Lactate metabolism

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Production of lactate

Lactate

- Two optical isomers
  - L-Lactate
  - D-Lactate (bacteria)
- pKₐ: 3.86
- Pyruvate⁻ + NADH + H⁺ ⇌ Lactate⁻ + NAD⁺
- Lactate as energy source
Glucose → 2 pyruvate → 2 ATP
FFK
LDH
2 lactate ↔ 2 pyruvate → alanine
RELATIONSHIPS OF PYRUVATE AND LACTATE DURING ANAEROBIC METABOLISM. I. EFFECTS OF INFUSION OF PYRUVATE OR GLUCOSE AND OF HYPERVENTILATION

WILLIAM E. HUCKABEE

J Clin Invest. 1958 Feb.;37(2):244-254
RELATIONSHIPS OF PYRUVATE AND LACTATE DURING ANAEROBIC METABOLISM. I. EFFECTS OF INFUSION OF PYRUVATE OR GLUCOSE AND OF HYPERVENTILATION

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Lactate production theoretically is not controlled exclusively by the adequacy of cellular oxygenation, and is demonstrably affected to a very significant extend by the pyruvate changes of over-ventilation or pH alterations of the body, of blood glucose changes and probably other stimuli. It would, therefore, seem quite inadvisable to draw any conclusions about tissue oxygen supply from determinations of lactate alone.
The effect upon blood lactic acid concentration of intravenous injection of isotonic NaCl solution and of adrenalin at rates of 0.00025, 0.00050, 0.00100, 0.00200, 0.00400, 0.00700 and 0.01000 mg/kg.min for 5 minutes.

II. The lower group of 3 curves: continuous line, values immediately upon completion of the 5-minute injection; dashed line, values 10 minutes after the end of injection; dotted line, values 30 min after the end of injection.

I. Upper single curve: total change during the 35-min period including the 5-min injection and the 30 min following.
In hemorrhage Lactate production is increased more in the absence of Ouabain

During Epinephrine: Lactate production is increased more in the absence of Ouabain

Relation between muscle Na⁺K⁺ ATPase activity and raised lactate concentrations in septic shock: a prospective study

Bruno Levy, Sébastien Gibot, Patricia Franck, Aurélie Cravoisy, Pierre-Edouard Bollaert

Ouabain-free infusion

Ouabain infusion

Lactate gradient (mmol/L)

Time (h)
INCREASED AEROBIC GLYCOLYSIS THROUGH BETA-2 STIMULATION IS A COMMON MECHANISM INVOLVED IN LACTATE FORMATION DURING SHOCK STATES

Bruno Levy, Olivier Desebbe, Chantal Montemont, and Sebastien Gibot
Groupe CHOC, Contrat AVENIR INSERM 2006, Faculté de Médecine, Nancy Université, Vandoeuvre les Nancy, France


Evolution of muscle lactate concentration (% of baseline value, y axis) measured by microdialysis during local pharmacological modulation of lactate metabolism. A, Hemorrhagic shock. B, Endotoxin. C, Peritonitis. In all models of shock, the use of ouabain, ICI-118551, or propranolol was associated to a decrease in muscular lactate. This demonstrates that lactate production during shock states is related, at least in part, to increased Na⁺K⁺ATPase activity under β2 stimulation induced by elevated endogenous epinephrine but independent of tissue hypoxia. Depicted are the mean values and SEM. Filled square indicates ouabain; triangle, propranolol; empty square, ICI; circle, Ringer *P G 0.01 vs. others groups.
Effect of prednisone on blood lactate concentrations in healthy dogs

![Graph showing effect of prednisone on blood lactate concentrations over time.](image-url)
The pattern of intermediary carbohydrate metabolism in Cushing’s syndrome

62 yr old male admitted with respiratory failure following 1st chemotherapy for B-cell lymphoma

High lactate levels

Lactate in B-cel lymphoma
The Warburg effect
Glucose $\rightarrow$ Pyruvate $\rightarrow$ 2 ATP $\rightarrow$ Lactate

Pyruvate $\rightarrow$ Alanine

Pyruvate $\rightarrow$ Acetyl CoA

Acetyl CoA $\rightarrow$ Electron Transport Chain $\rightarrow$ 36 ATP

Electron Transport Chain $\rightarrow$ H$_2$O $\rightarrow$ CO$_2$

Glycolysis

Oxidative Phosphorylation
Glucose $\rightarrow$ 2 ATP $\rightarrow$ Pyruvate $\rightarrow$ 2 Lactate $\rightarrow$ Alanine $\rightarrow$ Acetyl CoA $\rightarrow$ Oxidative Phosphorylation

Electron transport chain

36 ATP $\rightarrow$ H$_2$O $\rightarrow$ CO$_2$
Lactate shuttle

Lactate shuttle

Mitochondria

Lactate $\xrightarrow{LDH_i}$ pyruvate

Pyruvate $\xrightarrow{\text{monocarboxylate transporters}}$ Lactate

AcetylCoA

Krebs cycle
Gluconeogenesis

Lactate \[\rightarrow\] 6 ATP \[\rightarrow\] Cori cycle

LDH

glucose \[\rightarrow\] pyruvate
Glucose $\rightarrow$ 2 ATP

2 lactate $\rightarrow$ pyruvate $\rightarrow$ alanine

FFK $\rightarrow$ 2 ATP

LDH $\rightarrow$ pyruvate $\rightarrow$ alanine

sepsis $\rightarrow$ PDH $\rightarrow$ acetyl CoA

Electron transport chain

36 ATP

oxidative phosphorylation

glycolysis

H$_2$O $\rightarrow$ CO$_2$
Lactate in anemic and hypoxic hypoxia

Cain Am J Physiol 1965;209(3):604-610

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Lactate
intermediate fuel

- Glucose → red blood cell → lactate
- Glucose → astrocyte → lactate
- Glucose → neuron → lactate
- Glucose → cardiac muscle → lactate
- Glucose → striated muscle → lactate
- Glucose → liver → lactate
- Glucose → kidney → lactate

Cori cycle:
- Liver → Kidney
- Kidney → Liver

W. Nijsten, UMC Groningen

References:
- Stanley et al. Metabolism 1988;37:850-858
Increased lactate levels