Examination methods in DMP

Screening Methods Inherited Metabolic Disorders are a set of biochemical, genetic, physical-examination, anamnestic, and other procedures to determine a particular congenital enzymatic disorder, deficiency of transport or other protein.

Significance of the diagnosis

Diagnosis has an impact mainly on the choice of treatment, which is fundamentally different from diseases falling within the differential diagnosis of some inherited metabolic disorders (oncological diseases, neurodegenerative diseases, etc.). However, it is also important if there is no other than symptomatic treatment for the disease, which can be performed without knowledge of the diagnosis. Its importance lies not only in adjusting the treatment but also in improving the patient's mental state after explaining the causes of the disease and alleviating anxiety and uncertainty, as well as in preventing symptoms that have not yet manifested, unnecessary further examinations and risk assessment for the proband relative.

Diagnosis of DMP

- **Diagnosis of a specific patient**

  Based on the patient 's problems, medical history and physical examination, examinations are indicated that confirm or refute the initial **hypothesis**. In the first case, a diagnosis is made, in the second case, a new hypothesis is made and the process is repeated.

- **Selective screening**

  Laboratory examinations of some diseases are performed in a selected group of people in whom some manifestations of inherited metabolic disorders are manifested.

- **Population-wide screening**

  It is an active search for diseases in the whole population, it allows presymptomatic diagnosis.

  Laboratory tests for markers of diseases with a high incidence are performed in all newborns. The benefit (high incidence, serious illness) must outweigh the price (financial costs, burden on the patient and his family in the event of a false positive result).

Levels of diagnostics

An inherited metabolic disorder can be diagnosed in a patient at several levels that result from the pathogenesis of DMP: the cause is a gene mutation that results in an enzyme deficiency; this causes the accumulation of substrate and the absence of the product of the metabolic pathway, which then manifests as tissue, organ or general damage to the organism.

Used examinations

Procedure: organism level → metabolite level → enzymatic level → nucleic acid level.

- **genetic level**(DNA, mRNA): determination of a specific mutation by DNA diagnostic methods - polymerase chain reaction with primers specific for the given mutation; sequencing (common sequencing methods, next generation sequencing)
- **enzymatic level:** determination of the presence or better activity of a given enzyme - biochemical determination of enzyme activity: in time measured photometrically, radiometrically, fluorimetrically or by mass spectrometry loss of substrate or cofactor or formation of product of determined or coupled reaction. (Note: ELISA does not measure activity, but enzyme concentration.)
- **metabolites level:** determination of substrate accumulation and product absence, sometimes indirectly (eg NADH + H^+ accumulation in oxidative phosphorylation disorders by determination of lactate and 3-hydroxybutyrate) - biochemically, immunochemically, by chemical analysis methods:
  - for ***small molecules***, high-performance liquid chromatography, gas chromatography, widely used tandem mass spectrophotometry in screening
  - for ***complex molecules*** electrophoresis, immunochemistry
- **organism level:** physical examination, anamnesis, imaging methods (eg MRI in diseases of complex molecules replicating neurodegenerative diseases example!) - irreplaceable place. The doctor and his ability and ability to indicate selective screening play a big role.

The available laboratory tests have different sensitivities due to the nature of the laboratory method and analyte.

The output is a comprehensive picture of results that are difficult to interpret and require specialization.

Indications leading to suspicion of DMP

The reason for performing laboratory tests at the genetic, enzymatic and metabolite level is obtained by the doctor especially if:

- hereditary disorders are indicated by a *family history* - consanguinity, similar manifestations in relatives, unexplained deaths in the family,
- a disease considered to be *does not respond* to normal treatment,
- the disease is *multisystemic* ,
- the disease is affected by factors typical of DMP - catabolic conditions (fever, muscle strain), starvation, protein or carbohydrate intake,
- unexplained deviations from routine laboratory tests are found,
- Manifested manifestations of the disease are rare and at the same time typical for DMP - odor, urine color, specific dysmorphia (gargoilism), etc.

Manifestations differ in DMP small molecules and DMP complex molecules.

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Source

- ws:Vyšetřovací metody u DMP

Hereditary metabolic disorders (DMPs)	
In general	DMP of complex molecules • DMP of small molecules • Neonatal screening • Screening of hereditary diseases • **Examination methods at DMP**
DMP amino acids	Alkaptonuria
Organic aciduria	-
DMP urea cycle	Alcaptonuria • Ornithine transcarbamylase deficiency • Prolidase deficiency • Phenylketonuria • Glutaric aciduria • Hyperphenylalaninemia • Hyperornitinemia • Isovaleric aciduria • Leucinosis • Non-ketotic hyperglycemia • Cystinosis • Tyrosinemia
DMP propionate, biotin and cobalamin	Biotinidase deficiency • Methylmalonic acidemia • Propionic acidemia
DMP purines and pyrimidines	Liver porphyria • Skin porphyria • Mitochondrial neurogastrointestinal encephalomyopathy
DMP sugars	Glycogenoses • Fructosealdolase deficiency • Fructose-1,6-bisphosphatase deficiency • Essential fructosuria • Galactokinase deficiency • Galactose-1-phosphate uridyltransferase deficiency
DMP mitochondria	Phosphoenolcarboxykinase Deficiency • LCHAD Deficiency • MCAD Deficiency • Pyruvate Dehydrogenase Deficiency • Pyruvate Carboxylase Deficiency • SCAD Deficiency • Chronic Progressive External Ophthalmoplegia • Leber's Hereditary Optic Neuropathy • Leigh Syndrome • Maternally Hereditary Diabetes and Deafness • SayLC Syndrome
DMP peroxisomes	Neonatal adenodystrophy • Refsum's disease • Rhizomelic chondrodystrophia punctata • X-linked adrenoleukodystrophy • Zellweger syndrome
DMP of lysosomes	Fabry disease • Gaucher disease • Krabbe disease • Danon's disease • Mucolipidosis II • Metachromatic leukodystrophy • Mucopolysaccharidosis III • Niemann-Pick disease • Cystinosis • Tay-Sachs disease
Portal: Pathobiochemistry	