Lactic Acidosis

What is lactic acidosis?

Lactic acidosis is a life-threatening condition caused by too much lactate in the blood and low blood pH. Low blood pH means that your blood contains too much acid, which can be harmful to the cells of your body.

What is lactic acid?

Lactic acid is a chemical byproduct of energy production in cells. Cells contain mitochondria, rod-like structures that serve as a cell's powerhouse. Mitochondria help convert the food you eat into the energy you need to function.

The food you eat is broken down into glucose. Mitochondria use oxygen to turn glucose into energy. If there is not enough oxygen or if the mitochondria aren't working properly, cells must make energy in a different way. Making energy without oxygen produces lactic acid as a byproduct.

Lactic acid is quickly converted to lactate in the blood. Though lactic acid and lactate are not the same, the terms are often used interchangeably. Lactate is formed when lactic acid loses a hydrogen atom. The hydrogen atom lost by lactic acid stays in the blood; this decreases the blood's pH and makes it more acidic.

Your muscles produce lactic acid and lactate when you exercise. It is the lactate in your muscles that makes them feel sore after a workout. Lactate is broken down by your liver. If your body produces too much lactate, your liver may have a hard time keeping up.

What causes too much lactate?

High levels of lactate in the blood, referred to as *hyperlactatemia*, occur either when you make too much lactate or when your liver isn't working properly and can't break down lactate.

Terms Used in This Fact Sheet:

Liver function tests (LFTs): *tests that measure the blood levels of liver enzymes (proteins made and used by the liver) to determine if your liver is working properly.*

Mitochondrial toxicity: *also referred to as mitochondrial dysfunction. Damage to the mitochondria that can cause problems in the heart, nerves, muscles, pancreas, kidneys, and liver. It may also cause changes in the blood, such as thrombocytopenia (too few platelets), anemia (too few red blood cells), and neutropenia (too few neutrophils). Mitochondrial damage can lead to lactic acidosis and hepatic steatosis (fatty liver) and may also play a role in lipodystrophy* (see **Lipodystrophy Fact Sheet**).

Nucleoside reverse transcriptase inhibitor (NRTI): *class of anti-HIV medication. NRTIs are faulty versions of the building blocks (nucleosides) used by reverse transcriptase, a protein that HIV needs to make copies of itself. The NRTIs approved by the FDA are Combivir, Emtriva, Epivir, Epzicom, Hivid, Retrovir, Trizivir, Truvada, Videx, Viread, Zerit, and Ziagen.*

Nucleoside reverse transcriptase inhibitors (NRTIs) can cause hyperlactatemia by disrupting the function of the mitochondria. This is known as **mitochondrial toxicity**. NRTIs block the function of polymerase-gamma, a protein that mitochondria need to do their job properly. When the mitochondria don't work efficiently, excess lactate is produced.

NRTIs can also cause the liver to become fatty, a condition called *hepatic steatosis* (see **Hepatotoxicity Fact Sheet**). A fatty liver doesn't work well and can't break down lactate efficiently.

Severe hyperlactatemia leads to lactic acidosis. Lactic acidosis is a serious but very rare complication of treatment with NRTIs. Although all NRTIs are associated with hyperlactatemia and lactic acidosis, people taking Zerit (stavudine) and Videx (didanosine) seem to be at greater risk than people taking other NRTIs.

This information is based on the U.S. Department of Health and Human Services' *Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents* (available at **http://aidsinfo.nih.gov**).

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Lactic Acidosis (continued)

Are there other risk factors for lactic acidosis?

Yes. Women and people who are overweight have an increased risk of developing hepatic steatosis and lactic acidosis. Fatal lactic acidosis has also occurred in pregnant women taking both Zerit and Videx. HIV infected patients taking Rebetol (ribavirin) for hepatitis C virus infection may also be at increased risk for developing lactic acidosis.

What are the symptoms of hyperlactatemia and lactic acidosis?

You can have mild hyperlactatemia without experiencing any symptoms.

Signs and symptoms of severe hyperlactatemia and lactic acidosis are:

- persistent nausea, vomiting, and abdominal pain
- unexplained tiredness
- shortness of breath
- rapid breathing
- enlarged or tender liver
- cold or blue hands and feet
- abnormal heart beat
- weight loss

What should I do if I experience these symptoms?

Tell your doctor right away if you have any of the symptoms of lactic acidosis. Your doctor may order blood tests, including:

- **liver function tests (LFTs)**
- lactate level (this test is difficult to do and is not done routinely)
- electrolyte level
- blood pH level

Your doctor should also perform a physical exam to check for an enlarged liver and may order a CT scan or ultrasound of your liver.

What does my lactate level mean?

Lactate levels are usually reported as mmol/dL (millimoles of lactate per deciliter of blood). Lactate levels of 2 to 5 mmol/dL are elevated and should be evaluated along with any symptoms you have. Levels greater than 5 mmol/dL are abnormal, and levels greater than 10 mmol/dL indicate a serious and possibly life-threatening situation.

Lactate levels may vary depending on how the test was performed and which lab did the testing. Your doctor can help you understand what your lactate level means.

What is the treatment for lactic acidosis?

Lactic acidosis is treated by stopping any NRTIs you are taking. You may need to be hospitalized. Some people with lactic acidosis need intravenous (IV) fluids and a machine to help them breathe. Some doctors recommend giving riboflavin (vitamin B2), thiamine (vitamin B1), coenzyme Q, L-carnitine, or vitamins C, E, and K to patients with lactic acidosis, but the effectiveness of these treatments is uncertain.

You should not stop taking any anti-HIV medications without talking to your doctor, even if you have symptoms of lactic acidosis. If you are diagnosed with lactic acidosis, you and your doctor will decide how to stop your anti-HIV medications, when to restart medications, and which ones to take when you go back to treatment.

If you have only mild hyperlactatemia and no symptoms, you may not need to change your HIV treatment regimen. At this time, there is no evidence that people with mild hyperlactatemia are at increased risk for lactic acidosis.

For more information:

Contact your doctor or an *AIDSinfo* Health Information Specialist at 1–800–448–0440 or http://aidsinfo.nih.gov.

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