HUMAN MITOCHONDRIAL DISEASES

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Mitochondrial diseases are very diverse conditions due to dysfunction of mitochondria, specialized compartments in virtually every cell of the body. Mitochondria generate more than 90% of the energy required by the body. Mitochondrial dysfunction depletes cells of energy causing cell damage and even cell death. Due to the high energy requirements of brain and muscle, mitochondrial disease typically affect these parts of the body causing encephalomyopathies. Mitochondria are unique organelles because they are the products of their own genetic material (mitochondrial DNA or mtDNA) and nuclear DNA. Therefore, mitochondrial diseases are caused by mutations in either mtDNA or nuclear DNA.

Mitochondrial diseases are often difficult to diagnose and therefore, it is important for patients to be evaluated at a medical center with appropriate expertise. In some cases, symptoms and signs may suggest a particular mitochondrial disease. Physical examination and laboratory tests are necessary to characterize involvement of various organs and to reach the correct diagnosis. Laboratory studies typically include: blood tests, brain MRI or CT scans, heart tests (electrocardiogram and echocardiograms), ophthalmological and neurological evaluations, and hearing tests. Elevated lactic acid (lactate) or lactate to pyruvate ratio (>20:1) in blood or cerebrospinal fluid is a common sign of mitochondrial dysfunction. Muscle biopsy is the gold-standard for the diagnosis of many mitochondrial diseases and requires specialized microscopic analyses and biochemical tests (such as measurements of mitochondrial respiratory chain enzyme activities). Finally, genetic testing of blood, urine, or muscle is performed to pinpoint the exact mutation responsible for a specific disease. The most common symptoms of mitochondrial disorders are: muscle weakness, exercise intolerance, fatigue, cognitive difficulties, and neurological problems. The current genetic advice is that fathers with mtDNA mutations are at no risk of transmitting the defect to their offspring. Maternal transmission of mutated mtDNA occurs, but the risk depends on the type of mutation and possibly the segregation of the mutation within maternal tissues. Identifying specific mtDNA mutations and investigating family members for evidence of transmission will give guidance to the likelihood of transmission through the germline. Detailed studies of large patient cohorts provide invaluable information on the risk of transmission.