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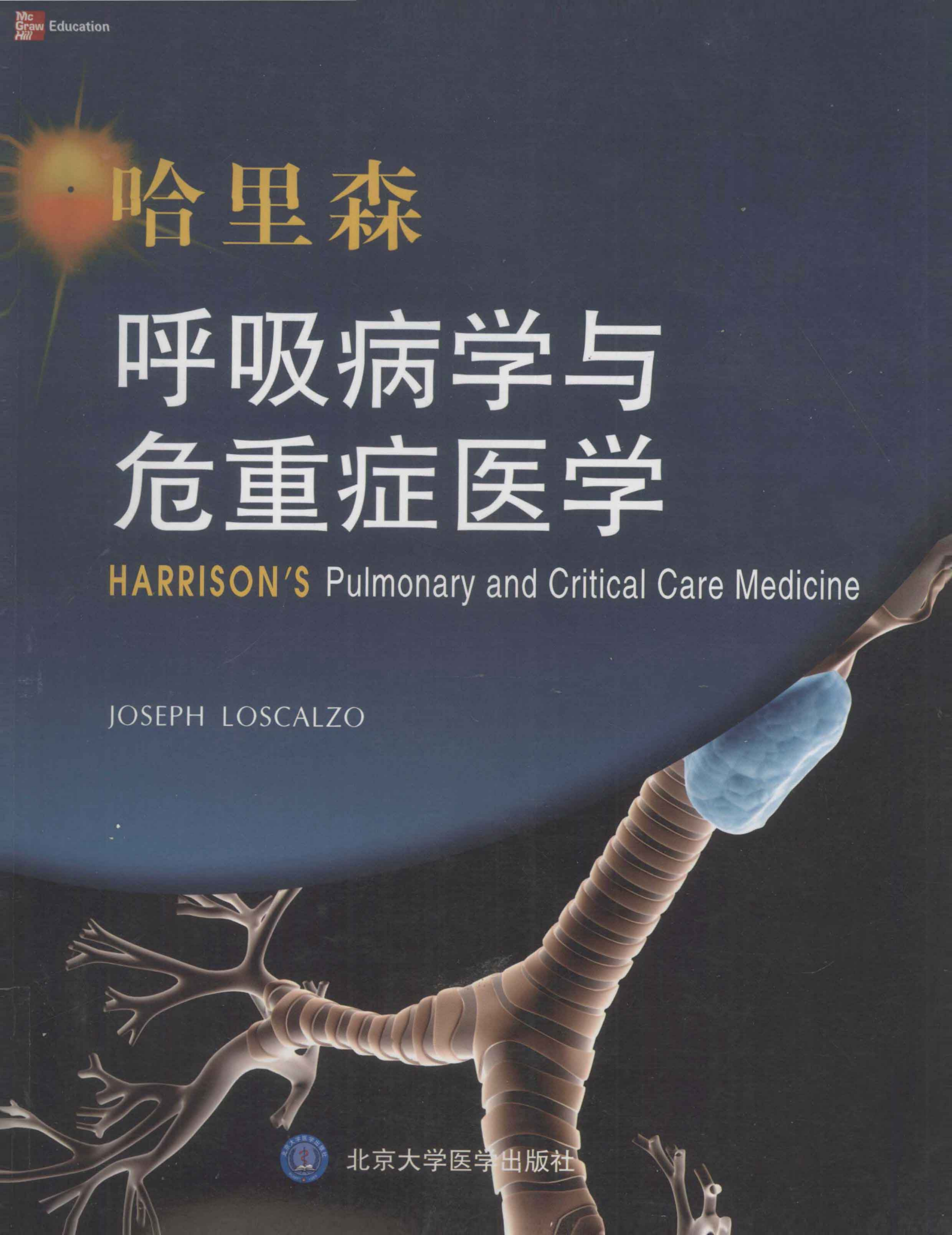
呼吸病学与危重症医学

HARRISON'S Pulmonary and Critical Care Medicine

JOSEPH LOSCALZO



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出版说明

《哈里森内科学》（Harrison's Principles of Internal Medicine）是一部内科学经典名著，也是美国及多个国家医学院校的首选内科学教科书。该书1945年由美国权威内科学家哈里森（Tinsley R. Harrison）首先提议并组织编写，第1版于1950年问世，并立即引起广泛的赞誉与好评。自此，随着医学科学的发展以及在市场的热销，该书每4年修订一次，历时半个多世纪，已出版至第17版，成为内科学发展的基石和风向标，享有“内科学著作之父”的美誉。

为了读者阅读和携带方便，更专注于内科学各亚科领域，《哈里森内科学》分册系列书问世了。该分册系列以《哈里森内科学》（第17版）中相关领域的内容为蓝本，并参考了《哈里森内科学》（第17版）出版以来的最新文献，强调基础与临床的整合，汇集了本领域内最新的进展，是内科学各亚科领域的权威教科书。

在医学领域，英文原版经典专著经过几十年甚至上百年的发展，在知识点的架构上形成了科学而完备的体系，不但语言规范、地道，而且更新及时，具有权威性和先进性。无论是临床医生、教师还是医学生，有这样一本经典专著放在案头，经常翻阅，不但可以获取医学知识，对提高专业外语水平也大有裨益。

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Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The authors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication. However, in view of the possibility of human error or changes in medical sciences, neither the authors nor the publisher nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they disclaim all responsibility for any errors or omissions or for the results obtained from use of the information contained in this work. Readers are encouraged to confirm the information contained herein with other sources. For example, and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this work is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

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The global icons call greater attention to key epidemiologic and clinical differences in the practice of medicine throughout the world.

The genetic icons identify a clinical issue with an explicit genetic relationship.

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PREFACE

Pulmonary diseases are major contributors to morbidity and mortality in the general population. Although advances in the diagnosis and treatment of many common pulmonary disorders have improved the lives of patients, these complex illnesses continue to affect a large segment of the global population. The impact of cigarette smoking cannot be underestimated in this regard, especially given the growing prevalence of tobacco use in the developing world. Pulmonary medicine is, therefore, of critical global importance to the field of internal medicine.

Pulmonary medicine is a growing subspecialty and includes a number of areas of disease focus, including reactive airways diseases, chronic obstructive lung disease, environmental lung diseases, and interstitial lung diseases. Furthermore, pulmonary medicine is linked to the field of critical care medicine, both cognitively and as a standard arm of the pulmonary fellowship training programs at most institutions. The breadth of knowledge in critical care medicine extends well beyond the respiratory system, of course, and includes selected areas of cardiology, infectious diseases, nephrology, and hematology. Given the complexity of these disciplines and the crucial role of the internist in guiding the management of patients with chronic lung diseases and in helping to guide the management of patients in the intensive care setting, knowledge of the discipline is essential for competency in the field of internal medicine.

The scientific basis of many pulmonary disorders and intensive care medicine is rapidly expanding. Novel diagnostic and therapeutic approaches, as well as prognostic assessment strategies, populate the published literature with great frequency. Maintaining updated knowledge of these evolving areas is, therefore, essential for the optimal care of patients with lung diseases and critical illness.

In view of the importance of pulmonary and critical care medicine to the field of internal medicine and the speed with which the scientific basis of the discipline is evolving, this *Sectional* was developed. The purpose of this book is to provide the readers with an overview of the field of pulmonary and critical care medicine. To achieve this end, this *Sectional* comprises the key pulmonary and critical care medicine chapters in *Harrison's Principles of Internal Medicine,* 17th edition, contributed by leading experts in the fields. This *Sectional* is designed not only for physicians-in-training, but also for medical students, practicing clinicians, and other health care professionals who seek to maintain adequately updated knowledge of this rapidly advancing field. The editors believe that this book will improve the reader's knowledge of the discipline, as well as highlight its importance to the field of internal medicine.

Joseph Loscalzo, MD, PhD

CONTENTS

SECTION IV

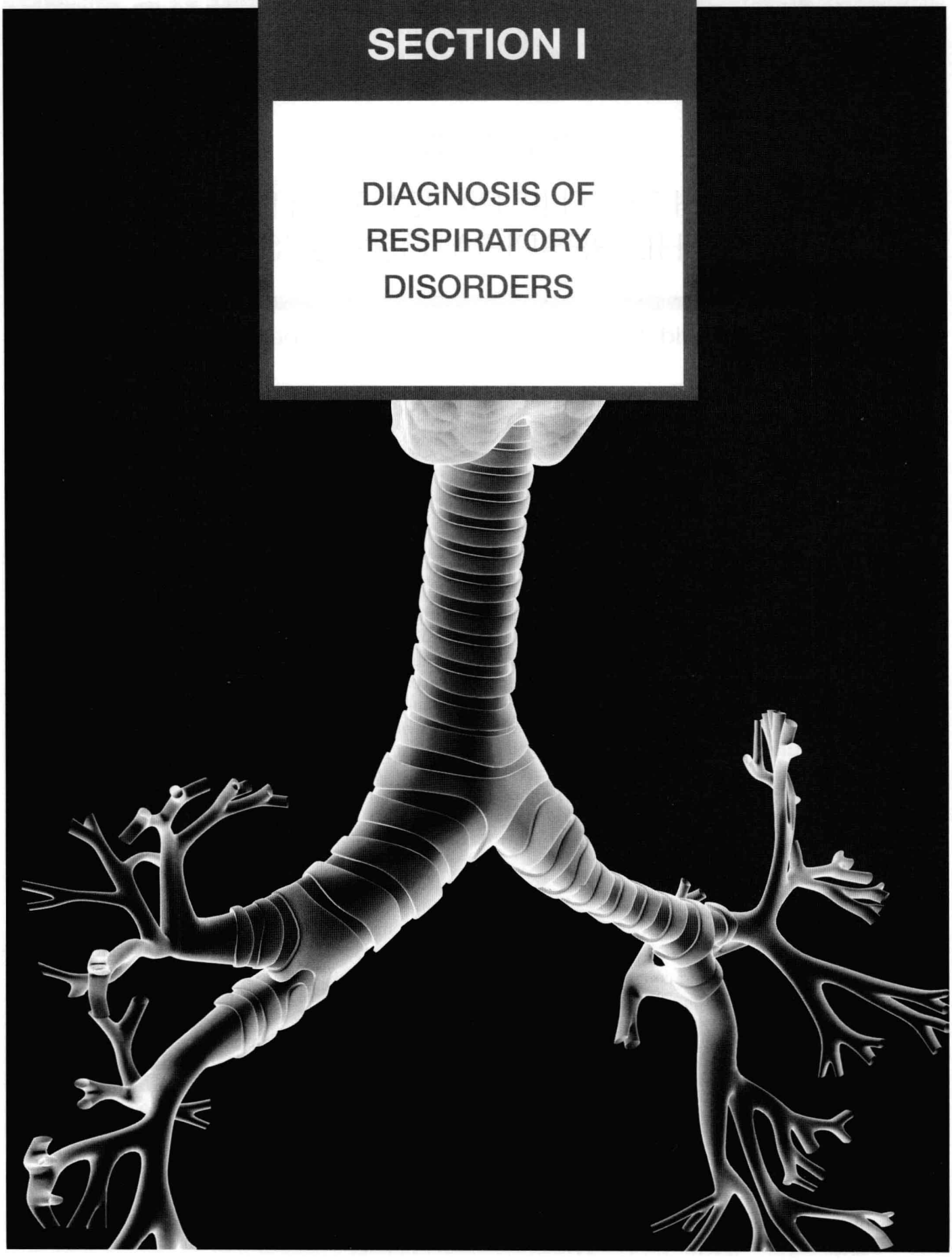
COMMON CRITICAL ILLNESSES AND SYNDROMES

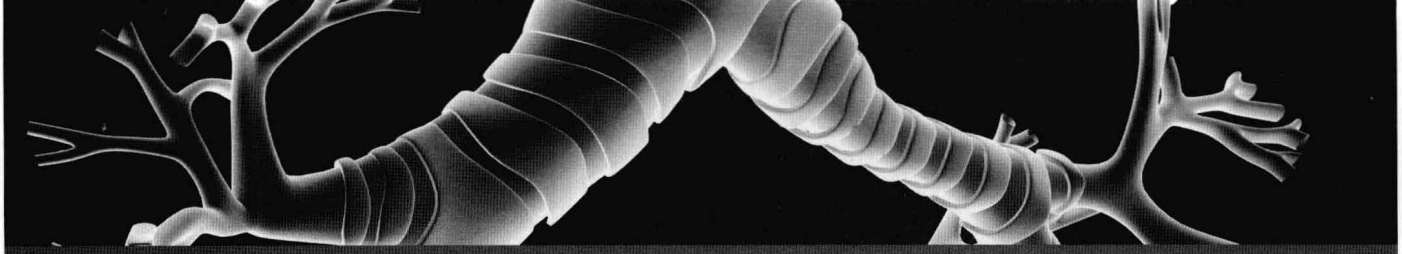
SECTION V

DISORDERS COMPLICATING CRITICAL ILLNESSES AND THEIR MANAGEMENT

SECTION I

DIAGNOSIS OF RESPIRATORY DISORDERS





CHAPTER 1

APPROACH TO THE PATIENT WITH DISEASE OF THE RESPIRATORY SYSTEM

David A. Lipson ■ Steven E. Weinberger

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. This chapter considers the approach to the patient based on the major patterns of presentation, focusing on the history, physical examination, and chest radiography. For further discussion of pulmonary function testing, see Chap. 5, and of other diagnostic studies, see Chap. 6.

CLINICAL PRESENTATION

History

Dyspnea (shortness of breath) and cough are nonspecific but common presenting symptoms for patients with respiratory system disease. Less common symptoms include hemoptysis (the coughing up of blood) and chest pain that often is pleuritic in nature.

Dyspnea

(See also Chap. 2.) When evaluating a patient with shortness of breath, one should first determine the time course over which the symptom has become manifest. Patients who were well previously and developed *acute* shortness of breath (over a period of minutes to days) may have acute disease affecting either the upper or the intrathoracic airways (e.g., laryngeal edema or acute asthma, respectively), the pulmonary parenchyma (acute cardiogenic or noncardiogenic pulmonary edema or an acute infectious process such as bacterial pneumonia), the pleural space (a pneumothorax), or the pulmonary vasculature (a pulmonary embolus).

A *subacute* presentation (over days to weeks) may suggest an exacerbation of preexisting airways disease (asthma or chronic bronchitis), an indolent parenchymal infection (*Pneumocystis jiroveci* pneumonia in a patient with AIDS, mycobacterial or fungal pneumonia), a noninfectious inflammatory process that proceeds at a relatively slow pace (Wegener's granulomatosis, eosinophilic pneumonia, cryptogenic organizing pneumonia, and many others), neuromuscular disease (Guillain-Barré syndrome, myasthenia gravis), pleural disease (pleural effusion from a variety of possible causes), or chronic cardiac disease (congestive heart failure).

A *chronic* presentation (over months to years) often indicates chronic obstructive lung disease, chronic interstitial lung disease, or chronic cardiac disease. Chronic diseases of airways (not only chronic obstructive lung disease but also asthma) are characterized by exacerbations and remissions. Patients often have periods when they are severely limited by shortness of breath, but these may be interspersed with periods in which their symptoms are minimal or absent. In contrast, many of the diseases of the pulmonary parenchyma are characterized by slow but inexorable progression. Chronic respiratory symptoms may also be multifactorial in nature

because patients with chronic obstructive pulmonary disease may also have concomitant heart disease.

Other Respiratory Symptoms

Cough (Chap. 3) may indicate the presence of lung disease, but cough per se is not useful for the differential diagnosis. The presence of sputum accompanying the cough often suggests airway disease and may be seen in patients with asthma, chronic bronchitis, or bronchiectasis.

Hemoptysis (Chap. 3) can originate from disease of the airways, the pulmonary parenchyma, or the vasculature. Diseases of the airways can be inflammatory (acute or chronic bronchitis, bronchiectasis, or cystic fibrosis) or neoplastic (bronchogenic carcinoma or bronchial carcinoid tumors). Parenchymal diseases causing hemoptysis may be either localized (pneumonia, lung abscess, tuberculosis, or infection with *Aspergillus* spp.) or diffuse (Goodpasture's syndrome, idiopathic pulmonary hemosiderosis). Vascular diseases potentially associated with hemoptysis include pulmonary thromboembolic disease and pulmonary arteriovenous malformations.

Chest pain caused by diseases of the respiratory system usually originates from involvement of the parietal pleura. As a result, the pain is accentuated by respiratory motion and is often referred to as *pleuritic*. Common examples include primary pleural disorders, such as neoplasm or inflammatory disorders involving the pleura, or pulmonary parenchymal disorders that extend to the pleural surface, such as pneumonia or pulmonary infarction.

Additional Historic Information

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 decreases progressively in the decade after 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 because it may be a risk factor for neoplasia or an exacerbating factor for airways disease.

A patient may have been exposed to other inhaled agents associated with lung disease, which act either via direct toxicity or through immune mechanisms (Chaps. 9 and 10). 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 because 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 because the lungs are not only the most common site of AIDS-defining infection but may also be involved by noninfectious complications of AIDS. Treatment of patients with nonrespiratory disease may 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) (Chap. 9).

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.

Physical Examination

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 caused by 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 may 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 the underlying air-containing lung is resonant. In contrast, consolidated lung or a pleural effusion sounds dull, and 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 free liquid or mucus is present 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.

A summary of the patterns of physical findings on pulmonary examination in common types of respiratory system disease is shown in **Table 1-1**.

A meticulous *general physical examination* is mandatory in patients with disorders of the respiratory system. Enlarged lymph nodes in the cervical and supraclavicular regions should be sought. Disturbances of mentation or even coma may occur in patients with acute carbon dioxide retention and hypoxemia. Telltale stains on the fingers point to heavy cigarette smoking; infected teeth and gums may occur in patients with aspiration pneumonitis and lung abscess.

Clubbing of the digits may be found in patients with lung cancer; interstitial lung disease; and chronic infections in the thorax, such as bronchiectasis, lung abscess, and empyema. Clubbing may also be seen with congenital heart disease associated with right-to-left shunting and with a variety of chronic inflammatory or infectious diseases, such as inflammatory bowel disease and endocarditis. A number of systemic diseases, such as systemic lupus erythematosus, scleroderma, and rheumatoid arthritis, may be associated with pulmonary complications, even though their primary clinical manifestations and physical findings are not primarily related to the lungs. Conversely, patients with other diseases that most commonly affect the respiratory system, such as sarcoidosis, may have findings on physical examination not related to the respiratory system, including ocular findings (uveitis, conjunctival granulomas) and skin findings (erythema nodosum, cutaneous granulomas).

Chest Radiography

Chest radiography is often the initial diagnostic study performed to evaluate patients with respiratory symptoms, but it may also provide the initial evidence of disease in patients who are free of symptoms. Perhaps the most common example of the latter situation is the

TABLE 1-1

TYPICAL CHEST EXAMINATION FINDINGS IN SELECTED CLINICAL CONDITIONS

CONDITION	PERCUSSION	FREMITUS	BREATH SOUNDS	VOICE TRANSMISSION	ADVENTITIOUS SOUNDS
Normal	Resonant	Normal	Vesicular (at lung bases)	Normal	Absent
Consolidation or atelectasis (with patent airway)	Dull	Increased	Bronchial	Bronchophony, whispered pectoriloquy, egophony	Crackles
Consolidation or atelectasis (with blocked airway)	Dull	Decreased	Decreased	Decreased	Absent
Asthma	Resonant	Normal	Vesicular	Normal	Wheezing
Interstitial lung disease	Resonant	Normal	Vesicular	Normal	Crackles
Emphysema	Hyperresonant	Decreased	Decreased	Decreased	Absent or wheezing
Pneumothorax	Hyperresonant	Decreased	Decreased	Decreased	Absent
Pleural effusion	Dull	Decreased	Decreased[a]	Decreased[a]	Absent or pleural friction rub

[a]May be altered by collapse of underlying lung, which increases transmission of sound.
Source: Adapted from Weinberger, with permission.

finding of one or more nodules or masses when radiography is performed for a reason other than evaluation of respiratory symptoms.

A number of diagnostic possibilities are often suggested by the radiographic pattern (Chap. 7). A localized region of opacification involving the pulmonary parenchyma may be described as a nodule (usually <3 cm in diameter), a mass (usually ≥3 cm in diameter), or an infiltrate. Diffuse disease with increased opacification is usually characterized as having an alveolar, interstitial, or nodular pattern. In contrast, increased radiolucency may be localized, as seen with a cyst or bulla, or generalized, as occurs with emphysema. Chest radiography is also particularly useful for the detection of pleural disease, especially if manifested by the presence of air or liquid in the pleural space. An abnormal appearance of the hila or the mediastinum may suggest a mass or enlargement of lymph nodes.

A summary of representative diagnoses suggested by these common radiographic patterns is presented in Table 1-2, and an atlas of chest radiography and other chest images can be found in Chap. 7.

Additional Diagnostic Evaluation

Further information for clarification of radiographic abnormalities is frequently obtained with CT scanning of the chest (see Figs. 6-1, 6-2, 19-1, 19-2, 30-3). This technique is more sensitive than plain radiography in detecting subtle abnormalities and can suggest specific diagnoses based on the pattern of abnormality.

For further discussion of the use of other imaging studies, including MRI, scintigraphic studies, ultrasonography, and angiography, see Chap. 6.

Alteration in the function of the lungs as a result of respiratory system disease is assessed objectively by pulmonary function tests, and effects on gas exchange are evaluated by measurement of arterial blood gases or by oximetry (Chap. 5). As part of pulmonary function testing, quantitation of forced expiratory flow assesses the presence of obstructive physiology, which is consistent with diseases affecting the structure or function of the airways, such as asthma and chronic obstructive lung disease. Measurement of lung volumes assesses the presence of restrictive disorders seen with diseases of the pulmonary parenchyma or respiratory pump and with space-occupying processes within the pleura. Bronchoscopy is useful in some settings for visualizing abnormalities of the airways and for obtaining a variety of samples from either the airway or the pulmonary parenchyma (Chap. 6).

INTEGRATION OF THE PRESENTING CLINICAL PATTERN AND DIAGNOSTIC STUDIES

Patients with respiratory symptoms but a normal chest radiograph often have diseases affecting the airways, such as asthma or chronic obstructive pulmonary disease. However, the latter diagnosis is also commonly associated with radiographic abnormalities, such as diaphragmatic flattening, an increase in the retrosternal air space, and attenuation of vascular markings. Other disorders of the respiratory system for which the chest radiograph is normal include disorders of the respiratory pump (either the chest wall or the neuromuscular apparatus controlling the chest wall) or pulmonary circulation and occasionally interstitial lung disease. Chest examination and pulmonary

TABLE 1-2

MAJOR RESPIRATORY DIAGNOSES WITH COMMON CHEST RADIOGRAPHIC PATTERNS
Solitary circumscribed density—nodule (<3 cm) or mass (≥3 cm)
Primary or metastatic neoplasm
Localized infection (bacterial abscess, mycobacterial or fungal infection)
Wegener's granulomatosis (one or several nodules)
Rheumatoid nodule (one or several nodules)
Vascular malformation
Bronchogenic cyst
Localized opacification (infiltrate)
Pneumonia (bacterial, atypical, mycobacterial, or fungal infection)
Neoplasm
Radiation pneumonitis
Bronchiolitis obliterans with organizing pneumonia
Bronchocentric granulomatosis
Pulmonary infarction
Diffuse interstitial disease
Idiopathic pulmonary fibrosis
Pulmonary fibrosis with systemic rheumatic disease
Sarcoidosis
Drug-induced lung disease
Pneumoconiosis
Hypersensitivity pneumonitis
Infection (pneumocystis, viral pneumonia)
Langerhans cell histiocytosis
Diffuse alveolar disease
Cardiogenic pulmonary edema
Acute respiratory distress syndrome
Diffuse alveolar hemorrhage
Infection (pneumocystis, viral or bacterial pneumonia)
Sarcoidosis
Diffuse nodular disease
Metastatic neoplasm
Hematogenous spread of infection (bacterial, mycobacterial, fungal)
Pneumoconiosis
Langerhans cell histiocytosis

function tests are generally helpful in sorting out these diagnostic possibilities. Obstructive diseases associated with a normal or relatively normal chest radiograph are often characterized by findings on physical examination and pulmonary function testing that are typical for these conditions. Similarly, diseases of the respiratory pump or interstitial diseases may also be suggested by findings on physical examination or by particular patterns of restrictive disease seen on pulmonary function testing.

When respiratory symptoms are accompanied by radiographic abnormalities, diseases of the pulmonary parenchyma or the pleura are usually present. Either diffuse or localized parenchymal lung disease is generally visualized well on the radiograph, and both air and liquid in the pleural space (pneumothorax and pleural effusion, respectively) are usually readily detected by radiography.

Radiographic findings in the absence of respiratory symptoms often indicate localized disease affecting the airways or the pulmonary parenchyma. One or more nodules or masses may suggest intrathoracic malignancy, but they may also be the manifestation of a current or previous infectious process. Multiple nodules affecting only one lobe suggest an infectious cause rather than malignancy because metastatic disease would not have a predilection for only one discrete area of the lung. Patients with diffuse parenchymal lung disease on radiographic examination may be free of symptoms, as is sometimes the case in those with pulmonary sarcoidosis.

FURTHER READINGS

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