EIGHTH EDITION

Pulmonary Pathophysiology

THE ESSENTIALS

John B. West

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PULMONARY PATHOPHYSIOLOGY

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PULMONARY PATHOPHYSIOLOGY

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To R.B.W.

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Preface

This book is a companion to *Respiratory Physiology: The Essentials*, 9th edition (Lippincott Williams & Wilkins, 2012), and is about the function of the diseased lung as opposed to the normal lung. It is intended primarily for medical students in their second and subsequent years. However, a concise, amply illustrated account of respiratory function in disease will prove useful to the increasingly large number of physicians (such as anesthesiologists and cardiologists) and other medical personnel (including intensive care nurses and respiratory therapists) who come into contact with respiratory patients. In addition, postgraduate students will find this brief account valuable for reviewing material before examinations.

Many medical schools are constantly trying to emphasize the relevance of the basic science of the first two years to the practice of medicine. Respiratory function can be a model for this. A discussion of a patient with asthma, for example, can quickly and painlessly cover the basic physiology of the airways, blood gases, and lung volumes. I hope that this little book will be helpful in such a course that bridges the preclinical and clinical disciplines.

This book emphasizes the relations between structure and function in the diseased lung. Indeed, readers will find more anatomic pathology than might be expected in a book about pathophysiology. However, function cannot be understood properly without knowledge of structure. It is assumed that students who read this book are also exposed to teaching in pathology.

For this eighth edition, the text has been thoroughly revised and brought up to date in a number of areas including exercise testing, control of ventilation, pathogenesis of asthma, and bronchoactive drugs. However, the length of the book has been kept almost the same in sympathy with the plight of modern medical students.

Other changes improve the didactic nature of the book. All the questions are now in the USMLE format, lists of key concepts have been added at the end of each chapter, and important points are highlighted. In addition there is a brief discussion of the answers to the questions.

I would be grateful for any comments on the selection of material and any factual errors, and I respond to all emails on these subjects.

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Contents

Reviewers vi

Preface vii

PART ONE Lung Function Tests and What They Mean

Chapter 1 **Ventilation** 3

Chapter 2 **Gas Exchange** 16

Chapter 3 **Other Tests** 34

PART TWO Function of the Diseased Lung

Chapter 4 **Obstructive Diseases** 47

Chapter 5 **Restrictive Diseases** 74

Chapter 6 **Vascular Diseases** 91

Chapter 7 **Environmental, Neoplastic, and Infectious Diseases** 110

PART THREE Function of the Failing Lung

Chapter 8 **Respiratory Failure** 129

Chapter 9 **Oxygen Therapy** 141

Chapter 10 **Mechanical Ventilation** 153

Appendix A: Symbols, Units, and Normal Values 163

Appendix B: Further Reading 166

Appendix C: Answers to Chapter Questions 167

Index 177

PART ONE

Lung Function Tests and What They Mean

1 ■ **Ventilation**

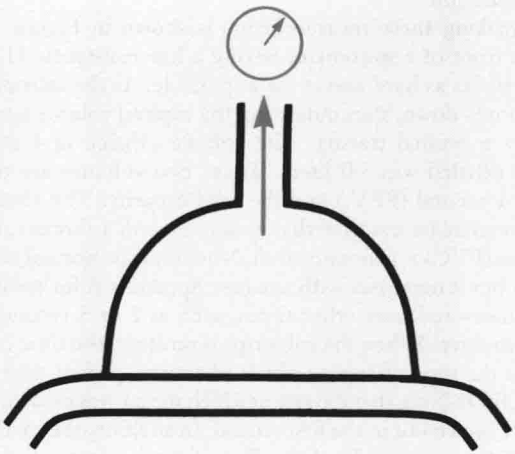
2 ■ **Gas Exchange**

3 ■ **Other Tests**

We learn how diseased lungs work by doing pulmonary function tests. Accordingly, Part One is devoted to a description of the most important tests and their interpretation. It is assumed that the reader is familiar with the basic physiology of the lung as contained in the companion volume, West JB. *Respiratory Physiology: The Essentials*, 9th ed. Baltimore, MD: Lippincott Williams & Wilkins, 2012.

Ventilation

1



The simplest test of lung function is a forced expiration. It is also one of the most informative tests and it requires minimal equipment and trivial calculations. The majority of patients with lung disease have an abnormal forced expiration volume and, very often, the information obtained from this test is useful in their management. In spite of this, the test is not used as often as it should be. For example, it can be valuable in detecting early airway disease, an extremely common and important condition. This chapter also discusses a simple test of uneven ventilation.

- **Tests of Ventilatory Capacity**
  - Forced Expiratory Volume
  - Forced Expiratory Flow
  - Interpretation of Tests of Forced Expiration
  - Expiratory Flow-Volume Curve
  - Partitioning of Flow Resistance from the Flow-Volume Curve
  - Maximum Flows from the Flow-Volume Curve
  - Peak Expiratory Flow Rate
  - Inspiratory Flow-Volume Curve
- **Tests of Uneven Ventilation**
  - Single-Breath Nitrogen Test
  - Closing Volume
  - Other Tests of Uneven Ventilation
  - Tests of Early Airway Disease

Tests of Ventilatory Capacity

Forced Expiratory Volume

The *forced expiratory volume* (FEV) is the volume of gas exhaled in *1 second* by a forced expiration from full inspiration. The *vital capacity* is the *total* volume of gas that can be exhaled after a full inspiration.

A simple way of making these measurements is shown in Figure 1-1. The patient is comfortably seated in front of a spirometer having a low resistance. He or she breathes in maximally and then exhales as hard and as far as possible. As the spirometer bell moves up, the kymograph pen moves down, thus indicating the expired volume against time.

Figure 1-2A shows a normal tracing. The volume exhaled in 1 second was 4.0 liters and the total volume exhaled was 5.0 liters. These two volumes are therefore the forced expiratory volume in 1 second (FEV_1) and the vital capacity. The vital capacity measured with a forced expiration may be less than that measured with a slower exhalation, so that the term *forced vital capacity* (FVC) is generally used. Note that the normal ratio of FEV_1 to FVC is approximately 80% but it decreases with age (see Appendix A for normal values).

The FEV can be measured over other times, such as 2 or 3 seconds, but the 1-second value is the most informative. When the subscript is omitted, the time is 1 second.

Figure 1-2B shows the type of tracing obtained from a patient with chronic obstructive pulmonary disease (COPD). Note that the rate at which the air was exhaled was much slower, so that only 1.3 liters were blown out in the first second. In addition, the total volume exhaled was only 3.1 liters. FEV_1/FVC was reduced to 42%. These figures are typical of an *obstructive* pattern.

Contrast this pattern with that of Figure 1-2C, which shows the type of tracing obtained from a patient with pulmonary fibrosis. Here, the vital capacity was reduced to 3.1 liters, but a large percentage (90%) was exhaled in the first second. These figures mean *restrictive* disease.

The simple water-filled spirometer shown in Figure 1-1 is now seldom used and has been replaced by electronic spirometers, which often provide a graph to be filed with the patient's chart.

The patient should loosen tight clothing and the mouthpiece should be at a convenient height. One accepted procedure is to allow two practice blows and then record three good test breaths. The highest FEV_1 and FVC from these three breaths are then used. The volumes should be converted to body temperature and pressure (see Appendix A).

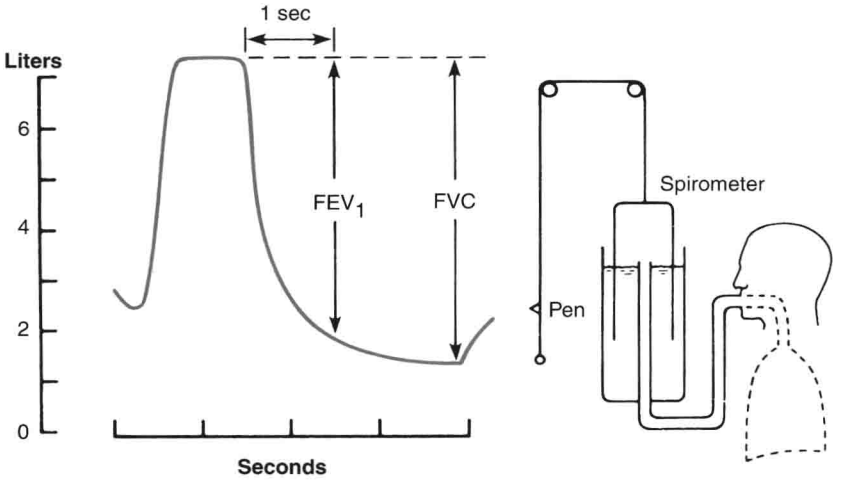


Figure 1-1. Measurement of Forced Expiratory Volume (FEV_1) and Vital Capacity (FVC).

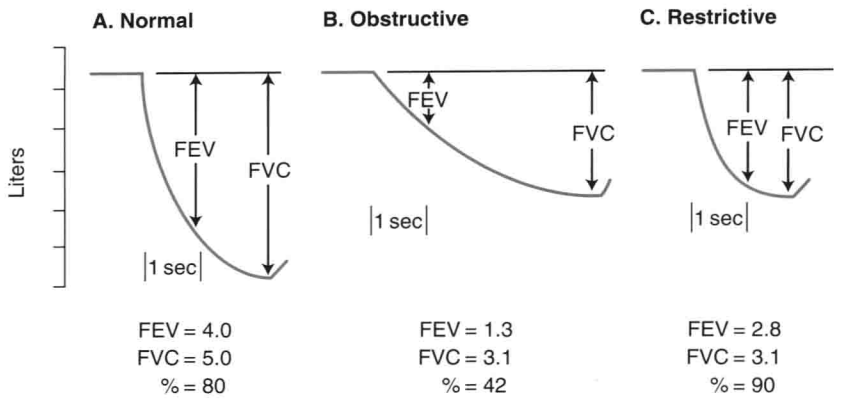


Figure 1-2. Normal, Obstructive, and Restrictive Patterns of a Forced Expiration.

The test is often valuable in assessing the efficacy of bronchodilator drugs. If reversible airway obstruction is suspected, the test should be carried out before and after administering the drug (e.g., 0.5% albuterol by nebulizer for 3 minutes). Both the FEV_1 and FVC usually increase in a patient with bronchospasm.

FEV_1 and FVC

The one-second forced expiratory volume together with the forced vital capacity is

- a simple test.
- often informative.
- abnormal in many patients with lung disease.
- often valuable in assessing the progress of disease.

Forced Expiratory Flow

This index is calculated from a forced expiration, as shown in Figure 1-3. The middle half (by volume) of the total expiration is marked and its duration is measured. The $FEF_{25-75\%}$ is the volume in liters divided by the time in seconds.

The correlation between $FEF_{25-75\%}$ and FEV_1 is generally close in patients with obstructive pulmonary disease. The changes in $FEF_{25-75\%}$ are often more striking, but the range of normal values is greater.

Interpretation of Tests of Forced Expiration

In some respects, the lungs and thorax can be regarded as a simple air pump (Figure 1-4). The output of such a pump depends on the stroke volume, the resistance of the airways, and the force applied to the piston. The last factor is relatively unimportant in a forced expiration, as we shall presently see.

The *vital capacity* (or forced vital capacity) is a measure of the stroke volume, and any reduction of it affects the ventilatory capacity. Causes of stroke volume reduction include diseases of the thoracic cage, such as kyphoscoliosis, ankylosing spondylitis, and acute injuries; diseases affecting the nerve supply to the respiratory muscles or the muscles themselves, such as poliomyelitis and muscular dystrophy; abnormalities of the pleural cavity, such as pneumothorax and pleural thickening; disease in the lung itself, such as fibrosis, which reduces

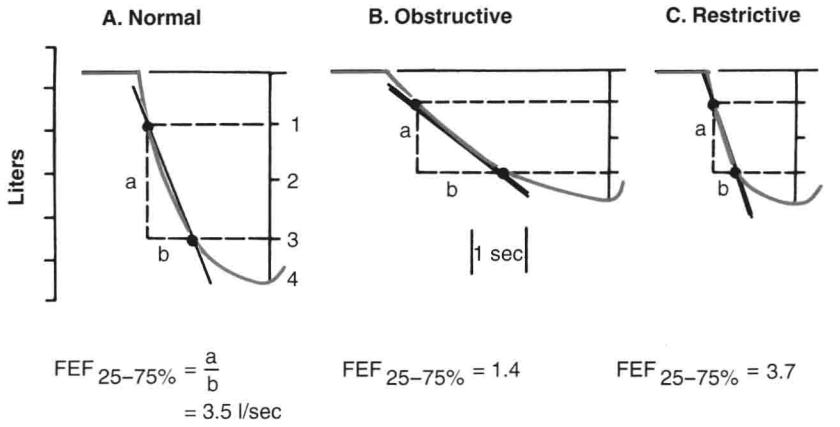


Figure 1-3. Calculation of Forced Expiratory Flow ($FEF_{25-75\%}$) from a Forced Expiration.

its distensibility; space-occupying lesions, such as cysts; or an increased pulmonary blood volume, as in left heart failure. In addition, there are diseases of the airways that cause them to close prematurely during expiration, thus limiting the volume that can be exhaled. This occurs in asthma and bronchitis.

The *forced expiratory volume* (and related indices such as the $FEF_{25-75\%}$) is affected by the airway resistance during forced expiration. Any increase in resistance reduces the ventilatory capacity. Causes include bronchoconstriction, as in asthma or following the inhalation of irritants such as cigarette smoke; structural changes in the airways, as in chronic bronchitis; obstructions within the airways, such as an inhaled foreign body or excess bronchial secretions; and destructive processes in the lung parenchyma, which interfere with the radial traction that normally holds the airways open.

The simple model of Figure 1-4 introduces the factors limiting the ventilatory capacity of the diseased lung, but we need to refine the model to obtain a better understanding. For example, the airways are actually *inside*, not *outside*, the pump, as shown in Figure 1-4. Useful additional information comes from the flow-volume curve.

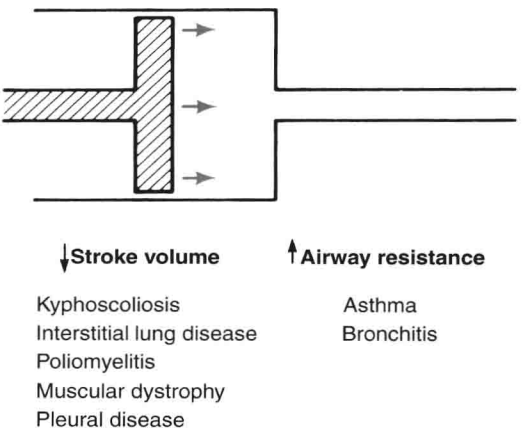


Figure 1-4. Simple Model of Factors That May Reduce the Ventilatory Capacity. The stroke volume may be reduced by diseases of the chest wall, lung parenchyma, respiratory muscles, and pleura. Airway resistance is increased in asthma and bronchitis.

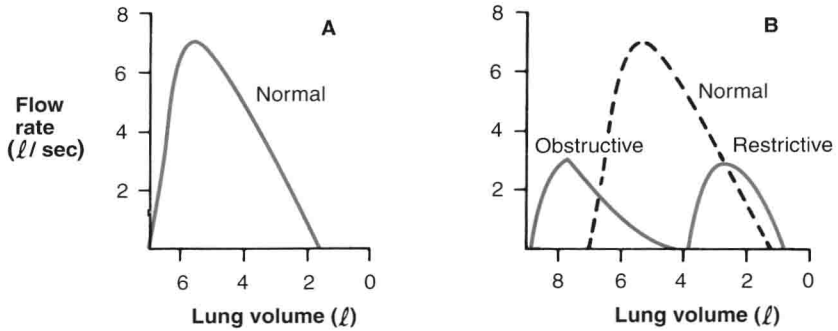


Figure 1-5. Expiratory Flow-Volume Curves. A. Normal. **B.** Obstructive and restrictive patterns.

Expiratory Flow-Volume Curve

If we record flow rate and volume during a maximal forced expiration, we obtain a pattern like that shown in Figure 1-5A. A curious feature of the flow-volume curve is that it is virtually impossible to get outside it. For example, if we begin by exhaling slowly and then exert maximum effort, the flow rate increases to the envelope but not beyond. Clearly, something very powerful is limiting the maximum flow rate at a given volume. This factor is *dynamic compression of the airways.*

Figure 1-5B shows typical patterns found in obstructive and restrictive lung disease. In obstructive diseases, such as chronic bronchitis and emphysema, the maximal expiration typically begins and ends at abnormally high lung volumes, and the flow rates are much lower than normal. In addition, the curve may have a scooped-out appearance. By contrast, patients with restrictive disease, such as interstitial fibrosis, operate at low lung volumes. Their flow envelope is flattened compared with a normal curve, but if flow rate is related to lung volume, the flow is seen to be higher than normal (Figure 1-5B). Note that the figure shows absolute lung volumes, although these cannot be obtained from a forced expiration. They require an additional measurement of residual volume.

To understand these patterns, consider the pressures inside and outside the airways (Figure 1-6) (see *Respiratory Physiology: The Essentials*, 9th ed., p. 121). Before inspiration (A), the pressures in the mouth, airways, and alveoli are all atmospheric because there is no flow. Intrapleural pressure is, say, 5 cm H_2O below atmospheric pressure, and we assume that the same pressure exists outside the airways (although this is an oversimplification). Thus, the pressure difference expanding the airways is 5 cm H_2O. At the beginning of inspiration (B), all pressures fall and the pressure difference holding the airways open increases to 6 cm H_2O. At the end of inspiration (C), this pressure is 8 cm H_2O.

Dynamic Compression of the Airways

limits flow rate during a forced expiration.

causes flow to be independent of effort.

may limit flow during normal expiration in some patients with COPD.

is a major factor limiting exercise in COPD.

Early in a forced expiration (D), both intrapleural and alveolar pressures rise greatly. The pressure at some point in the airways increases, but not as much as alveolar pressure because

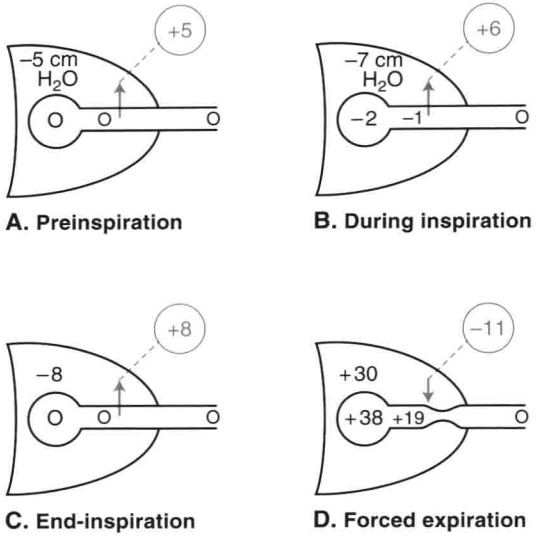


Figure 1-6. Diagram to Explain Dynamic Compression of the Airways during a Forced Expiration (see text for details).

of the pressure drop caused by flow. Under these circumstances, we have a pressure difference of 11 cm H_2O, which tends to *close* the airways. Airway compression occurs, and now flow is determined by the difference between alveolar pressure and the pressure outside the airways at the collapse point (Starling resistor effect). Note that this pressure difference (8 cm H_2O in D) is the static recoil pressure of the lung and it depends only on lung volume and compliance. It is *independent* of expiratory effort.

How then can we explain the abnormal patterns in Figure 1-5B? In the patient with chronic bronchitis and emphysema, the low flow rate in relation to lung volume is caused by several factors. There may be thickening of the walls of the airways and excessive secretions in the lumen because of bronchitis; both increase the flow resistance. The number of small airways may be reduced because of destruction of lung tissue. Also, the patient may have a reduced static recoil pressure (even though lung volume is greatly increased) because of breakdown of elastic alveolar walls. Finally, the normal support offered to the airways by the traction of the surrounding parenchyma is probably impaired because of loss of alveolar walls, and the airways therefore collapse more easily than they should. These factors are considered in more detail in Chapter 4.

The patient with interstitial fibrosis has normal (or high) flow rates in relation to lung volume because the lung static recoil pressures are high and the caliber of the airways may be normal (or even increased) at a given lung volume. However, because of the greatly reduced compliance of the lung, volumes are very small, and absolute flow rates are therefore reduced. These changes are further discussed in Chapter 5.

This analysis shows that Figure 1-4 is a considerable oversimplification and that the forced expiratory volume, which seems so straightforward at first, is affected both by the airways and by the lung parenchyma. Thus, the terms "obstructive" and "restrictive" conceal a good deal of pathophysiology.

Partitioning of Flow Resistance from the Flow-Volume Curve

When the airways collapse during a forced expiration, the flow rate is determined by the resistance of the airways up to the point of collapse (Figure 1-7). Beyond this point, the