INTRODUCTION

Metabolic acidosis is defined by an arterial blood pH of less than 7.35 with a plasma bicarbonate concentration of less than 22 mmol/L (see related article Metabolic Acidosis). Loss of lactate equilibrium is a common cause of metabolic acidosis and is addressed in this article. Hyperlactatemia is defined as a plasma lactate concentration of 2-5 mmol/L. Lactic acidosis is a disease characterized by a pH less than 7.25 and a plasma lactate greater than 5 mmol/L.

PATHOPHYSIOLOGY

Hyperlactatemia results from abnormal conversion of pyruvate into lactate. Lactic acidosis results from an increase in blood lactate levels when body buffer systems are overcome. This occurs when tissue oxygenation is inadequate to meet energy and oxygen need as a result of either hypoperfusion or hypoxia. Lactate is cleared from blood, mainly by the liver, kidney, and skeletal muscles. Cardiopulmonary failure, side effects of drugs and toxins, and various acquired and congenital diseases can lead to lactic acidosis.

In 1976, Cohen and Woods developed a widely accepted classification system that divides lactic acidosis into 2 categories:

- Type A is lactic acidosis occurring in association with clinical evidence of poor tissue perfusion or oxygenation.
- Type B is lactic acidosis occurring when clinical evidence of poor tissue perfusion or oxygenation is absent. Type B is divided into 3 subtypes.
  - Type B1 occurs in association with underlying diseases.
Type B2 is due to drugs and toxins.
Type B3 is due to inborn errors of metabolism.

In many cases of Type B lactic acidosis, occult tissue hypoperfusion is now recognized to accompany the primary etiology.

More recent classification schemes divide lactic acidosis cases into those associated with hypoxia versus nonhypoxic mechanisms and those secondary to increased production of versus decreased clearance of lactate.

Frequency:
Disordered lactate metabolism frequently is encountered among critically ill patients.

Mortality/Morbidity:
Patients exhibiting a disorder of lactate metabolism suffer a high hospital mortality rate and are at risk for developing multiple organ failure. The mortality rate of critically ill patients with a blood lactate level greater than 5 mmol/L and an arterial pH less than 7.35 is 75% at 6 months.

History:
The history is largely dependent on the etiology of lactic acidosis. A careful history may indicate the underlying pathology. The onset of acidosis may be rapid (ie, within minutes to a few hours) or progressive (ie, over a period of several days).

Physical Findings:
The physical examination also varies according to the underlying cause of lactic acidosis. Cardiovascular compromise is a frequent finding, explaining many of the associated signs, which include cyanosis, cold extremities, tachycardia, hypotension, signs of dehydration, hyperventilation or dyspnea, lethargy, stupor or coma, vomiting, and/or abdominal pain.

Pathophysiological classification of lactic acidosis
See Picture 1 for a table classifying causes of lactic acidosis.

The most frequent cause of lactic acidosis is poor perfusion, which is induced by various shock states, overwhelming infection, or other causes of hypoxia. Medicinal and toxic causes of lactic acidosis are quite numerous, including aceterminophen, alcohols and glycols (ethanol, ethylene glycol, methanol, propylene glycol), almitrine, antiretroviral nucleoside analogs (zidovudine, delavirdine, didanosine, lamivudine, stavudine, zalcitabine), beta-adrenergic agents (eg, epinephrine, ritodrine, terbutaline), biguanides (phenformin, metformin), cocaine, cyanogenic compounds (eg, cyanide, aliphatic nitriles, nitroprusside), diethyl ether, 5-fluorouracil, halaethane, iron, isoniazid, nalidixic acid, propofol, sugars and sugar alcohols (fructose, sorbitol, and xylitol), salicylates (eg, Reye syndrome), strychnine, sulfasalazine, and valproic acid.

Lactic acidosis also may occur in association with an underlying disease, such as diabetes mellitus, severe iron-deficiency anemia, liver diseases, alcoholic ketoacidosis, pancreatitis, malignancy (eg, leukemias, lymphomas, lung cancer), alkalosis, infections (malaria, cholera), renal failure, pheochromocytoma, thiamine deficiency, short gut syndrome and other carbohydrate malabsorption syndromes (eg, d-lactic acidosis), and milk protein intolerance.

Inborn errors of metabolism also may be responsible for lactic acidosis. These include glucose-6-phosphatase deficiency (von Gierke disease), fructose-1,6-diphosphatase deficiency, pyruvate carboxylase deficiency, pyruvate dehydrogenase deficiency, oxidative phosphorylation deficiency, and methylmalonic aciduria.

Lactic acidosis rarely may present as the so-called MELAS syndrome (mitochondrial encephalopathy, lactic acidosis, and strokelike episodes), which appears to be caused by a point mutation in mitochondrial DNA tRNAlep (UUR) gene. This has been reported in association with valproate use and has been reported as occurring in pregnancy and childhood.

Laboratory Studies:
- Serum electrolytes (ionogram) with calculation of the anion gap (AG = sodium - [total CO₂ + chloride]).
- Arterial blood gases (ABG): The correlation between arterial pH and serum lactate is weak.
- Serum lactate: No significant differences in lactate levels are noted in arterial and venous blood samples. The
concentration of lactate in blood must be measured as quickly as possible, within 4 hours of collection. The blood specimen collected for the measurement of lactate should be brought to the lab on ice. The serum lactate reference range is less than 2 mmol/L.

Other Tests:
- Other tests may be useful; they may be selected on the basis of suspected underlying etiology of lactic acidosis.

Prehospital Care:
Maintenance of airway patency and oxygen delivery are critical. Supplement patient with 100% oxygen by mask. Intubate if the patient is unconscious, in severe shock, or otherwise in unstable condition.

Establish an intravenous (IV) line. Give a fluid bolus if the patient has tachycardia, hypotension, or other signs of poor tissue perfusion (eg, poor capillary refill).

Monitor the cardiac rhythm. Acidosis predisposes to dysrhythmias. Administer sodium bicarbonate only in conjunction with on-line or off-line medical control.

Emergency Department Care:
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.

Thiamine deficiency may be associated with cardiovascular compromise and lactic acidosis. The response to thiamine (given as 50-100 mg IV followed by 50 mg/d orally for 1-2 wk) may be dramatic and potentially life saving.

The use of sodium bicarbonate is controversial and generally should be avoided (see Medications). Sodium bicarbonate administration results in the production of carbon dioxide, which leads to subsequent intracellular acidosis. Prospective studies of bicarbonate use in lactic acidosis have shown no improvement in outcome, even in cases of severe acidosis. Toxic etiologies of lactic acidosis, such as methanol, ethylene glycol, and cyanide poisoning may justify administration of bicarbonate (see articles on Toxicity, Cyanide, Toxicity, Ethylene Glycol, and Toxicity, Alcohols).

Continuing Care:
In addition to general supportive measures, other treatments to consider include the administration of appropriate antibiotics, surgical drainage or debridement, chemotherapy for malignant disorders, discontinuation of causative drugs, and dietary modification in certain types of congenital lactic acidosis.

Procedures:
Consider hemoperfusion or hemodialysis in association with ethylene glycol and methanol poisoning. Dialysis or continuous hemofiltration also may be a useful mode of therapy when severe lactic acidosis exists in conjunction with renal failure or congestive heart failure.

MEDICATIONS
Sodium bicarbonate: The use of this agent to treat lactic acidosis is controversial. The starting dose is one third to one half of the calculated extracellular bicarbonate deficit:

\[ \text{HCO}_3 \text{ deficit (in mEq)} = 0.5 \times (\text{wt in kg}) \times (\text{desired HCO}_3 - \text{measured HCO}_3) \]

Metabolic alkalosis can ensue after bicarbonate administration if correction is complete rather than partial. This result can be avoided by titration of the bicarbonate dose to modest therapeutic end points (eg, arterial pH of 7.20). In cardiopulmonary resuscitation, sodium bicarbonate generally is not recommended. In severe hypoxemia, sodium bicarbonate should be administered by slow infusion to minimize any increase in PvCO\(_2\), and minute ventilation must be increased in order to eliminate generated CO\(_2\) and avoid respiratory acidosis. Bicarbonate does not improve hemodynamics in critically ill patients exhibiting lactic acidosis. Because of increased CO\(_2\) production, sodium bicarbonate may precipitate ventilatory failure.

file:///D|/X. SOLER/BIBLIO2/Lactic acidosis.htm (3 de 5) [18/09/2001 18:12:30]
Tris-[hydroxymethyl] aminomethane (THAM): This agent has theoretical advantages over bicarbonate, as CO₂ is not generated. It has been studied in animals and humans but, to date, has not been proven to be more effective than bicarbonate.

Carbicarb: This agent is a combination of sodium carbonate and sodium bicarbonate that does not generate CO₂. While this theoretical advantage should favor its use over bicarbonate, evidence that it alters morbidity or mortality rates is lacking.

Dichloroacetate (DCA): This agent is not a buffer, but it stimulates the oxidation of pyruvate. This has resulted in improved lactate utilization and increased tissue levels of ATP. Prospective studies have failed to demonstrate its efficacy.

Miscellaneous agents: Thiamine, coenzyme Q, I-carnitine, and riboflavin have been used to treat lactic acidosis due to antiretroviral therapy, without definitive demonstration of efficacy.

**PROGNOSIS, COMPLICATIONS, AND FOLLOW-UP**

In lactic acidosis associated with ischemia, the blood lactate concentration has prognostic value, although the etiology of the shock state influences the probability of survival as well. Serum lactate levels greater than 2.5 mmol/L have been associated with increases in mortality rate.

Severe metabolic acidosis with arterial pH of less that 7.20 is associated with impaired cardiac contractility and altered responses to exogenous catecholamines. Elevated serum lactate concentrations may have negative inotropic effects, independent of pH. Electrolyte disturbances, such as hypokalemia and hypocalcemia, and a decrease in ionized calcium have been described as complications of bicarbonate therapy.

The patient may be discharged when acidosis has been corrected, as evinced by a return to normal lactate concentrations, and when the underlying disease process has been addressed adequately.

**PICTURES**

Caption: Picture 1.

![Image](Picture1.jpg)

**BIBLIOGRAPHY**


NOTE:
Medicine is a constantly changing science and not all therapies are clearly established. New research changes drug and treatment therapies daily. The authors, editors, and publisher of this journal have used their best efforts to provide information that is up-to-date and accurate and is generally accepted within medical standards at the time of publication. However, as medical science is constantly changing and human error is always possible, the authors, editors, and publisher or any other party involved with the publication of this article do not warrant the information in this article is accurate or complete, nor are they responsible for omissions or errors in the article or for the results of using this information. The reader should confirm the information in this article from other sources prior to use. In particular, all drug doses, indications, and contraindications should be confirmed in the package insert. FULL DISCLAIMER