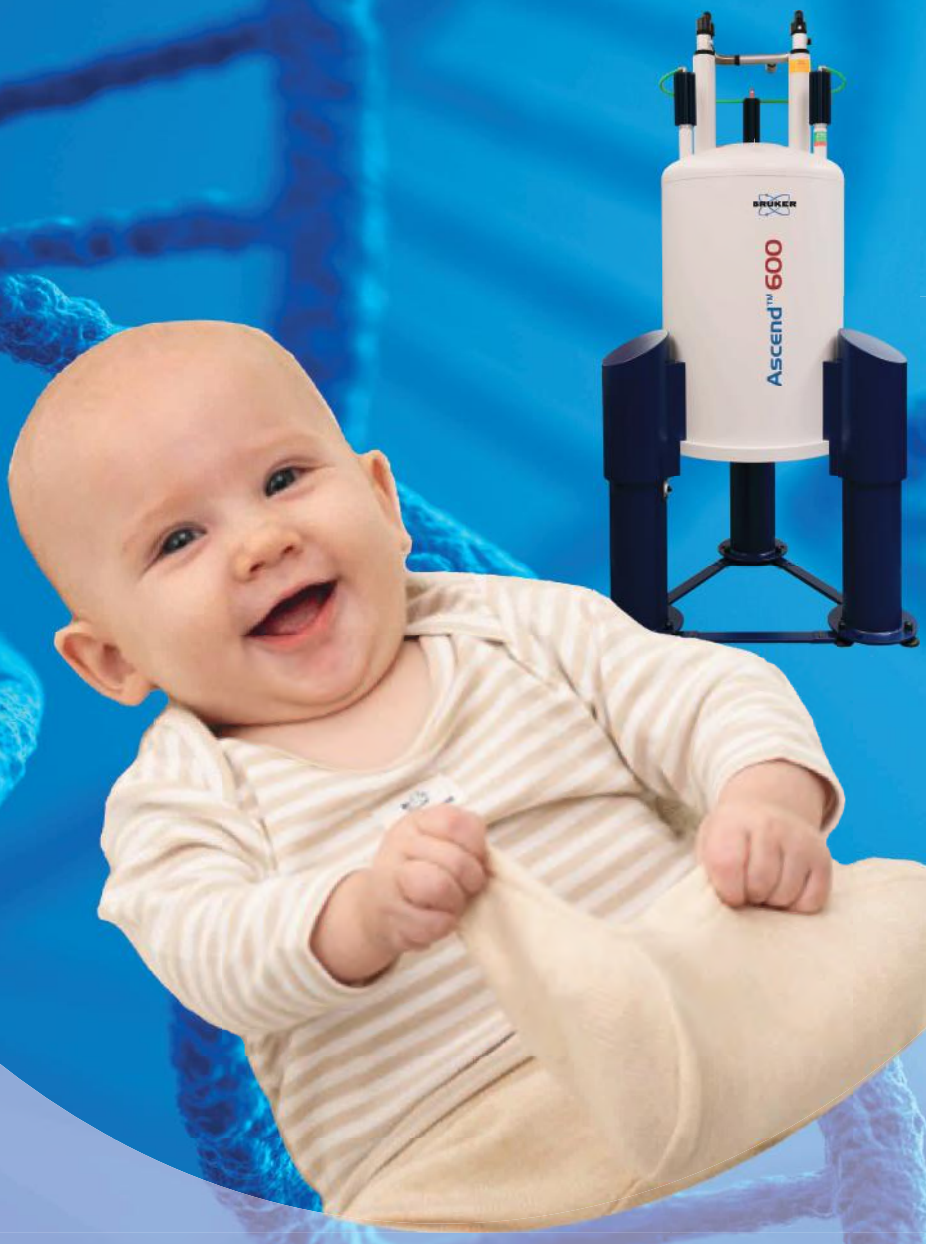
Metabo Test INFAI®

NMR-based screening for inborn errors of metabolism



Inborn errors of metabolism:
A worldwide problem for children

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What are congenital metabolic diseases?

As a result of inherited erroneous genes, your child can not utilize for his/her body some of the substances taken up with food. These substances accumulate, may harm your child's various organs and tissues, and symptoms and signs related to these organs and tissues emerge. Sometimes the cause of these symptoms is because of not being able to produce an end-product which is vital for the body.

What is the prevalence in Turkey?

The newborn screening studies being conducted nowadays (phenylketonuria, congenital hypothyroidism and biotinidase deficiency), pilot screenings for other metabolic diseases and clinical observations; indicate that the frequency of congenital metabolic diseases in our country is high. Interpersonal erroneous gene carrying for inherited metabolic diseases and the high consanguineous marriage rate in our country, play a role in high frequency. The frequency of congenital metabolic diseases in Turkey is approximately 1 in 400.

What are metabolites?

Metabolites are all small molecules that are used to build up bigger molecules or structures, such as cells or even organs. They are either produced in the body or are taken up by food. In urine, these metabolites can be observed as normal or pathological metabolites, which can cause different diseases.

What is newborn screening?

It is a standardized examination performed in every newborn. It is the examination of newborn babies for some inherited diseases that can be treated when detected early, and may cause irreversible damage (e.g. mental deficiency) when detected late, and have a convenient marker for the diagnosis in asymptomatic period. Newborn screenings in Turkey is routinely being performed for three inherited diseases (phenylketonuria, congenital hypothyroidism and biotinidase deficiency). The screenings of some other inherited metabolic diseases are performed optionally or within the scope of "selective screening".

Why is it necessary?

Because congenital metabolic disease can cause irreversible organ damage, disability, or death for some individuals, it is crucial to screen each newborn for these diseases. If your baby has one of these diseases which is detected early before some of the symptoms are emerging, and if it is treated properly, the progression of the disease can be stopped and any further damage for your baby can be prevented. For instance, if the detected disease prohibits a convertion from metabolite A to metabolite B, you just use a special diet providing your baby with metabolite B by food. This will make you happy as parents and improve the quality of life in your family.

Which methods are used for newborn screening?

Presently, tandem-mass spectrometry (MS-MS) is the most used method for newborn screening. Additionally, gas chromatography combined with mass spectrometry (GC-MS) can be used. However, Tandem-MS can only investigate a total of approximately 40 metabolites at a time. Only investigations in suspected disease are feasible. One of the effective and newest methods for newborn screenings is NMR spectroscopy.

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What is NMR Spectroscopy?

NMR stands for nuclear magnetic resonance. NMR spectroscopy of the body fluids, with respect to being noninvasive, is a promising alternative approach for the targeted or non-targeted analyses of the metabolites in known and unknown diseases. The 1H-NMR spectroscopy of body fluids shows the majority of proton-containing compounds, and therefore it presents an overall picture about the metabolism. Compared to other techniques, this is a great advantage in the diagnosis of inherited metabolic diseases. NMR spectroscopy of body fluids can be considered as an alternative analytic approach in the diagnosis of both known and not yet known congenital metabolic disorders.

What are the advantages of NMR screening?

More than 1000 metabolites can be observed in the urine spectrum obtained with NMR, and their concentrations can easily be detected. The analysis takes only 15 minutes, and provides a rapid and cost-effective diagnostic screening with one measurement. This method, non-invasive by nature, does not require derivatization and has a rapid measuring rate, and because of these, it is a great advantage compared to other techniques. Statistical analyses used in the device, allows examination not only for known metabolic diseases but also for the selective and non-selective metabolites, and therefore it can also indicate unknown diseases.

When are further examinations necessary?

Methods like tandem mass spectrometry and NMR may be insufficient for the identification of some metabolites. Despite all analyses, if the disease of your child could not be diagnosed specifically; enzyme activity measurements and advanced gene sequence analysis techniques may be helpful. If there is an inherited metabolic disease suspected; the gene associated with this disease can be evaluated for erroneousness, if a disorder is detected then it implies that the suspected disorder is proven to be inherited by your child. If it was not focused on a certain inherited metabolic disease; then a whole gene analysis must be performed. The suspected genetic disorder can be associated with the symptoms and signs of your child. Sometimes; it might be new disease which is not diagnosed before and diagnosed for the first time in your child. We kindly submit for your information that we provide diagnostic enzyme activity measurements regarding the suspected inherited metabolic disease together with the various genetic analyses services.

Suggestions

With early diagnosis, therapy and special medication, these developmental disorders can be prevented in most cases and may be treated successfully - which can greatly increase the quality of life of both the newborn and its parents. Therefore, all newborns should be tested for such congenital metabolic disorders.

INFAI and Bruker BioSpin conducted a multi-center study with the participation of 10 centers in Turkey to demonstrate the usability of NMR spectroscopy in newborn screening. Urine samples taken from 989 newborn babies were assessed with NMR spectroscopy in high fidelity. At the end of the research, it was understood that known and unknown inherited metabolism disorders can be detected early with fully automated and NMR spectroscopy.

Due to our long standing experience in investigation body fluids by NMR spectroscopy, we can rely on our database with more then 600 normal and pathologic metabolites, currently correlating with nearly 200 metabolic diseases.

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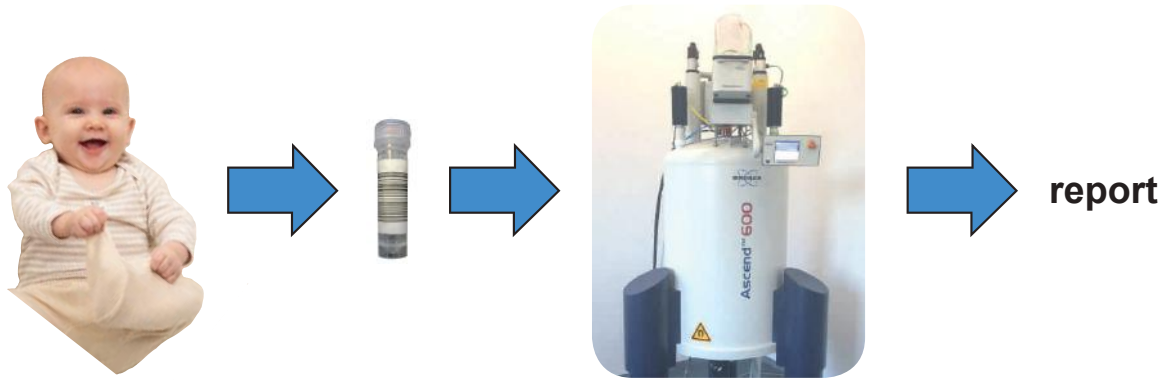
We offer

- Targeted and non-targeted screening for inborn metabolic diseases.
- Identification of 250 pathological metabolites used as disease markers, currently correlating with more then 190 inborn metabolic diseases.
- Research tool for metabolite search related to diseases on our homepage (www.infai.com).
- Additional analysis, such as gene sequence (full exome, next generation sequencing), enzyme analysis or tandem-MS.



Quality management

INFAI has established an integrated quality management system based on ISO 9001:2008, in compliance with national and international regulations. The high quality standards defined within this framework ensure the production of reliable and high-quality pharmaceutical products. Customer satisfaction is at the centre of all our activities. The permanent improvement of our quality management system enables us to act quickly upon changing market conditions.

Metabo Test INFAI in Turkey will be performed in cooperation with Bruker Biospin.

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