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CLINICAL ASPECTS OF MITOCHONDRIAL DISORDERS IN CHILDHOOD

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Mitochondrial disorders of energy metabolism represent a heterogeneous group of diseases. We analysed clinical symptoms in 210 children and adult patients with mitochondrial disturbances. Methods: Symptoms, body fluids metabolites, activities of respiratory chain complexes and molecular analyses were evaulated. Results: First clinical symptoms in children were failure to thrive, progressive hypotonia, respiratory problems and developmental delay, but other symptoms in various combinations including cardiomyopathy, seizures, microcephaly, strabismus, optic atrophy, ptosis and nystagmus were observed. Blood and CSF lactate and alanine were increased in 75-90% of children. Respiratory chain complex I deficiency was found in 17 patients, complex II 4x, complex III 7x, complex IV 48x, combinated deficiencies 55x. Mutations in SURF1 gene was found in 9 children with Leigh syndrome, mutations in SCO2 gene in 7 children with encephalopathy and hypertrophic cardiomyopathy, mtDNA mutations G3460A and G11778A in 65 patients with LHON syndrome, A3243G in 30 patients with MELAS syndrome, A8344G in 10 patients with MERRF syndrome, T8993G in 7 children with NARP syndrome, mtDNA deletion in 6 patients with Kearns-Sayre syndrome, mtDNA depletion in 2 boys with Alpers disease and mtDNA deletion 9204delAT in two boys with maternally inherited encephalopathy. In families with different mtDNA mutations, various patterns of intergenerational transmission were observed, increased level of heteroplasmy was found in all offspring of mothers with mtDNA mutations T8993G. Conclusions: Progressive course of the disease, family history, clinical investigation and increased lactate and alanine in blood and cerebrospinal fluid have a high predictive value for diagnostics. Supported by VZ 111100003.