Shedding Light on Mitochondrial NADH in Vivo:

From experimental animals to clinical applications

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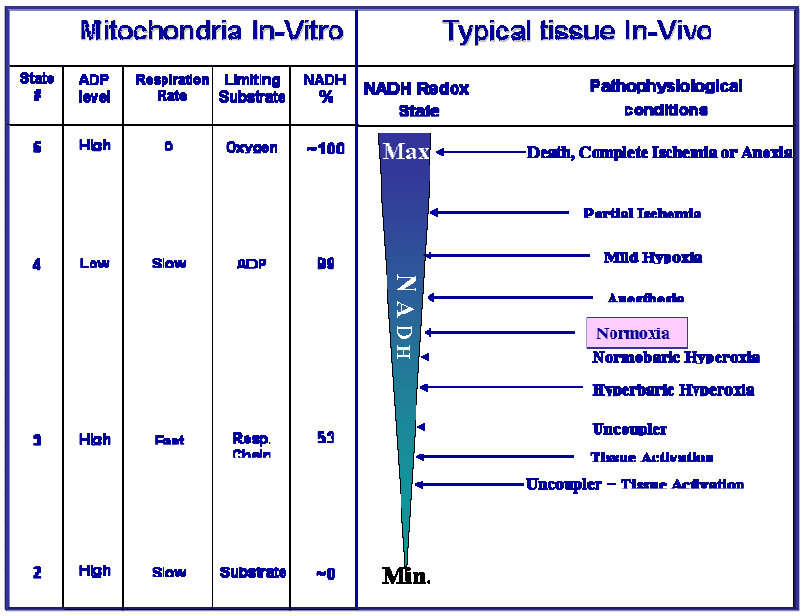
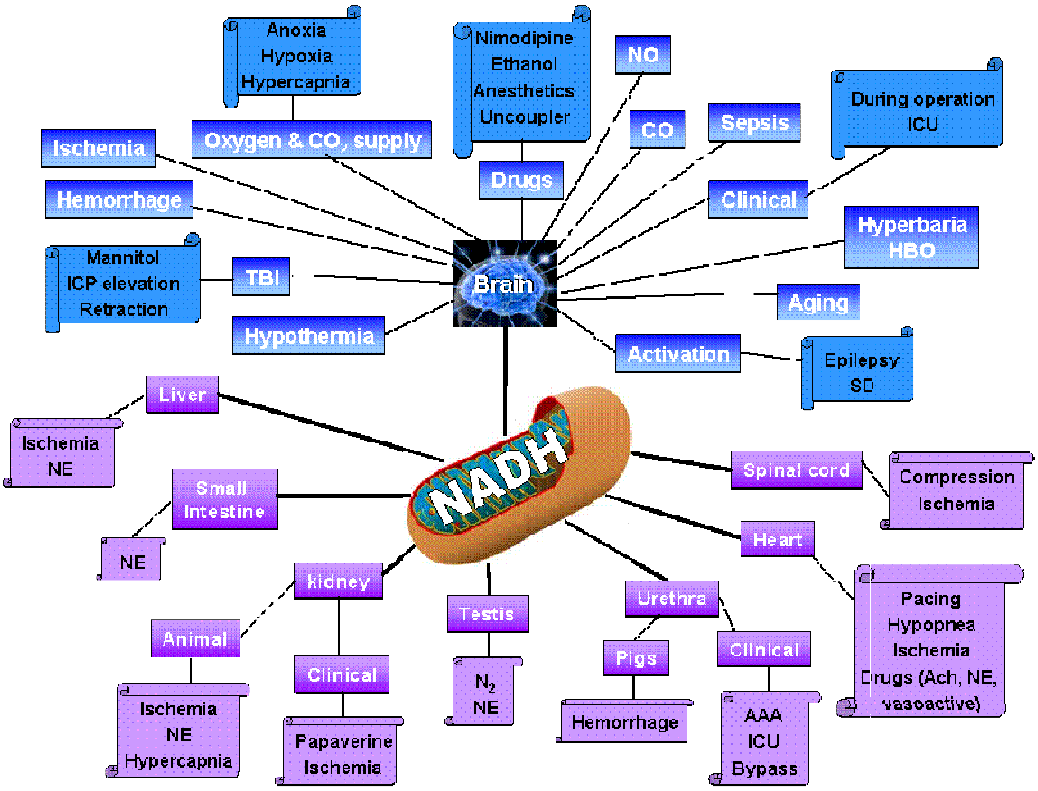
Understanding the mitochondrial function has been a challenge for many investigators, since its discovery more than 120 years ago. The description of pyridine nucleotides (i.e. NADH) by Harden and Young 100 years ago led the complete understanding of their structure by Warburg and collaborators 30 years later. In 1955, the seminal work of Chance and Williams defined for the first time the metabolic states of isolated mitochondria *in vitro*, and correlated these states to the oxidation-reduction levels of respiratory enzymes including the NADH. The physiological significance of these metabolic states was elaborated, by Chance and collaborators, to the In Vivo monitoring of NADH fluorescence resulted in 1,000 relevant publications on NADH fluorescence monitored *in vitro* and *in vivo*. The comparison between the metabolic states under the 2 conditions is presented in the next Scheme.



More recently, this technique was adapted for clinical applications (in intra-operative and intensive care units). In this lecture I will summarize my almost 40 years of activities and contributions to the understanding of mitochondrial redox state and tissue functions In Vivo. Normal mitochondrial function is a critical factor in maintaining cellular homeostasis in various organs of the body. Due to the involvement of mitochondrial dysfunction in many pathological states, the real-time *in vivo* monitoring of the mitochondrial metabolic state is crucially important. This type of monitoring in animal models as well as in patients provides real-time data that can help interpret experimental results or optimize patient treatment. The monitoring of NADH levels in the tissue provides the most important information on the metabolic state of the mitochondria in terms of energy production and intracellular oxygen levels.

In addition to NADH, we measured, optically, the microcirculatory blood flow and volume, as well as HbO_2 oxygenation, from the same tissue area. The four detected parameters provide real time data on tissue viability, which is critical for patients monitoring.



Monitored organs and perturbations measured by Mayevsky et al in experimental animals as well as in patients during the last 40 years.