



# Clinical Pharmacology & Toxicology Pearl of the Week

## ~ Drug-induced hyperlactatemia ~

### Lactate Production & Metabolism

- ✓ Lactate is formed when pyruvate is reduced via  $\text{NADH} \rightarrow \text{NAD}^+$ , which is facilitated by the enzyme Lactate Dehydrogenase (LDH).
- ✓ Lactate elevation can be classified as either Type-A or Type-B:
  - Type-A lactate production results from tissue hypoxia.
  - Type-B lactate production occurs despite normal tissue oxygenation in the setting of genetic/metabolic diseases, malignancy & drug-induced causes.
- ✓ Normally, lactate is taken up by the liver where it undergoes enzymatic transformation  $\rightarrow$  pyruvate  $\rightarrow$  glucose as part of the Cori Cycle.

### Drug-induced lactate production

- ✓ Drug-induced hyperlactatemia is typically a type-B hyperlactatemia resulting in tissue hypoxia *independent* of tissue oxygen availability.
- ✓ Hyperlactatemia results from medication induced imbalance between lactate production and metabolism.

**Table 1: Causes of drug-induced hyperlactatemia**

Cause of lactate elevation	Proposed mechanism	Culprit Medications
Increased pyruvate production	Cells shunt pyruvate $\rightarrow$ lactate to regenerate $\text{NAD}^+$	Beta-2 agonists
Metabolism of drug into lactate	Direct hepatic metabolism of parent drug to racemic mixture of D-lactate & L-lactate	Propylene glycol
Interference with Cori cycle	Inhibition of Cori cycle leads to reduced oxidation of lactate to pyruvate in liver	Biguanides (metformin)
Inhibition of mitochondrial protein synthesis	Increased drug-ribosome binding and reduced activity of the electron transport chain	Oxazolidinone antibiotics (linezolid)
Inhibition of electron transport chain	Direct inhibition of electron transport chain leading to decreased ATP synthesis	Propofol, sodium nitroprusside, barbiturates, valproic acid
Uncoupling of oxidative phosphorylation	Inhibition of ATP synthesis via uncoupling of the electron transport chain in mitochondria	Salicylates

## Management

- ✓ Rule out causes of a potential Type-A lactic acidosis before considering Type-B causes.
- ✓ Identify & discontinue the offending drug in the event of a suspected drug-induced hyperlactatemia.
- ✓ Supportive care, including hydration where indicated & monitoring for resolution vs. progression.
- ✓ Renal replacement therapy is indicated in cases of severe refractory lactic acidosis such as in the setting of metformin overdose.

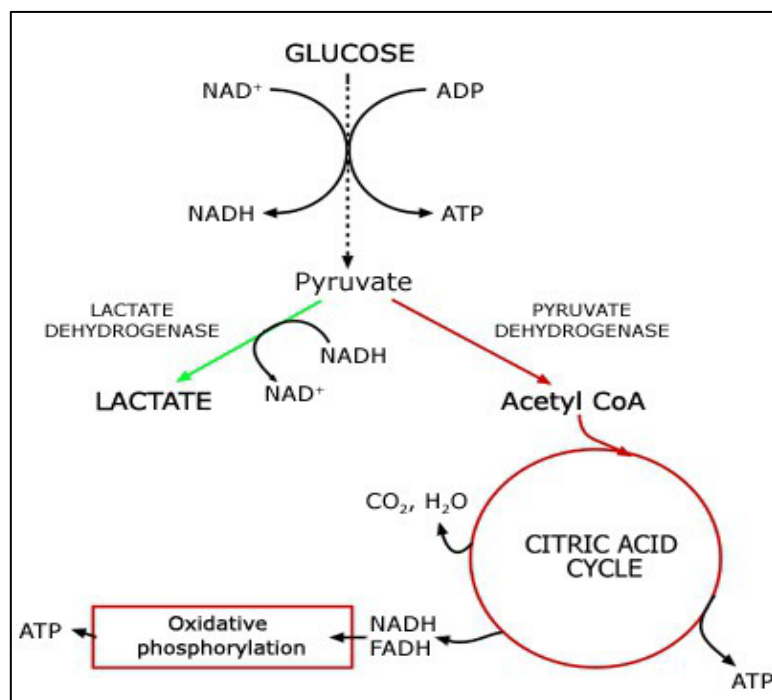
## References

1. Blohm E, Lai J, Neavyn M. Drug-induced hyperlactatemia. *Clinical Toxicology*. 2017; 55(8):869-878. DOI: 10.1080/15563650.2017.1317348

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching "Pharmacology" from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching "Toxicology" from the ARD home page.

More CPT Pearls of the Week can be found [HERE](#).



Lactate and lactic acidosis (acute-care-testing.org)

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