Examination methods of inherited metabolic disorders

This article has been translated from WikiSkripta; ready for the **editor's review**.

Examination methods of inherited metabolic disorders are a set of biochemical, genetic, physical-examination, anamnestic and other procedures to determine a specific 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 IMD

- **Determining the diagnosis in a particular patient**

🔎 *For more information see Diagnosing.*

  Based on the problems the patient is experiencing, the anamnesis and the 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 entire population, it allows pre-symptomatic diagnosis.

🔎 *For more information see Screening of the newborn.*

  Laboratory tests for markers of diseases with a high incidence are performed on 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).

Diagnostic levels

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, 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 the product of determined or coupled reaction. (Note: ELISA does not measure activity, but enzyme concentration.)
- **Level of metabolites:** determination of substrate accumulation and lack of product, sometimes indirectly (eg accumulation of NADH + H + 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, for screening widely used tandem mass spectrophotometry
  - for ***complex molecules*** electrophoresis, immunochemistry
- **Level of the organism:** physical examination, anamnesis, imaging methods (eg. MRI in diseases of complex

molecules copying 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 IMD

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
- The disease considered normal **does not respond** to the usual treatment
- The disease is **multi-systemic**
- Diseases are affected by factors typical of IMD- 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 IMD - odor, urine color, specific dysmorphia (gargoilism), etc.

Manifestations differ between IMD small molecules and IMD complex molecules.

Template:Netisknout