Pulmonary Assessment/Dyspnea

Learning Objectives:

1. Understand the key components of the history and physical exam of the patient with signs or symptoms of pulmonary disease.

2. Understand the mechanisms of dyspnea as they apply to common respiratory disorders such as COPD, asthma, neuromuscular weakness and pulmonary embolism.

3. List the 5 causes of hypoxia and the clinical syndromes that correlate with each. Understand how to differentiate these based on A-a gradient, response to supplemental oxygen, and pulmonary function testing/lung diffusion.

Required Reading:

George RB. History and Physical Examination, in Chest Medicine: Essentials of Pulmonary and Critical Care Medicine, 1995, Williams and Wilkins, 81-91.

Manning HL, Schwartstein RM. Pathophysiology of Dyspnea. NEJM 1995;333:1547-1553.

For Additional Study:

1. American Thoracic Society. Dyspnea: Mechanisms, Assessment, and Management: A Consensus Statement. Am J Resp Crit Care Med 1999;159:321-340.

2. Weisman IM, Zeballos RJ. Clinical Evaluation of Unexplained Dyspnea. Cardiologia 1996;41:621-634.

~~Related MKSAP~~ **Questions:** 6, 10, 49

Chapter 5

History and Physical Examination

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Obtaining a Useful History
Occupational and Exposure History
Symptoms of Respiratory Diseases
Upper Respiratory Tract Symptoms
Chest Pain
Breathlessness
Cough
Sputum Expectoration
Hemoptysis
Physical Examination
Inspection and Palpation
Percussion
Auscultation
Extrapulmonary Signs
Bedside Assessment of Critically Ill Patients

The process of obtaining a meaningful history, performing a good physical examination, and putting the information together to form an initial impression is an art that must be learned by experience. The history and physical examination should lead to a reasonable list of differential diagnoses. This list of impressions, in turn, forms the basis for a diagnostic plan, whereby the number of possible diagnoses is gradually decreased by the results of selected laboratory tests, radiographs, and specialized procedures. This chapter includes some guidelines for this important task.

Obtaining a Useful History

The interview is designed to identify the important symptoms and determine their duration. To do this without being led into blind areas of discussion is an important step toward identifying the problem. The interviewer must lead the discussion, avoiding lengthy digressions; on the other hand, the patient must have the freedom to mention items that may prove important as the history unfolds. The patient should not be badgered, but should be made to feel that the interviewer is truly interested in his or her problems. The interviewer should not yawn or act bored, but should instead appear interested in the patient's story.

The chief complaint—the symptom that caused the patient to seek help—and its duration should be identified. Frequently the patient will say that he or she was referred because of an abnormal finding on a chest film or some other laboratory test. However, it is important to determine why that test was made and, if it was part of a routine examination, what changes from previous films resulted in referral.

Once the major complaint and its duration are identified, the development of the patient's symptoms should be investigated chronologically, beginning at the time that the patient first noted a departure from feeling well. The patient should be questioned concerning current and past medications, any allergic reactions or intolerance to foods or drugs, or exposure to contagious illnesses. It is important to determine if other members of the household or coworkers have similar symptoms. It is also useful to obtain information from previous examinations or diagnostic tests. For instance, a previously negative tuberculin skin test is important if tuberculosis is suspected. Elements of the personal, occupational, and social history should be included in the present illness if they are directly pertinent to the patient's current symptoms.

A systematic review of the symptoms of respiratory illnesses and their character and duration should be

reported. Nonrespiratory symptoms should also be reviewed, since they may be related to the respiratory disease. Patients with carcinoma of the lung may present with complaints of headaches or seizures related to cerebral metastases; ankle swelling or a history of injury to the lower extremities is important if the patient has a suspected pulmonary embolism. Ascites and edema of the legs may be secondary to heart failure, cor pulmonale, or liver disease, all of which may cause abnormalities on the chest film, while joint pain may be caused by hypertrophic pulmonary osteoarthropathy. It is important to determine if a patient's complaints are seasonal, especially in patients with hay fever, sinusitis, postnasal drip, or asthma.

Previous illnesses and operations should be recorded, since they may be related to the present illness. For instance, childhood measles or pertussis may be the origin of bronchiectasis, and asthma during childhood that disappeared at puberty may return at a later age. Patients with reinfection tuberculosis often relate a history of household contact during their childhood years. Previous operations and biopsies may be the source of pathologic specimens that might be useful for reexamination. If previous chest films are available, they should be obtained for comparison with recent ones.

OCCUPATIONAL AND EXPOSURE HISTORY

Cigarette smoking is the most common preventable cause of death in the United States today (1). A smoking history is especially important in patients with respiratory complaints. Passive exposure to cigarette smoke in the home or the workplace is an increasingly recognized cause of respiratory symptoms in children whose parents smoke, and passive smoking has been shown to increase the incidence of respiratory infections (2).

The occupational history is especially important in patients with lung problems, since the lungs are constantly in contact with the environment. The patient should be encouraged to relate his or her job history in chronologic order. Occupational exposure may have occurred many years ago; exposure to asbestos may result in the development of a pleural mesothelioma 25 years or more after the exposure has ceased. It is important to ask the patient if he or she was advised to wear a mask at work or whether his or her fellow workers did so. The type of mask worn and the air source should be identified. Construction workers who are not directly involved in hazardous activities may work in closed areas containing toxic materials; for instance, carpenters, plumbers, and welders often work in areas where sandblasting is occurring. While the sandblaster may have extensive protection, the workers nearby may be exposed.

Some symptoms of toxic reactions are not related to the lungs. Patients working with galvanized metal (zinc fumes) may complain of nausea, vomiting, and other systemic symptoms. Allergic alveolitis due to thermophilic actinomycetes in workers exposed to moldy hay (farmer's lung) or sugar cane residue (bagassosis) is associated with fever, malaise, and headache in addition to nonproductive cough. The patient should be questioned about particularly irritating odors or upper respiratory symptoms, since toxic fumes usually affect the eyes, nose, and throat and this serves as an early sign of chemical exposure. Upper respiratory symptoms are common in toxic smoke inhalation.

Workers may not be aware of exposures to toxic materials. For instance, office workers have developed allergic alveolitis from air conditioners and humidifiers that were contaminated with fungal spores (3).

The family history is often useful. Cystic fibrosis and the immotile cilia syndromes are inherited, as are the hemoglobinopathies and α_1-antitrypsin deficiency. Patients with asthma often have a family history of allergic rhinitis, asthma, or other allergic symptoms. In addition, family members may have similar exposure. Tuberculosis is often spread by household contact, and viral respiratory diseases often affect several family members. Families may be exposed to the oxides of nitrogen (silo filler's disease) or moldy hay while working together on a farm.

SYMPTOMS OF RESPIRATORY DISEASES

UPPER RESPIRATORY TRACT SYMPTOMS

Rhinorrhea, conjunctivitis, and sneezing are common in patients with allergic rhinitis (hay fever), who may also have asthma; the two syndromes often coincide. Postnasal drip occurs in patients with upper respiratory disease and is manifested during the daytime by frequent clearing of the throat rather than by actual coughing. A postnasal drip is often a problem at night, and eventually may produce a "morning cough" due to chronic irritation of the upper airways.

Nosebleeds (epistaxis) may be a symptom of sinusitis or may be produced by trauma, foreign bodies, or tumors of the nose and nasopharynx. Systemic diseases such as hypertension, polycythemia, and bleeding disorders can also lead to bouts of epistaxis. Wegener's granulomatosis causes necrotizing granulomas

of the upper respiratory tract as well as of the lungs. Blood from the nose and nasopharynx sometimes accumulates in the oropharynx and is "coughed up," so the patient thinks that it is coming from the lungs. A history of epistaxis and the finding of blood clots in the nose or nasopharynx are clues that the expectorated blood may be coming from the upper respiratory tract. Hoarseness may result from lesions of the recurrent laryngeal nerve (surgical trauma, mediastinal tumors, or infections) or from diseases of the larynx (tuberculosis, tumors, or allergy).

Patients who present with anaerobic infections of the lungs and pleura (lung abscess, empyema) often have upper respiratory abnormalities leading to aspiration of oral secretions. The patient should be questioned concerning recent mouth or dental surgery, anesthesia, aspiration of a foreign body, neurologic abnormalities, periods of unconsciousness, and seizures.

CHEST PAIN

Thoracic pain is an alarming symptom, since most people are aware of its association with cardiac disease, lung tumors, and other serious life-threatening diseases. There are two basic types of chest pain: that which arises in the chest wall structures and is conducted through the intercostal and phrenic nerves (lateral or chest wall pain) and that which arises in the internal organs and is conducted through the afferent fibers of the vagus nerve (central or visceral pain). These two types of chest pain will be discussed separately.

Visceral chest pain occurs with neoplasms of the major bronchi or mediastinum; abnormalities of the heart, aorta, and pericardium; or diseases that cause esophageal pain, especially reflux esophagitis or tumors. Pain associated with acute bronchitis is usually central and is often accentuated by coughing.

Pain in the substernal area may indicate disease of the heart, pericardium, aorta, or esophagus. Angina pectoris is usually an effort-induced pain that is relieved by rest and vasodilators. It is often referred to the neck, shoulder, or arm. Pericardial pain is sometimes relieved by sitting up or leaning forward. Pain associated with a dissecting aortic aneurysm is frequently reported as severe and deep, and may be referred to the interscapular area of the back. Esophageal pain may mimic angina pectoris and may be relieved by sublingual nitroglycerine, which relaxes esophageal spasm. It is often related to meals and relieved with antacids. Patients with significant esophageal reflux are subject to aspiration, especially at night, and may present with recurrent bouts of acute bronchospasm and cough, mimicking asthma attacks.

Chest wall pain is sharp, often well localized, and is increased by deep breathing or coughing (pleuritic pain or pleurisy). Pleuritic pain is associated with any disease that causes inflammation of the parietal pleura such as infections (pneumonia, empyema, tuberculosis), trauma (pneumothorax, hemothorax, rib fracture), or tumors (cancer, lymphoma, mesothelioma). Older patients may suffer rib fractures following minor trauma or even severe coughing bouts. These fractures may not be visible on the initial chest film, but later callus formation around the fracture may make it apparent in retrospect. Irritation of the intercostal nerves (herpes zoster, spinal nerve root disease) may also lead to localized chest wall pain. Costochondritis of the second to fourth costosternal articulations (Tietze's syndrome) is common and may mimic the pain of myocardial ischemia or other serious diseases. The pain is clearly localized to the costal cartilage, and there is tenderness to pressure and often a palpable enlargement of the costosternal junction.

The peripheral innervation of the diaphragm is from the local intercostal nerves, and irritation of the peripheral diaphragm is referred to the adjacent chest wall. The central diaphragmatic pain fibers are conducted through the phrenic nerves, and pain in the central diaphragm is often felt in the ipsilateral trapezius region at the base of the neck and the shoulder, an area also supplied by the phrenic nerve.

BREATHLESSNESS

Breathlessness (dyspnea) is the sensation of difficulty in breathing, sometimes interpreted as the inability to take a deep breath. It is one of the most common reasons that patients with chest diseases consult a physician. Breathlessness is difficult to quantitate, since it is subjective and in certain situations (e.g., during and following exercise and at high altitudes) it is normal. While exercise normally produces dyspnea, a rapid increase in breathlessness or a decrease in exercise tolerance is an important symptom. Breathlessness may occur intermittently, as with attacks of asthma, or it may be persistent, as with chronic obstructive pulmonary disease (COPD). It may be influenced by position, as in patients with left heart failure, who complain of orthopnea (dyspnea when lying flat). Orthopnea may also be seen in patients with asthma or chronic airway obstruction.

There are three basic causes of the sensation of breathlessness: an increased awareness of normal breathing, an increase in the work of breathing, and an abnormality of the ventilatory system itself. Increased

awareness of normal breathing is usually a result of anxiety, and in this situation the common complaint is that the patient cannot take a satisfactorily deep breath. The breathing pattern is often irregular, with frequent sighs. Severe psychogenic breathlessness is associated with rapid breathing, tingling of the hands and feet, circumoral numbness, respiratory alkalosis, and occasionally tetanic seizures. This *hyperventilation syndrome* is diagnosed only after organic causes, both respiratory and nonrespiratory, have been excluded and the respiratory mechanics and blood oxygen level have been determined to be normal.

The second cause of breathlessness is an increase in the work of breathing. This may be due either to airways obstruction, in which case greater pressures are required to move air into and out of the lungs, or restriction of lung volumes and loss of compliance, in which case greater effort is required to expand the lungs and chest wall.

The third cause of breathlessness is an abnormality of the ventilatory apparatus. This involves dysfunction of the nerves, the respiratory muscles, or the thoracic cage itself. Neurologic abnormalities producing breathlessness include spinal cord injury, ascending polyneuritis, myasthenia gravis, amyotrophic lateral sclerosis, poliomyelitis, and exposure to paralytic agents or neurotoxins. Primary diseases of the respiratory muscles include polymyositis and muscular dystrophy, while examples of chest wall abnormalities include extreme obesity, kyphoscoliosis, large pleural effusions, and space-occupying lesions of the thorax.

COUGH

Cough receptors are located in the large bronchi, trachea, and larynx and respond to respiratory secretions in the large airways. Irritation of the cough receptors may occur in the absence of abnormal secretions as with inhalation of toxic fumes or a mild asthma attack. In such cases the nonproductive cough serves no useful purpose and may cause mechanical trauma, leading to more coughing. A nonproductive cough may also be a manifestation of anxiety. In such instances it may be useful to suppress the cough, but in most cases coughing aids in airway clearance and suppression is not indicated.

A change in the character or frequency of cough is a common complaint in patients with pulmonary diseases. Most acute and self-limiting coughs are secondary to a viral respiratory infection (4), while chronic and persistent coughs are most often secondary to chronic bronchitis or postnasal drip. Patients who smoke cigarettes have a characteristic "smoker's cough," a manifestation of chronic bronchitis, most noticeable in the morning on awakening. This cough may be productive of mucoid sputum and is often ignored by the chronic cigarette smoker.

Cough may be the sole complaint in patients with mild asthma (5). In such patients the cough may be relieved by a bronchodilator or the avoidance of inhaled allergens. If bronchospasm is not present at the time of examination, reversible airway obstruction may be demonstrated with the use of a nonspecific bronchial challenge such as methacholine (6). Cough with or without bronchospasm may occur as a side effect of β-adrenergic antagonists as well as the angiotensin converting enzyme (ACE) inhibiting drugs (7).

SPUTUM EXPECTORATION

If the patient has a productive cough, the duration of sputum expectoration, the character of the sputum, and the presence or absence of blood should be determined. Cigarette smokers with chronic bronchitis have mucoid or occasionally purulent sputum without much change for months or years and without hemoptysis. The sputum is the result of chronic stimulation and hypertrophy of the bronchial glands as a defense mechanism (8).

In patients with COPD and chronic sputum production, it is important to examine grossly the character of an expectorated sputum sample (color, opacity, and consistency). The patient should be asked about any changes in the quantity, color, or opacity, which may indicate an acute infectious exacerbation requiring antibiotic therapy. It is useful to look at an unstained wet preparation of purulent-appearing sputum to identify neutrophils or eosinophils as the cause of the purulence, since therapy is with antibiotics in the case of neutrophils, and with anti-inflammatory agents in the case of eosinophils (9). It is not usually necessary to obtain a Gram stain in cases of chronic bronchitis with acute exacerbation, and the results usually indicate a mixed flora with both Gram-positive and Gram-negative organisms. Likewise, a sputum culture and sensitivity are rarely indicated; antibiotic therapy is empiric, based on the usual causes of such exacerbations.

Viral infections of the lower respiratory tract are associated at first with scant mucoid sputum, which may contain a few streaks of blood. Later the sputum may become copious and purulent with or without bacterial superinfection. Patients recovering from influenza who begin to produce large volumes of purulent sputum associated with a febrile relapse most likely have a bacterial superinfection. Viral and mycoplasmal pneumonias are associated with relatively scant sputum production initially.

Patients with acute lower respiratory tract infections usually produce sputum containing neutrophils. A Gram stain of grossly purulent sputum may help to identify a predominant bacterial organism. In pneumococcal lobar pneumonia the sputum produced early is usually scanty and composed of mucus tinged with blood ("rusty"); later, sputum may become purulent. As opposed to the scant mucoid sputum in early lobar pneumonia, the sputum in patients with bronchopneumonia (frequently a complication of chronic bronchitis) is usually copious and purulent. The chronic production of purulent sputum with episodes of blood streaking is suggestive of severe bronchitis, bronchiectasis, a bronchogenic tumor, or the presence of an aspirated foreign body. Suppurative lung diseases, including bronchiectasis, lung abscess, or bronchopleural fistula with empyema, are associated with expectoration of large volumes of yellow or green sputum. The color is produced by pigments released from degenerating neutrophils. Approximately 60% of patients with lung abscess will have foul-smelling sputum associated with bad breath, anorexia, and weight loss (10).

Asthmatics who are recovering from an acute attack usually produce sputum that is thick and tenacious and contains bronchial mucus plugs. The sputum may be purulent but, when examined, is found to contain predominantly eosinophils rather than neutrophils. A simple wet preparation or a Wright stain allows ready determination of the predominant cell type (9).

Lung tumors and tuberculosis are associated most often with the chronic production of mucoid sputum that may be associated with blood streaking. Hemoptysis is an important symptom in such patients, and it is the appearance of bloody sputum that often brings the patient to the physician.

Sputum Induction

If the patient is unable to produce sputum, inhalation of a nebulized solution of 3 or 4 ml distilled water or 10% sodium chloride results in the induction of an adequate specimen for examination in over 90% of cases. Any type of nebulizer may be used; however, ultrasonic nebulizers, which produce a concentrated mist, are preferred. The patient should be placed in a private room or isolation booth if he or she is suspected of having a contagious disease. The patient inhales the nebulizer mist deeply and is encouraged to cough frequently, saving all material produced. Chest percussion and/or postural drainage may be used. The procedure is terminated when an adequate specimen is obtained, the nebulizer solution is exhausted, or after a maximum of 15 to 20 minutes. The procedure is most often used for patients suspected of having tuberculosis or a lung malignancy, and to search for *Pneumocystis carinii* infection in patients with the acquired immunodeficiency syndrome (AIDS).

Gastric Lavage

Aspiration of stomach contents may be used to obtain specimens for mycobacteria or fungi, especially in children who will not produce coughed sputum specimens. The usefulness of gastric washings is based on the fact that most coughed secretions are swallowed rather than expectorated. The procedure is performed immediately upon awakening, before the stomach has emptied. The material must be processed immediately to avoid destruction of the organisms by gastric acidity and enzymes. The presence of acid-fast bacilli in gastric washings is not diagnostic of mycobacterial disease, because saprophytic mycobacteria are often present in the stomach. The procedure has been largely replaced by sputum induction, since sputum induction results in higher yield and less patient discomfort (11).

HEMOPTYSIS

The term hemoptysis means simply the coughing of blood, and to say that a patient has hemoptysis is not enough. It is important to determine the duration of the hemoptysis and to note whether there is gross blood, blood-tinged sputum, or blood-streaked sputum. An attempt should be made to determine the amount of blood produced and to record whether it is bright red or dark and whether or not it contains blood clots.

Hematemesis, or vomiting of blood, may be confused with hemoptysis; however, hemoptysis tends to produce bloody sputum that is at least partly frothy, while hematemesis does not. Hematemesis more often produces dark red blood that is usually acid, while hemoptysis is alkaline. With hematemesis blood streaking of sputum is unusual, while with hemoptysis it is common. Vomited blood frequently contains food particles, while this is rare with hemoptysis.

The common causes of hemoptysis are shown in Table 5.1. While the majority of episodes in earlier

TABLE 5.1
INCIDENCE OF CAUSES OF HEMOPTYSIS

Cause	Percent of Cases
Bronchogenic carcinoma	13
Chronic bronchitis	53
Bronchiectasis	1
Tuberculosis	3
Other	30
Total cases	320

Data compiled from two published series (12, 13).

years were due to bronchiectasis, tuberculosis, or unknown causes, in more recent reports (following the appearance of fiberoptic bronchoscopy), the most common causes are bronchitis and carcinoma (12, 13). One-third of cases are still due to unknown causes. Grossly bloody sputum is often seen in patients with tuberculosis, pulmonary infarction, bronchial adenoma, mitral stenosis, and lung abscess. A ruptured aortic aneurysm communicating with a bronchus usually results in exsanguination. Recurrent episodes of hemoptysis, sometimes massive, may occur in mycetomas that invade air spaces caused by inactive tuberculosis or sarcoidosis.

Bleeding may occur with tumors of the larynx, and in this case hoarseness is frequently present. Problems in the nasopharynx and oropharynx are usually associated with obvious abnormalities of these areas on physical examination. Bleeding dyscrasias often cause hemoptysis, in which case there is usually evidence of hemorrhage elsewhere, for example, in the skin or gastrointestinal tract.

PHYSICAL EXAMINATION

As in recording the medical history, it is important to develop an organized, systematic approach to examining the patient. Initially, the patient's general condition should be observed and his or her body habitus and state of nutrition noted. The presence of acute distress, such as pain, dyspnea, or mental confusion, should be recorded. Evidence of chronic illness, such as weight loss or debilitation, should also be noted. The patient's psychological attitude, awareness and appreciation of events, handicaps, and use of prosthetic devices should be noted. If the patient is receiving oxygen the amount and method of administration should be recorded.

INSPECTION AND PALPATION

During the inspection and palpation of the head, neck, and chest, it is useful to have the chest radiograph handy. This is true during the entire examination of the chest because it allows correlation of physical and radiographic findings. In examining the chest, it is useful to recall the normal location of the five lobes of the lungs and their areas of contact with the chest wall (Fig. 5.1).

The nose, throat, and ears should be examined carefully, since lower respiratory diseases are often associated with upper respiratory tract abnormalities. Rhinorrhea and the presence of pale, edematous nasal mucosa occur with allergic rhinitis. Nasal polyps occur with respiratory allergies and may cause epistaxis. The frontal, ethmoid, and maxillary sinuses are often tender in the presence of sinusitis, which may produce postnasal drip or bleeding. A red, edematous throat may be due to infection, toxic fume exposure, or chronic postnasal drip. Patients with pneumonia often have inflamed mucous membranes due to associated viral or bacterial upper respiratory infections. Oropharyngeal candidiasis (thrush) may be associated with inhaled steroids or antibiotic therapy and is also common in immunosuppressed patients. Tumors, strictures, or inflammation of the oropharynx can cause upper airway obstruction leading to extreme breathlessness, and sleep-related disorders of breathing may occur in the presence of lesions that obstruct the upper airway. Patients with lung abscess or empyema frequently have poor dental hygiene and foul-smelling breath, and may have problems with swallowing.

Sarcoidosis may involve the salivary and lacrimal glands, with dryness of the oral mucosa and conjunctivae; involvement of the parotid gland may be associated with paralysis of the facial nerve (Bell's palsy). Inflammation of the uveal tract in sarcoidosis is detected by slit lamp examination. Drying of the oral mucous membranes may also be associated with anticholinergic drug therapy or with rheumatoid disease (keratoconjunctivitis sicca), which may affect the lungs also.

The position and mobility of the trachea should be determined, since shift of the mediastinum is associated with shift of the trachea, while fixation of the mediastinum by carcinoma or mediastinal fibrosis is associated with decreased tracheal mobility. The position of the trachea is easily ascertained from the front by comparing the distance from the trachea to each clavicular head. Nodes and masses in the neck and supraclavicular areas are usually best palpated from the rear.

An examination of the neck veins is important in patients with lung diseases. Right heart failure and severe obstructive airway disease are associated with neck vein distention. With airway obstruction the veins usually collapse during inspiration unless elevated venous pressure is also present. With obstruction of the superior vena cava there is marked distention of neck veins, sometimes associated with edema of the neck, eyelids, and hands, and dilation of veins over the anterior chest wall.

The presence of tenderness, discoloration, bruises, or scars over the chest wall should be noted. If there is a history of recent trauma and if chest pain is present, an attempt should be made to palpate the chest wall for crepitus indicating the presence of a rib fracture or subcutaneous emphysema. If scars from previous surgery are noted, the patient should be questioned about this. Examination of the spine for kyphoscoliosis

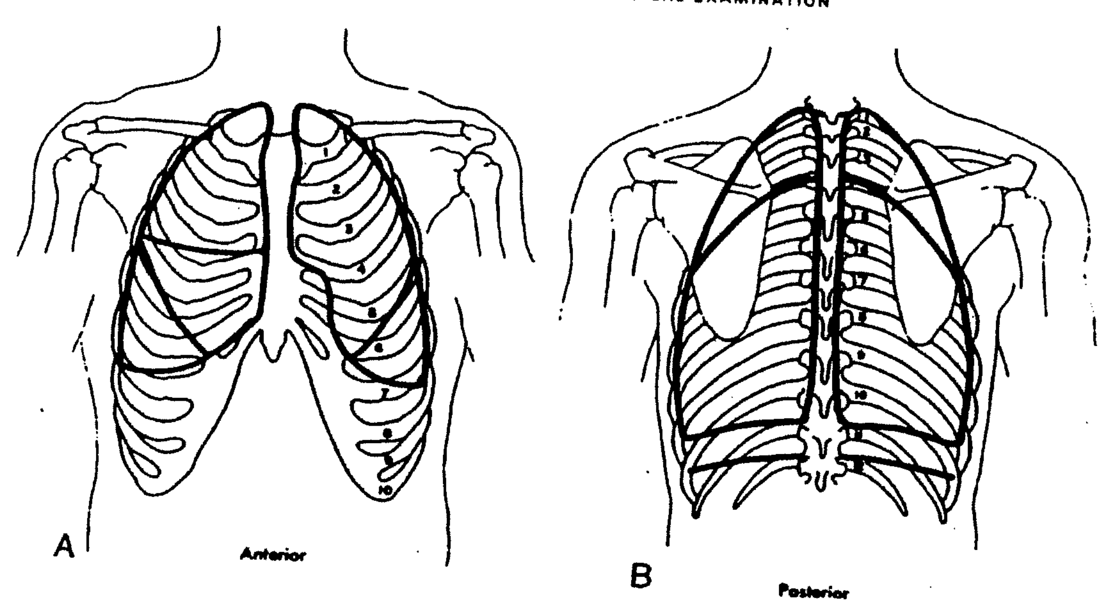

FIGURE 5.1. A, Normal relationship of the lungs to the anterior chest wall. The upper part of the chest overlies the upper lobes. The middle lobe lies under the fourth and fifth interspaces to the right of the heart. The lower lateral chest wall lies over the anterior and lateral basal segments of the lower lobes. B, Normal relationship of the lungs to the posterior chest wall. The upper lobe areas are covered by the bones and muscles of the shoulder girdle and are therefore not readily accessible to percussion and auscultation. Most of the posterior chest wall overlies the lower lobes. Diaphragm positions at inspiration and expiration are shown. (Modified from Prior JA, Silberstein JS, Stang JM: *Physical Diagnosis, the History and Examination of the Patient*, ed 6. St. Louis, CV Mosby, 1981.)

may reveal the cause in patients with restrictive lung disease. Expansion of the chest wall should be evaluated both by inspection and by palpation. In patients with severe hyperinflation of the chest due to COPD or asthma, the chest is rounded and "barrel shaped," and because the diaphragm is low and flat there may be inward deflection of the lower chest with inspiration (Hoover's sign). In each step of the physical examination, advantage should be taken of the fact that the chest is a bilaterally symmetrical structure, and each side should be compared with the other as a control. For example, tension pneumothorax produces an ipsilateral hyperinflation of the chest, with hyperresonance and decreased breath sounds.

In patients with significant emphysema and air trapping, pneumothorax may occur spontaneously or with minor trauma, such as chest physical therapy. The presence of a pneumothorax may be difficult to detect on physical examination in such patients, because the findings are similar to those of the underlying COPD (increased thoracic diameter, hyperresonance, decreased breath sounds, decreased fremitus) (14). The pneumothorax may not be evident on inspiratory chest films, because of the pulmonary hyperinflation; an expiratory film is useful in such cases.

PERCUSSION

Percussion of the chest is useful because the chest contains structures of both air and fluid density, and in the presence of disease their relationships may vary. With pleural effusions, consolidation, large intrathoracic masses, or atelectasis, the chest is dull to percussion. With pneumothorax or hyperinflation, the chest is hyperresonant. The generalized hyperresonance in patients with emphysema may cause the examiner to miss a small pneumothorax; in such patients, mediastinal shift may be limited due to air trapping on the opposite side (14).

Percussion over the area of the diaphragm during maximal inspiration and expiration allows the examiner to estimate the extent of diaphragm motion. This is one of the few objective measurements for assessing diaphragm movement. With emphysema, the diaphragm is low and flat and movement is minimal.

AUSCULTATION

The examiner should become familiar with the character of normal breath sounds. In the average resting person, inspiration involves approximately one-third

TABLE 5.2
LUNG SOUND NOMENCLATURE

Description	Term	Time Expanded Waveform
Discontinuous		
Fine (high pitch, low amplitude, short duration)	Fine crackles	
Coarse (low pitch, high amplitude, long duration)	Coarse crackles	
Continuous		
High-pitched	Wheezes	
Low-pitched	Rhonchus	

of the respiratory cycle and expiration the remaining two-thirds. Breath sounds vary according to the site of auscultation. Over the trachea, bronchial breath sounds are a normal finding.

Transmission of voice-generated sounds to the chest wall can be evaluated by either palpation or auscultation. Again, it is important to compare the two sides when listening for the conduction of voice sounds. A localized increase in the clarity of whispered or spoken sounds is associated with bronchial breathing and occurs with consolidation around open airways. Several words have been devised to describe this increased conduction of sound through fluid; these include bronchophony, egophony, and whispered pectoriloquy. Decreased conduction of whispered or spoken sounds occurs in the presence of obstructed bronchi, pneumothorax, or large collections of fluid or tissue between the lung and the chest wall.

The terminology of adventitious sounds in the chest has been confusing in the past, and there are still differences in terminology in different countries. In an attempt to unify the terminology a series of symposia have been held in several countries. The recommendations of the International Lung Sounds Association are those used in this chapter (Table 5.2) (15).

Discontinuous Sounds

The word "rale" was originally devised by Laennec to signify a variety of abnormal chest sounds. Because of the confusion associated with this term, Robertson and Coope introduced the term "crackles" to describe the series of tiny explosions heard over the chest wall during inspiration (16). A number of qualifying adjectives have been used, such as crepitant, subcrepitant, dry, and wet. To avoid confusion only the terms coarse and fine should be used.

A careful analysis of chest physical findings with waveform analysis has revealed that the *timing* of crackles is important. Those that begin early in inspiration are likely to be associated with airway obstruction (Table 5.3). Early, fine crackles are usually caused by small airway closure at end-expiration and disappear after a few deep breaths. Coarse, early inspiratory crackles are usually associated with bronchitis or bronchopneumonia. Fine, superficial crackles that occur late in inspiration ("Velcro") are usually associated with diseases that cause a restrictive ventilatory defect, such as idiopathic diffuse interstitial fibrosis, asbestosis, and sarcoidosis.

TABLE 5.3
CLINICAL CONDITIONS AND TIMING OF CRACKLES

Early Crackles	Late Crackles
Chronic bronchitis	Diffuse interstitial fibrosis
Asthma	Airspace pneumonia
Emphysema	Pulmonary congestion and edema
"Atelectatic crackles"	Sarcoidosis
Bronchopneumonia	Scleroderma
	Rheumatoid lung
	Asbestosis

Continuous Sounds

These sounds have a longer duration than crackles, usually lasting more than 250 msec. They have a musical quality that crackles do not have. Continuous breath sounds are either wheezes, which are high-pitched and arise in small airways, or rhonchi, which are low-pitched and occur in large airways (17). Wheezes generally occur in the presence of bronchospasm and are an important finding in asthma. Occasionally, a wheeze may begin with an audible pop as a small airway opens during inspiration. This crackle,

followed by a high-pitched wheeze, has been called a "sibilant crackle" and has the same significance as a wheeze.

The word rhonchus means snore; rhonchi are common in severely ill patients whose secretions have collected in proximal airways. They occur in the presence of large-airway disease (stricture, foreign body, tumor, or mucus secretions), and those that clear with coughing are associated with sputum in larger airways. The presence of a localized wheeze or rhonchus that does not clear with coughing and does not change from one examination to another suggests an intrinsic defect in a large airway, such as a bronchogenic neoplasm. Because of the constricting nature of these lesions, the rhonchus usually occurs during both inspiration and expiration.

Other Adventitious Sounds

In the presence of air in the pericardium or mediastinum, a coarse, crackling sound called a "mediastinal crunch" may be heard that is synchronous with systole. This sound may be associated with a pericardial friction rub.

A pleural friction rub is a grating sound associated with breathing. Rapid tape recordings have demonstrated that pleural friction rubs are actually a series of tiny explosions, just as crackles are (17). Pleural friction rubs are generally loud and sound as if they are immediately under the stethoscope. They occur during both inspiration and expiration, generally at the end of inspiration and the beginning of expiration. If a patient has pleuritic chest pain, it is useful to ask him or her to point to the location of the pain and to listen over that area, since the rub will be loudest there. The rub will often occur simultaneously with the patient's chest pain.

Pericardial friction rubs are similar to pleural rubs except that they occur with atrial and ventricular systole and diastole. They are best heard at the left sternal border at about the third interspace. It is useful to have the patient stop breathing, at which time the pericardial friction rub should persist. Pericardial and pleural friction rubs may occur simultaneously.

EXTRAPULMONARY SIGNS

A wide variety of physical findings outside the thorax may occur in patients with pulmonary diseases. Hypoxemia is associated with cyanosis if 5 g/dl or more of reduced hemoglobin is present in the capillary blood. Central cyanosis implies involvement of gas transfer in the lungs and affects the tongue as well as the extremities. Peripheral cyanosis without central cyanosis implies a circulatory problem such as vascular spasm or shock.

Clubbing of the digits may or may not be associated with cyanosis. It is seen with many chest diseases, including neoplasms, bronchiectasis, and lung abscess. It may be inherited as a familial trait or may occur with diseases of other organs such as the liver. The most reliable evidence of digital clubbing is an increase in the ratio of the diameter of the digit at the base of the nail to the diameter of the distal interphalangeal joint (Fig. 5.2). This ratio is always less than unity unless clubbing is present.

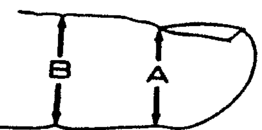

FIGURE 5.2. Clubbing of the fingers is best assessed by determining the ratio of the diameter at the base of the nail (A) to the diameter at the distal interphalangeal joint (B). This ratio is normally less than 1.

Patients who have pulmonary neoplasms may have one of several paraneoplastic syndromes, which are usually related to the production of hormones by tumor cells (see Chapter 17). Horner's syndrome occurs when apical lung tumors invade outside the pleura and into the superior cervical ganglion. There is ipsilateral enophthalmos, loss of sweating, and meiosis. Invasion of the brachial plexus nerves by these tumors may produce pain, atrophy, and loss of function in the ipsilateral arm.

BEDSIDE ASSESSMENT OF CRITICALLY ILL PATIENTS

The development of the modern intensive care unit (ICU) has allowed us to monitor the physiologic processes electronically in severely ill patients. Too often, electronic monitors replace clinical examination. A number of factors interfere with the clinical examination in the ICU, including the condition of the patient, the ICU environment, and the equipment surrounding the patient (Table 5.4). It is a mistake to rely solely on information from sophisticated monitoring devices and laboratory flow sheets, since errors may occur if the data derived are not interpreted in the light of clinical findings. A rapid but careful examination of the patient remains an important diagnostic tool, and should be a part of daily rounds.

Several scoring systems, including APACHE (18) and SAPS (19), have been devised to give baseline information regarding the severity of illness. While there is some debate regarding their prognostic value, it is helpful to have some initial scoring system in order to follow serial changes in the patient's condition.

TABLE 5.4
PROBLEMS ENCOUNTERED IN THE PHYSICAL EXAMINATION OF CRITICALLY ILL PATIENTS

Environmental interference, such as ambient light and noise, lack of privacy
Reduced cooperation from the patient resulting from impaired consciousness, altered mental state, pain, drug effects
Difficulties in positioning the patient caused by orthopedic traction, abrasion, burns
The presence of therapeutic devices, such as the ventilator, drains, dressings, plaster casts, peritoneal dialysis machines, intra-aortic balloon pump, stomas, catheters, splints
The presence of monitoring devices, including arterial and venous lines, pulse oximeters, spectrometers, blood pressure cuff, electrocardiographic leads
Time limitations caused by nursing procedures, personal hygiene regimens (such as bathing and turning, during which the physician is unable to observe the patient), dressing changes, position changes, physiotherapy, electrocardiograms, bedside procedures, surgical evaluation, visits from friends and family

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Visual assessment of the overall status is important. Is the patient awake or comatose? Is he or she receiving mechanical ventilation? What types of tubes are connected to the patient? Is the patient pallid, cyanotic, or jaundiced? Are there rashes or signs of trauma? Cool, cyanotic extremities indicate a low cardiac output (20), but also are found in the presence of peripheral vascular disease and in patients receiving vasopressor therapy. Muscle wasting indicates protein-calorie malnutrition; purpura and bruising suggest a coagulopathy; axillary petechiae suggest fat embolism.

A simple assessment of the patient's level of consciousness, including orientation and response to commands, can yield vital diagnostic and prognostic information. The neurologic status may be assessed using the Glasgow coma scale (Table 5.5) (21). This scale, originally proposed for use in victims of head trauma, is helpful for detecting and quantifying serial changes in the neurologic status. Coma scale scores range from 3 to 15 points; scores below 5 are associated with a very poor prognosis (21).

The vital signs often change rapidly in ICU patients. Palpate the peripheral pulse while watching the ECG monitor to check for a pulse deficit. Check all distal pulses in cannulated arteries. A weak, thready pulse indicates a low cardiac stroke volume, as is seen in cardiogenic or hypovolemic shock. A bounding pulse is common in sepsis associated with a low vascular resistance and a high cardiac output. Pulsus alternans (every other pulse is weak) is associated with severely depressed left ventricular function. Pulsus paradoxus (a decline in systolic arterial pressure greater than 10 mm Hg with normal inspiration) is present in patients with severe airways obstruction (as in status asthmaticus), as well as in those with pericardial tamponade. High airway pressures during mechanical ventilation may produce pulsus paradoxus.

The rate and depth of respiration should be noted in spontaneously breathing patients. Rapid, shallow breathing is an early and reliable sign of respiratory muscle fatigue. A respiratory rate above 30 per minute suggests that mechanical ventilation should be considered, especially in the presence of abnormal arterial blood gases (22). Evidence of inspiratory muscle fatigue includes use of accessory respiratory muscles, respiratory alternans, and paradoxical abdominal motion. Respiratory alternans, a shift back and forth from chest wall to abdominal breathing, is likely a method of periodically resting certain muscle groups (23). Paradoxical abdominal motion consists of a movement inward rather than outward of the abdomen during inspiration, due to failure of the diaphragm to contract.

Pupils should be checked for size, equality, and reaction to light. Pupil size may be affected by drugs such as opiates that cause constriction, or those that cause dilatation such as catecholamines. Dilated, unreactive pupils are a late sign of brain stem herniation. They may also occur after local trauma, use of mydri-

TABLE 5.5
THE GLASGOW COMA SCALE

Verbal response (choose one)	
Oriented	5
Confused	4
Inappropriate words	3
Incomprehensible	2
None	1
Eye opening (choose one)	
Spontaneously	4
To speech	3
To pain	2
None	1
Motor response (choose one)	
Obeys commands	6
Localizes pain	5
Withdraws	4
Abnormal flexion	3
Abnormal extension	2
None	1
Total	3–15

Adapted from Teasdale G, Jennett B: Assessment of coma and impaired consciousness: a practical scale. *Lancet* 2:81–84, 1974.

atic agents, third nerve lesions, seizures, or cerebral hypoxia.

Eye reflexes should be noted serially in comatose patients. The pupillary light reflex and corneal touch reflex may be absent initially after a cardiac arrest, but should return within 1 hour. Absence of these reflexes 6 or more hours after cardiac arrest is a very poor prognostic indicator for cerebral recovery. Rapidly rotating the head from side to side stimulates both the vestibular apparatus and proprioceptors in the neck, resulting in the **oculocephalic** or "doll's eye" reflex. The presence of a doll's eye reflex (movement of the eyes in the direction opposite that of head rotation) indicates that brain stem function is intact.

Clinicians should become familiar with the normal ventilator sounds and should be aware of any alarms, auditory or visual. Check the mode of ventilation, the airway pressure, and the exhaled volume indicator. Several of the current ventilators monitor both peak and plateau airway pressures and can quantify the patient's spontaneous efforts versus ventilator-delivered breaths. About 40% of functional ventilator problems occur in the external circuitry. Be alert for leaking humidifiers, disconnections, valve failures, and leaking tubing. Bubbling or gurgling sounds at the mouth indicate a leaking cuff or migration of the cuff outside the larynx. Make sure the alarms have not been manually deactivated.

Migration of the endotracheal tube into a bronchus is a common problem in the ICU. Asymmetric chest expansion and diminished breath sounds over the left hemithorax are characteristic of right main bronchus intubation, which is more common than left main bronchus intubation, due to the architecture of the bronchial tree. The normal tendency of endotracheal tubes is to migrate toward the carina.

When examining the limbs, observe the response to painful stimuli, assess muscle tone and range of joint movement, and check tendon reflexes. Many patients are hypotonic due to metabolic or toxic encephalopathy, drug overdose, anesthesia, or the use of sedatives or neuromuscular blocking drugs. Increased muscle tone is the classic finding in upper motor neuron lesions.

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REVIEW ARTICLE

MECHANISMS OF DISEASE

FRANKLIN H. EPSTEIN, M.D., *Editor*

PATHOPHYSIOLOGY OF DYSPNEA

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PATIENTS with cardiopulmonary disease often have respiratory distress, which physicians refer to as dyspnea. Dyspnea is responsible for substantial disability and for millions of patient visits each year. Although dyspnea has been defined in several ways,[1-4] we define it as "an uncomfortable sensation of breathing." This review will focus on the mechanisms of dyspnea, because a greater understanding of those mechanisms may lead to better therapy for this often troubling symptom.

PROBLEMS IN THE STUDY OF DYSPNEA

Dyspnea differs from other sensations in that the neural pathways underlying it are not well understood. For example, free nerve endings transmit pain signals to the central nervous system, but there are no specialized dyspnea receptors. Similarly, although the auditory, visual, olfactory, and somatosensory portions of the cerebral cortex have all been mapped, the region of the cerebral cortex that processes information related to dyspnea remains unidentified. There is no area of the cortex that when stimulated causes dyspnea or any other respiratory sensation, nor is there a cortical lesion that abolishes the sensation of dyspnea or the perception of other respiratory-related stimuli.

The study of dyspnea is further complicated by difficulty in defining the precise physical stimulus that causes it. When a person inadvertently touches a hot stove, pain arises from a quantifiable thermal stimulus. However, when a patient with chronic obstructive pulmonary disease (COPD) becomes dyspneic walking up a flight of stairs, is his or her respiratory discomfort due to the metabolic work of the task, increased airway resistance, weakened or mechanically disadvantaged ventilatory muscles, or changes in arterial blood gases? Often there is no single easily identifiable stimulus comparable to temperature to explain respiratory sensations.

Much of our understanding of the pathophysiology of dyspnea is derived from studies of respiratory sensations induced in young, healthy subjects. The studies that have been conducted in patients have focused largely on those with COPD and have used chemical stimuli (hypercapnia or hypoxia), added respiratory loads, breath holding, or exercise as the stimulus for dyspnea. The studies have used the techniques of psychophysics[5,6] and scales such as the Borg scale (a category scale that denotes the intensity of sensation with numbers and descriptive terms)[7] and visual analogue scales[8] to describe the relation between external stimuli (such as resistive loads) or internal measures (such as pleural pressure) and the intensity of respiratory discomfort. The relevance of many of these experimental models of dyspnea to spontaneously occurring dyspnea in patients is uncertain. For example, breathing through a narrow orifice may reasonably approximate the increased work of breathing experienced by patients with obstructive lung disease, but the pressure changes along the airway in normal subjects breathing through an external resistance are quite different from those in patients with narrowed bronchi or diminished elastic recoil of the lungs. Thus, caution must be exercised in extrapolating from normal subjects or patients with COPD to patients with other disorders associated with dyspnea.

MECHANISMS OF DYSPNEA

Dyspnea includes several qualitatively distinct sensations that probably arise from different pathophysiologic mechanisms. When normal subjects were made breathless by performing eight respiratory tasks, they selected different groups of phrases to characterize their dyspnea with each task.[9] In two studies of patients with dyspnea caused by cardiopulmonary disorders, the various patient groups selected unique combinations of qualifying phrases to characterize their breathing discomfort (Table 1).[10,11]

Dyspnea is frequently associated with conditions in which respiratory drive is increased or the respiratory system is subject to a mechanical load. These conditions are characterized by a sensation of air hunger or increased effort or work of breathing.[10,11] Some disorders are associated with the stimulation of irritant receptors in the lungs; patients with these disorders may describe their discomfort by phrases such as "breath stops," "chest tightness," and "constriction." In addition to these qualitative factors, the intensity of dyspnea may be modified by the relative match between the respiratory motor command or signal originating in the central nervous system and afferent feedback arising from various receptors in the respiratory system. Figure 1 summarizes the signals that contribute to the sensation of dyspnea, which will be discussed below.

Sense of Respiratory Effort

The sense of muscular effort is the conscious awareness of the voluntary activation of skeletal muscles. Although in theory the sense of effort could arise from either the central nervous system or the muscles, the bulk

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Table 1. Respiratory Sensations Associated with Various Conditions.*

Sensation	COPD	Congestive Heart Failure	Interstitial Lung Disease	Asthma	Neuromuscular and Chest-Wall Disease	Pregnancy	Pulmonary Vascular Disease
Rapid breathing		X					X
Incomplete exhalation				X			
Shallow breathing				X	X		
Increased work or effort	X		X	X	X		
Feeling of suffocation	X	X					
Air hunger	X	X				X	
Chest tightness				X			
Heavy breathing				X			

*Adapted from Simon et al.[10] and Elliott et al.[11]

of evidence suggests that it arises from simultaneous activation of the sensory cortex at the time the muscles are signaled to contract.[12] We have all experienced the sense of muscular effort: a very heavy object requires great effort to move, whereas little effort is expended to move a light object. However, under some circumstances, such as muscle weakness or fatigue, even a small task may involve substantial effort.

The sense of effort is related to the ratio of the pressure generated by the respiratory muscles to the maximum pressure-generating capacity of the muscles.[13] The sense of respiratory effort increases whenever the central motor command to the respiratory muscles must be increased — that is, when the muscle load is increased, or when the muscles are weakened by fatigue, paralysis, or an increase in lung volume. There is a striking overlap between the settings in which the motor command to the respiratory muscles is increased and those in which normal subjects or patients become breathless. For example, in normal subjects breathing at both normal and increased lung volumes, effort and breathlessness closely parallel one another over a range of added loads.[14]

There are, however, other clinical and experimental observations that the sense of effort fails to explain. For a given level and pattern of ventilation, both patients and normal subjects are more breathless when they are hypercapnic than when they are eucapnic,[15] even though respiratory effort should not differ between the two conditions, since respiratory motor output, and presumably motor command, are similar. If ventilation is suppressed below the level dictated by chemical drive,

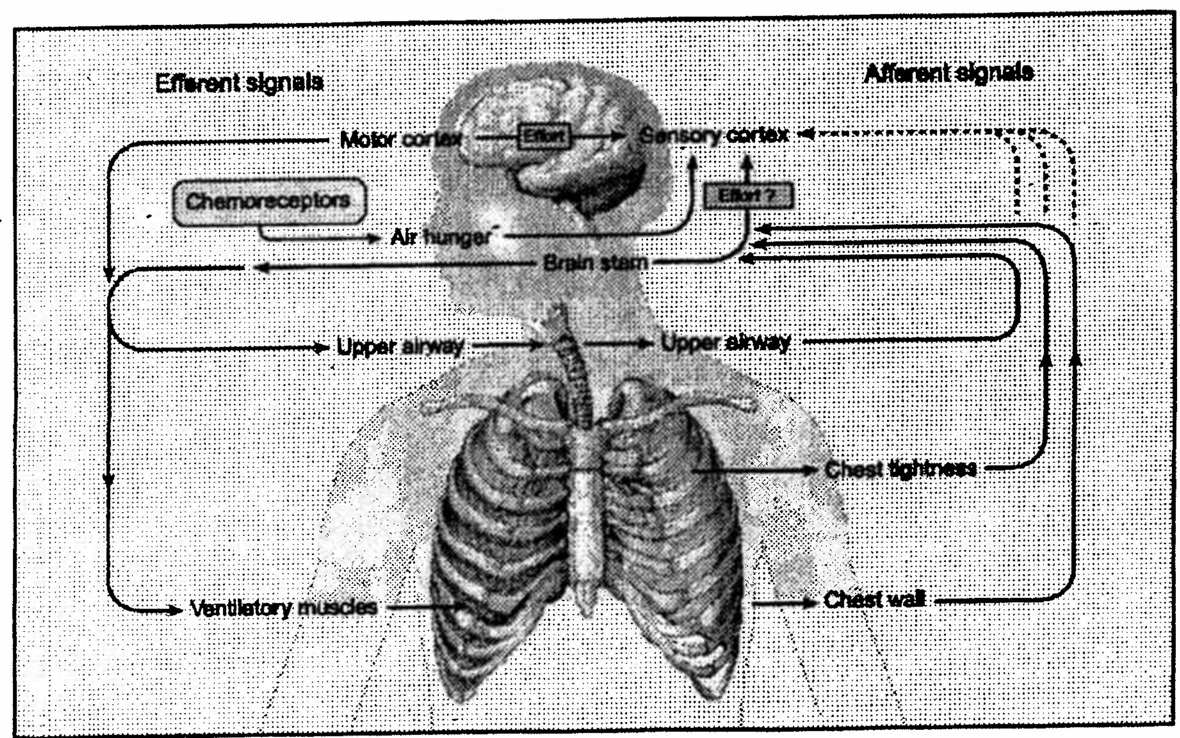

Figure 1. Efferent and Afferent Signals That Contribute to the Sensation of Dyspnea.

The sense of respiratory effort is believed to arise from a signal transmitted from the motor cortex to the sensory cortex coincidently with the outgoing motor command to the ventilatory muscles. The arrow from the brain stem to the sensory cortex indicates that the motor output of the brain stem may also contribute to the sense of effort. The sense of air hunger is believed to arise, in part, from increased respiratory activity within the brain stem, and the sensation of chest tightness probably results from stimulation of vagal-irritant receptors. Although afferent information from airway, lung, and chest-wall receptors most likely passes through the brain stem before reaching the sensory cortex, the dashed lines indicate uncertainty about whether some afferents bypass the brain stem and project directly to the sensory cortex.

a marked increase in breathlessness occurs, even though indexes of respiratory effort (such as ventilation) decrease.[16,17] When the relation between effort and breathlessness was studied in normal subjects maintaining a constant level of ventilation, the two sensations were dissociated; as end-tidal carbon dioxide increased, breathlessness also increased, but the sense of effort decreased.[18]

Thus, although the weight of evidence suggests that effort and breathlessness are not the same, the sense of effort may be the predominant factor contributing to breathlessness when the respiratory muscles are fatigued or weakened or when the load on them is increased. There are other settings, however, in which the sense of effort seems to play a less important part.

Chemoreceptors

Hypercapnia

Hypercapnia has long been known to cause dyspnea. Early studies suggested that stimulation of chemoreceptors itself was not a direct cause of dyspnea; rather, dyspnea was thought to arise only as a consequence of the evoked changes in respiratory-muscle activity. This interpretation was supported by studies in a normal subject who was paralyzed[19] and in a patient with quadriplegia[20] in whom large increases in end-tidal carbon dioxide produced no respiratory discomfort. Thus, in the absence of respiratory-muscle activity, hypercapnia appeared not to cause dyspnea.

More recent work, however, has established that hypercapnia causes dyspnea independently of any associated reflex increase in respiratory-muscle activity. Ventilator-dependent patients with quadriplegia who lack inspiratory-muscle function had air hunger when end-tidal carbon dioxide was raised by 7 to 11 mm Hg.[21] In a similar study in four normal subjects who were receiving mechanical ventilation after the induction of paralysis by a neuromuscular-blocking drug, all had severe air hunger when end-tidal carbon dioxide was raised by 5 to 10 mm Hg. The subjects likened the sensation to that experienced while hypercapnic before they were paralyzed.[22] Thus, in these studies, hypercapnia caused breathlessness in the absence of respiratory-muscle activity.

Although both normal subjects and patients with pulmonary disease become breathless when carbon dioxide is added to their inspired gas, it is not clear how hypercapnia relates to dyspnea in patients. Patients with COPD, neuromuscular disease, and other disorders associated with chronic hypercapnia and metabolic compensation may have little dyspnea at rest. It seems likely that the effects of carbon dioxide on dyspnea are mediated through changes in pH at the level of the central chemoreceptors, and on that basis one might expect acute and chronic (compensated) hypercapnia to differ markedly in the respiratory sensations they elicit. There are also many clinical settings (e.g., asthma) in which dyspnea develops under eucapnic or hypocapnic conditions.

Hypoxia

Among the lay public and many health care providers, there is a widely held belief that breathlessness arises primarily from lack of oxygen. Although the beneficial effects of oxygen therapy on longevity in patients with chronic hypoxia due to COPD are well established,[23] few studies have formally examined the effects of hypoxia on breathlessness. Normal subjects are more breathless during exercise when breathing a hypoxic gas mixture, and less breathless when breathing 100 percent oxygen, than they are when breathing air.[24] In patients with COPD, the administration of oxygen improves breathlessness,[25] probably in part because of an oxygen-induced decrease in exercise ventilation.[26] However, there also appears to be a direct effect, independent of any change in ventilation.[25] Despite these observations, hypoxia may play a limited part in the breathlessness experienced by patients with cardiopulmonary disease. Some patients with hypoxia do not have dyspnea; many patients with dyspnea are not hypoxic, and those who are often have only a slight improvement in their symptoms after the hypoxia is corrected.

Mechanoreceptors

Upper-Airway Receptors

Clinical observations suggest that upper-airway and facial receptors modify the sensation of dyspnea. Patients sometimes notice a decrease in the intensity of their dyspnea when sitting by a fan or open window. Conversely, the dyspnea of some patients worsens when they breathe through a mouthpiece during pulmonary-function tests. Studies of induced dyspnea in normal subjects indicate that receptors in the trigeminal-nerve distribution influence the intensity of dyspnea.[27,28] The same mechanism may also be operative in patients with COPD in whom exercise tolerance increases and dyspnea decreases when they breathe cold air.[29] It is unclear whether the receptors responsible for the effect of airflow on dyspnea sense the mechanical effect of airflow or the temperature changes that accompany it.

Lung Receptors

The lung contains a variety of receptors that transmit information to the central nervous system. Pulmonary stretch receptors in the airways respond to lung inflation and participate in the termination of inspiration; irritant receptors in the airway epithelium respond to a variety of mechanical and chemical stimuli and mediate bronchoconstriction; and C fibers (unmyelinated nerve endings) located in the alveolar wall and blood vessels respond to interstitial congestion.[30] Information from these receptors may also play a part in dyspnea.

Dynamic airway compression occurs in many patients with COPD and may contribute to their dyspnea. One mechanism by which dynamic airway compression might cause dyspnea is through the simple mechanical distortion of the airways during exhalation. Breathing with pursed lips, a breathing strategy adopted spontaneously by some patients with COPD and learned by others (e.g., during a pulmonary-rehabilitation program), may derive its effect by altering the changes in transmural pressure along the airway. When a negative pressure is applied at the mouth in patients

with severe COPD in such a way that dynamic airway compression increases, the sensation of breathlessness increases.[31] Presumably, receptors sensitive to the deformation of the airway or to changes in transmural pressure across the airway wall transmit the information that mediates the sensation of dyspnea.

Afferent information from the lung reaches the central nervous system by way of the vagus nerve. Although vagal input alters the pattern of breathing in humans,[32,33] relatively little is known about the contribution of vagal afferents to the sensation of dyspnea. Anesthesia of the vagus nerve increases breath-holding time in normal subjects,[20] and in uncontrolled studies it decreased breathlessness in some patients with cardiopulmonary disease.[32,34]

Studies comparing the sensations associated with bronchoconstriction and those associated with breathing through an external resistance help shed light on the role of vagal afferents. Induced bronchoconstriction causes greater dyspnea than breathing through an external resistance of comparable magnitude; inhaled lidocaine ameliorates the sensation associated with bronchoconstriction but has no effect on the discomfort associated with the external resistive load.[35] When qualitative aspects of sensation were examined in patients with asthma, the patients described a sensation of chest tightness or constriction in only 3 percent of the trials involving an external resistive load, as compared with 92 percent of the trials involving induced bronchoconstriction.[36] These studies suggest that information from vagal irritant receptors increases the intensity of dyspnea and alters its quality as well. In contrast, when information from pulmonary stretch receptors is reduced, dyspnea at a given chemical drive to breathe increases.[37,38]

Thus, the effect on dyspnea of vagally transmitted afferent information from the lungs probably depends on which receptors are stimulated. Stimulation of vagal irritant receptors appears to intensify the sensation of dyspnea and may impart a sense of chest tightness or constriction, whereas stimulation of pulmonary stretch receptors probably decreases the sensation of dyspnea.

Chest-Wall Receptors

The brain receives projections from a variety of receptors in the joints, tendons, and muscles of the chest wall that might influence the sensation of dyspnea. In normal subjects, hypercapnic tolerance increases when they are allowed to take larger breaths.[39,40] In normal subjects in whom dyspnea was induced by a combination of hypercapnia and inspiratory resistive loading, application of a physiotherapeutic vibrator over the parasternal intercostal muscles reduced dyspnea, whereas vibration over the deltoid muscles had no effect.[41] Similar findings have since been reported in patients with chronic lung disease.[42] However, vibration of the parasternal region during expiration increased dyspnea.[43] These studies suggest that afferent information from the chest wall modifies the intensity of dyspnea and that the temporal relation of the information to neuromotor output is an important determinant of the effect on dyspnea.

Afferent Mismatch

The concept of length–tension inappropriateness as the cause of dyspnea was proposed in 1963.[44] According to this theory, dyspnea arises from a disturbance in the relation between the force or tension generated by the respiratory muscles and the resulting change in muscle length and lung volume. This theory has since been refined to incorporate the general concept of a mismatch between outgoing motor signals to the respiratory muscles and incoming afferent information.[17,45] Although the hypothesis has not been tested directly, a number of clinical observations are consistent with this theory. In both patients and normal subjects, temporary suppression of ventilation during speaking or eating causes a mismatch between the respiratory motor command and afferent feedback from receptors in the lungs, airways, and chest wall and may cause dyspnea. An analogous phenomenon may occur in patients receiving mechanical ventilation in whom the ventilator settings (e.g., inspiratory flow rate and tidal volume) selected by the physician or respiratory therapist may not match those desired by a patient with heightened respiratory drive; under those conditions, the patient may experience dyspnea.

Experimental data are also consistent with the concept of afferent mismatch. When normal subjects breathe carbon dioxide, their ventilation increases and most experience dyspnea. However, if minute ventilation is reduced but end-tidal carbon dioxide is maintained at a constant level, the subjects report a marked increase in the intensity of breathlessness, even though the chemical drive to breathe has not changed.[16,17] Other aspects of afferent information more subtle than the global level of ventilation may also modify dyspnea. For example, when normal subjects are forced to breathe at an inspiratory flow rate lower than that which they have chosen as most comfortable, they experience a sense of air hunger.[46] These studies and the aforementioned clinical observations suggest that under a given set of conditions, the brain "expects" a certain pattern of ventilation and associated afferent feedback and that deviations from this pattern cause or intensify the sensation of dyspnea.

Dyspnea in Some Common Disorders

Although none of the factors outlined above appear to explain the pathogenesis of dyspnea in all patients, each may contribute to the sensation under some circumstances. Unfortunately, our understanding of dyspnea has not reached the point where we can conclusively link a specific disease with a specific mechanism of dyspnea. Furthermore, in most diseases associated with dyspnea the discomfort is probably caused by more than one of these mechanisms. Nonetheless, knowledge of the pathophysiology of a disorder sometimes allows us to formulate rational hypotheses about the underlying mechanisms of dyspnea (Table 2).

In asthma, a number of factors increase the burden

Table 2. Possible Mechanisms of Dyspnea in Selected Conditions.

CONDITION	MECHANISM
Asthma	Increased sense of effort
	Stimulation of irritant receptors in airways
Neuromuscular disease	Increased sense of effort
COPD	Increased sense of effort
	Hypoxia
	Hypercapnia
	Dynamic airway compression
Mechanical ventilation	Afferent mismatch
	Factors associated with the underlying condition
Pulmonary embolism	Stimulation of pressure receptors in pulmonary vasculature or right atrium (?)

on the inspiratory muscles, which must generate greater tension to overcome the increase in airflow resistance that accompanies bronchoconstriction. When hyperinflation occurs, the inspiratory muscles become shorter and therefore less effective in generating tension. Hyperinflation may change the radius of curvature of the diaphragm, thereby placing it at a mechanical disadvantage, and it represents an additional threshold load for the inspiratory muscles to overcome. As a result, respiratory motor output increases, and the accompanying increased sense of respiratory-muscle effort probably contributes to dyspnea. However, the sense of effort cannot explain the chest tightness experienced by many patients with asthma; rather, the sensation of chest tightness or constriction probably arises from the stimulation of irritant (vagal) receptors in the airways.[36]

In patients with neuromuscular disorders, such as amyotrophic lateral sclerosis or myasthenia gravis, the mechanical properties of the respiratory system may be normal, but greater neural drive is needed to activate the weakened respiratory muscles. This heightened neuromotor output is sensed as increased respiratory-muscle effort and is probably the principal mechanism of breathlessness in patients with uncomplicated neuromuscular disease.

In patients with COPD, the sense of effort as well as airway-receptor and chemoreceptor stimulation may all contribute to dyspnea. The respiratory muscles have many of the same loads already mentioned in the discussion of asthma. Some patients with COPD may have acute or chronic hypoxia, though hypoxia probably plays only a small part in their dyspnea. During severe exacerbations of COPD, new or worsening hypercapnia may develop in some patients and may also contribute to their breathlessness. Finally, in patients with dynamic airway compression, the mechanical compression of the airways may be sensed through vagal afferents as yet another stimulus for dyspnea.

Patients receiving mechanical ventilation are often breathless, despite a reduction in the work performed by the respiratory muscles. The process that necessitated mechanical ventilation in the first place is often responsible for the symptoms, but additional factors may play a part. For example, unless the output of the ventilator is matched to the patient's requirements for flow and tidal volume, afferent mismatch may intensify the sensation of dyspnea.

Finally, pulmonary embolism is an example of a disorder in which none of the mechanisms of dyspnea discussed thus far clearly apply. Although the dyspnea associated with pulmonary embolism has not been studied systematically, it often appears out of proportion to any derangement in respiratory mechanics or gas exchange. Anecdotal reports of patients undergoing thrombolysis indicate that dyspnea may be rapidly relieved by clot lysis (Markis J: personal communication). One possibility is that pressure receptors in the pulmonary vasculature or right atrium or C fibers in pulmonary vessels mediate the sensation of dyspnea.

APPROACH TO PATIENTS WITH DYSPNEA

A detailed discussion of the evaluation and treatment of dyspnea is beyond the scope of this article; interested readers are referred to any of several textbooks.[47,48] Instead, we focus briefly on a few selected aspects of treatment that are most closely linked to an understanding of the pathophysiology of dyspnea.

The initial goal of the treatment of dyspnea is to correct the underlying disorder causing the symptoms. Unfortunately, in all too many patients, treatment of the underlying disorder is ineffective or only partly effective, and dyspnea persists. For example, in many patients with COPD, therapy with bronchodilators and corticosteroids results in only minor improvement, and airflow obstruction and dyspnea persist. In these patients, a number of strategies may reduce dyspnea. Since, for any given muscular task, greater effort is required if the muscle is weak than if it is strong, one potential approach is to strengthen the respiratory muscles. In some studies, inspiratory-muscle training reduced dyspnea in patients with COPD.[49,50] Although one might predict a beneficial effect of respiratory-muscle rest on the sense of effort and dyspnea, a randomized, double-blind study found that respiratory-muscle rest did not reduce dyspnea.[51] In some patients with COPD, theophylline improves dyspnea independently of its role as a bronchodilator,[52] possibly by decreasing neural drive and the sense of effort through its effects on respiratory-muscle performance.

One can also attempt to alleviate dyspnea by minimizing the role of chemoreceptor stimulation. The administration of oxygen reduces dyspnea in patients with hypoxia who have COPD or interstitial lung disease.[53] Supplemental oxygen may also benefit patients with COPD and only mild hypoxia[54] for whom oxygen would not be prescribed to reduce mortality. Patients can minimize the discomfort arising from dynamic airway collapse by learning the technique of pursed-lips breathing. Finally, the ability of many drugs, including opioids,[55] benzodiazepines,[56] and phenothiazines,[57] to relieve dyspnea has been studied, but only opioids were effective in controlled studies.[55]

CONCLUSIONS

Dyspnea has been described as a "synthetic sensation, like thirst or hunger"[58] that is the result of a com-

plex interaction of signals arising from within the central nervous system, both from the automatic centers in the brain stem and from the motor cortex, and from a variety of receptors in the upper airway, lungs, and chest wall (Fig. 1). Most conditions that cause breathlessness probably do so by more than one mechanism, and different conditions share common mechanisms. However, each condition probably has a unique combination of physiologic factors that determines the quality and intensity of dyspnea in a particular patient at a given time. Our capacity to alleviate the symptom of dyspnea depends in large part on our ability to define these mechanisms in our patients.

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