Case 24

Chronic Obstructive Pulmonary Disease

Bernice Betweiler is a 73-year-old retired seamstress who has never been married. She worked in the alterations department of a men's clothier for 48 years. Bernice is a chain smoker. On the job, she was never found without a cigarette hanging from her lips. When her employer announced that smoking would no longer be allowed in the store, Bernice retired. Since her retirement 3 years ago, Bernice has not been feeling well. She fatigues easily, even with light exertion. She has shortness of breath and recently has begun to sleep on two pillows. However, despite these problems, she has refused to stop smoking.

Bernice made an appointment with her physician, who noted a prolonged expiratory phase in her breathing, expiratory wheezes, and increased anteroposterior chest diameter. Her nail beds were cyanotic, and she had moderate pitting edema of her ankles. Based on these observations and the results of laboratory and pulmonary tests, the physician concluded that Bernice has a combination of emphysema and bronchitis, called chronic obstructive pulmonary disease (COPD), which resulted from her long history of smoking.

The results of pulmonary function and laboratory tests are shown in Tables 3-7 and 3-8, respectively.

<table>
<thead>
<tr>
<th>TABLE 3-7</th>
<th>Bernice's Pulmonary Function Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital capacity</td>
<td>Decreased</td>
</tr>
<tr>
<td>Residual volume</td>
<td>Increased</td>
</tr>
<tr>
<td>Functional residual capacity</td>
<td>Increased</td>
</tr>
<tr>
<td>Expiratory flow rate</td>
<td>Decreased</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 3-8</th>
<th>Bernice's Laboratory Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>14.5 g/dL (normal for women, 12-15 g/dL)</td>
</tr>
<tr>
<td>$P_{O_2}$ (arterial $P_{O_2}$)</td>
<td>48 mm Hg (normal, 100 mm Hg)</td>
</tr>
<tr>
<td>$O_2$ Saturation</td>
<td>78% (normal, 98%-100%)</td>
</tr>
<tr>
<td>$P_{CO_2}$ (arterial $P_{CO_2}$)</td>
<td>69 mm Hg (normal, 40 mm Hg)</td>
</tr>
<tr>
<td>$HCO_3^-$</td>
<td>34 mEq/L (normal, 24 mEq/L)</td>
</tr>
</tbody>
</table>

QUESTIONS

1. Bernice's chronic bronchitis is associated with inflammation of the airways and hypersecretion of mucus, which led to obstruction of her airways and increased airway resistance. Her emphysema is associated with loss of alveolar-capillary units and decreased lung elasticity. How do these changes in airway resistance and lung elasticity explain the results of Bernice's pulmonary function tests?

2. The curves in Figure 3-9 show expiratory airflow during forced expiration in a healthy person and in a person with COPD. Each subject first inspired maximally (not shown) and then expired forcibly. The curves show the expiratory flow rates and lung volumes during forced expiration.
What is the value for forced vital capacity (FVC) in the healthy person and the person with COPD? What is the value for peak expiratory flow rate in each person? What is the value for residual volume in each person?

3. How is Bernice’s increased anteroposterior (AP) chest diameter explained by the results of her pulmonary function tests and by your answers to Question 1?

4. Why does Bernice have a decrease in arterial $P_{O_2}$ ($P_{aO_2}$)?

5. Why is her percent $O_2$ saturation decreased, and what are the implications for $O_2$ delivery to the tissues?

6. Why are Bernice’s nail beds cyanotic (blue)?

7. Bernice’s hemoglobin concentration is normal. If her hemoglobin concentration had been decreased, would that have altered her $P_{aO_2}$? If so, in what direction?

8. Why does Bernice have an increase in arterial $P_{CO_2}$ ($P_{aco_2}$)?

9. What is Bernice’s arterial pH? (Assume that the $CO_2$ concentration of arterial blood is $P_{aco_2} \times 0.03$.) What acid–base disorder does she have, and what is the cause? Why is her $HCO_3^-$ concentration increased?

10. How does respiratory acidosis alter the delivery of $O_2$ to the tissues? (Think about the effect of $CO_2$ on the $O_2$–hemoglobin dissociation curve.) Is this effect helpful or harmful?

11. Why does Bernice have ankle edema? (Hint: Think sequentially, starting with her lungs.)
1. The pulmonary function tests showed that Bernice had increased residual volume, increased functional residual capacity (FRC), decreased vital capacity, and decreased expiratory flow rate. Recall that residual volume is the volume that remains in the lungs after forced maximal expiration; FRC is the volume that remains in the lungs after expiration of a normal tidal volume. Two components of Bernice's disease led to these pulmonary changes: increased resistance of her airways and decreased elasticity of her lung tissues.

The bronchitic component of Bernice's pulmonary disease caused narrowing and obstruction of her airways. The resulting increased resistance of the airways caused a decrease in airflow, especially during expiration. Because the expiratory phase was compromised, air was trapped in the lungs and residual volume was increased. Because FRC includes residual volume, FRC was also increased.

The emphysematous component of Bernice's disease caused decreased elasticity of her lung tissues, which also compromised expiration. To understand how lung elasticity is related to expiratory function, it is necessary to recall that elastance is inversely correlated with compliance (where compliance = volume/pressure). To illustrate the relationship between elastance and compliance, consider two rubber bands, one thick and one thin. The thick rubber band has a large amount of elastic “tissue”; thus, it has high elastance and high elastic recoil strength, but low compliance. The thin rubber band has a smaller amount of elastic “tissue;” thus, it has lower elastance and lower elastic recoil strength, but high compliance. In emphysema, there is loss of elastic tissue in the lung structures; as a result, elastance is decreased and compliance is increased. These changes in elastance and compliance have two important implications for the expiratory functions of the lungs: (1) Normal expiration is driven by elastic recoil forces that compress the air in the lungs, increase alveolar pressure, and drive the air out of the lungs. When elastic tissue is lost, elastic recoil force is decreased and expiration is impaired. (2) Normally, the airways are kept open during expiration by radial traction. This traction is created by elastic recoil forces acting on the airway walls. When elastic recoil strength decreases, the airways are deprived of this radial traction. As a result, they may collapse and close during expiration. When the airways collapse, airway resistance increases, expiration ends “early,” and air that should have been expired is trapped in the lungs.

One consequence of air being trapped in the lungs, which increases the residual volume, is that the vital capacity is decreased. (Recall from Case 20 that vital capacity is the maximal volume of air that can be inspired above the residual volume.) Because the residual volume occupies a greater fraction of total lung capacity, it encroaches on and decreases the vital capacity.

2. To answer these numerical questions, first note that the curves show expiratory airflow as a function of lung volume. Each person has just inspired maximally. The curves show the lung volume and airflow during the forced expiration that follows.

The healthy person inspired maximally to a lung volume of 6.8 L, and then started the forced expiration. During expiration, the peak (maximal) expiratory flow rate was 8 L/sec. At the completion of the forced expiration, 2 L remained in the lungs. Thus, the healthy person's residual volume was 2 L, and his FVC (the total volume expired) was 4.8 L (6.8 L – 2 L).

The person with COPD inspired maximally to a lung volume of 9.3 L, and then started the forced expiration. The peak expiratory flow rate was much less than in the healthy person (3 L/sec). At the completion of the forced expiration, 5.8 L remained in the lungs. Thus, the person with COPD had a higher residual volume (5.8 L) and a lower FVC [3.5 L (9.3 L – 5.8 L)] than the healthy person.

3. Bernice's anteroposterior (AP) chest diameter was increased because her expiratory functions were compromised. As a result, Bernice had air trapping, increased residual volume, and increased FRC. Because of air trapping and increased FRC, people with COPD have barrel-shaped chests and are said to “breathe at higher lung volumes.”
4. Bernice's arterial P$_{O_2}$ (Pao$_2$) was 48 mm Hg, much lower than the normal value of 100 mm Hg. In other words, she was hypoxemic. Recall that a normal value of Pao$_2$ indicates normal oxygenation of blood in the lungs. Normal oxygenation requires ventilation–perfusion (V/Q) matching, whereby ventilated alveoli lie in close proximity to perfused capillaries. Bernice had a V/Q defect as a result of impaired ventilation. A portion of her pulmonary blood flow perfused lung regions that were not ventilated (intrapulmonary shunt). Those regions had a decreased V/Q ratio. In other words, the denominator (Q) became relatively higher than the numerator (V). The blood serving these lung regions could not be oxygenated. This poorly oxygenated blood from shunt regions mixed with blood from regions of the lung that were well oxygenated. As a result, the overall P$_{O_2}$ of blood leaving the lungs (and becoming systemic arterial blood) was decreased.

5. The percent saturation of hemoglobin was reduced because Bernice's P$_{O_2}$ was reduced. Recall the important relationship between P$_{O_2}$ and percent saturation from the discussion of the O$_2$–hemoglobin dissociation curve in Case 22 (see Figure 3-5).

According to the curve, percent saturation is approximately 80% at an arterial P$_{O_2}$ of 48 mm Hg. This number is in good agreement with Bernice's measured value of 78%. This percent saturation is clearly reduced from the normal value of 100%, and it corresponds to about three O$_2$ molecules per hemoglobin molecule (rather than the normal four O$_2$ molecules per hemoglobin molecule). Such a change would impair O$_2$ delivery to the tissues because the O$_2$ content of the blood is largely dependent on the amount of O$_2$ bound to hemoglobin. Thus, at 78% saturation, the delivery and content of O$_2$ are approximately 78% of normal. (Recall that dissolved O$_2$, the other form of O$_2$ in blood, contributes little to the total O$_2$ content.)

6. Bernice's nail beds were cyanotic (they had a dusky blue appearance) because there was an increased concentration of deoxygenated hemoglobin in her blood. This deoxygenated hemoglobin was visible in capillary beds near the skin surface. Oxygenated hemoglobin is red; deoxygenated hemoglobin is blue. Because Bernice's P$_{O_2}$ was decreased, she had a decreased percent saturation of hemoglobin. With less hemoglobin present in the oxygenated form, more hemoglobin was present in the deoxygenated form. As a result, the blood appeared blue rather than red.

7. You may have thought that a decrease in hemoglobin concentration automatically means there is a decrease in Pao$_2$; however, this is not the case. Although decreased hemoglobin causes decreased O$_2$ content of blood (because the total amount of O$_2$ bound to hemoglobin is decreased), Pao$_2$ is determined by the free, unbound O$_2$ (see Case 21), which is not directly affected by the hemoglobin concentration.

8. Bernice's P$_{CO_2}$ was increased (hypercapnia) because she could not eliminate all of the CO$_2$ that her tissues produced. As her disease progressed, she was unable to maintain alveolar ventilation (due to increased work of breathing), and thus retained CO$_2$.

9. Bernice had respiratory acidosis secondary to CO$_2$ retention. Her arterial pH can be calculated with the Henderson-Hasselbalch equation as follows:

$$\text{pH} = 6.1 + \log \frac{\text{HCO}_3^-}{\text{P}_{CO_2} \times 0.03}$$

$$= 6.1 + \log \frac{34 \text{ mM}}{69 \text{ mm Hg} \times 0.03}$$

$$= 6.1 + \log \frac{34 \text{ mM}}{2.07 \text{ mM}}$$

$$= 6.1 + 1.22$$

$$= 7.32$$

An arterial pH of 7.32 is considered acidemia because it is lower than the normal pH of 7.4. Bernice had acidemia secondary to an elevated P$_{CO_2}$, which increased the denominator of the Henderson-Hasselbalch equation.
Bernice’s \( \text{HCO}_3^- \) concentration was increased because she has *chronic* respiratory acidosis, in which *renal compensation* occurs. The renal compensation for respiratory acidosis is increased reabsorption of \( \text{HCO}_3^- \) (a process that is aided by the high level of \( P_{\text{CO}_2} \)). When \( \text{HCO}_3^- \) reabsorption increases, the blood \( \text{HCO}_3^- \) concentration increases. This increase in \( \text{HCO}_3^- \) concentration is “compensatory” in the sense that it helps to restore normal arterial pH. Amazingly, although Bernice had a severely elevated \( P_{\text{CO}_2} \), her pH was only *slightly* acidic. This is explained by the fact that her \( \text{HCO}_3^- \) concentration was also elevated, almost to the same extent as her \( P_{\text{CO}_2} \). As a result, the ratio of \( \text{HCO}_3^- \) to \( \text{CO}_2 \) was nearly normal, and her pH was nearly normal.

10. The only “good news” for Bernice is that her increased \( P_{\text{CO}_2} \) caused a *right shift* of the \( O_2 \)-hemoglobin dissociation curve (see Figure 3-5). Increases in \( P_{\text{CO}_2} \) (and acidosis) cause a decrease in the affinity of hemoglobin for \( O_2 \) (*Bohr effect*), which appears as a right shift of the curve. For a given value of \( P_{\text{O}_2} \), the percent saturation of hemoglobin is decreased. In Bernice’s case, the right shift was helpful; although the \( O_2 \) content of her blood was significantly decreased (secondary to hypoxemia), the *decreased affinity* made it easier for hemoglobin to unload \( O_2 \) in the tissues. The “bad news” is that the right shift with its decreased affinity also made it more difficult to load \( O_2 \) in the lungs.

11. The “hint” in the question suggests that Bernice had edema on the systemic side of the circulation (in the ankles) because of problems in her lungs. In patients with COPD, pulmonary artery pressure is often elevated secondary to *increased pulmonary vascular resistance*. Pulmonary vascular resistance is increased for two reasons: (1) COPD is associated with loss of alveolar–capillary units. The loss of capillary beds increases pulmonary resistance. (2) Alveolar hypoxia (secondary to hypoventilation) causes *hypoxic vasoconstriction*. The increased pulmonary vascular resistance leads to increased pulmonary artery pressure, which is the afterload of the right ventricle. Increased afterload on the right ventricle causes decreased *cardiac output*, or *cor pulmonale* (right ventricular failure secondary to pulmonary hypertension). Blood that is not ejected from the right ventricle “backs up” into the right atrium and the systemic veins. Increased systemic venous pressure increases capillary hydrostatic pressure, leading to increased filtration of fluid into the interstitium (*edema*).

Although hypoxic vasoconstriction (discussed earlier) is “bad” in the sense that it causes pulmonary hypertension and subsequent right ventricular failure, it is “good” in the sense that it is attempting to improve \( V/Q \) matching. Poorly ventilated regions of the lung are hypoxic; this hypoxia causes vasoconstriction of nearby arterioles and directs blood flow away from regions where gas exchange cannot possibly occur. Therefore, this process attempts to redirect (or shunt) blood flow to regions that are ventilated.

A final note on this case: patients with COPD are classified as “pink puffers” (type A) or “blue bloaters” (type B), depending on whether their disease is primarily emphysema (pink puffers) or bronchitis (blue bloaters). Bernice is a *blue bloater*: she has severe hypoxemia with cyanosis, hypercapnia, right ventricular failure, and systemic edema. *Pink puffers* are tachypneic (have an increased breathing rate), have mild hypoxemia, and are hypocapnic or normocapnic.
Key topics

Anteroposterior (AP) chest diameter
Bohr effect
Bronchitis
Chronic obstructive pulmonary disease (COPD)
Compliance
Cor pulmonale
Cyanosis
Elastance
Emphysema
Functional residual capacity (FRC)
Heart failure
Henderson-Hasselbalch equation
Hypercapnia
Hypoxemia
Hypoxic vasoconstriction
Peak expiratory flow rate
Percent saturation
Physiologic dead space
Physiologic shunt
Pulmonary hypertension
Pulmonary vascular resistance
Residual volume
Respiratory acidosis
Right ventricular failure
Right shift of the O₂-hemoglobin dissociation curve
Ventilation-perfusion (V/Q) defect
V/Q ratio