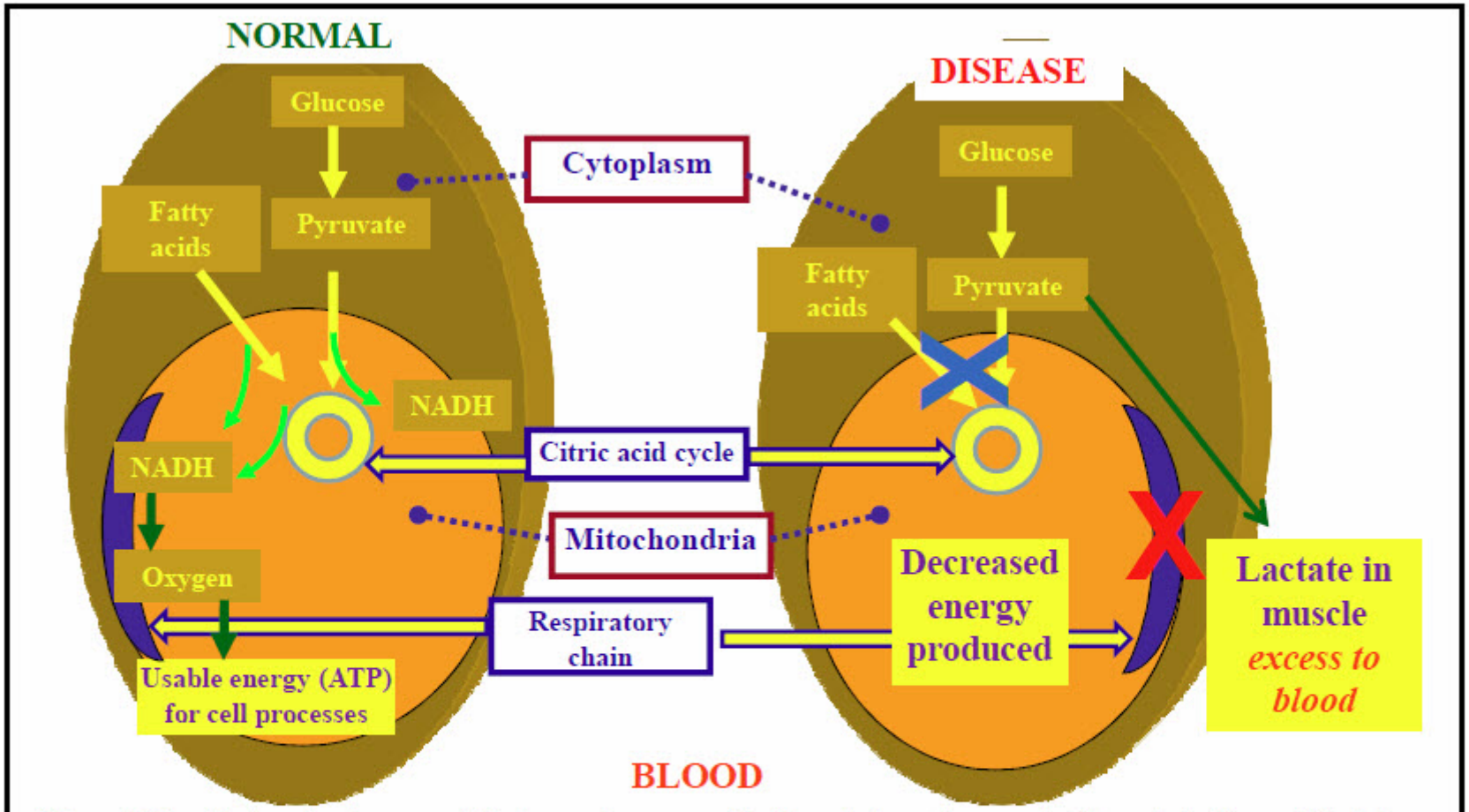

Figure 1. In cells (e.g., brain or muscle) glucose is processed in the cytoplasm to pyruvate. Pyruvate is then oxidized in the mitochondria via the citric acid cycle producing NADH. NADH is oxidized by oxygen using the respiratory chain to generate energy (ATP). Likewise fatty acids are oxidized in muscle (but not brain) mitochondria producing NADH to ultimately produce ATP for energy (left). The most common deficiency in Leigh Syndrome is of **complexes I or IV** of the respiratory chain (**X**). When either complex is not functioning, the respiratory chain cannot produce ATP and oxidation of pyruvate and/or fatty acids diminishes markedly. Lack of energy leads to muscle symptoms of **weakness, hypotonia, movement disorders** and **overproduction of lactic acid** from the pyruvate that cannot be oxidized. In nervous tissue the energy deficit leads to the **progressive nerve degeneration, spasticity** and **peripheral neuropathy**.

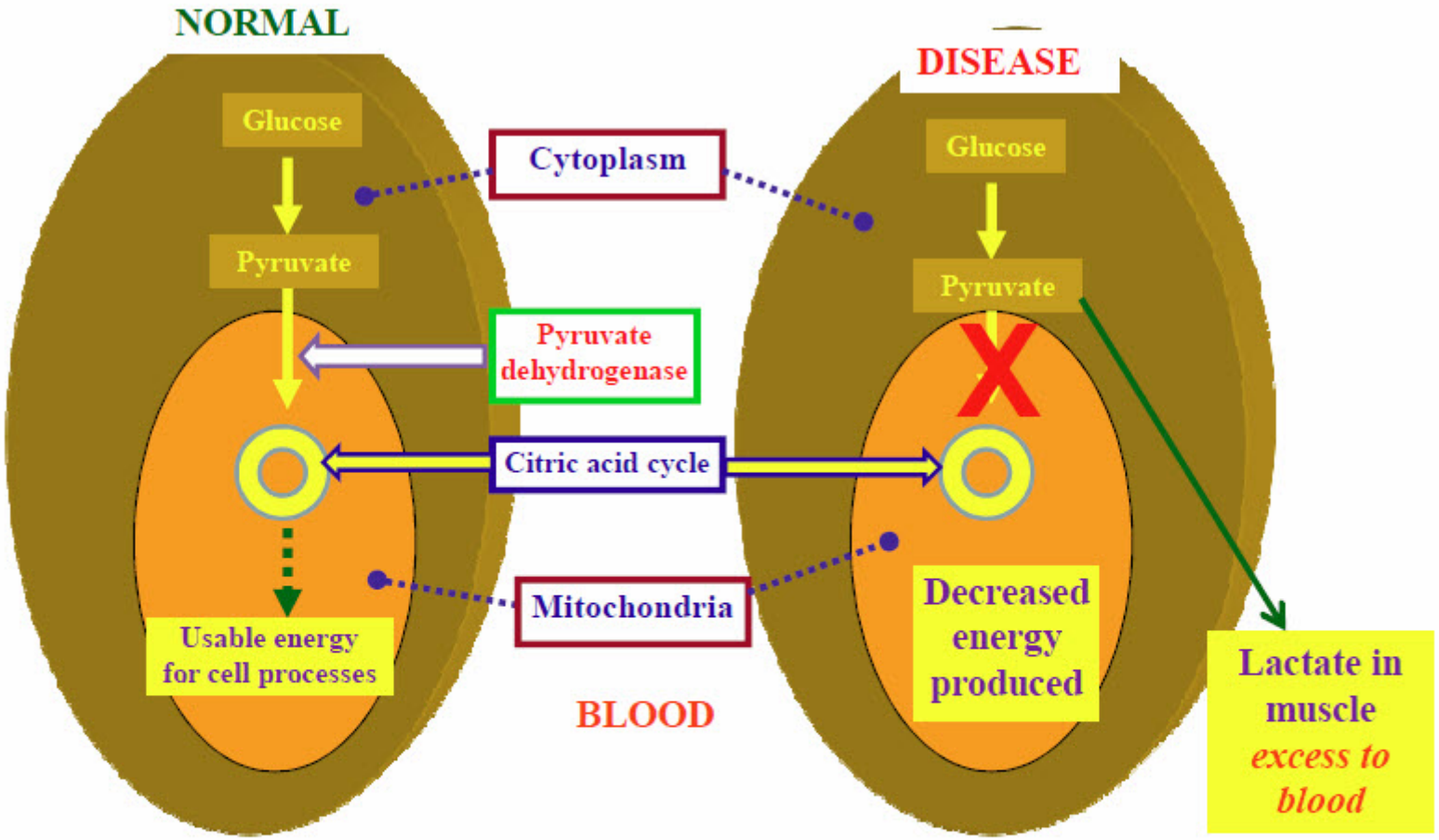

Figure 2. In cells (e.g., brain or muscle) glucose is processed in the cytoplasm to pyruvate. The pyruvate then enters the mitochondria where it is oxidized via pyruvate dehydrogenase to produce a product used to generate energy via the citric acid cycle (left). In some types of Leigh Syndrome, pyruvate dehydrogenase is deficient (X) so that pyruvate cannot be oxidized to produce energy. The lack of energy leads to muscle symptoms of weakness, hypotonia, movement disorders and the notable overproduction of lactic acid from the pyruvate that cannot be oxidized. In nervous tissue the energy deficit leads to the progressive nerve degeneration, spasticity and peripheral neuropathy.