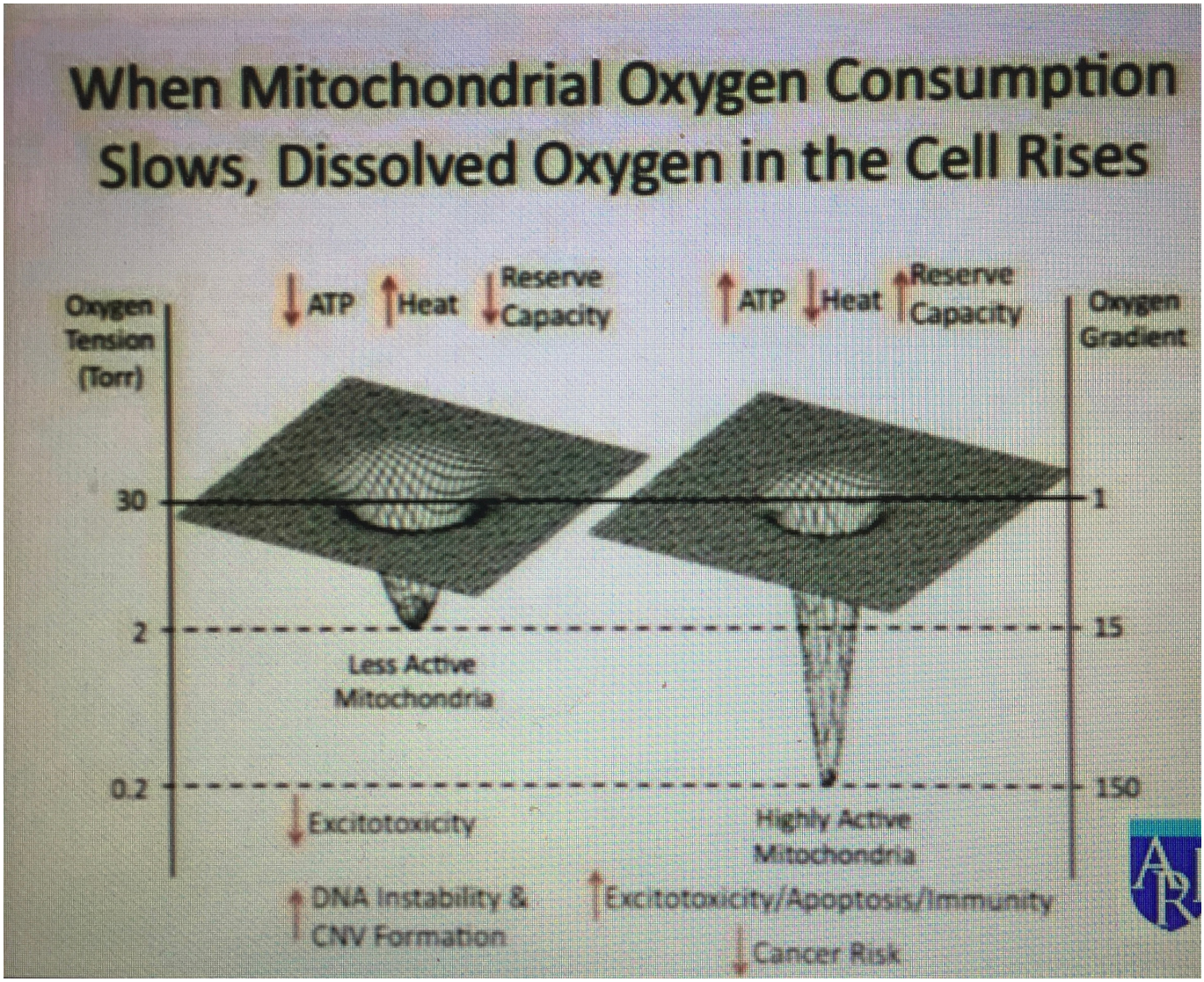
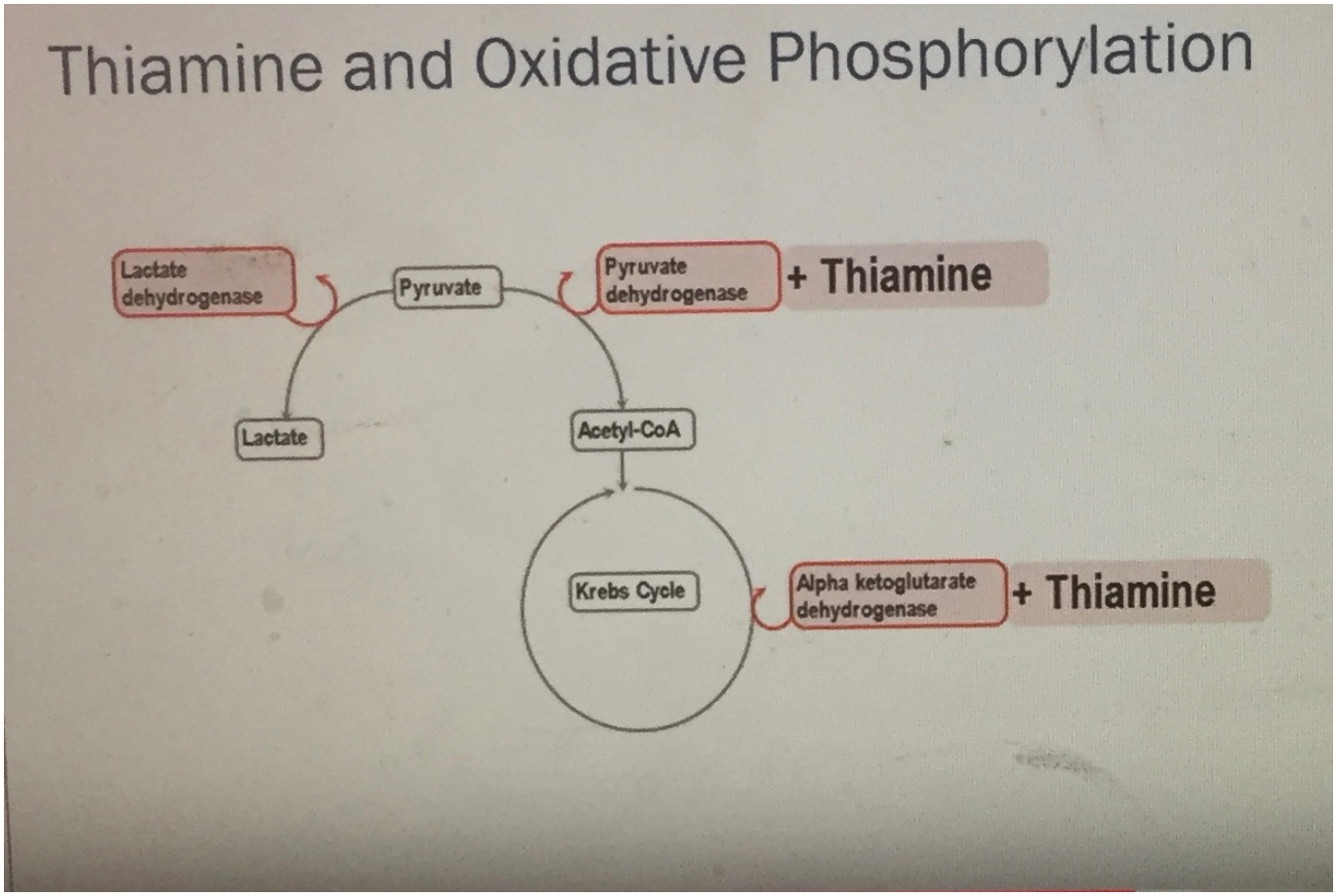
I covered this in Levee 25 of the Quilt long ago and now this series will visit this in depth:

Hypoxia/pseudohypoxia. Hypoxia is a cellular state that disrupts normal oxygen supply to the tissue (mitochondria), causing cellular dysfunction. Examples of t 25.his are altitude sickness at high elevations and clots in a blocked artery in an organ causing an organ to fail and die. Apoptosis and autophagy allow cells to adapt over their lifespan to many situations. Hypoxia is directly toxic to mitochondrial energy production. In humans, when oxygen is in short supply we can shift to anaerobic energy production, but it is not as efficient as mitochondrial energy production. Athletes with proper training can perform well in anaerobic conditions but it does appear that they pay a steep price for this adaptation by depleting their stem cell supply. The gateway in mitochondria for hypoxia is pseudohypoxia by blockade of pyruvate which sits atop the TCA cycle inside the matrix. The gatekeeper of the creation of Acetyl-CoA from pyruvate is *thiamine.* It is the major controller of substate movements in the matrix. As it drops we lose control of UCP-2 and this alters the matrix concentration of hydrogen isotopes.

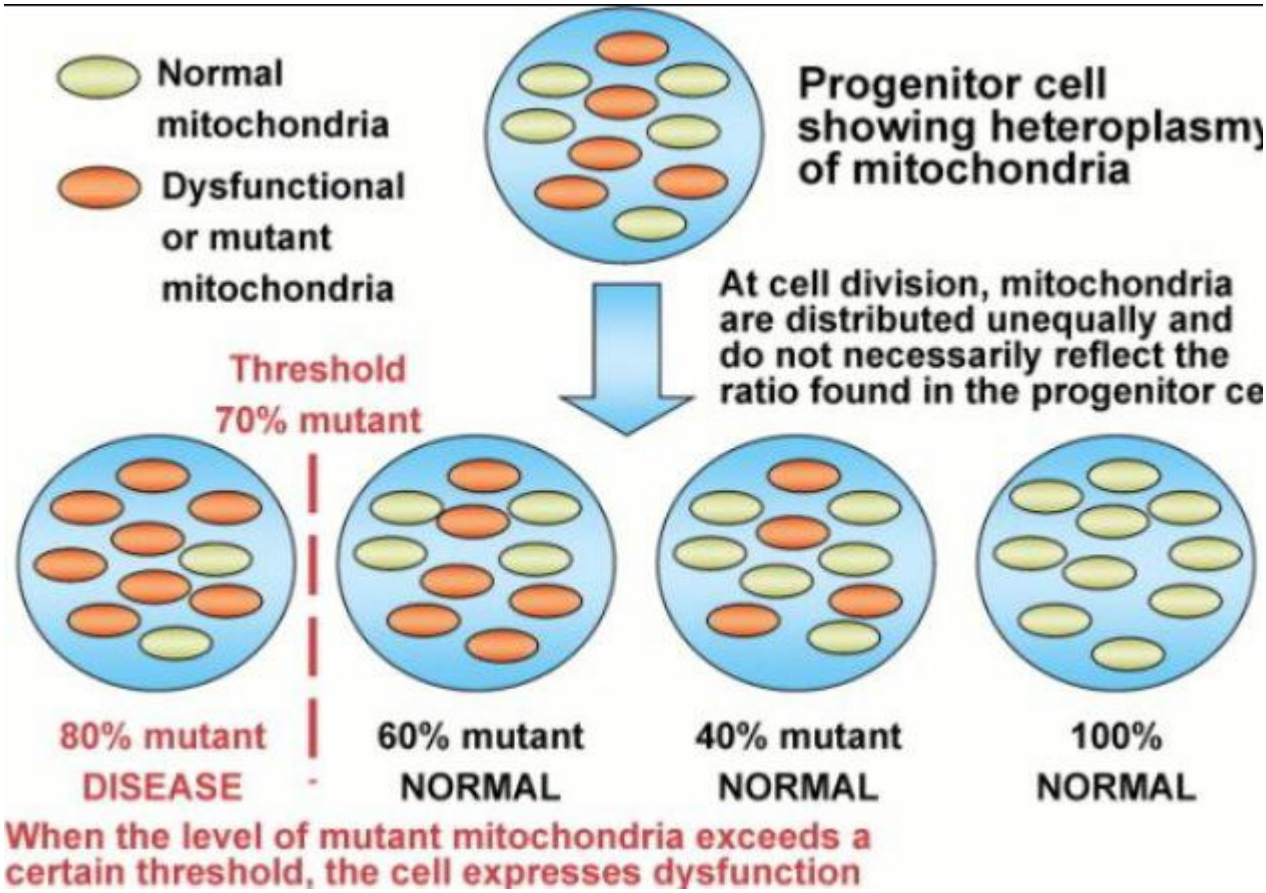


Thiamine deficiency causes a relative pseudohypoxia and is closely linked to heteroplasmy rate elevation in aging. Coffee and polyphenols destroy thiamine levels. As this occurs there is massive signaling to the SIRT system to affect mitochondrial biology.



As a consequence of pseudohypoxia, NAD+ levels drop and this funnels all the way back to how the aromatic amino acid tryptophan is catabolized in cells. It has multiple pathways it can travel and the pathway chosen will lead to the cell's fate.

Hypoxia plays a role in aging because as one age the amount of blood to organs declines as the heart fails to deliver the same amount of blood through a stiffened arterial tree throughout the body. THIS IS A PROTECTIVE STATE FOR POOR MITOCHONDRIAL FUNCTION = higher heteroplasmy rate.



This causes cellular oxygen levels to fall and usually is a signal to mitochondrial biogenesis to offset the deficits. As one age, this signaling system is not as accurate in sensing changes to the oxygen level. This can be measured in the pyruvate/lactate levels. Low oxygen tension is a signal to autophagic pathways that normally help repair cells. If this gets impaired, signaling autophagy becomes less effective as we age and results in more organ failure and diseases of aging. Hypoxia is critical signaling in the cell for repair processes. This is disordered in heart disease and in sleep abnormalities such as sleep apnea. Hypoxia decreases cell mass and improves leptin resistance by forcing a calorie restriction via a relative thiamine deficiency state. This only operates well if the person remains in a strong solar environment.

This, below, is the deep lesson of levee 25.