Detecting and correcting tissue hypoxia is a primary concern in critically ill patients. Measurement of blood lactate as an indirect indicator of tissue oxygenation has been used in human medicine for over 30 years. However, veterinary medicine has only recently followed suit. With the advent of inexpensive, easy-to-use portable lactate meters, serial lactate measurements in critically ill patients are becoming commonplace in veterinary emergency hospitals and referral centers. Blood lactate measurement in veterinary patients is a useful adjunct in determining the severity of certain conditions and guiding therapeutic decisions.

**ABSTRACT:** With the advent of accurate, affordable, point-of-care lactate monitors, use of plasma or blood lactate measurements can provide valuable diagnostic information in treating critically ill patients. Tissue hypoxia causes anaerobic metabolism, which increases lactate production. Decreased perfusion is the most common cause of hyperlactatemia in critically ill patients; however, there are other causes of hyperlactatemia besides tissue hypoxia (i.e., mitochondrial dysfunction, hypermetabolic states), and collection techniques and sample handling can also affect results. Serial blood lactate measurements can guide treatment by allowing clinicians to assess improvements in tissue oxygenation and provide prognostic information to clients.

Detecting and correcting tissue hypoxia is a primary concern in critically ill patients. Measurement of blood lactate as an indirect indicator of tissue oxygenation has been used in human medicine for over 30 years. However, veterinary medicine has only recently followed suit. With the advent of inexpensive, easy-to-use portable lactate meters, serial lactate measurements in critically ill patients are becoming commonplace in veterinary emergency hospitals and referral centers. Blood lactate measurement in veterinary patients is a useful adjunct in determining the severity of certain conditions and guiding therapeutic decisions.

LACTATE PRODUCTION AND METABOLISM

During glucose metabolism, glucose is converted into pyruvate, which is then mostly converted into water and carbon dioxide (CO₂) with production of energy in the form of ATP. During aerobic conditions, pyruvate crosses into the mitochondria and is converted to acetyl coenzyme A, which then enters the citric acid cycle. The final step of ATP production occurs via oxidative phosphorylation by the electron transport chain. Through aerobic glycolysis, one molecule of glucose yields a total of 38 molecules of ATP, two ATP molecules are generated from glycolysis of glucose into two pyruvate molecules, and 36 ATP molecules are produced from the citric acid cycle and oxidative phosphorylation¹⁻⁴ (Figure 1).

Lactate production is traditionally considered an anaerobic event. However, even in aerobic conditions, a portion of pyruvate is converted into lactate by the enzyme lactate dehydrogenase. Skeletal muscle and the gastrointestinal tract are the major sites of lactate production in the body, whereas other tissues and cells,
including the brain, skin, and erythrocytes, also contribute to lactate production during homeostasis. In cells and tissues lacking mitochondria, such as erythrocytes and fast-twitch or white muscle fibers, anaerobic glycolysis is the main route of energy production.

Lactate clearance involves conversion of lactate to pyruvate, which may then be used for energy production via oxidative phosphorylation or glucose production via gluconeogenesis in the liver and renal cortex. Fifty percent of lactate metabolism occurs in the liver and 30% in the kidneys. The normal basal production and clearance of lactate is referred to as the Cori cycle (Figure 2). Under conditions of physiologic hyperlactatemia, such as exercise, an elevated lactate concentration quickly resolves because of normal blood flow and oxygen delivery to the liver, resulting in normal lactate clearance. However, pathologic conditions such as shock result in prolonged hyperlactatemia because the liver becomes a net producer of lactate, thus impairing clearance of lactate being produced by all hypoperfused tissues.

Pyruvate production through anaerobic glycolysis yields only two ATP molecules per glucose molecule, and lactate production yields no additional ATP. However, this process provides more rapid energy production than the citric acid cycle and electron transport chain. More important, glycolysis does not require oxygen, thus enabling hypoxic tissues to produce energy. The oxidized form of nicotinamide adenine dinucleotide (NAD+) is necessary for ATP production from ADP. Under aerobic conditions, reduced nicotinamide adenine dinucleotide (NADH) is oxidized to NAD+ via the electron transport chain. In the absence of oxygen, conversion of pyruvate to lactate regenerates NAD+ from NADH, thereby allowing continued ATP production.
through anaerobic glycolysis through anaerobic glycolysis (Figure 1).

In the presence of sustained tissue hypoxia, anaerobic metabolism generates lactate more rapidly than it can be metabolized, resulting in hyperlactatemia. Lactate production results in hydrogen ion (H+) production, resulting in metabolic acidosis during periods of prolonged anaerobic metabolism. This condition is known as lactic acidosis.

Increased lactate concentration in the absence of tissue hypoxia can also occur. This can be caused by a variety of metabolic alterations, such as increased glycolysis, decreased cellular extraction, or use of oxygen. Increased glycolysis leads to an elevated pyruvate concentration, which in turn results in an elevated lactate concentration, even when tissue oxygenation is adequate. An increased pyruvate concentration can occur in response to catecholamines and with alkalosis. Also, various conditions and drugs can cause derangements in aerobic glycolysis. For example, cyanide toxicity interferes with the electron transport chain, which in effect blocks aerobic glycolysis.

There are two isomers of the lactate molecule: D-lactate and L-lactate. D-Lactate is produced by some bacteria and is the isomer found in most lactated Ringer’s solutions. L-Lactate is the isomer produced by mammalian lactate dehydrogenase. All modern point-of-care lactate monitors measure L-lactate.

**CLASSIFICATIONS OF HYPERLACTATEMIA**

Hyperlactatemia can be a result of increased lactate production, decreased clearance of lactate, or a combination of the two (see box on page 290). When tissue hypoxia results in increased lactate production, it is referred to as type A hyperlactatemia. This type is the most common cause of lactic acidosis and is discussed in the following section. Type B hyperlactatemia refers to any cause of hyperlactatemia in which tissue hypoxia is not apparent. There are three subcategories of type B hyperlactatemia, which are based on underlying cause. Type B1 hyperlactatemia includes hyperlactatemia caused by certain disease processes, such as diabetes mellitus, severe liver disease, sepsis, malignancy, and pheochromocytoma. Hyperlactatemia caused by drugs or toxins, such as cyanide, acetaminophen, ethylene glycol, salicylates, and morphine, constitutes type B2 hyperlactatemia. Type B3 hyperlactatemia refers to inborn metabolic defects primarily involving abnormal mitochondrial function. Other processes that can lead to type B hyperlactatemia that do not fit into any of the subtypes include hypoglycemia, alkalosis–hyperperfusion, thiamine deficiency, and D-lactate hyperlactatemia.

Hyperlactatemia caused by increased D-lactate isomer is uncommon and can be caused by intestinal diseases such as short-bowel syndrome, which results in absorption of bacteria-generated lactate from the intestinal lumen. Propylene glycol, which is found in semimoot pet foods and a variety of injectable medications, can also lead to D-lactate production. Some D-lactate is also produced with ketoacidosis.

**CAUSES OF TYPE A HYPERLACTATEMIA**

Any process that negatively affects cellular oxygen delivery can cause type A hyperlactatemia. Oxygen delivery to the tissues depends on cardiac output and oxygen content in the arterial circulation (Figure 3). Cardiac output is a function of heart rate and stroke volume, the latter of which is a function of preload, afterload, and cardiac contractility. The oxygen content of blood is present as a dissolved gas and is bound to hemoglobin in the form of oxyhemoglobin. The oxygen carried by hemoglobin constitutes most of the total oxygen content.
In normal physiologic situations, oxygen consumption by tissues is independent of oxygen delivery. Therefore, tissue oxygen demand can increase or tissue oxygen delivery can decrease within a reasonable range without necessarily resulting in tissue hypoxia. In more extreme pathophysiologic conditions, when tissue oxygen consumption becomes dependent on oxygen delivery, tissue hypoxia likely ensues.\(^6,10\) (Figure 4).

Causes of type A hyperlactatemia include systemic or local hypoperfusion, severe hypoxemia (partial pressure of arterial oxygen <40 mm Hg), severe anemia (packed cell volume <15%), and carbon monoxide toxicosis; however, the most common cause of lactic acidosis is hypoperfusion.\(^4\) Also, relative tissue hypoxia may cause hyperlactatemia due to increased oxygen demand. Excessive muscle activity caused by seizures, extreme exercise, and even trembling increases oxygen demand relative to oxygen delivery, leading to anaerobic metabolism.\(^1–5\) However, it has been shown that even with adequate oxygen delivery, increased muscle activity elevates lactate production. This is due to increases in glycolysis and conversion of pyruvate to lactate in muscle.\(^11\)

Certain pathologic conditions cause hyperlactatemia through a combination of both type A and type B mechanisms. Neoplasia is one example. If a neoplastic mass outgrows its blood supply, type A hyperlactatemia results secondary to tissue hypoxia. More commonly, however, neoplastic cells may block NAD+ regeneration or preferentially use anaerobic glycolysis for energy production, constituting type B hyperlactatemia.\(^2,12\)

Sepsis is another condition by which hyperlactatemia may be multifactorial. Septic shock can create tissue hypoxia due to one or more of the following: hypovolemia, decreased cardiac contractility, and maldistribution of the circulating blood volume. However, hyperlactatemia also occurs in septic patients with adequate tissue oxygenation. Lactate clearance can decrease as much as 50% in sepsis.\(^13\) Impairment of pyruvate dehydrogenase, the enzyme responsible for conversion of pyruvate to acetyl coenzyme A, can elevate pyruvate concentrations. This elevation subsequently increases lactate concentrations, even in the absence of tissue hypoxia. Cytopathic hypoxia can lead to reduced oxygen metabolism due to impairment of mitochondrial enzyme function, even in the presence of adequate oxygen delivery. The degree to which tissue hypoxia is responsible for hyperlactatemia in septic patients has not been completely determined and may vary significantly from patient to patient.\(^13–16\)
Lactate Measurement as an Indicator of Perfusion

The use of a lactate:pyruvate (L:P) ratio to discriminate between type A and type B hyperlactatemias has been proposed. Studies indicate the L:P ratio is more specific for tissue hypoxia than evaluation of the lactate concentration, but unfortunately, the sensitivity of the L:P ratio is significantly less. In addition, measurement of pyruvate requires special sample handling and is not currently available as a point-of-care test. Therefore, the L:P ratio is impractical for clinical use at this time.

COMPARISON OF LACTATE VERSUS OTHER INDICATORS OF HYPOPERFUSION

In addition to lactate measurement, other indirect measurements of tissue oxygenation include oxygen-derived variables, such as saturated oxygen concentration (S\text{VO}_2), partial pressure of venous oxygen (P\text{VO}_2), and oxygen extraction ratio, as well as gastric tonometry, base deficit, and anion gap. Measuring venous oxygen levels by evaluating S\text{VO}_2 or P\text{VO}_2 can give clinicians insight into the oxygen concentration in tissues. Dual oximetry involves measuring the percentage of arterial oxygen saturation (S\text{aO}_2) and S\text{VO}_2. The oxygen extraction ratio can then be calculated from these measurements and increases with increased tissue oxygen consumption (V\text{O}_2) or decreases in oxygen delivery. When cardiac output is also measured with the use of a pulmonary artery catheter, oxygen delivery can be calculated. Unfortunately, S\text{VO}_2 measurements require sophisticated instrumentation in the form of specially modified pulmonary artery catheters, which are invasive and relatively cost prohibitive in clinical practice.

Alternatively, venous oxygen concentration can be evaluated using a mixed venous (obtained from the pulmonary artery) or central venous blood gas measurement (i.e., P\text{VO}_2). Whereas S\text{VO}_2 refers to the percentage of hemoglobin saturation in venous blood, P\text{VO}_2 is a measure of the partial pressure of dissolved oxygen in venous blood. An advantage of P\text{VO}_2 over S\text{VO}_2 is that a modified pulmonary artery catheter is not needed to measure P\text{VO}_2. A normal P\text{VO}_2 is in the range of 40 to 50 mm Hg. Any situation that decreases oxygen delivery or increases oxygen consumption by the tissues could lead to decreased P\text{VO}_2. Causes of decreased P\text{VO}_2 include hypoxemia, anemia, or any condition that may lead to decreased cardiac output, such as hypovolemia, decreased cardiac contractility, and cardiac arrhythmia. The increased oxygen use by tissues that occurs in hypermetabolic states such as hyperthyroidism, seizures, or pyrexia can also reduce P\text{VO}_2 levels. Alternatively, increased P\text{VO}_2 can be caused by increased oxygen delivery to the tissues, arteriovenous shunting, or failure of the tissues to extract the oxygen that is being delivered. Although an abnormal P\text{VO}_2 measurement may indicate abnormal tissue perfusion or oxygenation, lack of specificity limits overall usefulness. Human studies comparing the use of oxygen-derived variables with lactate measurements in various forms of circulatory shock demonstrate that lactate is a better predictor of mortality.

In patients experiencing shock, splanchnic perfusion is often disproportionately compromised. Gastric pH may indicate local hypoperfusion before significant changes in global parameters. Gastric tonometry involves placing a modified nasogastric tube with a gas-permeable balloon that permits measurement of gases within the stomach. This balloon must then be in contact with the gastric mucosa for 30 minutes while a gas sample is extracted to determine the partial pressure of carbon dioxide (P\text{CO}_2). Gastric P\text{CO}_2 correlates with mucosal P\text{CO}_2 because of the high solubility of CO\text{2}. With this information and that from arterial blood gas analysis, a gastric pH value can be extrapolated. Gastric tonometry requires time, specialized equipment, and patient tolerance of nasogastric tube placement.
studies suggest concurrent evaluation of blood lactate and gastric tonometry may be better at predicting mortality than either measurement alone.

Because lactic acidosis is a form of metabolic acidosis, a base deficit should exist, and because lactate is an unmeasured anion, there should also be an increase in the anion gap. Both base deficit and anion gap have been used as indirect estimates of hypoperfusion. Although experimental studies indicate a correlation between lactate concentration and base deficit as well as anion gap, this correlation seems to be lost in clinical studies. Although the latter measurements lack specificity and sensitivity, studies suggest that evaluation of base deficit in conjunction with lactate may provide a better indication of oxygen debt than either measurement used alone.

USES OF LACTATE MEASUREMENT

The use of lactate measurement in veterinary medicine can provide helpful diagnostic and prognostic information. In clinical practice, lactate measurement is useful as an aide in differentiating conditions that result in metabolic acidosis and in detecting the severity of certain conditions. For example, lactate measurement may help a clinician determine the need for a blood transfusion in an anemic patient. Although hematocrits above 15% rarely cause lactic acidosis, in certain patients with concurrent underlying conditions that prevent compensatory increases in cardiac output, lactate levels can become elevated with less severe anemia. Sepsis, general anesthesia, and underlying heart disease are examples of conditions or circumstances that sometimes cause moderate anemia in which an elevated lactate measurement may serve as a transfusion trigger.

When used in conjunction with clinical signs, serial lactate measurements may be used to gauge response to treatment and provide a resuscitation endpoint. For example, shock with persistent hyperlactatemia, even after aggressive fluid therapy, is suggestive of ongoing anaerobic metabolism possibly caused by inadequate volume resuscitation. If hypovolemia is corrected based on other indices (e.g., central venous pressure) but the lactate concentration remains elevated, other causes of decreased oxygen delivery or increased lactate production should be pursued and other treatment modalities (e.g., positive inotropes or vasopressors) may be instituted as indicated. Conversely, normalizing lactate concentrations indicate successful resuscitation, especially in light of improvement of other perfusion parameters, such as blood pressure, heart rate, pulse quality, and urine output. This has been demonstrated in several human studies in which decreasing serum lactate levels during resuscitation were associated with improved outcomes.

In humans, normal lactate concentration is considered to be 1 ± 0.5 mmol/L. Normal lactate concentrations reported for horses, dogs, and cats vary slightly but are comparable, with lactate concentrations above 2.5 mmol/L considered abnormal in unstressed patients (Table 1). Lactate concentrations of 2.5 to 4.9 mmol/L are considered mild elevations. Lactate concentrations of 5 to 7 mmol/L are considered moderate elevations and are usually associated with acidemia. Lactate concentrations greater than 7 mmol/L are considered severe elevations. Normal lactate concentrations may be significantly higher in neonatal and pediatric patients.

Lactate measurement can be used as a prognostic indicator. Studies in both humans and animals have demonstrated the value of lactate measurements in providing prognostic information in a variety of situations, including gastric dilatation–volvulus, caval syndrome, and babesiosis. A retrospective study examining the usefulness of plasma lactate concentrations as a predictor of survival among dogs with gastric dilatation–volvulus showed a 99% survival rate among dogs with plasma lactate concentrations below 6 mmol/L compared with a 58% survival rate if plasma lactate concentrations were above 6 mmol/L. Another study...
Lactate Measurement as an Indicator of Perfusion

Lactate measurement can be a useful adjunct in evaluating perfusion in critically ill patients.

Table 1. Interpretation of Lactate Concentrations in Mature Dogs and Cats

<table>
<thead>
<tr>
<th>Lactate Concentration (mmol/L)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2.5</td>
<td>Normal</td>
</tr>
<tr>
<td>2.5–4.9</td>
<td>Mild elevation</td>
</tr>
<tr>
<td>5–7</td>
<td>Moderate elevation</td>
</tr>
<tr>
<td>&gt;7</td>
<td>Severe elevation</td>
</tr>
</tbody>
</table>

Examining lactate concentrations in critically ill and injured dogs found significantly higher lactate concentrations in nonsurvivors than in survivors. It is important to recognize that although elevated lactate concentrations may correlate with the severity of a certain condition, many factors play a role in determining the prognosis for each patient. Several human studies suggest that trends in lactate concentrations are more predictive of outcome than are single measurements. These studies indicate that rapid correction of hyperlactatemia confers an improved outcome compared with persistent lactate elevations despite aggressive resuscitative efforts. A recent study looking at lactate levels in dogs with babesiosis illustrated the increased prognostic value in conducting serial lactate measurements.

**METHODOLOGY**

Two methodologies are currently being used to determine lactate concentrations: spectrophotometry and amperometry. Some portable lactate meters use both technologies. With spectrophotometry, lactate concentration is determined by reflectance photometry of a reduced mediator. The mediator is reduced in a lactate oxidase–mediated colorimetric reaction in which lactate is converted into pyruvate. The amount of reduced mediator measured is proportional to the original lactate concentration. When lactate is determined amperometrically, lactate oxidase is used again to convert lactate to pyruvate. A by-product of this reaction (i.e., hydrogen peroxide or another reduced mediator) is then oxidized on an electrode, producing a current that is proportional to the original lactate concentration. Both of these methodologies have been compared in clinical studies in both humans and horses with comparable results. According to a study conducted in horses, hemocrit concentrations greater than 10 mmol/L may falsely decrease lactate when measured spectrophotometrically. Studies validating both amperometric and spectrophotometric handheld lactate meters in dogs are underway.

**LIMITATIONS**

Lactate measurement may lack sensitivity in certain situations. Hyperlactatemia occurs when oxygen delivery diminishes to the point of altering oxygen consumption. In addition, lactate production must exceed functional capacity to metabolize the lactate that is produced. Thus lactate measurement may fail to detect early or regional hypoperfusion.

In some situations, lactate measurement may lack specificity as a measure of decreased cellular oxygen delivery. As discussed earlier, many conditions causing hypoperfusion can also contribute to hyperlactatemia through other mechanisms. In other words, one disease process or condition may cause hyperlactatemia through both type A and type B mechanisms. Although hypo-
ing tissue hypoxia in shock. This is especially concerning if lactate concentrations are used as the sole resuscitation endpoint. If the lactate concentration is elevated despite adequate tissue oxygenation, unnecessary and potentially harmful aggressive resuscitative efforts could continue even after other parameters, such as blood pressure, central venous pressure, urine output, pulse quality, and heart rate, have normalized.

Sample collection and handling techniques affect lactate concentrations to a certain extent. Patient trembling or excessive struggling causes moderate elevation in plasma lactate concentration. Vascular occlusion and patient restraint for phlebotomy can be associated with an elevation in measured plasma lactate, although the elevation is usually mild. Blood samples drawn and not separated in a timely fashion have elevated lactate concentrations due to glycolysis within blood cells. Therefore, it is recommended to immediately separate the plasma or serum from the sample or store the sample on ice until it can be tested. If point-of-care lactate measurement is available, glycolysis should not be a concern because there should be no in vitro elevation of lactate concentration if the sample is run within 30 minutes. Arterial sampling has been recommended to ensure that the measurement reflects global tissue oxygenation. However, jugular venous samples have been shown to yield lactate concentrations comparable with arterial samples. Placing an indwelling arterial catheter or central venous catheter may facilitate sample collection for serial lactate measurements as well as minimize erroneous elevations in lactate due to venous occlusion or animal restraint.

**TREATING LACTIC ACIDOSIS**

As with most conditions, treating hyperlactatemia involves treating the underlying cause. Correcting hyperlactatemia involves reestablishing normal perfusion by either improving preload through volume resuscitation or enhancing contractility with positive inotropic therapy. In hypotensive patients, vasopressors
should be considered only after correcting deficits in preload and contractility. When vasopressors are needed, doses should be titrated to effect to avoid excessive increases in vascular resistance, which may result in decreased perfusion and increased afterload. Oxygen content can be increased by whole blood or packed erythrocyte transfusion therapy, increasing the fraction of inspired oxygen, or mechanical ventilation. Ideally, improvement of tissue oxygen delivery should resolve acidosis caused by hyperlactatemia.\textsuperscript{2,4,6,13,38}

Specifically treating lactic acidosis with administration of sodium bicarbonate is contraindicated by many and should be reserved for patients with severe acidemia.\textsuperscript{6,38} Correcting acidemia to alleviate adverse metabolic and cardiovascular effects may seem advantageous; however, several undesirable effects of bicarbonate administration may occur when it is used to treat lactic acidosis. One of these effects, referred to as paradoxic acidosis, occurs when CO\textsubscript{2} produced in the circulation following bicarbonate administration diffuses into cells. This worsens intracellular acidosis despite improvement in acidemia in circulating blood. Bicarbonate administration can also shift the hemoglobin–oxygen dissociation curve to the left, decreasing oxygen release from hemoglobin at the tissue level, which is detrimental to patients already experiencing decreased oxygen delivery.\textsuperscript{11} Nevertheless, some clinicians still advocate bicarbonate use with severe acidemia to correct depression of myocardial performance and a lack of responsiveness to catecholamines caused by acidemia.\textsuperscript{3,4,38} If a clinician believes bicarbonate therapy is indicated to correct severe acidemia, sodium bicarbonate should be administered judiciously while efforts are made to resolve underlying tissue hypoxia. Once the underlying cause of acidemia is corrected and aerobic conditions are restored at the tissue level, lactate clearance by the liver results in bicarbonate production, which can cause an “overshoot” metabolic acidosis.\textsuperscript{6}

It may also be prudent to supplement thiamine in patients with lactic acidosis, as thiamine is an important cofactor in pyruvate oxidation; however, there is no evidence that thiamine supplementation is beneficial unless a thiamine deficiency is present.\textsuperscript{4,6}

**CONCLUSION**

An ideal measure of tissue oxygenation should be sensitive and specific with results obtained easily, quickly, and cost effectively and with minimal risk to the patient. Because of the availability of fast, affordable, and reliable portable lactate meters, lactate measurement is becoming more common in veterinary critical care medicine. As lactate meters become more accessible, lactate measurement should prove to be an essential clinical tool in assessing global perfusion and tissue hypoxia in critically ill patients. However, interpretation of lactate results should be made with consideration of concerns with sensitivity and specificity in individual patients and in conjunction with close patient evaluation and other diagnostics. As with any diagnostic test, knowledge of all of the factors that can affect the results and experience with interpretation are paramount to the utility of lactate measurement as a diagnostic tool.

**REFERENCES**


---

ARTICLE #3 CE TEST

This article qualifies for 2 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. Paid subscribers may purchase individual CE tests or sign up for our annual CE program. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. To participate, fill out the test form inserted at the end of this issue or take CE tests online and get real-time scores at [CompendiumVet.com](http://CompendiumVet.com).

---

1. **Production of lactate from pyruvate**
   a. requires the presence of oxygen.
   b. only occurs in the presence of tissue hypoxia.
   c. replenishes NAD⁺ in the absence of oxygen.
   d. occurs via oxidative phosphorylation.

2. **D-lactate is**
   a. produced by mammalian lactate dehydrogenase.
   b. the lactate isomer measured by modern lactate monitors.
   c. produced in increasing rates with tissue hypoxia.
   d. the isomer of lactate produced by propylene glycol metabolism.

3. **NAD⁺ is**
   a. necessary for ATP production.
   b. produced via lactate production from pyruvate.
   c. replenished in the presence of oxygen through oxidative phosphorylation.
   d. all of the above

4. **Type B hyperlactatemia**
   a. is a more common cause of lactic acidosis than is type A.
   b. is a direct result of tissue hypoxia.
   c. is most commonly associated with an increase of the D-lactate isomer.
   d. includes hyperlactatemia caused by drugs and toxins that increase muscle glycolysis.

5. **Oxygen delivery to tissues is not affected by**
   a. decreases in cardiac output.
   b. decreases in hemoglobin concentrations.
   c. decreases in arterial oxygen content.
   d. cytopathic hypoxia.

6. **Sepsis can**
   a. lead to both type A and type B hyperlactatemia.
   b. decrease lactate clearance by the liver as much as 50%.
   c. lead to a condition known as cytopathic hypoxia.
   d. all of the above

7. **An abnormal Pvo₂ level**
   a. may be an indication of abnormal tissue perfusion or oxygenation.
   b. has been shown to be a better predictor of mortality than is lactate.
   c. is a specific and sensitive indicator of abnormal tissue oxygen delivery.
   d. must be measured via a modified pulmonary artery catheter.
8. When using lactate measurements as a resuscitation endpoint,
   a. an elevated lactate level is a definitive indicator of tissue hypoxia in septic patients.
   b. they should be evaluated concurrently with other resuscitative endpoints, such as heart rate, blood pressure, pulse quality, and urine output.
   c. the use of catecholamines should not affect lactate levels.
   d. none of the above

9. When collecting lactate samples,
   a. only arterial samples should be used.
   b. excessive patient trembling or restraint does not affect results.
   c. tourniquets should be avoided.
   d. lactate levels decrease in vitro if the plasma is not separated in a timely fashion.

10. When treating hyperlactatemia,
    a. bicarbonate should be administered to any patient with lactic acidosis.
    b. treatment should be aimed at correcting hypoperfusion and arterial oxygen content.
    c. determining the cause of hyperlactatemia is usually not helpful.
    d. all of the above