Lactic acidosis: Causes, Types, Symptoms and Treatment

Lactic acidosis is a form of **high anion gap metabolic acidosis** characterized by a **serum lactate level >4 mmol/L**. It occurs due to:

- Excessive **lactate production** (often from tissue hypoxia),
- Impaired **lactate clearance** (commonly hepatic or renal dysfunction),
- Or both mechanisms combined.

It is the **most common cause of metabolic acidosis in hospitalized patients**.

Pathophysiology

What is Lactic Acid?

- **Lactate** is the end-product of **anaerobic glycolysis**, a normal metabolic process where **glucose** is broken down to **pyruvate** and then reduced to lactate.
- In anaerobic conditions, pyruvate is converted to lactate via the **Embden-Meyerhof pathway**.
- The **lactate:pyruvate ratio** in tissues is about **25:1**.
- Lactate is transported to the **liver**, where it undergoes **oxidation to pyruvate** and is then converted back to glucose via the **Cori cycle**.

Lactic Acid Isomers

- **L-lactate**: The physiologic form produced by human metabolism and the one typically measured clinically.
- **D-lactate**: Produced by bacterial metabolism; found in excess in patients with **short bowel syndrome** or a history of **gastric bypass surgery**.

Types of Lactic Acidosis (Cohen and Woods Classification)

Type A – Hypoxic Lactic Acidosis

- Due to **tissue hypoperfusion** or **hypoxia**.

- Associated with:
    - Shock (septic, cardiogenic, hypovolemic)
    - Severe hypoxemia or anemia
    - Cyanosis
    - Cool, mottled extremities
    - Excess catecholamines (e.g., intense exercise, seizures)

Mechanisms:

- **Overproduction** of lactate due to anaerobic metabolism.
- **Underutilization** due to impaired hepatic clearance or inhibited gluconeogenesis.

Type B – Non-Hypoxic Lactic Acidosis

- Occurs **without clinical signs of hypoperfusion**.
- Subtypes:
    - **Type B1** – Associated with systemic diseases:
        - Renal failure
        - Hepatic failure
        - Diabetes mellitus
        - Malignancy (e.g., leukemia, lymphoma)
    - **Type B2** – Induced by drugs/toxins (see below).
    - **Type B3** – Caused by **inborn errors of metabolism**.

Note: In **sepsis**, initial lactic acidosis may be Type A (hypoxic), but with resuscitation, ongoing acidosis may persist as Type B due to **mitochondrial dysfunction** and **altered oxidative phosphorylation**.

Common Causes of Lactic Acidosis

? Endogenous Causes

- **Shock states** (hypovolemic, cardiogenic, septic)
- **Severe hypoxia**
- **Liver failure** (reduced clearance)
- **Renal failure**
- **Thiamine deficiency**
- **Uncontrolled diabetes mellitus**
- **Malignancies**
- **Acute pancreatitis**
- **Short bowel syndrome**

? Drugs and Toxins (Type B2)

Drug Class/Type	Examples
Antiretrovirals	Zidovudine, Didanosine, Lamivudine, Zalcitabine
Biguanides	Metformin, Phenformin
Alcohols & Glycols	Ethanol, Methanol, Ethylene glycol, Propylene glycol
Analgesics	Paracetamol (Acetaminophen), Salicylates
Beta-agonists	Epinephrine, Ritodrine, Terbutaline
Anticonvulsants	Valproic acid
Others	Isoniazid, Iron, 5-Fluorouracil, Cyanide, Cocaine, Diethyl ether, Propofol, Strychnine, Sorbitol, Xylitol, Halothane, Sulfasalazine

Special Situations

- **Starvation Ketoacidosis**: Often seen in neonates, pregnancy, lactation, or prolonged fasting.
- **Alcoholic Ketoacidosis**: Follows binge drinking and chronic malnutrition.
- **D-Lactic Acidosis**: Occurs in patients with **jejunoileal bypass** or **short bowel syndrome**, due to **bacterial fermentation** of carbohydrates to D-lactate.
- **Pyroglutamic Acidemia**: Rare cause seen in **acetaminophen toxicity** due to glutathione depletion.

Clinical Presentation

- Symptoms often reflect the **underlying condition** causing lactic acidosis.
- May present acutely or progressively, especially in **critically ill** patients.
- Common signs:
    - **Altered mental status**
    - **Tachypnea (compensatory)**
    - **Hypotension**
    - **Cool extremities**
    - **Cyanosis**
    - **Nausea, vomiting**

In Severe Cases:

- Seizures
- Coma
- Multiorgan failure
- Disseminated intravascular coagulation (DIC)
- Poor prognosis with persistently high lactate

Diagnosis

- **Serum lactate >4 mmol/L**
- **High anion gap metabolic acidosis**

    AG = Na? - (Cl? + HCO??)

- pH typically <7.35 (in metabolic acidosis)
- **Evaluate underlying cause** through:
    - Drug/toxin history
    - Sepsis screen

- Organ function panels (renal, liver)
- Nutritional status (thiamine levels)

Management

1. **Treat the underlying cause**:
    - Restore perfusion in shock
    - Discontinue causative drugs/toxins
    - Correct hypoxemia
    - Manage infections or organ dysfunction
2. **Supportive therapy**:
    - Intravenous fluids
    - Oxygen therapy
    - Vasopressors if needed
    - Hemodialysis (for metformin or toxic alcohols)
3. **Supplementation**:
    - **Thiamine** in deficiency or suspicion
    - **Bicarbonate therapy** (controversial, reserved for pH <7.1)

Prognosis

- Dependent on etiology and speed of correction.
- **Persistent lactic acidosis** in critically ill patients is associated with **high mortality**.
- Early recognition and **aggressive treatment** of underlying cause improve outcomes.