Hi clinical problem solvers! My name is Maani Kamal. I am a fourth year at the University of Alabama School of Medicine, and I'm going to talk to you about lactic acidosis.

Lactic acidosis occurs when lactic acid production exceeds lactic acid clearance. There are two big categories of lactic acidosis. Type A which is characterized by tissue hypoxia and Type B which is lactic acidosis in the absence of tissue hypoxia. Easy enough right?

When thinking about type A lactic acidosis, or lactic acid from tissue hypoxia, think about decreased O2 supply and increased O2 demand.

Decreased oxygen supply can result from decreased perfusion-- this can be diffuse resulting from a systemic drop in blood pressure, like from sepsis or hypovolemia, or you can have normal blood pressure but low perfusion because of cardiac pathology that reduces cardiac output – such as cardiogenic shock.

A patient may also have normal blood pressure, but a localized decrease in perfusion resulting in tissue hypoxia, like in mesenteric ischemia or compartment syndrome.

Tissue hypoxia can also result from cellular hypoxia, when blood is perfusing the body, but the amount of oxygen available from the blood is decreased. This can be due to a low PaO2 from decreased oxygenation from the lungs or a decreased oxygen carrying capacity of the blood. Think about things like severe anemia, carbon monoxide poisoning, or methemoglobinemia where the hemoglobin-oxygen dissociation curve, and thus oxygen delivery, is altered.

The final cause of type A lactic acidosis is from anything that increases metabolic oxygen demand like seizures or shivering. Even exercise can do this, although it isn't in our schema because it doesn't usually cause a hospital stay. Here, cells are not getting adequate oxygen to meet their increased demand for tissue metabolism

Now moving on to Type B lactic acidosis, which is lactic acidosis in the absence of tissue hypoxia. We have to think about biochemically how we create lactate. Glucose moves through glycolysis to create pyruvate and then pyruvate (with the help of NADH) can be turned to lactate. Sorry I know biochem is the ghost from the past. Let's focus in on the conversion of pyruvate (with NADH)→ lactate. Keeping the law of equilibrium in mind, each time we increase production of pyruvate or NADH or decrease utilization of these molecules we move the equation to the right towards lactate production resulting in type B lactic acidosis.

Pyruvate generally has 2 fates, or two ways of being utilized, moving though the krebs cycle (with the help of thiamine) or moving through gluconeogenesis. Therefore, anything that decreases these two processes results in an increased pyruvate and increased lactate.

Things that might inhibit the Krebs cycle are ingestion of ethanol (by increasing NADH production), cyanide toxicity by directly inhibiting enzymes, and sepsis which alters

mitochondrial function. Medications like metformin, propofol, and linezolid can also inhibit the Krebs cycle.

Genetic disorders that affect the mitochondria can result in lactic acidosis, and anything that decreases thiamine, which is a necessary cofactor for the pyruvate dehydrogenase complex, can also push the equation to the right. So decreased thiamine means decreased Krebs cycle which means increased pyruvate and the law of equilibrium says that means increased lactate!

The other pathway for pyruvate is through gluconeogenesis so anything that decreases gluconeogenesis will increase lactate, most notably liver disease.

Let's think back to our initial equation and remember that anything that increases production of pyruvate increases lactate. The end product of glycolysis is pyruvate so anything that increases glycolysis like cancer's Warburg effect (which is increased glycolysis in malignant cells) or Beta 2 adrenergic activation (from albuterol, cocaine, caffeine, or a pheochromocytoma) may lead to a lactic acidosis.

Also, exogenous ingestion of propylene glycol (often in lorazepam drips), which is directly metabolized to lactate, and infusion of LR in patients with cirrhosis can also lead to lactic acidosis.

Finally, I want to mention that lactic acidosis is most commonly due to decreased perfusion, ethanol consumption, or an increased adrenergic state.

We have covered a lot of ground, so let's take a step back and remember there are two types of lactic acidosis. First, there is type A which results from impaired tissue oxygenation either due to increased O2 demand or decreased supply. Then there is type B lactic acidosis (think B for biochemistry - just kidding I won't say the B word anymore) which is mainly caused by increased pyruvate production through increased glycolysis, or decreased utilization of pyruvate through a decrease in gluconeogenesis or the Krebs cycle.

Thank you all for listening and until next time Clinical Problem Solvers!