REFRESHER COURSE FOR TEACHING RESPIRATORY PHYSIOLOGY

This report presents highlights of a refresher course presented at Experimental Biology '97 on Sunday, April 6, 1997, in New Orleans, Louisiana.

The teaching of respiratory physiology was the focus of the 1997 refresher course at EB '97. Organizer Stephen DiCarlo (Northeastern Ohio University) issued a “call for papers” that resulted in responses from 14 poster presenters. Their posters and accompanying demonstrations formed the backdrop for the formal remarks made by three invited speakers.

Poster presentations were, for the most part, demonstrations of computer-assisted instruction in respiratory physiology. Computer animations, simulations, and customization techniques were on display. They addressed the teaching of acid-base physiology, the chemical and neural control of respiration, ventilation/perfusion relationships, and the use of multimedia resources to create customized lecture presentations. A new text on the physiology of respiration and the use of small groups to solve respiratory problems were featured in two of the exhibits.

The poster session portion of the refresher course exposed viewers to the use of instructional programs in presenting respiratory physiology. The omnipresence of computers in the exhibit area led to spirited discussions on the use of computers in the classroom and laboratory. Refresher course participants could be overheard speculating on the effectiveness of computer-assisted instruction relative to more traditional teaching modes.

After the 1.5-hour poster session, organizer DiCarlo invited all present to hear presentations by Harold Modell, Jay Farber, and Michael Maron. Harold Modell (National Resource for Computers in Life Science Education, Seattle, WA) noted that helping students to learn has replaced his goal of helping us to teach. He reminded the audience of students’ problems with the interpretation of language and with the extensive use of symbols and notation. He also noted that the student perspective on learning is influenced by preexisting models and by prior learning. Modell recommended active learning that engages the instructor in a dialogue with students. He suggested that as physiologists we act more as facilitators by motivating students and providing resources and less as teachers who see their function as the delivery of content.

Jay Farber (University of Oklahoma Health Science Center) asserted that clinically relevant issues can be used to teach the control of breathing. He presented a series of slides that illustrated pacemaker neuronal activity by describing disordered function in perinatal asphyxiation. He indicated that coughing could be used to teach the normal function of tracheobronchial tree receptors. Finally, he demonstrated the usefulness of a discussion of chronic obstructive pulmonary disease to illustrate the effects of CO₂ retention and chemoreceptor activity.

Michael Maron (Northeastern Ohio University) related basic concepts in pulmonary mechanics to clinical situations. He considered the factors that determine total lung capacity, functional residual capacity, and residual volume and related changes in these three volumes to emphysema and pulmonary fibrosis. Maron’s presentation included a demonstration of his development of pressure-volume relationships in class.

Lively discussion followed the three presentations; it reinforced the need for more such interactions dealing with process and content. Marsha Matyas (APS Education Officer) developed a feedback form that was made available to all refresher course participants. Responses indicated that participants came largely from medical school, college, and university faculties (93%) and that respiratory physiology was not necessarily the primary field of the participants (63%). There was general satisfaction with both the
format and the content of the refresher course. Given the number of participants, the positive reaction to the program, and the many suggestions for future APS refresher courses, the APS Education Committee is convinced of the merits of continuing the tradition of refresher courses at EB meetings.

A final note, perhaps the most challenging aspect of this year’s refresher course (confirmed by the experience of Steve DiCarlo) was meeting the hardware needs of the many poster presentations that depended on computers. Steve was faced with an early morning deadline for being “up and running.” He rose to the occasion and managed to coordinate a successful poster session. Kudos Steve!

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ABSTRACTS OF POSTERS AND DEMONSTRATIONS

Interactive computer simulations for teaching basic concepts in respiratory physiology
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Over the years, we have become aware that classes are not the same as they once were. Class size continues to grow, students are unaware of fundamental concepts of math, physics, and chemistry, and many students lack the zeal or inspiration to “put their noses to the grindstone.” To compensate, we continually adjust our teaching strategies to meet these changing conditions.

Presenting information in a lecture format in a large amphitheater has come under fire as being archaic and inefficient. Some universities have started to replace lectures with other learning techniques, such as problem-based learning (PBL). This or other formats may work well in some settings as a replacement for lectures, but in others it can be a scheduling nightmare. We favor a combination of teaching methods, rather than supplanting one with another. At the University of Puerto Rico, we are reducing the number of formal lectures, replacing those hours with other activities, such as PBL, small group discussions of case studies, computer-simulation labs, etc. To this end, we have developed a series of interactive computer simulations that can be integrated into lectures, used in computer labs, or used by students as a study aid.

Our intent when designing these programs was to present concepts that, in our experience, are poorly understood by students. Although these models produce results that are reasonable, we avoided the inclusion of complex interactions among several variables. To do so would have produced more accurate results, but would promote confusion among students. We also felt strongly that these programs be interactive. That is, that the user be able to alter conditions and observe their effects. An interactive approach is also necessary if these programs are to be used as an aid to lectures. Finally, we decided that all of the programs will present information graphically to familiarize our students in the art of extracting information from line graphs.

Whenever possible, we begin a series of programs with a model that presents a concept using a physical or chemical analog, or at least, begins with a simple representation of a physiological system, building to more complex arrangements of variables. For example, students are uncomfortable with pressure-flow relationships. To introduce them to the work of breathing, we begin with a block sitting on the floor. This block is also attached to the wall with a spring. With this analog, we can discuss compliance and resistance (friction) and develop the principle of hysteresis before moving on to airway resistance and lung elasticity. The acid-base series begins with a titration program demonstrating the influence of pK and [buffer] on buffer power. The next program walks students through the construction of the Davenport diagram (or Siggaard-Andersen) before they move on to acid-base disturbances.

The following is a list of the currently available modules:

- Work of Breathing and Ventilation
  - Work using a block and spring
  - Work of breathing and optimal breathing frequency
  - Ventilation using a syringe pump
- Blood Gas Transport
  - Oxygen dissociation and Bohr effect
  - Oxygen transport
Carbon dioxide equilibrium and Haldane effect
Carbon dioxide transport
Acid-Base Programs
Buffer titration
Constructing the Davenport diagram
Acid-base disturbances
Acid-base self test
CSF and plasma disturbances
Pulmonary Shunts and V/Q Inequalities
In vitro blood mixing program
V/Q inequalities
Pulmonary shunts

As educators, we try to create an atmosphere that will excite and challenge students, and promote active participation by the students in the learning process. However, regardless of the format that is used to transmit information, the ultimate responsibility for acquiring and retaining that material lies with the students. The old adage “you can lead a horse to water, but you can’t make it drink” seems especially relevant here.

Computers improved my communication with students (and it’s fun)
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Introduction of computer interactive/educational programs has produced an increase in both quantity and quality of content of a graduate level nursing course I teach. For background, this course covers basic and advanced topics in cellular, autonomic, cardiovascular, renal, respiratory, acid-base, endocrine, and reproductive physiology. We (the students and I) conduct the class in discussion format. While a text is required to provide a framework of basic concepts, much of the didactic material is presented using computer instructional programs, including CD-ROM dynamic animations of physiological processes. Multiple copies of all computer programs are provided for the students to review on computers available to them. This report is a brief description of some of the respiratory computer materials used.

We all know a basic for teaching physiology is the use of appropriately detailed anatomical structures as a framework for understanding functional association of organ systems. To meet this need in a uniform manner and at the professional level required for this course, I use human anatomical material as formatted on CD-ROM (I use A.D.A.M. Comprehensive, but other products are available). An important feature of this software is that it contains a programmable tool (A.D.A.M. Studio) that has enabled me to integrate my lecture notes and other digital material with A.D.A.M., anatomical figures into customized multimedia presentations. Presentations are saved as “books” located on a virtual image “bookshelf” within the A.D.A.M. Comprehensive program. A short demonstration of this material, as it pertains to respiration, is planned at the EB ’97 refresher course. Recently the ADAM software company released an animated CD-ROM on respiration and a demonstration of this software is possible.

The use of a second computer program, (SimBioSys Physiology Lab) helps to meet another need in the teaching of physiology. This need is the training experience for each student that leads to comprehension of how cardiovascular, respiratory, and renal responses are integrated during normal conditions, disease states, and following medicinal interventions. Traditionally (before use of computer simulations), this training experience required laboratory procedures with the use of animals. These laboratory experiences, while useful, are expensive in both time and money and appear to many to be distasteful. With the use of computer-based, “SimBioSys Physiology Lab” I have designed class room ‘dry labs’ with dynamic simulations that I feel avoid the negative aspects of an animal laboratory yet, provide valuable training experience for the student. A short demonstration of one of these “dry labs,” with focus on respiratory and cardiovascular responses, is also planned.

As time and interest permit, other computer animations and clinical cases used in this course can also be demonstrated. So far, it appears that the use of multimedia presentations has not only improved transmission of information but has also provided a more enjoyable experience for the students (and me) than was found with the more traditional methods (lectures, slides, handouts, etc.) I previously used.
A visual model for understanding ventilation/perfusion relationships
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In an attempt to accommodate the various learning styles of students at the University of New England College of Osteopathic Medicine, I have developed a visual scheme to supplement the teaching of ventilation/perfusion relationships to students taking the second-year “Respiratory System” course. For some students, the concept of the ventilation/perfusion ratio and the effect that V\textsubscript{A}/Q mismatching has on pulmonary gas exchange has remained an unfathomable mystery even after my best attempts to explain it. An approach that has proved useful to students who are primarily visual learners is the incorporation of a visual “sliding rectangles” model describing the ventilation/perfusion relationship into my classroom presentations. This model is presented at the start of a 10-hour sequence of Respiratory Physiology and Pathophysiology that takes place at the beginning of the Respiratory System course, and is referred to repeatedly as the concepts of ventilation, perfusion, and gas exchange are developed.

Two rectangles are used in this model, one on top representing ventilation, the other below it representing perfusion. The Introduction to the Respiratory Physiology sequence begins with the two boxes perfectly aligned, indicating the “ideal” situation of perfect matching of ventilation and perfusion. The boxes are then depicted as sliding past one another, so that a portion of the ventilation rectangle is not touching the perfusion rectangle and vice versa. The concepts of “dead space” and “shunt” are introduced at this point and are further developed and expanded upon in later lectures.

The concepts of anatomical and physiological dead space and the effects of dead space ventilation on expired and alveolar gas values are included in the classroom sessions on pulmonary ventilation. The “overhang” representing the dead space is further subdivided into anatomical and alveolar dead spaces, and combinations of these, along with the appropriate equations, are used to show the effects of alveolar dead space on alveolar PO\textsubscript{2} and PCO\textsubscript{2} (and their movement away from the “ideal” point), and the effects of dead space ventilation as a whole on expired gas concentrations.

Similarly, the concept of “shunt” and methods of quantifying anatomical and physiological shunts are included in the lectures on pulmonary blood flow and are again presented using the visual model (subdividing the shunt overhang into anatomical and functional shunts) and applying the appropriate mathematical expressions.

By the time the students get to the classroom sessions devoted to pulmonary gas exchange, the visual model is well established in their minds, and is used to reinforce the reasons for the normal A-a PO\textsubscript{2} difference and the effects of ventilation/perfusion mismatching on alveolar and arterial PO\textsubscript{2} and PCO\textsubscript{2}. The concept of pulmonary diffusion capacity is also brought into the discussion at this point and is related visually to the overlap between the ventilation and perfusion rectangles (available area for diffusion) and the thickness of the line separating the two rectangles (diffusion distance).

After the first 6 hours of using the visual model to supplement the usual presentations regarding ventilation, perfusion, and gas exchange, the students seem well prepared to understand the major causes of low arterial PO\textsubscript{2} (hyperventilation, shunts, V\textsubscript{A}/Q mismatching, diffusion abnormalities, and ambient hypoxia) and to distinguish among these causes using additional information about arterial PCO\textsubscript{2}, the A-a PO\textsubscript{2} difference, and the effects of supplemental oxygen administration.

I have found that such a visual model is definitely not for everyone and is viewed by some students as an unnecessary or complicating addition. But for others,
the “sliding rectangles” concept of ventilation/perfusion matching has made all the difference and has enabled them to grasp this traditionally difficult area of Physiology.

\[ V_{A}/Q \]

Ideal high low dead space

VENTILATION

PERFUSION

shunt

Using multimedia resources to create customized lecture presentations in respiratory physiology
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A complete multimedia textbook of physiology entitled Essentials of Human Physiology: a Multimedia Resource has been developed by faculty members at the Medical College of Georgia. Essentials was written in Multimedia Toolbook (Asymetrix) and designed to run in the Windows (3.1 or 95) environment. It is available on CD-ROM from Visible Productions (Fort Collins, CO). We will demonstrate novel features of the respiration section of Essentials, which contains eight chapters with 335 screen displays, most of which are split between text and illustrations or animations. The respiration section includes 310 illustrations and 26 animations, as well as 118 interactive test questions. An instructor’s resource for Essentials is also available on CD-ROM, which contains full screen displays of all the illustrations and animations without textual material. The instructor’s resource was designed for use in the classroom with the aid of television monitors or computer projection equipment. We will demonstrate how figures and animations contained in the instructor’s resource can be selected and easily incorporated into presentation programs such as PowerPoint (Microsoft) for customized classroom presentations. The instructor can annotate the PowerPoint slides and combine illustrations and multimedia aspects of the Essentials with materials obtained from other sources to create personalized lecture presentations that meet unique needs.

“Virtual physiology”: contributions of computer simulations to respiratory education
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Traditionally, animal laboratories have been an integral part of physiology courses, providing students with active participation, exposure to experimental design, and a “hands on” experience. Unfortunately, costs, animal concerns, and increasing demands on faculty time and university resources are causing traditional laboratories to be offered less frequently. Alternatively, computer simulations of physiological systems have been proposed as a substitute for traditional laboratories. These “virtual laboratories” solve many of the problems with traditional laboratories and have the further advantage that students can access the software independently and more physiological parameters can be manipulated. The aim of our presentation will be to describe the design, implementation, and outcome of our experience with incorporating computer simulations into the teaching of respiratory physiology.

Simulations were incorporated into three physiology courses (600–700 medical, dental, nursing, pharmacy, graduate, and undergraduate students). The required laboratories were based on two commercial products: Simbiosys and Virtual Heart. Each laboratory was held in a computer classroom (24 computers), with two or three students (40–60/session) at each computer and six faculty/instructors. Like traditional laboratories, students were provided with specific instructions for each experiment. Currently, two respiratory (mechanics and blood gases) and three cardiovascular laboratories have been developed. Based on attitude questionnaires, students strongly believed that the computer simulation experiments helped them to understand the course material.

GASP: a computer program for teaching about the chemical control of breathing
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GASP is a computer program that helps students to integrate the knowledge that they have about the
chemical control of breathing into a coherent unit. The program works by having the student solve a set of problems about situations that initiate corrective reflex respiratory responses. The student solves each problem by predicting the qualitative changes in the values of 10 variables. The variables are components of breathing (VT, f, VE, and Va), oxygen-related variables (arterial PO2, Hb saturation, and O2 content), and CO2-related variables (PCO2, [HCO3], and pH). Predictions must be made for the three phases of the reaction: the immediate or direct response to the stimulus, the changes produced by the reflex response, and the final steady state. GASP evaluates these entries in three ways: 1) the internal logic of the predictions for each variable over the three time intervals, 2) the conformity of individual predictions to identified respiratory relationships, and 3) the correctness of the predictions about the response to the stimulus situation. Corrective instruction is provided for any errors. It is structured to help the student to develop a method for solving problems that involve physiological systems in general and the respiratory system in particular.

**Learning to solve respiratory problems in a small group, cooperative setting**

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Practicing problem solving can help students to integrate their “textbook” knowledge into useable mental models. We have evolved a format for small group, cooperative problem solving in which faculty model the solutions to problems and facilitate student problem solving. Students receive the problems at the beginning of the session. The instructor often begins by modeling one part of the problem. Then the 20–25 students in each session break up into groups of 4–6 students and attempt to solve the next part of the problem. After each group is done they post their answers on the board. A discussion of all the posted answers ensues, facilitated by the instructor. Another part of the problem may be modeled by the instructor followed by the students again working together in their small groups to solve additional parts of the problem. Student interaction results in appreciable peer teaching. The group work encourages student participation in the problem solving and the discussion because everyone “owns” the answer generated.

We have written problems that deal with: 1) alveolar ventilation, 2) oxygen transport, 3) hypoxia, 4) chronic hypoxemia and hypercapnia, and 5) pulmonary effusion. An example of one of these problems is displayed in the poster.

**Computer-assisted teaching in respiratory physiology**

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As the first step in generating an interactive module for teaching respiratory physiology, I have created a series of 15 programs that cover the key aspects of the topic. They are currently used in a classroom setting, the graphic output being projected on a 10’ × 10’ screen in front of the audience. A handout provides an anchor for the material. The main advantages of the approach are: 1) the possibility of developing complex relationships step by step; 2) the use of animation; and 3) the fact that the programs are stored in the school’s computer network and are always available to students who wish to review or preview the lectures.

**Structure and function of pulmonary pressure-volume relationships**

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This graphical computer program is designed to correlate the gross structural features of the thorax learned in anatomy to the functional performance of the lungs, chest wall, and diaphragm learned while studying the physiology of pulmonary mechanics. The following points are demonstrated for rib cage motion: shortening of external intercostal muscles raises the ribs, the lower ribs rise more than upper ribs, intercostal muscle contraction leaves diaphragm length virtually unchanged; the dome of the diaphragm descends slightly during accessory muscle breathing, accessory muscles increase lung volume without the aid of the diaphragm. With regard to the diaphragm: during contraction, the diaphragm dome travels a great distance; at the peak of expiration, the heart is forced to lie almost horizontally on the diaphragm; when the diaphragm descends, the heart becomes...
vertically oriented; thoracic volume changes are greater when the diaphragm is allowed to move; the diaphragm moves away from lower chest wall (zone of apposition) changing a “potential” space into a real space for lung expansion and the base of the lung moves more than the apex. When both chest wall and diaphragm are in motion the following may be observed: thoracic volume excursions are largest when both diaphragm and accessory muscles contract, the lungs slide along the chest wall, and diaphragm and the lungs normally fill the thoracic cavity. In addition, animated gauges continuously track pressure and volume excursions during the respiratory cycle. Moving bar graphs and pressure-volume plots show diaphragm length and the static compliance of the lungs and thoracic cage while breathing. This DOS-based program requires less than 640Kb RAM, a 80286 or better CPU, and VGA screen capability.

Using clinical correlation to teach cardiopulmonary physiology
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Clinical correlations during basic science courses not only aid students in the assimilation and retention of newly learned information but also help develop clinical problem-solving skills. An ideal clinical correlation would require students to weave together many recently learned basic science principles to diagnose and treat a living patient. The ability to interview and touch a patient with authentic medical problems validates the science and forms a lasting impression.

The specific goals of this clinical correlation in the second semester of the freshman year of medical school are to reinforce previously learned cardiopulmonary physiology and to provide these students with their first exposure to the basic methods of clinical problem solving. A patient with complex cardiopulmonary disease is introduced to the entire class by a clinical faculty member. The patient’s medical history is elicited by the faculty member who encourages the participation of the students and basic science faculty in the process. After obtaining the history, appropriate physical findings are demonstrated and laboratory data are presented. This session lasts approximately 30 minutes. Next, the class is divided into small groups of 12-15 students. Each small group is facilitated by a clinical and basic science faculty member. During these interactive sessions, a patient problem list is developed that consists of all the abnormal symptoms and signs elicited during the large group session. This problem list emphasizes any recently learned cardiopulmonary pathophysiology. Problems are then placed into relevant groups; disease entities, which explain the syndromes, are suggested by the faculty. Finally, treatment strategies, intuitively based on reversing the pathophysiology, are proposed by the students.

The patient currently presented is that of a 38-year-old native American male with 3-year history of depression, drug, tobacco and alcohol abuse, and progressive hypersomnolence who presented to the emergency room in a stuporous condition. A history of recent weight gain, loud snoring, morning headaches, and hypertension was obtained. Pertinent physical exam observed in the emergency room: weight 400 lbs (photo), injected conjunctiva, central cyanosis, distended neck veins, hepatomegaly, severe leg edema, persistently split second heart sound with loud P2 component, parasternal heave, and wheezes on chest auscultation. Pertinent lab data on presentation were: Hct 60%; Na+ 142 meq/l; Cl− 95 meq/l; serum HCO3− 35 meq/l; BUN 35 mg/dl; creatinine 1.4 mg/dl; ABG pH 7.20, Pco2 100, Po2 35 on room air; EKG, right ventricular hypertrophy (shown); spirogram, reversible expiratory airflow obstruction (shown); flow/volume loop, extrathoracic inspiratory airway obstruction (shown); sleep study, frequent, nocturnal, obstructive apneas associated with oxyhemoglobin desaturations and miniarousals (shown).

The specific objectives of the small group are three-fold: 1) to review the following physiological principles: relationship between pressure, flow, and resistance; transmural pressure gradients and upper airway closure; spirometry, flow volume loops, diffusing capacity; control of breathing, arterial chemoreceptors and respiratory drive; acid-base disturbances and compensation; causes of hypoxemia; oxyhemoglobin dissociation curve; hypoxic pulmonary vasoconstriction; Frank Starling relationships; right ventricular failure; EKG interpretation; and renin-angiotensin-aldosterone system; 2) to practice clinical problem
solving by grouping-related problems, e.g. cyanosis, hypoxemia, and erythrocytosis; leg edema, hepatomegaly, and distended neck veins; and 3) to review the following diseases/conditions, what tests are used to diagnose them, and what therapies are useful to reverse the pathophysiology in each: obstructive sleep apnea; obesity-hypoventilation syndrome; asthma and COPD; cor pulmonale; neuropsychiatric effects of chronic hypoxemia and REM sleep deprivation; and the synergistic roles of drug and alcohol abuse.

**Physiology of respiration**
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Physiology of Respiration was written with the student in mind. The purpose in creating this book was to provide students with many of the modern ideas necessary to understand the broad subject of respiratory physiology. The scope of the book is comprehensive yet not overwhelming in the depth in which it covers any one topic. The two authors have diverse teaching and research interests. The book provides up-to-date coverage of almost all major topics in respiratory physiology with a balanced perspective. The emphasis is on underlying physiological mechanisms.

The level of the text is appropriate for medical, dental, nursing, other allied health students, as well as graduate students. In addition, it is useful for scientists and clinicians who wish to review basic information on the respiratory system.

The first eight chapters present the basic concepts of lung structure, lung mechanics, ventilation, pulmonary blood flow, blood gas transport and exchange, as well as acid-base balance. Chapters 9–11 concern the neural and chemical control of the respiratory system. Chapters 12-14 cover some important examples of how the respiratory system works in an integrated manner during stresses such as hypo- and hyperbaric conditions, exercise, and during the in utero and early postnatal periods. Chapter 14 also discusses the important alterations in breathing that occur during sleep. Chapter 15 considers the significant role that cells within the lung have in the synthesis and conversion of many biologically active compounds. Finally, Chapter 16, by surveying comparative respiratory physiology, provides a wide perspective over the material presented in the preceding chapters on human respiratory physiology.

**The Mount Sinai respiratory physiology syllabus**
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About one-third of our first-year medical students seem to learn best by listening to a lecturer and taking notes in a traditional classroom setting, one-third prefer learning in small group seminars where they come prepared to present basic material to their classmates, and the remaining one-third choose to learn on their own by reading or by studying computer programs. Our students are permitted to choose between these three alternatives for most of the material covered during the respiratory section of the physiology course.

For these different approaches to work, there must be no ambiguity in what students are expected to know. For this reason, we provide a detailed syllabus that students can use in preparation for their seminars or lectures and for review. We also provide examples of multiple-choice and essay questions (and answers) that will be asked on examinations.

The physiology syllabus for the respiratory section of the course is 200 pages long. It is divided into five chapters with 76 figures. Each chapter is preceded by a clinical case. The case sets the stage for the basic principles of respiratory physiology that are to follow.

The cases (e.g., asthma, COPD, ARDS, heroin overdose) are discussed in small group problem-based learning sessions (4 or 5 students/group) led by second- and fourth-year medical students. The cases are also discussed in evidence-based medicine sessions that are led by joint faculty from courses running simultaneously with physiology, i.e., histology and epidemiology. Finally, the cases serve as a foundation for small group computer-assisted instruction.

All material contained in the syllabus is covered either in lecture or, alternatively, in a seminar track. About
one-third of the class signs up for the seminar track, which meets regularly in small groups (10 students/group) with the same faculty member throughout the physiology course. The same material is covered in lecture for the rest of the class.

**Computer animations of the CNS respiratory network. A new didactic approach for visualizing cellular and network processes underlying the neural control of breathing in mammals**

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The neural activity underlying respiratory movements in mammals is generated by complex dynamic interactions of cellular and network processes in the brain stem that are difficult to understand. We have developed neurobiologically “realistic” models of the brain stem respiratory network that capture what is currently postulated to be the main features of these dynamic interactions. The models incorporate the essential biophysical properties of the seven main types of respiratory interneurons and their synaptic interactions in the medulla within a network architecture that is consistent with current experimental data. To enhance visualization of the cellular and network dynamics, we have developed methods for animating the model simulations, which allow visualization of neuron activity and interactions in a computer-generated movie format. To produce the animations, we used Mathematica to construct a virtual elastic surface on which the seven different types of interneurons in the network were arrayed. Neuron activity is represented by upward surface motions described by a Gaussian-like function where the amplitude of the motion scales with the instantaneous neuronal spiking frequency. Functional synaptic interactions between neurons (excitatory or inhibitory) are represented as colors (red and blue, respectively) that flow in “synaptic traffic lanes” on the surface from presynaptic to postsynaptic neurons. The color intensities and speed in these lanes change with the strength of synaptic activation, allowing the activation patterns to be visualized dynamically. Changes in excitatory and inhibitory postsynaptic conductances are also separately color encoded, where the color intensity scales with the summated inhibitory or excitatory conductance. These conductance color changes are superimposed on the surface motions, providing a visual correlation of the regulation of neuron activity by synaptic inputs. Images are computed every 30 ms during the rhythmic respiratory cycle (2-to 3-s period) and are compiled as a QuickTime movie/video on a Macintosh computer and include sound generated from the membrane potential of selected neurons. As a didactic tool, these animations rely on the parallel processing capabilities of the observer’s brain to comprehend a number of simultaneous complex dynamic processes that are inherent in neurobiological mechanisms. The animations represent the prototype of a new didactic medium that exploits the evolving audiovisual capabilities of desktop computers.
How can we help students learn respiratory physiology?

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Why should it be necessary to devote a whole morning’s session to teaching respiratory physiology? The general concepts underlying respiratory physiology are not new to students. They have encountered them many times in their lives in a variety of contexts. They encounter and have experience with elastic structures throughout their childhood, from using pacifiers as infants to playing with balloons as children and engaging in sports that use various types of balls (e.g., tennis, soccer, volleyball, basketball, football) to taking advantage of the recoil characteristics of rubber bands. Popular children’s books contain examples of reservoirs, illustrating steady-state mass balance relationships (5). All through their childhood, students encounter examples of pressure-flow relationships; they use garden hoses, blow horns, and squeeze toothpaste from a toothpaste tube. They also encounter numerous examples of control systems, and they learn about diffusion and chemical interactions long before they arrive in our classrooms.

In fact, students are often first introduced formally to ideas related specifically to respiratory physiology as early as the first grade. Figure 1 shows the report of a first-grade student whose classroom assignment was to tell what the class learned about the day before. The report indicates that the previous day’s discussion included aspects of pulmonary anatomy, gas exchange, and pulmonary mechanics. So students are well on their way toward developing a knowledge base in respiratory physiology at a very young age.

When students finally arrive in our classrooms, we have aids to help them organize their knowledge base into functional models of the respiratory system. In 1962, Comroe and his colleagues (1) presented simple pictorial representations of models of gas exchange and mechanics that were very helpful in conceptualizing the principles and relationships involved in respiratory physiology. These illustrations, examples of which are shown in Fig. 2, were so helpful that they are still used, some 35 years later, as the templates for many illustrations in current texts.

Despite all this prior knowledge and the clarity of our models, students have a very difficult time translating what we tell them into functional models that they can use for solving problems related to the respiratory system. Obviously we are doing something wrong when we teach respiratory physiology, or we are not doing something that we should be doing.

Why should we devote a session to teaching respiratory physiology? The answer is clear. Many students still seem to have more difficulty understanding the physiology of the respiratory system than they do any of the other organ systems, and until this situation is remedied, we must examine why our attempts to help students learn fall short of reaching our educational goals. In this communication, I would like to raise some relevant issues that, I suspect, some faculty may have reflected upon, but that most faculty have not yet considered regarding how we talk about respiratory physiology and how we approach the classroom.

The title of this presentation is “How can we help students learn respiratory physiology?” rather than “How can we best teach respiratory physiology?” In my mind, there is a critical difference between these two questions, and that difference is that, in the first question, the primary focus is on the student and his or her learning. Unfortunately, in most discussions of teaching among physiologists, the focus seems to be more on the presentation of information rather than the specific needs of the students. Let us explore some issues facing students in respiratory physiology, and then, I would like to propose an approach to dealing with these issues.
WHY IS RESPIRATORY PHYSIOLOGY DIFFICULT FOR STUDENTS?

Certainly the difficulties do not arise from the complexities of the underlying concepts. As we have already noted, most of these concepts are not new to students, and they have been able to deal successfully with them in other contexts. But we tend to obscure the familiarity of these concepts by introducing the concepts with an elaborate set of symbols and abbreviations. Upon opening any textbook of respiratory physiology or examining the respiratory section of a general physiology book, one of the first things that the student encounters is an extensive table of symbols and abbreviations. Most of these abbreviations and the conventions governing their use were adopted following a meeting of respiratory physiologists intended to establish standard terminology (4), but they are far from standard for the student who has not only never seen them before, but who, more than likely, just finished cardiovascular physiology, where many of the same words (e.g., blood flow, cardiac output, blood volume) are associated with a different set of symbols.

The problem gets worse for the student because, with the continuing trend toward use of acronyms and abbreviated speech, communication has been reduced to “buzz” words. For example, the student no longer reads about inspiratory and expiratory neurons, words that they can associate directly with an action. Instead, they read about the more abstract “I neurons” and “E neurons.” Furthermore, there are two types of I neurons, “I alpha” and “I beta” neurons. The authors have, of course, defined these terms the first time that they are used. However, when the student reads the text, the label is most likely read as a label rather than a concept (i.e., I neuron rather than inspiratory neuron). In addition, some of these abbreviations resemble different abbreviations used in other contexts. While this is not a source of confusion for the physiologist who is focused on his or her area of expertise, it confuses students who have recently been introduced to other areas of physiology and who, more than likely, have not really mastered any of them. For example, the student may wonder how these “I alpha” neurons relate to the “type Ia” nerve fibers that they were told about when they read about muscle spindles. After all, they are both neurons, and they are designated in the reading with the symbol “I.” At this point, students have several options. If they want to gain an understanding of the topic, they can continually revisit previous pages seeking the first use of the abbreviations, but this can become tedious and distracting as the number of abbreviations increases. Another option is to memorize the relationships involving the abbreviations without attaching any meaning to them. Yet another option is to stop reading altogether and adopt the attitude that, “If I wait until class, the instructor will tell me what I need to memorize to pass the exam.”

Another source of confusion and student stress related to respiration seems to be the quantitation associated with respiratory physiology. We want our students to

FIG. 1.
Report of a first-grade student on health science lesson from the previous day.
Static Relationships

Ventilation-Perfusion Maldistribution

FIG. 2.
Conceptual aids presented by Comroe et al. (1) that have become “standard” in presentations of respiratory physiology. (Reprinted with permission from Ref. 1.)
understand steady-state mass balance relationships. Yet, when we show relationships, we present equations without presenting the underlying concept (that is, in the steady state, the amount of mass entering a “compartment” per minute must equal the amount of mass leaving the compartment per minute). Furthermore, we show more abbreviations and symbols that lead to memorization and confusion rather than understanding. The mass balance equations applied to alveolar and mixed expired gas deal with the same concept, only the location of the “compartment” is different. However, the student interprets the different subscripts indicating the different compartments as constituting two very different sets of equations.

The first step to helping students understand respiratory physiology, then, is to explain the mechanisms in “everyday” English. In this way, students can draw on their previous understanding and vocabulary to build their mental models of the system in their own set of words. Having established an understanding in their own frame of reference, it is a small step to introduce our labels and jargon. However, most faculty will report that they are explaining mechanisms using everyday language and common analogies. For example, many faculty use balloons when they talk about elastic structures. Faculty will also report that taking this first step doesn’t remedy the apparent problems the students have understanding the simplest of concepts. Hence, while potentially helpful, minimizing jargon and trying to relate the physiology to the students’ previous knowledge and mental models do not solve the problem. So, what is the answer?

To solve the problem, we must gain a better understanding of the problem. To do this, we must have a better understanding of our students. Our students come to us with varied backgrounds and various levels of understanding. Some of this understanding is based on appropriate models of the system, but some is based on inappropriate models of the system. If we start with the first grader’s report shown in Fig. 1, we can see how the seeds of inappropriate models, that is, misconceptions, may be sown. The student said that she learned that, if you squeeze a sponge, all the water will come out and if you don’t squeeze a sponge, it will fill with water just like the lungs. Does this mean that when we breathe, we first force out gas, that is, squeeze the sponge, and then relax, don’t squeeze the sponge, to draw air into the system?

The first grade student also remembered that you breathe out corvidoxi. Later on in this young person’s education, she received clarification of this. She was taught that we eliminate carbon dioxide through the lungs. If we eliminate it, how can there still be carbon dioxide left in arterial blood? It has been eliminated, it’s gone!

The student was also taught that oxygen is delivered to the tissues by arterial blood. If the blood picks up the oxygen in the lungs and delivers it to the tissues, there must not be any oxygen left in venous blood.

**WHAT’S IN A WORD?**

Students learn that blood participates in gas exchange. “Exchange” is an essential word in the respiratory physiologist’s vocabulary. What does the word, exchange, mean to the student? The dictionary definition of “exchange” is to transfer one thing for another thing in return. We exchange currency, receiving an equivalent valued foreign currency for US currency. We exchange sweaters at the store, receiving a blue sweater in exchange for a green sweater or a large sweater in exchange for a medium sweater.

What model emerges from the use of the word “exchange”? We continually encounter students who, even after transport mechanisms involving hemoglobin have been discussed, believe that oxygen and carbon dioxide compete for the same binding site. Hemoglobin “exchanges” oxygen for carbon dioxide. Obviously this must involve the same carrying site. We continually encounter students who, even after discussing the gas exchange process, believe that if alveolar PO2 increases, alveolar PCO2 must decrease regardless of the mechanism by which the PO2 change came about. Ask these students what happens to alveolar PCO2 if the inspired gas is switched from room air to 100% oxygen. They will tell you that PCO2 decreases because “exchange” implies a coupling, and if something is exchanged for something else, they must move in opposite directions. So if oxygen goes up, carbon dioxide must go down.
AN EXPERIMENT

Consider another example. Show students (or colleagues, for that matter) a rubber tie-down strap, easily purchased at a home improvement or auto supply store, and a length of waistband (e.g., as found in underwear) material purchased from a fabric store. Ask which item is more elastic. The answer that is offered depends on interpretation of the word elastic. Is something that is “more elastic” more “stretchable” or less “stretchable”? According to the physicist, something that is elastic exhibits recoil. The more elastic something is, the more recoil it exhibits. The rubber strap is more elastic. However, according to the clerk at the fabric store, and according to most students (and some colleagues), something that is elastic is stretchable, and the more elastic something is, the easier it is to stretch. The waistband material is more elastic. Is it any wonder that students have a difficult time with respiratory mechanics?

All of these examples have, to one extent or another, depended on interpretation of language. They illustrate why it is important to choose language carefully and why it is critical that we interact with students to make sure that their interpretation of our language is the same as our interpretation.

OTHER SOURCES OF INAPPROPRIATE MENTAL MODELS

Are there other sources of potential misconceptions that students encounter before they come to our classrooms? The answer is, “Of course!” and the inappropriate models that they form are reinforced in their everyday lives. Figure 3 shows an excerpt from an article that appeared recently in The Seattle Times (3). The article clearly tells the reader that lung tissue is very elastic (easily stretched or exhibiting considerable recoil?) and that it stiffens as a result of emphysema (more recoil?). The article goes on to tell the reader that lung-reduction surgery allows the remaining lung to expand more, increasing its elasticity, but increased elasticity means increased recoil. What impact do this and other descriptions of physiological relationships encountered in the media have on the mental models that our students bring to our classrooms?

Before students arrive in our classrooms, they have formed very definite ideas about how the respiratory system works. They have formed these ideas from experiences in school, from exposure to information in the media, from experiences with friends and family, and from interpretation of language in all of these settings. Some of these models are appropriate, many are not. When students arrive in our classrooms, few of us recognize that these preexisting models exist, or we ignore them and assume that by telling students about the way things really are, they will correct their models.

How good is the assumption that students will correct their faulty models as a result of faculty lectures and course exams? Diane Halpern, chair of the Psychology Department at California State University at San Bernardino, addressed this problem in an article that appeared recently in the Chronicle of Higher Education (2). An excerpt from her article follows.

"About 2 million Americans suffer from emphysema, a stiffening and weakening of the lungs resulting primarily from smoking.

Lung tissue is normally very elastic, and when it stiffens with emphysema, not enough air can be expelled, pushing the diaphragm down in the abdomen and lessening the muscles’ ability to contract.

In the lung-reduction operation, severely damaged tissue is removed. That allows the remaining lung to expand more, increasing its elasticity and freeing up space for the diaphragm to return to its normal position."

FIG. 3.
Excerpt from an article in The Seattle Times reporting on a new study involving radical new lung surgery (3).
they believed that the sun revolved around the earth; an additional 7 per cent said they did not know which revolved around which.

I have no doubt that virtually all of these adults were taught in school that the earth revolves around the sun; they may even have written it on a test. But, in fact, they never altered their incorrect mental models of planetary motion because their everyday observations didn’t support what their teachers told them: People see the sun “moving” across the sky as morning turns into night, and the earth seems stationary while that is happening.

Students can learn the right answers, even recite them in class, and yet never incorporate them into their working models of the world. The objectively correct answer that the professor accepts and the student’s personal understanding of the world can exist simultaneously, each unaffected by the other. Outside of class, the student continues to use the personal model because it has always worked well in that context. Unless professors address specific errors in their students’ naive models of the world, the students are not likely to replace their own models with the correct one promoted by the professor.

I would go a step further than Dr. Halpern and say that, unless we force students to test their models of the world, they will not recognize their errors and will not even attempt to correct them.

**SOLVING THE PROBLEM**

If we want to help students learn respiratory physiology, we must recognize that students have preconceived notions of how the respiratory system works and that many of these notions are based on a teleological view of the world. We must also recognize that the language that we use on an everyday basis may not have the same meaning to students as it does to us. So, how can we meet this challenge? How can we address the specific errors in our students’ naive models of the respiratory system, and how can we address different interpretations of the language that we use?

The answer is that we must transform our classrooms into active learning environments. We must carry on a dialogue with our students. Normally, we wait until a student asks a question, and we answer the question based on our interpretation of the language that they use. But what we hear does not always reflect the student’s intent. We need to seek clarification from us. We need to ask questions, and we need to listen to the students’ answers. The interaction provides us with an opportunity to learn more about the student’s mental model. In this way, we can arrive at a common understanding, and the class, as well as the student asking the question, benefits from the interchange.

For example, I am responsible for the respiratory section of the physiology course that dental students and nursing graduate students take at the University of Washington. Early in the discussion, before we get to the topic of alveolar PCO₂, it is common for a student to ask what happens when we hyperventilate. Before I attempt to answer the question, I ask the student, “What does hyperventilation mean to you?” Last year, the questioning student told me that hyperventilation is when the body needs more oxygen (a teleologic view) and so your ventilation increases (a common, but erroneous interpretation of hyperventilation). This year, a student answered the question by saying that hyperventilation is when you breathe into a bag. By interacting with the student in this way, that is, asking him or her what the words mean to them, I learn more about the student’s misconceptions, and, to some extent, I can begin to address them. This also benefits other students who may hold a similar view or who do not have confidence in their mental models.

In addition to this questioning type of interaction, we must also encourage students to test their mental models. For it is only through this testing process that students can recognize the limitations of their models and correct them. There are many ways that we can do this in the classroom. We can present students with an observation and ask the student to explain what led to the current situation. Many people use clinical cases in this way. We can ask the students to make predictions about how the system will behave if it is perturbed. Another way of uncovering misconceptions is to ask students to explain aspects of familiar phenomena (e.g., exercise, going to altitude).

In each case, we, as facilitators of learning, must carry on a dialogue with students, we must listen to what our students are saying, and we must seek clarification so that we can better understand their needs with respect to learning. We are faced with a formidable challenge, and if we expect to help students learn
respiratory physiology, or anything else for that matter, we must recognize that they have prior knowledge, that this prior knowledge may be faulty, and that communication is often limited by the language that we use. We must also learn from our students. We must learn how they interpret our language. We must learn about their mental models and how they apply them. In short, to help students learn, we must learn more about what kind of help they need. The only way we can do this is to carry on a dialogue with them.

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When teaching control of breathing we have traditionally considered three aspects: 1) how the breathing pattern is generated by the brain, 2) how reflexes from the lungs influence breathing pattern, and 3) how stimulation of chemoreceptors increases ventilation. Within each of these areas there is the opportunity to bring relatively new ideas from both clinical and basic science and use them to add clinical relevance and better insight into physiological mechanisms. For the present discussion, we will use responses to perinatal asphyxiation to show that pacemaker neurons in the medulla may participate in the formation of breathing patterns. The common event of coughing will illustrate the function of receptors in the airways and larynx, and chronic obstructive lung disease will provide a “real world” context for the function of chemoreceptors. These explanations are appropriate for first-year medical students.

A refresher course for teaching respiration should include ways to teach material that is well established in medical school teaching programs. It should also reexamine what we teach, as well as the examples we use for illustration, on the basis of lessons learned from clinical and basic research. Most medical physiology courses include the following three topics in control of breathing: how the breathing pattern is generated by the brain, how reflexes from the lungs influence breathing pattern, and how stimulation of chemoreceptors increases ventilation. Updates are proposed here for each of these three topics. The first update considers the idea that pacemaker neurons in the medulla contribute to the expression of breathing pattern. The illustrative example is the gasping breaths that occur during perinatal asphyxiation. The second update considers the reflex responses we use to teach about the function of airway receptors. Currently, the Hering-Breuer reflexes are most often characterized, but they do not represent the most prominent consequences of airway receptor activation in adults. Instead, a discussion of coughing allows consideration of receptor activation in the tracheobronchial tree and larynx within a context that can be readily appreciated by most students. The third update advocates expanding what we teach about the relationship between chemoreceptor stimulation of breathing and ventilatory response. We have typically ignored important clinical circumstances whereby stimulation of chemoreceptors does not result in the expected increase in breathing. An illustrative case is chronic obstructive lung disease with CO₂ retention.

FORMATION OF BREATHING PATTERN BY THE CENTRAL NERVOUS SYSTEM

A major issue confronting the instructor is how deeply to pursue the cellular and network mechanisms underlying the respiratory cycle. One solution is to present the respiratory cycle in broad overview, considering arrays of brain stem neurons associated with inspiration and expiration. Such a model, adapted from more detailed presentations (2, 9), is shown in Fig. 1, where selected neuronal activities at the beginning, during, and at the termination of inspiration (Fig. 1, top left, steps a-c) and expiration (Fig. 1, top right, steps d-f) are correlated with motor events of breathing (Fig. 1, bottom, steps a-f). This model emphasizes that at the beginning of inspiration several different types of neurons become active (step a). At the beginning of expiration, inhibition affects several (but not all) respiratory neuronal populations (step d). The model also shows a rapid withdrawal of neuronal excitation to the diaphragm at the end of inspiration (step c) and a similar withdrawal of excitation to major expiratory muscles at the end of expiration (step f). Activation of expiratory muscles occurs during exercise or when airway resistance is
increased. This is noted in Fig. 1 (bottom right) as "load," but expiration is passive at rest.

The actual neuronal events that cause transitions between inspiratory and expiratory phases are controversial. Groups of inhibitory interneurons acting as inspiration and expiration off switches may play a role. Membrane properties of excitability, including spike frequency adaptation and postinhibitory rebound, could also help induce phase transitions. A recent idea is that medullary neurons with pacemaker properties may participate in the transition from expiration to the next inspiration (13). Pacemaker neurons spontaneously depolarize at regular intervals, producing bursts of action potentials. Such events do not require periodic inhibition of the cell. Numbers of spontaneous depolarizations over time vary with resting membrane potential, with a less polarized cell having more spontaneous depolarizations and a more polarized cell having fewer spontaneous depolarizations (13). Pacemaker events most likely produce gasping in the asphyxiated neonatal brain stem. This extreme, but clinically relevant case, can be used to introduce the idea of neural pacemakers to students.

Perinatal asphyxiation can result from a number of causes, including an upper airway defect, obstruction of the nose (babies are obligate nose breathers), and episodes of apnea, especially in premature infants. The respiratory response to asphyxiation is typically characterized by increasing respiratory efforts, but this is followed by cessation of breathing (apnea). After an interval of apnea, breaths of a gasping nature (short but forceful inspiratory efforts) occur for a period of time. Because these breaths might be useful to reestablish an airway or to terminate a prolonged apneic episode, some investigators have used the term autoresuscitation to describe their occurrence (4, 10, 14). Autoresuscitation has been considered as a mechanism for protection against sudden infant death syndrome. Gasping breaths are also significant in a clinical setting because they warn the neonatologist that strong intervention is required.

The circumstances that induce autoresuscitation in the neonate are comparable in several respects to the experimental conditions for in vitro experiments using superfused rodent brain stems, where pacemaker activity clearly drives respiratory output. For in vitro studies, the brain stem is considered to be in a functionally reduced state because neuronal connections are lacking to other brain regions and the periphery. Furthermore, some of the brain tissue is...
hypoxemic. Raising extracellular $K^+$ concentration helps bring out pacemaker activity because of neuronal asphyxiation. Events during progressive neonatal asphyxiation at the gross behavioral and cellular levels are illustrated in Fig. 2. On the left from the top down are successive behavioral events during asphyxiation, including stimulation of breathing and apnea that is accompanied first by increased motor activity and then by collapse of motor activity. After the collapse of motor activity, gasping begins (7). As with the in vitro preparation, the asphyxiated brain stem in vivo is now in a functionally reduced state (7). At the cellular level (Fig. 2, events on the right from the top down), apnea is associated with suppression of rhythmic discharge of neurons producing the respiratory output. As tissue hypoxemia continues, there is a rise in extracellular $K^+$ concentration ($[K^+]_o$) (15) that contributes to neuronal depolarization (5). Depolarization of pacemaker neurons is expected to bring out pacemaker-driven breathing. Effects of hypoxia on neuronal depolarization and especially $[K^+]_o$ around selected brain stem neurons are substantially less in the newborn than the adult (5). This may help explain the ability of newborns to take gasping breaths for a prolonged period of time, thereby making autoresuscitation more effective (14).

When teaching medical students, the preceding rationale can be replaced by an example showing the occurrence of autoresuscitation in a neonatal animal
(Fig. 3). The potential role of pacemakers during normal breathing and gasping can then be discussed. To integrate this example with other course material, students can be reminded of the occurrence of cellular pacemakers with respect to cardiac rhythmicity. Also, the depolarization of neurons due to increased extracellular $K^+$ can be predicted using the Nernst equation.

**REFLEXES FROM THE LUNGS AND UPPER AIRWAY**

The rate and depth of breathing are weakly influenced by vagally mediated pulmonary reflexes in healthy persons (3). Nonetheless, we teach about the consequences of airway receptor activation using Hering-Breuer inspiratory and expiratory reflexes. These reflexes are more potent in infants (3), but illustrating the effects of pulmonary receptor activation with respect to a very familiar event, namely cough, is more interesting and more relevant for medical students. Coughing moves secretions from smaller to larger airways and also helps prevent aspiration of material into the lungs. Stimulating receptors in either the tracheobronchial tree or larynx can provoke cough.

Cough elicited from the tracheobronchial tree involves slowly and rapidly adapting airway receptors, as well as unmyelinated free nerve endings (11). All have afferents in the vagus nerves and can be characterized conventionally in terms of their responses to lung inflation, as illustrated in Fig. 4. The receptors with myelinated afferents have either slowly or rapidly adapting responses to lung inflation, but unmyelinated endings have weak and inconsistent responses to changes in lung volume. Figure 5, left, shows typical endogenous and exogenous stimuli for tracheobronchial cough (11). The exogenous examples of water and sulfur dioxide, which could be aspirated or inhaled, have been characterized by their instillation into the tracheobronchial tree and are known to elicit cough. The contributions of the specific receptor types to cough are listed in Fig. 5, right. Slowly adapting airway receptor discharge is minimally affected by substances that elicit cough, but blockade of these receptors in the single species where such a block can be performed (rabbit), prevents coughing. For that reason, the slowly adapting airway receptors are said to exert a permissive effect on cough or facilitate cough (11).

Cough can also be stimulated from the larynx by irritant receptors that respond to water in the larynx and by unmyelinated free nerve endings that respond to other potential irritants (11). Figure 6 summarizes familiar stimuli and their responses. Most people have coughed when water has reached the larynx. Anybody roasting hot peppers, in Chinese or Mexican cooking, has had the experience of coughing as vaporized capsaicin is inhaled. The latter can be blocked by anesthetizing the larynx, presumably through blockade of unmyelinated free nerve endings (11).

Once the subject of cough is introduced, it can be used to illustrate an important principle in respiratory system mechanics. Figure 7 summarizes neuromuscular and mechanical events of a cough (11). The feature of particular interest for teaching basic pulmonary physiology is that dynamic compression of the airways is induced because pleural space and alveolar pressures are forced to increase during the period of glottis closure before expiratory airflow occurs (8, 11). High flow velocities due to airway compression may then assist in moving material toward larger airways.
RELATIONSHIP OF CHEMORECEPTOR STIMULATION TO VENTILATION

Chemoreceptor function is usually taught in the context of how blood gases stimulate breathing, but chemoreception is also important in a common clinical circumstance where increased stimulus to breathe does not result in increased ventilation. This occurs in chronic obstructive pulmonary disease (COPD). Patients with COPD have arterial hypoxemia (reduced arterial \( P_{O_2} \)). Importantly, some of these patients also have elevated levels of arterial \( P_{CO_2} \), indicating that hypoventilation or \( CO_2 \) retention is occurring. That is, alveolar ventilation is insufficient to eliminate resting metabolic \( CO_2 \) production at normal arterial \( P_{CO_2} \) values.

We teach that peripheral arterial chemoreceptors, particularly the carotid bodies, respond mostly to decreases in arterial \( P_{O_2} \) but also to elevations in \( P_{CO_2} \) and acidity. When stimulated, the arterial chemoreceptors can be shown to elicit an increase in breathing. Chemoreceptors in the medulla respond to elevations in blood \( CO_2 \) levels, presumably through acidification of brain interstitial fluid, leading to an increase in breathing. Students could conclude that failure to increase breathing with COPD is due to a defect in stimulation of chemoreceptors. The more typical situation, however, is that in patients with COPD and \( CO_2 \) retention the drive to breathe is usually greater than for normal individuals at rest (1, 12).

To understand how chronically elevated arterial \( P_{CO_2} \) affects both receptors and motor output, we compare respiratory stimulus and response in a normal individual when \( CO_2 \) is acutely inhaled and then after \( CO_2 \) has remained elevated for a period of time (Fig. 8). All four panels in Fig. 8 show effects of \( CO_2 \) inhalation compared with normal resting conditions (horizontal arrows). Figure 8, top, shows strong stimulation of medullary chemoreceptors along with a smaller stimulation of arterial chemoreceptors with acute inhalation of \( CO_2 \) (left columns; open plus signs).
Figure 8, bottom, shows a large increase in pulmonary ventilation, but arterial PCO₂ remains elevated because CO₂ is in the inspired air (left columns; open symbols). With chronic CO₂ inhalation, increases in HCO₃⁻ result in an increase in blood pH when compared with acute values. We will assume that increases in HCO₃⁻ of brain interstitial fluid (6) likewise increases pH in the region of chemoreceptors with respect to acute

**FIG. 5.**
Summary of stimuli and receptor responses that elicit tracheobronchial cough.

**FIG. 6.**
Summary of stimuli and receptor responses that elicit laryngeal cough.
conditions. As shown in Fig. 8, top (filled plus signs), stimulation of medullary and arterial chemoreceptors becomes less; this leads to loss of a ventilatory response and a further rise in arterial Pco₂ (Fig. 8, bottom; filled symbols).

The condition of chronically elevated Pco₂ represents the starting point for a patient with COPD breathing air (Fig. 9). Figure 9, top left (open plus signs), shows reduced stimulus to medullary chemoreceptors because of elevated brain interstitial fluid HCO₃⁻ levels.

**A Larger than normal inspiration is taken**

**The glottis closes briefly while expiratory muscles begin to contract**

**Pressure in the lungs rises**

**Glottis opens and air is rapidly expired**

**High pressures in the lungs and pleural space produce dynamic compression of airways**

**Where compression occurs, high flow velocity helps to move material towards larger airways**

**FIG. 7.**

Sequence of mechanical and motor events in cough.

**FIG. 8.**

Chemoreceptor stimulation and ventilatory responses to acute versus chronic CO₂ inhalation in normal individuals. For further explanation, see RELATIONSHIP OF CHEMORECEPTOR STIMULATION TO VENTILATION. ISF, interstitial fluid.
and increased pH. Because CO₂ retention in COPD is accompanied by low arterial Po₂ (arterial hypoxemia), arterial chemoreceptors will be stimulated as shown in Fig. 9, top right (open plus signs). Despite this, pulmonary ventilation is not consistently changed from normal values, and alveolar ventilation is actually lower than normal (Fig. 9, bottom left columns; open symbols). Relieving arterial hypoxemia by inhaling increased levels of O₂ will greatly reduce the stimulus to arterial chemoreceptors (Fig. 9, top right, filled plus signs). This reduces pulmonary and alveolar ventilation, causing more CO₂ retention (Fig. 9, bottom, filled plus signs, right columns). Increased levels of CO₂ are expected to provide an additional stimulus to medullary chemoreceptors (Fig. 9, top left, filled plus signs). Most individuals with COPD will hypoventilate when inspired O₂ is elevated, but severe decreases in ventilation occur in only a minority of these patients (1).

The flow chart in Fig. 10 explains how stimuli to breathe are uncoupled from respiratory responses in COPD with CO₂ retention. Starting from the top of the figure, there is stimulation to breathe caused by decreased arterial Po₂ and increased arterial PCO₂ (Fig. 10, plus signs). The former is mainly from regions of the lungs, where ratio of alveolar ventilation to alveolar capillary blood flow, V˙A/Q˙, is low (due to uneven V˙A/Q˙ distribution and hypoventilation) while chronic elevation of CO₂ causes partial adaptation of receptors. The result is increased activity of brain stem respiratory controllers, which, in turn, increases the neural output to respiratory muscles. This output is not successfully converted to airflow because of factors such as 1) lung hyperinflation that causes inspiratory muscles to be on a less efficient portion of their length-tension relationship, 2) respiratory muscles nearing the point of fatigue (12), and 3) increased airway resistance. This means that pulmonary ventila-
tion cannot be increased above resting values (Fig. 10, zero sign). Additionally, Va/Q abnormalities will include poorly perfused regions that act as alveolar dead space. This lowers the effective alveolar ventilation (Fig. 10, minus sign) and causes CO₂ retention.

This example could be used in lecture and/or small group conference settings after basic issues in ventilatory chemostimulation are discussed. A contrast to the preceding situation would be high-altitude exposure in normal individuals, where ventilation is increased as a result of chemoreceptor stimulation.

The issues and examples chosen for this presentation were meant to highlight areas of respiratory control, where newer ideas and their clinical applications can be incorporated into teaching basic physiological concepts. With the time limits typically applied to any section of a physiology course, the instructor must decide on the most effective methods to update course material while allowing students to begin to appreciate the clinical applications that are becoming a dominant feature of National Board exams.

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RELATING BASIC CONCEPTS OF PULMONARY MECHANICS TO CLINICAL SITUATIONS

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How the pressure-volume relationships of the lungs and chest wall interact to determine the compliance characteristics of the respiratory system is perhaps one of the more difficult conceptual areas in pulmonary physiology both to teach and for first-year medical school physiology students to master. An understanding of this material is nevertheless important, because it allows the student to integrate a large number of concepts in pulmonary mechanics that may not seem at first glance to be related. For example, in spirometry, the lung divisions, total lung capacity (TLC), functional residual capacity (FRC), and residual volume (RV) are frequently learned only in descriptive terms; e.g., FRC is the volume of air remaining in the lungs at the end of a normal expiration. An understanding of the pressure-volume characteristics of the respiratory system, however, allows these descriptive definitions to be replaced by more useful functional definitions; e.g., FRC is the lung volume at which the elastic recoils of the lungs and chest wall are equal in magnitude but opposite in direction. The latter has the distinct advantage in that it helps the student to understand why FRC is altered in such diseases as emphysema and pulmonary fibrosis, the clinical utility of determining FRC, and the calamitous consequences of a pneumothorax. An understanding of the compliance characteristics of the lungs is also critical for helping the student to understand why a vertical distribution of ventilation exists in the lungs and how, for example, in unilateral lung disease, arterial Po2 can have substantially different values depending on whether the patient is lying on the left or right side. Accordingly, the objective of this presentation is to provide a framework for teaching this material in a way that allows the student to understand the relationship of basic concepts to the disordered physiology that results from lung disease.

PLACING A DISCUSSION OF COMPLIANCE IN THE OVERALL CONTEXT OF FUNCTION: WORK OF BREATHING

The work required to ventilate the lungs can be divided into two major components, elastic and non-elastic work. Both of these components can be further divided. In this regard, the elastic work component is composed of work that must be done against lung elastic recoil, chest wall recoil, and surface tension. The nonelastic work component is primarily the effort required to overcome airway resistance but also has a small tissue resistance contribution. An understanding of how energy is expended in ventilating the lungs is important, because patients with lung disease may have a larger energy requirement to breathe than individuals with healthy lungs. Importantly, the precise mechanism responsible for the increased work of breathing may differ depending on which subcomponent is affected. For example, the work of breathing is increased in a patient with pulmonary fibrosis because of an abnormal reduction in lung compliance. In a patient with ankylosing spondylitis (a disease in which the vertebral joints and ribs become immobile), the work of breathing may be increased due to a reduction in chest wall compliance. Babies with infant respiratory distress syndrome have to work harder to breathe because of an increase in alveolar surface tension due to a deficiency of pulmonary surfactant. Finally, patients with asthma or bronchitis expend more energy breathing because of an increased airway resistance. These examples thus indicate that an understanding of the various components that contribute to the work of breathing allows the student to appreciate that patients with lung disease may be required to expend more respiratory energy but for very different reasons. In the remainder of this discussion, we will concentrate on developing an understand-
A “Time-Out” For Some Basic Definitions

At this time, it is important to define three of the lung capacities and volumes that are generally considered during a discussion of spirometry. These are TLC, FRC, and RV, and they are defined in Table 1. When introducing these concepts, I find it useful to have the students inhale maximally to TLC, exhale passively to FRC, exhale maximally to RV, and then finally inhale passively to FRC. This allows me to point out that they had to do considerable work in both reaching and maintaining TLC and RV. This sets the stage for a discussion of the factors that require this energy expenditure. I also point out that when they reached FRC (after either exhaling from TLC or inhaling from RV), their lungs automatically stopped at this position and that it takes no conscious work to keep the lungs at this volume. Note that the definitions given in Table 1 are purely descriptive. They give little insight into the functional significance of these capacities and volumes. As the discussion develops, these descriptive definitions will be replaced with functional definitions that have the advantage of allowing the student to understand the significance of measuring TLC, FRC, and RV in health and disease.

DISCUSSION OF COMPLIANCE: FROM SPRINGS AND BELLOWS TO ISOLATED LUNGS TO INTACT LUNGS

Figure 1 (top) shows a simple spring that is progressively being stretched in each succeeding frame by the addition of incremental amounts of weight. This behavior is plotted as a simple graph at the bottom, which shows that as the force (f) on the spring increases, the distance (d) the spring stretches also increases. For a while this relationship is linear, and the slope of this curve (Δd/Δf) is defined as the compliance of the spring. Note that after a critical amount of weight is added, the spring can no longer distend, and the curve becomes flat. At this point, we say that the spring has reached its elastic limit. The addition of further weight may cause the spring to break. This behavior has an analogy in the lung in that, in breath hold divers who do not exhale as they ascend from a dive, the air contained in the lungs expands. If this process continues, alveolar pressure may increase to values that exceed the elastic limits of the alveoli, and barotrauma may result. Finally, Fig. 1, middle, shows the effect of stretching a bellows, a structure that behaves in an analogous fashion to the spring. The compliance characteristics of the bellows are also shown on the graph plotted in Fig. 1. In this case, however, the data are plotted on volume (v)-pressure (p) axes (instead of the distance-force axes used for the spring), and the compliance is given as Δv/Δp. This representation is useful because this structure is more like a lung, i.e., air flows into the bellows as its volume is expanded.

Up to this point, we have discussed the compliance characteristics of a single spring or bellows with a set compliance. It is also possible to examine the pressure-volume characteristics of less compliant (stiffer) and more compliant (looser) springs and bellows (Fig. 2). As shown in Fig. 2, the compliance (Δd/Δf or Δv/Δp) is reduced for the stiff spring or bellows and is increased for the loose spring or bellows. In other words, it is harder to both stretch a stiff spring and to inflate a stiff bellows than it is to cause the same changes in normal springs or bellows.

It is also possible to measure the compliance of isolated lungs. An experimental setup for doing so is shown in Fig. 3, which depicts an isolated lung in a bell jar. The pressure surrounding the lung (pleural pressure) can be reduced in a step fashion by pumping air out of the jar. This causes the lung to inflate. In the figure, the volume of air entering the lungs is measured by a spirometer. The results of this maneuver are plotted on the graph at right and show the pressure-volume relationships of the lungs. Note that the inflation and deflation curves do not follow the

<table>
<thead>
<tr>
<th>Capacity or Volume</th>
<th>Definition</th>
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<tbody>
<tr>
<td>TLC</td>
<td>Volume of air contained in the lungs after a maximal inspiration</td>
</tr>
<tr>
<td>FRC</td>
<td>Volume of air remaining in the lungs after a normal passive expiration</td>
</tr>
<tr>
<td>RV</td>
<td>Volume of air remaining in the lungs after a maximal expiration</td>
</tr>
</tbody>
</table>

TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume.
same path. This is called “hysteresis” and is related to the presence of surface tension on the alveolar epithelial surfaces, because the degree of hysteresis is markedly reduced when the contribution of surface tension is eliminated by inflating the lungs with saline instead of air. For simplicity, a deflation compliance curve is shown in Fig. 4. This curve indicates that the lung exhibits nonlinear compliance characteristics. At low lung volumes, the compliance is high (i.e., a given change in pressure results in a relatively large change in volume), and at higher lung volumes, the compliance is reduced (i.e., the same change in pressure results in a smaller change in volume).

Another “Time-Out” For Some Basic Definitions

An often confusing aspect of understanding compliance is the term that is used to describe the pressure axis of the pressure-volume curve. In various text figures, the reader may see this axis labeled as “pressure surrounding the lung,” “pleural pressure,” “transpulmonary pressure,” or “elastic recoil pressure.” The first two of these terms are synonymous, i.e., pleural pressure is the pressure surrounding the lung. Likewise, under static conditions, transpulmonary pressure is synonymous with the term elastic recoil pressure. Pleural pressure and transpulmonary pres-
sure are two very different pressures, however. Pleural pressure is the pressure on the outside of the lung and during normal breathing is a negative (subatmospheric) value. The transpulmonary pressure, however, is a “transmural pressure,” i.e., the difference in pressure between the inside and outside of the lungs, and by convention is always positive. While we are breathing (when air is either flowing in or out of the lung), the two pressures are not the same, as shown in Fig. 5. If this is true, how can these terms be used interchangeably on the x-axis of the pressure-volume curve? The answer to this question is that they cannot, except under one unique set of conditions: when there is no airflow in or out of the lungs. Under these conditions, the pleural and transpulmonary pressures are equal in magnitude but opposite in sign (Fig. 5). Thus, when compliance is measured under conditions of zero airflow (i.e., “static conditions”), either measure of pressure may be used.

**BACK TO COMPLIANCE OF THE LUNGS:**

**MEASUREMENT OF COMPLIANCE IN THE INTACT LUNG WITHIN THE CHEST**

It is also possible to measure the compliance of the lungs in people. As with isolated lungs, this measurement requires knowledge of the lung volume and some measure of the distending pressure of the lungs. The former can be easily measured using a spirometer, but the latter is complicated because of the difficulty of measuring pleural pressure when the lungs are...
enclosed within the thoracic cavity. Although it is possible to insert a needle to measure the pressure between the visceral and parietal pleural membranes, this procedure carries the risk of either puncturing the lungs or creating a pneumothorax. Few people would be willing to have this measurement made on themselves, and it is not likely that an institutional human review board would readily approve such a procedure. A less onerous procedure for obtaining a measurement of pleural pressure is to measure changes in the pressure within the esophagus during the respiratory cycle. This measurement is obtained by having the subject swallow a balloon-tipped catheter so that the tip comes to rest within the esophagus. What does the measurement of esophageal pressure tell about pleural pressure? The answer is that the esophagus is actually located outside of the lung, but within the chest wall, i.e., within the pleural space! Because the esophagus is essentially a flaccid tube (but only when there is no esophageal muscular activity such as when the subject swallows), it expands as its outside pressure (pleural pressure) falls during inspiration, thus lowering its internal pressure. Thus the pressure within the esophagus changes as the pleural pressure changes during the respiratory cycle and can thus be used to track changes in pleural pressure.

**ALTERED LUNG COMPLIANCE IN INDIVIDUALS WITH LUNG DISEASE**

It is possible to use the above technique to determine the pressure-volume relationships of lungs of individuals with different lung diseases. Figure 6 shows representative compliance curves for an individual with normal lungs, a patient with pulmonary fibrosis, and another with emphysema. The figure shows that compliance is reduced in the patient with fibrosis and increased in the patient with emphysema. The work...
expended in overcoming the elastic recoil of the lungs is thus increased in the patient with fibrosis. This occurs because relatively noncompliant fibrotic tissue has been laid down in the lung, thus increasing its stiffness. On the other hand, the effort required to overcome the elastic recoil of the lungs is actually decreased in the patient with emphysema, because the lungs have lost elasticity due to tissue destruction. The figure also shows that TLC is reduced in the patient with fibrosis but may be greater than normal in the patient with emphysema. At this point, it is important to ensure that the student does not come away from this discussion with the idea that emphysema is a desirous condition to have because it is easier to inflate the lungs and TLC is greater. These effects are far outweighed by an increased work of breathing due to an increase in airway resistance caused by the loss of radial tension around noncartilaginous airways and disruptions in gas exchange due to loss of surface area for gas exchange and ventilation/perfusion inequality. Later in the discussion, we will discuss factors that may play a role in altering TLC in patients with these diseases.

COMPLIANCE CHARACTERISTICS OF THE CHEST WALL

Up to this point, we have discussed only the compliance characteristics of the lungs. When we breathe, however, we also have to expand the chest wall, which has its own unique set of compliance characteristics. (The term “chest wall” used in this context is a simplification and actually represents the rib cage, diaphragm, and abdomen.) The pressure-volume relationship for the chest wall is shown in Fig. 7. The curve shows that at ~55–60% of vital capacity, the transmural pressure of the chest wall is zero. This means that the pressures on the outside and inside of the chest wall are equal and that it requires no effort to keep the chest wall at this position. This is called the “resting position” of the chest wall. Work is required to either inflate or deflate the chest wall from this position, however. To deflate the chest wall, the transmural pressure must be made negative (outside greater than inside pressure), whereas to inflate the chest wall, the transmural pressure must be made positive.

COMPLIANCE OF THE RESPIRATORY (COMBINED LUNGS AND CHEST WALL) SYSTEM

As indicated earlier, when we breathe, we must do work against the elasticity of both the lungs and chest wall. Accordingly, it is useful to show both curves on the same pressure-volume graph (Fig. 8). To determine the pressure-volume relationship of the entire respiratory system, the lung and chest wall curves are added to create a third curve that defines the work required to inflate the combined lungs and chest wall. This graph also contains another piece of very important information. Note that all three structures at some point have a particular volume where the recoil (transmural) pressure is zero. This means that the pressure on the inside of each structure is equal to that on the outside and that there is thus no force to make the structure inflate or deflate. These points are “equilibrium points” and represent the volumes that occur in the absence of external forces. In this regard, they represent the “resting positions” of the chest wall, lungs, and respiratory system. As indicated above, the resting position of the chest wall is at ~55–60% of vital capacity, and the resting position of the lungs is actually at some value below the residual volume. (This volume is termed the “minimal volume” of the lungs and is analogous to the small...
Thus, under normal conditions, the lungs never reach their minimal volume. The resting position of the respiratory system is somewhere in between those of the lungs and chest wall. Figure 8 shows that, at this point, the elastic recoils of the lungs and chest wall are equal but opposite. In other words, at this volume, the tendency of the lungs to recoil inward toward their minimal volume is exactly balanced by the tendency of the chest wall to recoil outward to its resting position. A standoff is achieved, which requires no effort, and this creates the resting position of the respiratory system. This volume is FRC. Previously, we gave this volume a descriptive definition (Table 1). It can now be defined as the resting position of the respiratory system, i.e., the lung volume where the tendency of the lungs to recoil inward is exactly balanced by the tendency of the chest wall to recoil outward (Table 2).

**UNCOUPLING THE LUNGS FROM THE CHEST WALL: CREATION OF A PNEUMOTHORAX**

The pressure-volume curves of the lung, chest wall, and respiratory system can also be used to understand what happens when a pneumothorax is created. Normally, the pleural pressure is subatmospheric (negative). If the chest wall is injured in such a way as to create a passage between the atmosphere and pleural space, the higher atmospheric pressure causes air to rush into the pleural space. If the passage is

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3 This may not be strictly correct. Submaximal neuromuscular blockade in seated humans has been found to produce a small (15%) reduction in FRC that results from a decrease in the outward elastic recoil of the chest wall (2). These data suggest that involuntary respiratory muscle activity contributes to the elastic recoil of the chest wall and thus somewhat influences the value of FRC.
sufficiently large, this process results in the lung becoming uncoupled from the chest wall. When the normal coupling is severed, both the lungs and chest wall are free to move toward their respective resting positions. As a result, the lung collapses to its minimal volume and the chest wall recoils outward to its resting position. To reestablish the coupling between the lung and chest wall, it is necessary to reestablish the subatmospheric pleural pressure. This is what the surgeon does by inserting a chest tube before closing the chest after thoracic surgery. The chest tube is used to evacuate air from the thoracic cavity and thus reestablish a subatmospheric pleural pressure.

**FUNCTIONAL DEFINITIONS OF TLC, FRC, AND RV**

Based on the previous discussion, it is now possible to replace the descriptive definitions of TLC, FRC, and RV with functional definitions that result from considering these volumes as lung volumes at which static balances have been achieved between opposing respiratory forces (Table 2). Thus, as indicated above, FRC represents the volume at which the opposing elastic recoil pressures of the lungs and chest wall are of equal magnitude. At TLC, muscular effort is required to maintain the lungs (which have a relatively low compliance at this volume; see Fig. 8) and chest wall at this volume. The value for TLC is thus determined by how successful the inspiratory effort is in balancing the combined tendencies of the lungs and chest wall to recoil inward. Finally, at RV, the lungs still have a small but finite recoil pressure (tendency to collapse), but this is overwhelmed by the much greater tendency for the chest wall to recoil outward. RV in young individuals without pulmonary disease is thus determined by the ability of the respiratory muscles to

**TABLE 2**

Functional definitions of TLC, FRC, and RV based on the attainment of static balances between opposing respiratory forces

<table>
<thead>
<tr>
<th>Capacity or Volume</th>
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</tr>
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<tbody>
<tr>
<td>TLC</td>
<td>Lung volume at which a static balance has been achieved between the maximal inspiratory force that can be generated by the respiratory muscles and the expiratory force generated by the inward-directed elastic recoils of the lungs and chest wall.</td>
</tr>
<tr>
<td>FRC</td>
<td>Lung volume at which the elastic recoils of the lung and chest wall are equal but opposite.</td>
</tr>
<tr>
<td>RV</td>
<td>Lung volume at which a static balance has been achieved between the maximal expiratory force that can be generated by the respiratory muscles (and the elastic recoil of the lung) and the force generated by the outward-directed elastic recoil of the chest wall.</td>
</tr>
</tbody>
</table>
compress the chest wall. In older individuals and those with lung disease, however, RV may have additional determinants, which will be discussed in the next section.

These functional definitions have the advantage in that they provide the student with the means to begin to analyze how lung volumes may become altered in disease. For example, reductions in TLC could occur if the compliance of the lung or chest wall is reduced or if the inspiratory muscles become weakened.

INTERACTION OF LUNG AND CHEST WALL ELASTIC RECOILS IN HEALTH AND DISEASE

At this point, it is now possible to consider how the determination of FRC and TLC helps the physician to understand how the mechanical properties of the lungs can change with disease. In Fig. 9, FRC is depicted as a standoff between a tug-of-war between two rival individuals, lung and chest wall recoil. In emphysema, the elastic recoil of the lungs is reduced, because lung compliance is increased. The chest wall elastic recoil is thus proportionally greater, and the equilibrium point now occurs at a higher lung volume. Thus, in patients with emphysema, FRC is increased. Just the opposite occurs in pulmonary fibrosis, a disease where the lung becomes stiff and its elastic recoil is increased. The equilibrium standoff position has now been altered, because the increased elastic recoil of the lung results in the equilibrium position being at a smaller volume. Thus a hallmark of pulmonary fibrosis is a reduced FRC.

A similar approach can be used to describe the differences in TLC observed in these patients. If TLC represents the static balance between the combined tendency of the lungs and chest wall to recoil inward from TLC and the resisting maximal inspiratory effort required to keep the lungs at this volume, then changes in lung compliance and elastic recoil should result in changes in TLC. Thus TLC is reduced in the patient with pulmonary fibrosis because of a reduced lung compliance and may be increased in the patient with emphysema because of an increased lung compliance. Thus an abnormally high TLC and FRC lead the clinician to consider the possibility of emphysema, whereas reductions in these values suggest the presence of pulmonary fibrosis.

Thus far I have indicated that TLC, FRC, and RV can be considered to represent lung volumes at which static balances have been attained between opposing respiratory mechanical forces. It is important to note,
however, that under some conditions, dynamic factors may prevent these static balances from being achieved. For example, in older individuals with no lung pathology, expiration at low lung volumes is slower than normal due to an increased airway resistance, and the individual terminates expiration and begins to inspire before the static balance that determines RV in younger subjects is reached (5). Additionally, as indicated in footnote 5, FRC may be determined dynamically in some patients with emphysema. Finally, in some diseases, such as asthma, airway closure occurs and air trapping contributes to an increased RV (6). It is important to emphasize, however, that although these lung volumes and capacities may not always be determined by the static balances discussed above, an understanding of these basic interactions provides the initial critical first step in helping the student to understand more complicated changes that may occur during aging or the development of disease.

**ROLE THAT NONLINEAR LUNG COMPLIANCE PLAYS IN DETERMINING THE VERTICAL DISTRIBUTION OF VENTILATION IN THE LUNG**

Due to the weight of the lung, the hydrostatic pressure is greater at the base of the lung compared with the apex. As a result, pleural pressure is more positive (less negative) at the base of the lung. There is no vertical gradient of alveolar pressure, however. Because transpulmonary pressure is the difference between alveolar and pleural pressure, the vertical gradient of pleural pressure makes the transpulmonary pressure of alveoli at the base of the lung less than that of those located at the apex. Because the pressure-volume curve defines the relationship between transpulmonary pressure and volume, this must mean that alveoli at the base of the lung are less inflated than those at the apex. For example, Fig. 10, depicting the pressure-volume curve for the lung, shows the location on the curve of alveoli located at the apex (Fig. 10A) and those located at the base of the lung (Fig. 10B). Thus, at FRC, alveoli at the apex of the lung may be ~70% inflated, whereas those at the base may be only ~30% inflated.

These initial volumes would be of no consequence if the pressure-volume curve of the lung was linear. If so, the increase in volume in all regions of the lung would be identical, because a given change in pleural pressure caused by the inspiratory effort would result in the same incremental increase in volume in all alveoli. This would occur, because the relationship between pressure and volume would be identical for all lung regions. In reality, the pressure-volume curve is not linear. For alveoli located on the steep section of the curve (Fig. 10B), a given change in pressure will result in a relatively large increase in volume. For alveoli located at the apex, where the slope of the curve is flatter (Fig. 10A), the same change in pressure will result in a proportionally smaller increase in volume. Thus, when we inhale from FRC, more of the air goes to alveoli located at the base of the lungs.

**A POSSIBLE CONSEQUENCE OF THE NONLINEAR PRESSURE-VOLUME CURVE FOR ARTERIAL OXYGENATION IN UNILATERAL LUNG DISEASE**

Remolina et al. (9) measured arterial P\textsubscript{O\textsubscript{2}} in nine hospitalized patients with unilateral lung disease. These included cases of bacterial and aspiration pneumonia and bronchogenic and metastatic carcinoma. Large differences in arterial P\textsubscript{O\textsubscript{2}} were observed in these patients when they were lying on their right or left sides. When the sick lung was dependent, severe reductions in arterial P\textsubscript{O\textsubscript{2}} were observed that could be reversed if the patient rolled over to place the healthy lung in the dependent position (Fig. 11). These positional differences disappeared after recovery. The most likely explanation for this behavior is the development of regions of ventilation-perfusion heterogeneity when the sick lung was dependent. In this regard,
both blood flow and ventilation are normally higher at the bottom of the lung. When the sick lung was dependent, its blood flow was probably increased, but ventilation may not have been able to increase to maintain a normal ventilation-perfusion ratio. Placing the good lung down thus probably allowed ventilation to increase to more precisely match the larger blood flow.

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