BECAUSE LIFE BEGINS TODAY

CentoICU®
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Genetic testing for newborns or children <24 months admitted to the ICU

Complex and severe genetic disorders encompass diseases with complex phenotypic presentations and severe disease courses. A precise diagnosis of the underlying condition is especially important in serious and life threatening situations as found in the intensive care setting. Newborns and children presenting with life threatening metabolic, neurologic, gastrointestinal, or urogenital conditions need a fast and precise diagnosis in order to have optimal and efficient further diagnostic and therapeutic progress. Up to one third of all babies and children admitted to the intensive care unit (ICU) have a genetic disease. For many of them early identification can make the difference for their immediate and later health.

Statistics on genetic disorders in newborns admitted to the ICU

- About 3-4% of newborns will be born with a genetic disease or major birth defect
- Approximately 1% of all babies will be born with a chromosomal abnormality which can cause physical problems and mental retardation
- More than 20% of infant deaths are caused by birth defects or genetic conditions (e.g. congenital heart defects, abnormalities of the nervous system, or chromosomal abnormalities)
- 11.1% of pediatric hospital admissions are for children with genetic disorders and 18.5% are children with other congenital malformations
- Approximately 10% of all adults and 30% of children in hospitals are there due to genetically related problems; 12% of adult hospital admissions are for genetic causes.
How does CentoICU® differentiate from current newborn screening?

The term newborn screening refers to public health programs designed to screen newborns for treatable inherited conditions soon after birth. Usually newborn screening is conducted as a metabolic or biochemical test. Newborn screening is currently performed for selected conditions which can be analyzed by biochemical assays from blood and for which treatment options exist.

The selection of analyzed diseases varies between countries - i.e. recommendation guidelines (ACMG) differ. The analysis of DNA offers us a broader view of diseases which may not be identifiable by blood biochemistry. It also includes conditions which may be present acutely later in early childhood or which have a complex symptomatology. This can make differential diagnosis very difficult and can be quite challenging in an emergency setting, such as an ICU.

Who should consider CentoICU®?

- Parents and physicians providing treatment to newborns and children under 24 months admitted to the ICU and presenting with unclear symptomatology which can be part of a genetic condition, i.e.:
  - Bleeding Dyathesis
  - Blood Abnormalities (Anemia)
  - Bone Fragility
  - Failure to Thrive
  - Heart Abnormality/Arrhythmia
  - Hepatosplenomegaly
  - Hypotonia
  - Ichthyosis/Epidermolysis Bullosa
  - Metabolic Abnormalities
  - Microcephaly
  - Neutropenia
  - Abnormal Newborn Screening Results
  - Respiratory Failure
  - Skeletal Abnormalities/Craniosynostosis
  - Skin Fragility
  - Unclear Seizures

Why choose CentoICU®?

CentoICU® is our comprehensive NGS panel for the earliest and fastest diagnosis of critically ill newborns and children in intensive care units of hospitals. It offers:

- Short TATs: 10 days (CentoICU® FAST and CentoICU® Panel Genomic FAST) or 15 days (CentoICU® and CentoICU® Panel Genomic)7
- Add-on option of CGH array CentoArray® possible to complement copy number analysis with high density array8
- Exhaustive coverage of the coding regions within the 810 targeted genes
- Specialized technology that allows us to target genes that are clinically linked to the ACMG-recommended newborn screening conditions as well as conditions that have been nominated for the list
- Earlier detection of these conditions can also result in less invasive and lower cost treatments for patients
- Can be performed on as little as 1 µg DNA, 1 mL blood, or 1 filtercard

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5 Abnormal Acylcarnitine Profile, Amino Acidemia/Urea, Hyperbilirubinemia, Hyper-/Hypoinsulinism, Persistent Hypoglycemia, Organic Acidemia/Urea
6 CentoICU® includes genes to cover all ACMG core panel phenotypes for newborn screening except hearing loss
7 CentoICU® Panel Genomic and CentoICU® Panel Genomic FAST are performed on a Whole genome sequencing backbone, and when negative can be reflexed to WGS at a nominal cost to examine genes outside the panel that may explain the phenotype
8 Copy number variants calling with NGS has limited sensitivity over whole genome. We strongly recommend to complement the NGS Panel genomic option with aCGH for increased sensitivity for genome wide structural variants, wherever analysis of structural variants may have a significant bearing on the phenotype.
We offer NGS sequencing of all targeted genes in CentoICU® with exhaustive coverage of the coding regions.
What genes are included in CentoICU®?

CentoICU® is designed for analysis of 810 genes and more than 100 associated conditions/phenotypes. The list of included genes has been developed by our expert medical team based on several selection criteria, i.e.:

- Early onset
- Severe disease
- ICU related symptomatology
- Diseases/syndromes of differential diagnostic value

The following table indicates the distribution of genes depending on HPO terms in 14 categories:

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>NUMBER OF GENES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn Screening ++</td>
<td>25</td>
</tr>
<tr>
<td>Metabolism</td>
<td>538</td>
</tr>
<tr>
<td>Skeletal and Malformation</td>
<td>498</td>
</tr>
<tr>
<td>Blood Disorders</td>
<td>246</td>
</tr>
<tr>
<td>Immunodeficiencies</td>
<td>290</td>
</tr>
<tr>
<td>Lung Diseases</td>
<td>342</td>
</tr>
<tr>
<td>Cardiologic Disorders</td>
<td>351</td>
</tr>
<tr>
<td>Kidney Diseases</td>
<td>174</td>
</tr>
<tr>
<td>Liver Diseases</td>
<td>241</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>191</td>
</tr>
<tr>
<td>Skin Diseases</td>
<td>55</td>
</tr>
<tr>
<td>Neurologic Disorders</td>
<td>647</td>
</tr>
<tr>
<td>Muscular Disorders</td>
<td>143</td>
</tr>
<tr>
<td>Endocrinology</td>
<td>166</td>
</tr>
</tbody>
</table>

+) Due to overlapping phenotypes, particular genes are listed in more than one category.
++ Covering all core panel phenotypes as recommended by ACMG for newborn screening except hearing loss.

What type of test results can you expect?

Positive Result

Indicates that a well characterized and certain disease-causing mutation was identified. This result can help to assess the risk of experiencing certain symptoms and indicate the best way to treat the disease. A positive result may also identify family members who are at risk of having the mutation, therefore carrier testing may be recommended.

Inconclusive Result

Indicates a change in the DNA, but this change has not been proven thus far to be associated with any disorder. To clarify the clinical significance of the variant, testing of other family members may be helpful.

Negative Result

Does not necessarily rule out a disorder; the patient should be managed according to clinical symptoms. Further testing may be recommended.

We will be happy to provide detailed information on the genes within CentoICU® panels related to a specific set of HPO terms on request. For the full list of genes, please visit:

https://www.centogene.com/centogene/?centoicu
References:

Please visit our website for more information:

www.centogene.com

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