Case 13

Cardiovascular Responses to Exercise

Cassandra Farias is a 34-year-old dietician at an academic medical center. She believes in the importance of a healthy lifestyle and was intrigued when the division of cardiology recruited healthy female volunteers for a study on the cardiovascular responses to exercise. Cassandra met the study criteria (i.e., 25-40 years old, no medications, normal weight for height, normal blood pressure), and she was selected for participation.

Control measurements were taken of Cassandra's blood pressure, heart rate, and arterial and venous $P_O_2$; her stroke volume was estimated. Cassandra then walked on the treadmill for 30 minutes at 3 miles per hour. Her blood pressure and heart rate were monitored continuously, and her arterial and venous $P_O_2$ were measured at the end of the exercise period (Table 2-2).

### Table 2-2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (Pre-exercise)</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>110 mm Hg</td>
<td>145 mm Hg</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>70 mm Hg</td>
<td>60 mm Hg</td>
</tr>
<tr>
<td>Heart rate</td>
<td>75 beats/min</td>
<td>130 beats/min</td>
</tr>
<tr>
<td>Stroke volume (estimated)</td>
<td>80 mL</td>
<td>110 mL</td>
</tr>
<tr>
<td>Arterial $P_O_2$</td>
<td>100 mm Hg</td>
<td>100 mm Hg</td>
</tr>
<tr>
<td>Venous $P_O_2$</td>
<td>40 mm Hg</td>
<td>25 mm Hg</td>
</tr>
</tbody>
</table>

**QUESTIONS**

1. To set the stage for the following questions, describe the cardiovascular responses to moderate exercise, including the roles of the autonomic nervous system and local control of blood flow in skeletal muscle. What is the ultimate “purpose” of these cardiovascular responses?

2. What were Cassandra’s mean arterial pressure and pulse pressure for the control and exercise periods, respectively?

3. What was her cardiac output for the control and exercise periods, respectively? Of the two factors that contribute to cardiac output (stroke volume and heart rate), which factor made the greater contribution to the increase in cardiac output that was seen when Cassandra exercised, or do these factors have equal weight?

4. What is the significance of the observed change in pulse pressure?

5. Why was systolic pressure increased during exercise? Why did diastolic pressure remain unchanged?

6. If Cassandra had been taking propranolol (a $\beta$-adrenergic antagonist), how might the responses to exercise have been different? Would her “exercise tolerance” have increased, decreased, or remained the same?
7. Early in the exercise period, Cassandra's skin was cool to the touch. However, at the peak of exercise, her skin was flushed and very warm to the touch. What mechanisms were responsible for these changes in skin color and temperature as the exercise progressed?

8. Arterial and venous $P_{o_2}$ were measured before and after exercise. Explain why venous $P_{o_2}$ decreased, but arterial $P_{o_2}$ did not.
The "goal" of the cardiovascular responses to exercise is to increase O₂ delivery to muscles that are working harder (skeletal and cardiac muscle). The major mechanism for providing this additional O₂ is increased blood flow to the exercising skeletal muscle and the myocardium.

In principle, blood flow in an organ can be increased in two ways: (1) Total blood flow (cardiac output) can increase, which also increases blood flow to individual organs. (2) Blood flow can be redistributed so that the percentage of total flow to some organs is increased at the expense of other organs. During exercise, both of these mechanisms are utilized: cardiac output increases significantly (through increases in heart rate and stroke volume), and blood flow is redistributed to skeletal muscle and myocardium, so that these tissues receive a greater percentage of the (increased) cardiac output. Figure 2–9 summarizes these responses.

![Figure 2-9 Cardiovascular responses to exercise. TPR, total peripheral resistance.](image)

At the initiation of exercise, muscle mechanoreceptors and chemoreceptors trigger reflexes that send afferent signals to the cerebral motor cortex. The cerebral cortex then directs responses that include increased sympathetic outflow to the heart and blood vessels. (1) In the heart, increased sympathetic activity, through activation of β₁ receptors, produces an increase in heart rate and an increase in contractility. The increase in contractility results in increased stroke volume. Together with increased heart rate, this increased stroke volume produces an increase in cardiac output. (Recall that cardiac output = stroke volume × heart rate.) (2) In addition, increased sympathetic activity, through α₁ receptors, produces arteriolar constriction in some vascular beds (e.g., splanchnic, renal) and venoconstriction. (3) Venoconstriction (combined with compression of the veins by the squeezing action of skeletal muscle) increases venous return to the heart. Increased venous return is an essential component of the response.
to exercise; it provides the increased end-diastolic volume that is needed to produce the increase
in cardiac output (Frank-Starling mechanism).

In addition to these central responses that are orchestrated by the sympathetic nervous sys-

tem, local responses occur in skeletal and cardiac muscle to increase their blood flow. In skele-
tal muscle, as the metabolic rate increases, metabolites such as lactate, K+, nitric oxide, and
adenosine are generated. These metabolites produce vasodilation of skeletal muscle arterioles,
thereby increasing local blood flow. This local vasodilation in skeletal muscle is so prominent
that it is responsible for an overall decrease in total peripheral resistance (TPR). (If these local
responses in skeletal muscle did not occur, TPR would have increased as a result of sympathetic
vasoconstriction.) Local responses also dominate in the myocardium, where they are primarily
mediated by adenosine and decreased PO2 and cause vasodilation and increased coronary blood
flow.

2. Recall the calculations of pulse pressure and mean arterial pressure from Case 10:

\[
\text{Pulse pressure} = \text{systolic pressure} - \text{diastolic pressure} \\
\text{Mean arterial pressure} = \text{diastolic pressure} + \frac{1}{3} \times \text{pulse pressure}
\]

During the control period, Cassandra's pulse pressure was 40 mm Hg (110 mm Hg - 70 mm Hg). During exercise, her pulse pressure increased to 85 mm Hg (145 mm Hg - 60 mm Hg). During the
control period, mean arterial pressure was 83 mm Hg [70 mm Hg + \frac{1}{3} \times (40 mm Hg)]. During the
exercise period, mean arterial pressure increased to 88 mm Hg [60 mm Hg + \frac{1}{3} \times (85 mm Hg)]. You may wish to add this data on pulse pressure and mean arterial pressure to the
data provided in Table 2-2.

3. Cardiac output is the product of stroke volume and heart rate, as discussed in Case 10:

\[
\text{Cardiac output} = \text{stroke volume} \times \text{heart rate}
\]

Thus, in the control period, Cassandra's cardiac output was 6 L/min (80 mL/beat \times
75 beats/min = 6000 mL/min, or 6 L/min). During exercise, her cardiac output increased dra-
matically to 14.3 L/min (110 mL/beat \times 130 beats/min = 14,300 mL/min, or 14.3 L/min). Again,
you may wish to add these values to the data in Table 2-2.

To determine whether stroke volume or heart rate made the greater contribution to the
increase in cardiac output, it is helpful to evaluate the observed changes on a percentage basis. In
other words, during exercise, how much did cardiac output, stroke volume, and heart rate change
as a percentage of their control values? Cardiac output increased from a control value of 6 L/min
to 14.3 L/min during exercise. Thus, cardiac output increased by 8.3 L (14.3 L/min - 6 L/min =
8.3 L/min), or 138% above the control value (8.3 L/min + 6 L/min = 1.38). Stroke volume
increased from 80 mL/beat to 110 mL/beat, an increase of 30 mL/beat, or 38% above the control
value. Heart rate increased from 75 beats/min to 130 beats/min, or 73% above the control value.
Thus, the dramatic increase in cardiac output has two components, increased stroke volume and
increased heart rate, and the increase in heart rate is the more significant factor.

4. Cassandra's pulse pressure, the difference between systolic and diastolic pressures, increased
from a control value of 40 mm Hg to 85 mm Hg during exercise. To understand what this
change means, consider what the pulse pressure represents. Because of the large amount of
elastic tissue in the arterial walls, they are relatively stiff and noncompliant. (Yes! Compliance
is the inverse of elastance.) Therefore, during systole, when blood is rapidly ejected from the
left ventricle into the systemic arteries, arterial pressure increases rapidly from its lowest value
(diastolic pressure) to its highest value (systolic pressure). The magnitude of this increase in
pressure (i.e., pulse pressure) depends on the volume of blood ejected from the ventricle (stroke
volume) and the compliance of the arteries. Cassandra's pulse pressure increased during exercise
because her stroke volume increased.
5. The explanation for the increase in systolic pressure is the same as the explanation for the increase in pulse pressure: a larger stroke volume was ejected into the arteries during systole.

On the other hand, diastolic pressure was decreased, which may be surprising. However, think about what diastolic pressure represents: it is the pressure in the arteries while the heart is relaxed (in diastole) and blood is flowing from the arteries to the veins and back to the heart. During exercise, more blood is ejected into the arterial system during systole (i.e., cardiac output is increased), but this blood returns to the veins and eventually to the heart (i.e., venous return is also increased). Diastolic pressure can decrease during exercise because of the decrease in TPR.

6. Propranolol is a β-adrenergic receptor antagonist. Propranolol blocks β₁ receptors that mediate the sympathetic increases in heart rate and contractility. Recall that these effects on heart rate and contractility were the major mechanisms underlying Cassandra's increased cardiac output. Furthermore, increased cardiac output was a major mechanism for increasing O₂ delivery during exercise. Therefore, had Cassandra been taking propranolol, her exercise tolerance would have been significantly reduced.

7. Cutaneous blood flow exhibits a biphasic response to exercise. Early in exercise, vasoconstriction of cutaneous arterioles occurs as a result of the activation of sympathetic α₁ receptors. Blood flow is shunted away from the skin, and the skin is cool. As exercise progresses, body temperature increases secondary to increased O₂ consumption, and sympathetic centers controlling cutaneous blood flow in the anterior hypothalamus are inhibited. This selective inhibition of sympathetic activity produces vasodilation in cutaneous arterioles. As a result, warmed blood is shunted from the body core to venous plexus near the skin surface, as evidenced by redness and warmth of the skin.

8. Cassandra's skeletal and cardiac muscle performed increased work and used more O₂ during exercise than at rest. To help meet the increased demand for O₂, her skeletal and cardiac muscles extracted more O₂ from arterial blood. As a result, the PₐO₂ of venous blood was lower than normal; the normal PₐO₂ of venous blood is 40 mm Hg, and Cassandra's venous PₐO₂ was 25 mm Hg. (In the respiratory portion of your course, you will appreciate that this increased extraction of O₂ is accomplished by a right shift of the O₂-hemoglobin dissociation curve. Right shifts of this curve are produced by increased temperature, increased P₂CO₂ and decreased pH, all of which are consequences of an increased metabolic rate.) Thus, in addition to increased blood flow, which delivered more O₂ to the exercising muscles, more O₂ was extracted from the blood.

Now for a puzzling question. If Cassandra's venous PₐO₂ was decreased, shouldn't her arterial PₐO₂ also have been decreased? No, not if O₂ exchange in the lungs restored the PₐO₂ of the blood to its normal arterial value of 100 mm Hg. Mixed venous blood enters the right side of the heart and is pumped to the lungs for oxygenation. In Cassandra's case, even though this venous blood had a lower PₐO₂ than normal, the diffusion of O₂ from alveolar gas was rapid enough to raise PₐO₂ to its normal arterial value (100 mm Hg). This blood then left the lungs through the pulmonary veins, entered the left side of the heart, and became systemic arterial blood. (You may be correctly thinking that people with lung diseases that interfere with O₂ diffusion might not be able to restore their arterial PₐO₂ to the normal value of 100 mm Hg, especially during exercise, when more O₂ is extracted by the exercising tissues.)
Key topics

Adenosine
Cardiac output
Cutaneous blood flow
Exercise
Frank-Starling mechanism
Local control of muscle blood flow
Local metabolites
Mean arterial pressure
Nitric oxide
O₂ extraction
O₂–hemoglobin dissociation curve
Propranolol
Pulse pressure
α, Receptors
β, Receptors
Right shift of the O₂–hemoglobin dissociation curve
Total peripheral resistance (TPR)