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ST VINCENT'S PATHOLOGY

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LACTATE INFORMATION SHEET

PHYSIOLOGY

Lactate is a 3 carbon intermediary of carbohydrate metabolism which is formed from pyruvate by the reversible action of lactate dehydrogenase. Under normal circumstances it is produced in skeletal muscle, brain and erthrocytes and metabolised in the liver and kidney. The Cori cycle refers to the pathway whereby glycolysis in the muscle produces lactate, which is released into the bloodstream, transported to the liver and converted back to glucose for re-use in the muscle.

High levels of lactate may be produced in vigorous exercise. This occurs when energy requirements exceed oxygen supply and is known as oxygen debt. The lactate is rapidly cleared once the muscular activity ceases both by renal and hepatic clearance and by aerobic metabolism in the muscles. The half-life of serum lactate is about 60 minutes in these circumstances.

PATHOLOGY

Pathological lactate production occurs when there is inadequate tissue oxygen supply, or if there is defective pyruvate clearance or increased pyruvate production. Type A lactic acidosis occurs when there is obvious tissue hypoxia and Type B when tissue hypoxia is not apparent.

Hypoxia is by far the most common cause of lactic acidosis and can occur with shock from any cause. Other factors which may cause tissue hypoxia include severe asthma, severe anaemia, regional hyoperfusion and carbon monoxide poisoning. The rate of lactate recovery after shock is much slower than after exercise with an average clearance half-life of about 18 hours. Tissue hypoxia is probably a contributing factor in many patients with Type B lactic acidosis.

Other mechanisms of lactate accumulation include those causing a block in the further metabolism of pyruvate, eg cyanide toxicity, nucleoside analogues treatment, salicylates or mitochondrial cytopathies affecting the electron transport chain, thiamine deficiency reducing the activity of pyruvate dehydrogenase, and defects of gluconeogenic enzymes due to inborn errors or alcohol effects; and those leading to increased production of pyruvate, eg increased glycolysis with adrenaline treatment, and protein breakdown increasing the conversion of alanine to pyruvate in sepsis. The elevated pyruvate then equilibrates via LDH to produce increased lactate levels.

In the case of hypoxia, or other causes of inhibition of the electron transport chain, NADH accumulates, and the supply of NAD is depleted. This pushes the balance between pyruvate and lactate dramatically in favour of lactate further exacerbating its production in these circumstances. This change also occurs with alcohol abuse with alcohol dehydrogenase depleting NAD and producing NADH. A list of the common causes of elevated lactate is shown below.

CAUSES OF LACTIC ACIDOSIS

Type A: (clinical evidence of tissue hypoxia)

- Shock, sepsis, regional hypoperfusion, severe anaemia, CO poisoning, severe asthma

Type B: (no clinical evidence of tissue hypoxia)

- Diseases: eg diabetes, neoplasia, liver disease
- Drugs: eg ethanol, salicylates, methanol, cyanide, adrenaline, biguanides, nitroprusside, nucleoside analogues for HIV treatment
- Inborn errors: eg methylmalonic acidaemia, fatty acid oxidation defects, gluconeogenic enzyme defects
- Other: D-lactate, thiamine deficiency, sepsis

MEASUREMENT

Lactate is rapidly released from red cells in normal blood tubes. For accurate measurements, the following precautions must be observed:

- The patient must be at rest with no recent heavy exercise (eg not short of breath or tachycardic due to exertion).
- The tourniquet must be used minimally, and preferably not at all. Fist-clenching must be avoided.
- The sample must be collected into a fluoride-oxalate (grey-top) tube which blocks further glycolysis.