Acid Base Online Tutorial

University of Connecticut

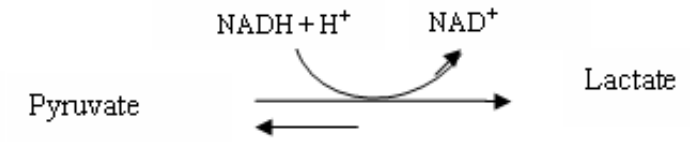
Lactic Acidosis

A commonly encountered cause of elevated anion gap metabolic acidosis, particularly in the ICU is lactic acid. Lactic acidosis is characterized by a pH < 7.36 and lactate level > **5mmol/L**

Lactic acid is produced under normal aerobic states in cells of the brain, retina, and erythrocytes. Under normal circumstances, lactate is circulated to the liver, and to a lesser degree the kidney, where it is converted into glucose or CO_2 and H_2O.

Lactate + $3O_2$ → HCO_3^- + $2CO_2$ + $2H_2O$
2 Lactate + $2CO_2$ + $2H_2O$ → $2HCO_3^-$ + glucose.

In hypoxic states (low O_2 supply) such as in strenuous muscle activity (seizure) or in low tissue perfusion states from circulatory failure, lactic acid is also produced anaerobically during glycolysis. This occurs via the following reaction:



This conversion of pyruvate to lactate in anaerobic conditions is promoted by the accumulation of NADH and the depletion of NAD+ which is needed as an electron acceptor so that glycolysis can continue. The conversion to lactate results in the regeneration of NAD+ so that minimal amounts of ATP can be made indefinitely from glycolysis in states of very low tissue oxygenation.

Lactate accumulation and lactic acidosis results because in states of low tissue perfusion such as shock, or in states of mitochondrion dysfunction, lactate cannot be recycled to the liver for conversion back to glucose or for further breakdown because both of these reactions as shown above require oxygen and both take place in the mitochondrion.

There are primarily 2 types of lactic acidosis:

Type A – Due to tissue hypoperfusion and hypoxia
Type B – Not due to tissue hypoperfusion and hypoxia.

Type A Lactic Acidosis

Most cases of lactic acidosis are due to reduced oxygen delivery as a result of reduced tissue perfusion from **shock** or cardiopulmonary arrest. Other conditions such as **acute pulmonary edema**, can cause severe hypoxemia leading to reduced O2 delivery. Other causes are carbon monoxide poisoning and **severe anemia**. Other causes of type A lactic acidosis which may not necessarily involve generalized tissue hypoxia are **severe seizure**, **severe exercize** and **hypothermic shivering**. All of which result in localized skeletal muscle hypoxia leading to increased lactic acid production.

The clinical signs usually indicate reduced tissue perfusion and include severe hypotension, tachypnea, oliguria or anuria, peripheral vasoconstriction and deteriorating mental status. **Sepsis**, particularly in critically ill patients is a very important cause of lactic acidosis and is often associated with fever (>38.5°C) or hypothermia (35°C). **Kussmaul hyperventilation** (deep sighing respiration) may be observed if the severity of the acidosis is sufficient to elicit a degree of respiratory compensation. Lactic acidosis is usually associated with laboratory abnormalities indicating organ failure or compromise such as abnormal liver function tests, elevated BUN and elevated creatinine. Lactate levels are usually greater than 5 meq/L. Upper limit of nl is 1.6 in plasma. Anion gap is classically elevated, > 16.

Type B Lactic Acidosis

Usually without clinically apparent tissue hypoxia and can be due to any number of conditions:

- Underlying diseases: DM, uremia, liver disease, infections, malignancies
- Drugs and toxins: ethanol, methanol, ethylene glycol, salicylates, metformin
- Inborn errors of metabolism: pyruvate dehydrogenase deficiency, glycogen storage disease, pyruvate carboxylase deficiency, etc.
- Other : **D-Lactic acidosis** (short bowel syndrome) *, idiopathic

Typical picture includes acute onset after nausea and vomiting, altered state of consciousness and hyperventilation. Laboratory findings are variable depending on underlying cause.

D-Lactic Acidosis*

Easily missed diagnosis, because the isomer responsible for the acidosis is the D- isomer which is not detected by the standard assay for lactate. This unique form of lactic acidosis can occur in patients with **jejunoilelal bypass**, or less commonly, **small bowel resection** or other causes of the **short bowel syndrome.**

In these settings, the glucose and starch are metabolized in the colon into D-lactic acid, which is then absorbed into the systemic circulation. The ensuing acidemia tends to persist, since D-lactate is not recognized by L-lactate dehydrogenase, the enzyme that catalyzes the conversion of the physiologically occurring L-lactate into pyruvate.

Two factors that tend to contribute to the accumulation of D-lactate systemically are 1) **an overgrowth of gram positive anaerobes**, such as lactobacilli that are most able to produce D-lactate and 2) **increased delivery of glucose and starch to the colon in the presence of a shorter small bowel transit.**

Patients typically present with recurring episodes of metabolic acidosis, usually after a carbohydrate meal, and characteristic neurologic abnormalities including confusion, cerebella ataxia, slurred speech, and loss of memory.

Criteria for D-lactic acidosis:

- Presence of short bowel syndrome with an intact colon.
- An acute episode of encephalopathic symptoms, such as confusion, slurred speech , ataxia, unsteady gait, abusive behavior and/or nystagmus
- Metabolic acidosis with an increased anion gap
- Normal L-lactate levels
- Serum D-lactate levels > 3 mmom/L
- Abnormal colonic flora, with a predominance of Gram positive anaerobic bacteria (Lactobacilli, which produce large amounts of lactic acid)

Treatment for Lactic Acidosis

Treatment of lactic acidosis requires identification of the primary illness and therapy directed toward correction of that disturbance. Restoration of tissue oxygen delivery through hemodynamic and/or respiratory support is the key therapeutic goal in type A lactic acidosis, which will reduce further lactate production and allow metabolism of excess lactate to HCO_3^- .

Unlike other forms of metabolic acidosis, the use of **sodium bicarbonate** in lactic acidosis is controversial, particularly in patients with circulatory and respiratory failure. Proponents argue that raising the arterial pH may improve tissue perfusion, by reversing acidemia induced vasodilatation and impaired cardiac contractility, and may diminish the risk of serious arrhythmias. Others argue that the $NaHCO_3$ administration may actually worsen acidosis, particularly in patients with respiratory compromise due to the generation of CO_2 from the metabolism of $NaHCO_3$. It is thought that this CO_2 accumulates in tissues leading to worsening intracellular acidosis. The intracellular acidosis leads to reduced lactate utilization in hepatic cells and a decline in cardiac contractility leading to reduced cardiac output and **paradoxically further promotion of lactic acid production**. Others also argue that $NaHCO_3$ administration carries with it a risk of volume overload and **overshoot metabolic alkalosis** after normal hemodynamic has been restored.

Despite the controversy most physicians support administration of $NaHCO_3$ for very severe acidemia and will give small amounts of $NaHCO_3$ to

maintain the arterial pH above 7.10, since a pH beyond this value will promote the development of arrhythmias and cardiac depression.

Treatment for D-Lactic acidosis

Spontaneous regeneration of HCO3- does not occur in D-lactic acidosis, since D-lactate cannot be metabolized. Therapy for D-lactic acidosis consists of sodium bicarbonate administration to correct the acidemia and **oral antibiotics** to decrease gram positive anaerobic colonic bacteria. A low carbohydrate diet is also helpful in the reducing carbohydrate delivery to the colon.

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