

This thesis has been worked out in The Laboratory for Study of Mitochondrial Disorders, Department of Paediatrics, 1st Faculty of Medicine, Charles University in Prague.

A retrospective multicentric study in 180 children with cytochrome *c* oxidase (COX) deficiency was designed in cooperation with the Division of Metabolic Diseases in Department of Paediatrics, The Children's Memorial Health Institute, Warsaw, Poland. The survey was focused on clinical manifestation, molecular background and prognosis of the disease and showed that COX deficiency in childhood represents a heterogeneous group of diseases with significantly unfavourable prognosis. Genetic counselling in affected families requires detailed characterization of COX deficiency at the molecular level. An underlying genetic defect was found in 42 % of patients by detection of mutation in mitochondrial DNA (mtDNA) or in nuclear coded genes for proteins *surf1* and *sco2* that contribute to COX assemblation. Isolated defects of COX were found in patients with mutations in *SURF1* or *SCO2* genes, whereas in the patients with mutations in mtDNA was the defect of COX combined with decreased activities of one or more other respiratory chain complexes. In the second part of the work, activities of respiratory chain complexes in isolated platelets were analysed in large control group of 161 children and adults in age between 0.5 and 35 years. We showed that isolated platelets are suitable biological material for diagnostics of generalized mitochondrial disorders. In addition, a significant difference in mitochondrial energetic metabolism with increased activities of respiratory chain complexes I and II was

found in a group of 36 females with anorexia nervosa and BMI 15 ± 1.7 in comparison with the age related controls.

In the last part of the work, the activities and protein amount of respiratory chain complexes and pyruvate dehydrogenase (PDH) were analysed in 19 premature neonates in isolated muscle mitochondria obtained at autopsy. Significant age-related differences between premature neonates and older children were observed. Especially, the activities of PDH and respiratory chain complexes III and IV were significantly lower in premature neonates.