, percussion, and auscultation apply to the examination of the respiratory system. However, the physical examination should be directed not only toward ascertaining abnormalities of the lungs and thorax but also toward recognizing other findings that may reflect underlying lung disease.

On *inspection*, the rate and pattern of breathing as well as the depth and symmetry of lung expansion are observed. Breathing that is unusually rapid, labored, or associated with the use of accessory muscles of respiration generally indicates either augmented respiratory demands or an increased work of breathing. Asymmetric expansion of the chest is usually due to an asymmetric process affecting the lungs, such as endobronchial obstruction of a large airway, unilateral parenchymal or pleural disease, or unilateral phrenic nerve paralysis. Visible abnormalities of the

thoracic cage include kyphoscoliosis and ankylosing spondylitis, either of which can alter compliance of the thorax, increase the work of breathing, and cause dyspnea.

On *palpation*, the symmetry of lung expansion can be assessed, generally confirming the findings observed by inspection. Vibration produced by spoken sounds is transmitted to the chest wall and is assessed by the presence or absence and symmetry of tactile fremitus. Transmission of vibration is decreased or absent if pleural liquid is interposed between the lung and the chest wall or if an endobronchial obstruction alters sound transmission. In contrast, transmitted vibration may increase over an area of underlying pulmonary consolidation. Palpation may also reveal focal tenderness, as seen with costochondritis or rib fracture.

The relative resonance or dullness of the tissue underlying the chest wall is assessed by *percussion*. The normal sound of underlying air-containing lung is resonant. In contrast, consolidated lung or a pleural effusion sounds dull, while emphysema or air in the pleural space results in a hyperresonant percussion note.

On *auscultation* of the lungs, the examiner listens for both the quality and intensity of the breath sounds and for the presence of extra, or adventitious, sounds. Normal breath sounds heard through the stethoscope at the periphery of the lung are described as *vesicular breath sounds*, in which inspiration is louder and longer than expiration. If sound transmission is impaired by endobronchial obstruction or by air or liquid in the pleural space, breath sounds are diminished in intensity or absent. When sound transmission is improved through consolidated lung, the resulting *bronchial breath sounds* have a more tubular quality and a more pronounced expiratory phase. Sound transmission can also be assessed by listening to spoken or whispered sounds; when these are transmitted through consolidated lung, *bronchophony* and *whispered pectoriloquy*, respectively, are present. The sound of a spoken E becomes more like an A, although with a nasal or bleating quality, a finding that is termed *egophony*.

The primary adventitious (abnormal) sounds that can be heard include crackles (rales), wheezes, and rhonchi. *Crackles* are the discontinuous, typically inspiratory sound created when alveoli and small airways open and close with respiration. They are often associated with interstitial lung disease, microatelectasis, or filling of alveoli by liquid. *Wheezes*, which are generally more prominent during expiration than inspiration, reflect the oscillation of airway walls that occurs when there is airflow limitation, as may be produced by bronchospasm, airway edema or collapse, or intraluminal obstruction by neoplasm or secretions. *Rhonchi* is the term applied to the sounds created when there is free liquid or mucus in the airway lumen; the viscous interaction between the free liquid and the moving air creates a low-pitched vibratory sound. Other adventitious sounds include pleural friction rubs and stridor. The gritty sound of a *pleural friction rub* indicates inflamed pleural surfaces rubbing against each other, often during both inspiratory and expiratory phases of the respiratory cycle. *Stridor*, which occurs primarily during inspiration, represents flow through a narrowed upper airway, as occurs in an infant with croup.

Diagnostic Tests

Radiology

Plain chest radiography (CXR), computed tomography (CT), magnetic resonance imaging (MRI), pulmonary angiography, and bronchial angiography are among the tests performed in the diagnosis of chest diseases.

Plain Chest Radiography

Internists should become familiar with the interpretation of common abnormalities on a plain CXR. Even normal CXRs should be viewed so that reading CXRs becomes routine. Many

of the radiographic diagnoses such as pneumothorax, pleural effusion, and lung nodule can be established by CXR. It is essential to correlate clinical and other laboratory data with CXR findings. It is important to compare the present film with previous films, particularly in assessing the seriousness of a newly identified abnormality. A lateral CXR is of most help in identifying retrocardiac and retrodiaphragmatic abnormalities.

The ability to identify normal radiographic anatomy is essential. A routine step-by-step method of interpretation should be developed so that subtle abnormalities are not missed. Initially, the CXR should be eyeballed, without focusing on any one area or abnormality. This is to ensure that the technical aspects are adequate and the patient identification markers and the orientation of the CXR (identification of the left and right sides) are correct. Next, the extrapulmonary structures are viewed. For instance, destructive arthritis of a shoulder joint seen on a CXR may be the result of rheumatoid arthritis and may prompt the CXR reader to look for pulmonary manifestations of this disease. The absence of a breast shadow on the CXR of a female patient suggests the need to look for signs of pulmonary metastases. The visualization of a tracheostomy stoma or cannula on the CXR may indicate previous laryngeal cancer, suggesting the possibility of complications such as aspiration pneumonia and lung metastases. Infradiaphragmatic abnormalities such as calcifications in the spleen, displacement of the gastric bubble and colon, and signs of upper abdominal surgery (metal staples or feeding tubes) may indicate the cause of a pleuropulmonary process.

The skeletal thorax should be viewed to exclude rib fracture, osteolytic and other lesions of the ribs, rib notching, missing ribs, and vertebral abnormalities. Changes due to a previous thoracic surgical procedure such as coronary artery bypass, thoracotomy, lung resection, or esophageal surgery may provide clues to the pulmonary disease. Next, the intrathoracic but extrapulmonary structures such as the mediastinum (great vessels, esophagus, heart, lymph nodes, and thymus) should be assessed. The superior mediastinum should be viewed to see whether the thyroid gland extends into the thoracic cage. A calcified mass in the region of the thyroid almost always indicates a goiter. The esophagus can produce important abnormalities in the CXR. A large esophagus, as in achalasia, may mimic a mass, and a large hiatal hernia with an air-fluid level may mimic a lung abscess. The aortopulmonary window (a notch below the aortic knob on the left, just above the pulmonary artery), if obliterated, may indicate a tumor or lymphadenopathy. Right paratracheal and paramediastinal lymphadenopathy can be subtle. Hilar regions are difficult to interpret because lymphadenopathy, vascular prominence, or tumor may make the hila appear larger. The retrocardiac region may show hiatal hernia with an air-fluid level; this may be helpful in the diagnosis of reflux or aspiration.

The pleural regions should be examined for pleural effusion, pleural thickening (particularly in the apices), blunting of costophrenic angles, pleural-based lesions such as pleural plaques or masses, and pneumothorax. A lateral decubitus film may be necessary to confirm the presence of free fluid in the pleural space. An air bronchogram depicting the major airways may indicate a large tumor (cut-off of air bronchogram), deviation of airways, signs of compression or stenosis, and the relation of major airways to the esophagus.

Finally, the lung parenchyma should be evaluated. Nearly 15% of the pulmonary parenchyma is located behind the heart and diaphragm; a lateral CXR is helpful in examining this region. It is important not to overinterpret increased interstitial lung markings.

Oligemia of the lung fields is difficult to assess because the clarity of the film depends on the duration of the exposure of the film. Generally, bronchovascular markings should be visible throughout the lung parenchyma. The complete absence of any markings within the lung

parenchyma should suggest a bulla or an air-containing cyst. Apical areas should be evaluated carefully for the presence of pleural thickening, pneumothorax, small nodules, and subtle infiltrates. If the apices cannot be visualized properly with a standard CXR, a lordotic view should be obtained.

Fluoroscopy

Fluoroscopy is useful in localizing lesions during biopsy and aspiration procedures. It also is valuable in assessing diaphragmatic motion and in diagnosing diaphragmatic paralysis by the sniff test. Paradoxic motion of the diaphragm suggests diaphragmatic paralysis (but it is present in up to 6% of healthy subjects).

Computed Tomography

Standard CT is useful in the staging of lung cancer and in assessing mediastinal and hilar lesions, solitary nodules, calcification in nodules, diffuse lung disease, and pleural processes. High-resolution CT (HRCT) demonstrates characteristic findings in pulmonary bronchiectasis (HRCT has replaced bronchography for diagnosing bronchiectasis), Langerhans cell granulomatosis (nodular-cystic spaces in the upper lung fields), lymphangitic carcinomatosis (nodular interlobular septal thickening), lymphangioleiomyomatosis (well-defined cystic spaces in lung parenchyma), and idiopathic pulmonary fibrosis (subpleural honeycombing). HRCT findings in pulmonary fibrotic diseases are more than 90% accurate; honeycombing may be seen in up to 90% of patients, as compared with 30% with traditional CXR. HRCT is also helpful in diagnosing certain granulomatous lung diseases (sarcoidosis and mycobacterial infections), asbestosis, pulmonary alveolar phospholipoproteinosis, chronic eosinophilic pneumonia, and bronchiolitis obliterans. Ultrafast CT with contrast media is better than a ventilation-perfusion (V/Q) scan in detecting pulmonary emboli in the main and lobar arteries.

Magnetic Resonance Imaging

MRI is recommended for the initial evaluation of superior sulcus tumors (Pancoast tumor), lesions of the brachial plexus, and paraspinal masses that on CXR appear most consistent with neurogenic tumors.

MRI is superior to CT in the evaluation of chest wall masses and in the search for small occult mediastinal neoplasms (e.g., ectopic parathyroid adenoma). MRI is useful when CT with contrast media is contraindicated for patients with renal failure or contrast allergy.

MRI may be superior to CT in evaluating pulmonary sequestration, arteriovenous malformation, vascular structures, and tumor recurrence in patients with total pneumonectomy.

Pulmonary Angiography

The main indication for pulmonary angiography is to detect pulmonary emboli. However, small peripheral emboli may not be seen.

Pulmonary angiography is also useful in the diagnosis of pulmonary arteriovenous fistulas and malformations, and it is usually a prerequisite if embolotherapy is planned.

Bronchial Angiography

Bronchial angiography is used to determine whether the bronchial arteries are the cause of massive pulmonary hemorrhage or massive hemoptysis. It is a prerequisite if bronchial arterial embolotherapy is planned.

Radionuclide Lung Scans

The V/Q scan is still commonly used in the diagnosis of pulmonary embolism, although CT angiography is assuming an increasingly larger diagnostic role. The likelihood of pulmonary embolism in a V/Q scan that shows "high probability" and a scan that shows "low probability" is greater than 90% and less than 5%, respectively. An "intermediate probability" scan usually is an indication for a CT scan with contrast medium or for pulmonary angiography. However, clinical suspicion of pulmonary embolism should guide the decision.

The quantitative V/Q scan is used to assess unilateral and regional pulmonary function by measuring V/Q relationships in different regions of the lungs. It is indicated for patients who are poor surgical candidates for lung resection because of underlying pulmonary dysfunction. If the lung region to be resected shows minimal or no lung function on a quantitative V/Q scan, the resection is unlikely to impair further the patient's pulmonary reserve. The gallium scan is of minimal or no use in the diagnosis of diffuse lung diseases. The technetium 99m scan is useful in detecting diffuse pulmonary calcification associated with chronic hemodialysis.

Ultrasound.

Because ultrasound energy is rapidly dissipated in air, ultrasound imaging is not useful for evaluation of the pulmonary parenchyma. However, ultrasound is helpful in the detection and localization of pleural abnormalities and is often used as a guide to placement of a needle for sampling of pleural liquid (i.e., for thoracentesis). Endobronchial ultrasound, in which the ultrasound probe is passed through a bronchoscope, is emerging as a valuable adjunct to bronchoscopy, allowing identification and localization of pathology adjacent to airway walls or within the mediastinum.

Sputum Microscopy

Simple microscopy with a "wet" slide preparation of sputum is helpful in assessing the degree of sputum eosinophilia and detecting the presence of Charcot-Leyden crystals. Gram staining of sputum should be used to evaluate suspected bacterial infections. However, routine examination with Gram stain is not necessary for all patients with COPD who present with acute exacerbations. Induced sputum is helpful in identifying mycobacteria, fungi, *Pneumocystis carinii*, and malignant cells. Gastric washings are used to identify mycobacteria and fungi. Hemosiderin-laden macrophages in sputum do not always indicate alveolar hemorrhage; smokers can have a large number of hemosiderin-laden macrophages in their sputum.

Pulmonary Function Tests

The major indication for PFTs is dyspnea. PFT results do not diagnose lung disease, but they are used to assess the mechanical function of the respiratory system and to quantify the loss of lung function. They can be used to separate obstructive dysfunction, which indicates airflow limitation (as in asthma, bronchitis, and emphysema) from restrictive phenomena. In restrictive phenomena, the lungs cannot fully expand because of a large pleural effusion or disease in the lung parenchyma, chest wall, or diaphragm, and the volumes are diminished. A combination of obstructive and restrictive patterns is also possible (e.g., COPD with pulmonary fibrosis). Bronchoprovocation testing with agents such as methacholine is useful in detecting airway hyperresponsiveness. An increase in flow rates (>12% and 200 mL) after bronchodilator therapy suggests reversible component airway disease, although the absence of response does not

preclude a clinical trial with inhaled bronchodilator medications. Results of previous PFTs are helpful in following the course of lung disease.

Provocation Inhalational Challenge

Provocation inhalational challenge is useful when the diagnosis of asthma or hyperreactive airway disease is uncertain. The test uses agents that elicit a bronchospastic response. A 20% decrease in forced expiratory volume in 1 second (FEV1) from baseline is considered a positive test result. Up to 10% of healthy subjects may exhibit a positive response to provocation challenge without symptoms of asthma. Thus, the strength of the test is in its high negative predictive value.

Interpretation of Pulmonary Function Tests

A simplified step-by-step approach to interpretation of PFT results is as follows:

1. Evaluate volumes and flows separately.

2. Total lung capacity (TLC), functional residual capacity (FRC), and residual volume (RV) indicate volumes. TLC = VC (vital capacity) + RV. Increases in TLC and RV suggest hyperinflation (asthma or COPD). If TLC and VC are decreased, consider restrictive lung disease (fibrosis) or loss of lung volume (surgery, diaphragmatic paralysis, or skeletal problems).

3. VC measured during a slow (not forced) expiration is not affected by airway collapse in COPD. Forced VC (FVC) may be low with forced expiration because of airway collapse. In healthy subjects, VC = FVC.

4. FEV1 and forced expiratory flow (FEF) between 25% and 75% of VC (FEF25%-75%) indicate flow rates. Flow rates are diminished in COPD, but smaller decreases can occur if lung volumes are low. Decreased FEV1/FVC (<70%) indicates obstruction to airflow.

5. The maximal voluntary ventilation (MVV) test requires rapid inspiratory and expiratory maneuvers and, thus, tests airflow through major airways and muscle strength. Disproportionately reduced MVV (MVV = FEV1 × 35) may be from poor effort, variable extrathoracic obstruction, and respiratory muscle weakness. Respiratory muscle weakness can be assessed by maximal inspiratory pressure (PImax) and maximal expiratory pressure (PEmax). Clinical features should be correlated with the results of PFTs.

Bronchoscopy

Common diagnostic indications for bronchoscopy include persistent cough, hemoptysis, suspected cancer, lung nodule, atelectasis, diffuse lung disease, and lung infections. Diagnostic yield is low in pleural effusion. Therapeutic indications include atelectasis, retained secretions, tracheobronchial foreign bodies, airway stenosis (dilatation), and obstructive lesions (laser therapy or stent placement). Bronchoscopy is valuable in the staging of lung cancer. Complications from bronchoscopy are minimal and include bleeding from mucosal or lung biopsy, pneumothorax (from lung biopsy), and hypoxemia.

Bronchoalveolar Lavage

Bronchoalveolar lavage (BAL) is performed by instilling 100 to 150 mL of sterile normal saline into the diseased segment(s) of the lung. The instilled saline is aspirated back via the bronchoscope. The aspirated effluent can be analyzed for cells, chemical constituents, and cultures for infectious agents. BAL in healthy subjects shows alveolar macrophages (93%±3%)

and lymphocytes (7%±1%). Other types of leukocytes (neutrophils <1%) are rarely found in healthy subjects.

Lung Biopsy

Lung biopsy can be performed via bronchoscopy, thoracoscopy, or thoracotomy. The indications for lung biopsy in diffuse lung disease should be based on the clinical features, treatment planned, and risks from biopsy and from treatment without a pathologic diagnosis.

Bronchoscopic lung biopsy can provide a diagnostic yield of up to 80% to 90% in sarcoidosis, pulmonary Langerhans cell granulomatosis, eosinophilic pneumonitis, lymphangioleiomyomatosis, infections, pulmonary alveolar proteinosis, lymphangitic carcinomatosis, drug-induced lung disease, and hypersensitivity pneumonitis, especially when performed in combination with special stains. The major complications after bronchoscopic lung biopsy are pneumothorax (<2%) and hemorrhage (<3%).

Arterial blood gases.

The most commonly used measures of gas exchange are the partial pressures of O_2 and CO_2 in arterial blood, i.e., Pa_{O2} and Pa_{CO2}, respectively. These partial pressures do not measure directly the quantity of O_2 and CO_2 in blood but rather the driving pressure for the gas in blood. The actual quantity or content of a gas in blood also depends on the solubility of the gas in plasma and the ability of any component of blood to react with or bind the gas of interest. Since hemoglobin is capable of binding large amounts of O_2, oxygenated hemoglobin is the primary form in which O_2 is transported in blood. The actual content of O_2 in blood therefore depends both on the hemoglobin concentration and on the Pa_{O2}.

Because measurement of Pa_{O2} requires arterial puncture, it is not ideal either for office use or for routine or frequent measurement in the inpatient setting. Additionally, because it provides intermittent rather than continuous data about the patient's oxygenation, it is not ideal for close monitoring of unstable patients. Pulse oximetry, an alternative method for assessing oxygenation, is readily available in many clinical settings. Using a probe usually clipped over a patient's finger, the pulse oximeter calculates oxygen saturation (rather than Pa_{O2}) based on measurements of absorption of two wavelengths of light by hemoglobin in pulsatile, cutaneous arterial blood.

Self-control questions.

1. What is dyspnea and what causes it?
2. Give the features of dyspnea that are important to distinguish in the pulmonary and respiratory history
3. What questions should be asked about a patient's smoking history?
5. What information should be obtained from a patient who complains of cough?
6. Define hemoptysis. How are the cause and severity assessed?
7. Can the causes of chest pain be reliably differentiated from one another?
8. What information should be obtained about potential environmental exposures and occupational history?
8. Which clinical signs best indicate respiratory distress?

9. What is the significance of paradoxical respiration?
10. How can inspection be useful in a patient with a chest disease?
11. What is the subcutaneous emphysema?
12. How is consolidation distinguished from pleural effusion on pulmonary examination?
13. What are rales, crackles, or crepitations?
14. How is airway obstruction identified?
15. Which findings in a patient with bronchospasm are most ominous?
16. Which findings in a patient with bronchospasm are most ominous?
17. What is the significance of hypertrophic pulmonary osteoarthropathy?
18. What are the usual clinical signs in emphysema?

Further reading:

1. Principles of Harrison's internal medicine, self-assessment and board review 18th editon /Edited by Charles Wiener etc. - The McGraw-Hill Professional. – 2012. – 514 p.
2. Board review from Medscape. Case-based internal medicine self-assessment questions / Editor-in-Chief David C. Dale. - WebMD. – 2005. – 592 p.
3. Kaplan Medical USMLE Step 2 Clinical Knowledge Qbook, 5th edition/ Edited by Kaplan inc. – Kaplan Publishing. – 2011. - 540 p.
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5. Davidson's Principles and Practice of medicine, 21st edition / Edited by Nicki R. Colledge, Brian R. Walker, Stuart H. Relston. - Churchill Livingstone – 2010. – 1376 p.
6. Goldman's Cecil Medicine, 24th edition / Edited by Lee Goldman, Andrew I. Schafer. – Saunders Ltd. – 2011. – 2672 p.
7. Kumar & Clark's Clinical Medicine, 8th edition / Edited by Parveen Kumar, Michael Clark. – Saunders Ltd. – 2012. – 1304 p.