Case Studies in Medical Physiology

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Preface

To distinguish normal physiology from pathophysiology is to fail to understand disease. Most of the functional disturbances a physician encounters at the bedside are manifestations of normal physiological mechanisms responding to the stresses of disease. These natural stresses are not fundamentally different from the artificial ones that the physiologist employs in the laboratory to analyze physiological function. A patient who is running a spiking fever, for example, provides an excellent opportunity for the study of how heat conservation and heat loss mechanisms regulate body temperature.

Unfortunately, the complexity of human disease and the priority that must be given to the well-being of the patient often obscure the nature of the physiological processes. The beginning student will therefore be wisely advised to confine his attention to such simplified models as squid axones, turtle hearts, and segments of guinea pig intestine until he has mastered the fundamental principles of physiological function. Yet achieving this mastery is a sterile accomplishment for the medical student unless these principles can be related to bedside medicine.

This book is designed to take the reader to the bedside and challenge him to identify the physiology encountered there. It should prove useful for the student who is just completing his basic mastery of the subject, as well as for the more advanced student or physician who wishes to review the physiology of disease in a context divorced from the practical problems of therapy and patient management. Knowledge of the physiology of the patient is essential for understanding of his disease, but it should be clearly recognized that physiology alone does not tell us how to practice medicine effectively.

The reader should be forewarned that these case histories have been severely edited to delete aspects that were not specifically relevant to the physiological problem. Because of these deletions, there is no pretense that the case descriptions in this book present acceptable diagnostic work-ups or appropriate therapeutic management of these clinical problems, matters that are remote from the author's competence.

Two departures from conventional units have been incorporated into the presentation of the data. Years of classroom frustration in teaching acid-base physiology have convinced me that a major source of difficulty in understanding this subject is the confusion inherent in the inverted log scale of pH. Acidity data are therefore expressed directly in units of nanomoles (nM) of hydrogen ion and can simply be manipulated by use of the linear form of the Henderson equation:

$Pco_2 = (H^+ \times HCO_3^-)/24$, in which the Pco_2 is expressed in mm Hg and the HCO_3^- is in units of millimoles. Since the normal plasma concentration of HCO_3^- is 24 mM, this system starts from the happy coincidence that both H^+ and Pco_2 have as their normal reference level the identical numerical value of 40. For readers familiar with the pH scale but unfamiliar with the H^+ scale, a conversion table is provided at the back of the book. Similarly, the widely used but potentially ambiguous "milliequivalent" unit has been replaced by the millimolar unit (mM). For readers not familiar with normal blood values, a table of these is also provided at the rear of the book.

The cases have been selected from a file of case histories that I have collected over a number of years because of their physiological interest. They have been grouped into eight sections to identify the system to which they relate. Questions are appended to each case history to encourage the reader to work through his own analysis of the case before accepting the crutch of the author's analysis.

I am deeply indebted to many clinical colleagues and upper-class medical students who have called these cases to my attention.

R. S. A.

Contents

Respiration

1

Police were called to a college fraternity house early one morning. They found the body of a student at the shallow end of a swimming pool in about 3 feet of water. Near the head of the student was the end of a length of garden hose, 1 inch in diameter and 6 feet long; the opposite end of the hose had been tied to a ladder at the edge of the pool several inches above the water line.

Questioning of the student's fraternity brothers revealed that during a party the previous evening some sort of a hide-and-seek game was initiated. Apparently the dead student had been a participant in this game and had not been seen since that time. Detailed reports were somewhat confused because appreciable amounts of alcohol had been consumed by all concerned. It was theorized that the student assumed he could hide at the bottom of the swimming pool by breathing through the length of garden hose.

Questions

What problems would be encountered in maintaining respiration under these conditions?

Would they have been of sufficient magnitude to account for the death of the student?

Analysis of Case 1

Two factors would have made it impossible for the student to maintain respiratory exchange under these conditions. A length of hose 6 feet long by 1 inch in diameter would contain a volume of approximately 1 liter, which would represent added dead space to the respiratory circuit. In the normal situation, an alveolar ventilation of about 350 ml per breath is achieved by a tidal volume of 500 ml, 150 ml of which is wasted in normal dead-space ventilation. To sustain the same alveolar ventilation with the dead space increased by 1 liter would require a threefold increase in tidal volume.

Complicating this requirement is an even more serious pressure problem. The musculature of the thoracic cage is designed as a bellows to move substantial air volumes at low pressures. In normal function these low pressures are sufficient to overcome elastic forces in the lungs of the order of 6 to 8 mm Hg and a small resistance to air flow that creates an additional pressure gradient of 1 to 2 mm Hg. The maximal inspiratory pressure the respiratory muscles are capable of developing

against a closed airway is some ten times this amount, or about 90 mm Hg at the full expiratory position. This capability for developing inspiratory pressure decreases significantly as the chest expands. The 3 feet of water in which the student was immersed represents a hydrostatic pressure equivalent to almost one-tenth of an atmosphere, or 70 mm Hg. To expand the chest by inspiring gas at atmospheric pressure, the respiratory muscles would have to create this additional pressure to displace the water surrounding the chest. An additional complication was created by the effects of the student's supine posture and the external hydrostatic pressure on the soft tissues of the body, which would counteract the normal gravitational forces tending to pool blood in the extremities. This would shift a significant volume of blood into his chest to congest the pulmonary vascular bed and decrease the compliance of his lungs. The student would, therefore, have been incapable of achieving any significant inspiration under these circumstances, and most certainly not the large tidal volume required to compensate for the dead space of the hose.

2

A 28-year-old man was admitted to the hospital for evaluation of his complaint of chronic cough. His examination included the initial pulmonary function studies listed in the table below. On the morning when he was scheduled for discharge, he suddenly had a severe bout of coughing and became extremely short of breath and cyanotic. Physical and fluoroscopic examination established the diagnosis of pneumothorax, and the patient was returned to bed rest. For academic purposes, the pulmonary function studies were repeated that afternoon. Examination of the patient two weeks later showed physical findings and an x-ray of the chest that were indistinguishable from those taken at the time of his original admission.

Pulmonary function studies	Expected normal	Initial study*	Repeat study
Respiration rate (breaths/min)	12	9	22
Tidal volume (ml)	600	760	240
Inspiratory reserve (ml)	3000	1880	1630
Expiratory reserve (ml)	1200	2330	610
Vital capacity (ml)	4800	4970	2480
Functional residual capacity (ml)	2400	3420	920
Forced expiratory volume in 1 sec (% VC)	85	40	31
Lung compliance (liters/cm H_2O)	0.20	0.19	0.08
Chest compliance (liters/cm H_2O)	0.20	0.17	0.19
Airway resistance (cm H_2O/ liter/sec)	1.0	3.2	4.2
Arterial saturation (%)	97	96	93

Questions

Explain the abnormalities in pulmonary function observed in the initial examination.

What accounts for the changes observed after the pneumothorax?

What happened to the pneumothorax during the subsequent two weeks?

Analysis of Case 2

The initial pulmonary studies of this patient can be explained as the manifestations of increased airway resistance, which could be compatible with chronic bronchitis. Vital capacity was a bit greater than the expected normal, a not uncommon finding in patients with moderate resistive airway disease, since their respiratory musculature has been well developed by the excess demand placed on it. The distribution of this vital capacity was significantly abnormal, however. The small inspiratory reserve and large expiratory reserve indicate that the tidal volume was riding up toward the full inspiratory position. Associated with this was a prolongation of the time required to exhale the vital capacity, with only 40% moved during the first second. All these elements reflect the fact that airway resistance impedes expiration more than inspiration. Resistance is minimal during inspiration, when the negative intrathoracic pressure dilates the bronchial tree, and becomes maximal during forced expiration, when positive intrathoracic pressures narrow the airway. The direct measurement of airway resistance confirmed this interpretation of the spirometric examination.

Patients with increased airway resistance learn that rapid expiratory efforts are futile because they lead to collapse of the smaller airways that lack cartilagenous support. It is, therefore, of interest that this patient exhibited a relatively slow respiratory rate with a correspondingly higher tidal volume than normal, which would reduce the tendency for airway collapse and require less work in breathing. The reduced chest compliance that was observed would relate to the patient's large functional residual capacity. The inflated chest position in which the patient is doing his tidal respiration represents a range of reduced distensibility of the chest wall as compared with that at normal lung volumes.

Hard coughing in the presence of obstructive bronchial disease makes a patient vulnerable to developing high pressures within a segment of the lung, which may tear the pleural lining. The pneumothorax this creates will produce relatively more positive intrathoracic pressures, which will further aggravate the airway narrowing and add to the already high airway resistance. In addition, the collapsed lung requires much greater pressures to inflate. Both the fall in the vital capacity and the drop in pulmonary compliance reflect this difficulty of inflating the collapsed lung, overinflating the opposite lung, or both.

Note that at the time of the acute episode the patient was described as being cyanotic, but by the time of the laboratory study the arterial saturation was almost normal. Blood flow to unventilated alveoli is sharply curtailed by a combination of neural, chemical, and humoral factors to shunt blood toward well-ventilated alveoli, thereby minimizing arterial desaturation.

The fate of a pneumothorax, or any other collection of gas trapped within body tissues, is explained by the equilibration of this gas with the surrounding tissue fluids. These fluids will have gas tensions of the same order as systemic capillary blood, which in turn should be the same as those in venous blood. At sea level, venous blood has a nitrogen tension of 573 mm Hg, an oxygen tension that averages 40 mm Hg, and a carbon dioxide tension of 46 mm Hg. Adding the water-vapor tension of 47 mm Hg yields a total gas tension of 706 mm Hg, some 54 mm Hg below the atmospheric pressure. This negative pressure, which develops in the trapped gas volume as it tends to equilibrate with the surrounding tissue fluid, is a very effective force to pull out a collapsed lung or, in other body tissues, to pull soft tissues into the gas cavity. Since the consequent reduction in the gas volume will increase its pressure, the total gas tension in the trapped gas will tend to rise above 706 mm Hg toward atmospheric tension. This rise will proportionately elevate the partial pressure of each of the contained gases to levels above the partial pressure of the same gases in the surrounding tissues. The trapped gas will, therefore, progressively diffuse into the tissues until the gas pocket disappears entirely. This "vacuum cleaner" characteristic of venous blood finds its explanation in the unique form of the hemoglobin dissociation curve. Blood oxygen tension falls some 60 mm Hg as oxygen is delivered to the tissues, while an essentially equivalent amount of carbon dioxide is picked up in the tissues with a rise of only 6 mm Hg in carbon dioxide tension in the venous blood. This large discrepancy in the changes in the tensions of the two respiratory gases creates the subatmospheric pressure in the venous blood.

3

A 24-year-old veteran contracted pulmonary tuberculosis shortly after entering the service and was treated for active disease for three years. X-ray examinations during this period demonstrated diffuse infiltrative lesions through all lung fields. His period of active disease was also complicated by repeated bouts of pleurisy. He had been free of evidence of active disease for the subsequent two years, but was seriously incapacitated by dyspnea on mild exertion. In current x-rays, there were multiple calcified scars throughout his left lung field, while the right side of his chest was virtually opaque to x-rays.

Analysis of the patient's pulmonary function in the laboratory gave the data shown in the table.

Pulmonary function studies	Expected normal	Observed
Respiratory rate (breaths/min)	12	19
Tidal volume (ml)	600	430
Inspiratory reserve (ml)	2200	400
Expiratory reserve (ml)	900	430
Vital capacity (ml)	3700	1260
Forced expiratory volume in 1 sec (% VC)	85	88
Maximum ventilatory volume (liters/min)	159	67
Arterial saturation – at rest (%)	95	89
Arterial saturation – exercise	97	88
Arterial saturation – breathing O_2	100	92

Bronchospirometry demonstrated that his right lung was responsible for 16% of his tidal volume, 18% of his resting oxygen consumption, and 9% of his vital capacity. An esophageal balloon was passed, which recorded a pressure of -4 cm H_2O at the end of expiration with atmospheric airway pressure. He was then instructed to inspire 500 ml of air from a spirometer. The expiratory valve in the spirometer circuit was closed, and he was told to relax his respiratory muscles completely. Esophageal pressure measured -7 cm H_2O and airway pressure rose to $+9$ cm H_2O when he relaxed his inspiratory muscles.

The patient was referred to surgery.

Questions

Analyze each of the measured variables of pulmonary function and explain its physiological implications.

What is the nature of the functional deficiency in this patient?

Analysis of Case 3

The clinical picture of this patient suggested that his right lung was encased in a fibrous scar, resulting from his repeated bouts of tuberculous pleurisy, and that this scar was restricting lung expansion and accounting for his exertional dyspnea. In view of the evidence of extensive scarring from old disease in the left lung, however, the surgeon wished to assess the functional status of this lung before committing himself to attempting resection of the fibrous scar that was restricting right lung expansion.

The deficiency in vital capacity and maximum ventilatory volume indicated severe mechanical restriction to ventilation. The low expiratory reserve volume, the high value (in percent of vital capacity) of his 1 sec forced expiratory volume, and the fact that his maximal ventilatory volume was proportionately greater than his vital capacity all indicate normal airways with low airway resistance. The deficiency in arterial oxygen saturation seems to reflect some shunting of blood past scarred areas of lung tissue. If it had been a sign of any generalized impairment in pulmonary diffusion capacity, we would have expected a much greater rise in saturation with oxygen breathing (a 400% increase in oxygen tension) and a greater fall in saturation with exercise. Recognizing that normally the right lung contributes some 55% of the ventilatory function, the bronchospirometry clearly indicated that the mechanical problem was essentially in the right lung. Nevertheless, the right lung was taking up oxygen well in proportion to its ventilation, suggesting that its problem was chiefly mechanical.

The esophageal pressure studies provided the direct confirmation of the patient's functional problem. In the expiratory position, there was a pressure of 4 cm H_2O across the lung. With the addition of 500 ml of air and the relaxation of the respiratory muscles, there was a pressure of $9 - (-7)$ or 16 cm H_2O across the lung. The volume increase of 500 ml was, therefore, associated with an increased pressure across the lung of $16 - 4 = 12$ cm H_2O. This yields a pulmonary compliance of 0.04 liters/cm H_2O, compared with the normal value of 0.20 liters/cm H_2O. It is interesting that to adapt to this low pulmonary compliance and the large amount of work necessary to stretch this restricted lung, the patient had adjusted to relatively rapid but shallow tidal respiration (compare with Case 2).

The laboratory data encouraged the surgeon to remove the fibrous scar encasing the right lung, and the patient's respiratory problems were greatly alleviated.