Neonatal and Adult Cholestasis: Deletion/Duplication Panel

**Test Code:** MD340  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81222 x1, 81228 x1, 81405 x1, 81406 x1

### Condition Description

Neonatal cholestasis is often clinically defined as the prolonged occurrence of conjugated hyperbilirubinemia in the newborn period, due to impairments in the flow of bile. It is caused by a diverse group of hepatobiliary diseases with overlapping clinical presentations, supporting a need for multi-gene diagnostic panel.

The incidence of neonatal cholestasis is estimated to be 1 in 2500 live births. Genetic and metabolic causes account for at least 25-30% of all cases of neonatal cholestasis, generally due to impairments of hepatobiliary transport, intermediary metabolism, storage disorders, or bile duct dysgenesis. Several of these disorders are life-threatening and benefit from early diagnosis and intervention, yet diagnosing the specific cause via routine serum chemistries or by evaluation of liver biopsies is not as definitive as direct genetic testing. Moreover, several cholestatic entities develop in adults that are caused by variants in these same genes.

Highlights for pediatricians, internists, gastroenterologists, and hepatologists include:

- PFICs, Alagille syndrome, A1AT, bile acid synthetic disorders, CF, etc., all on one platform
- Extremely rare cholangiopathies, (nephronophthises, ARPKD) as well as causes of neonatal liver failure (DGUOK and others)
- Opportunities to diagnose adult-onset cholestatic syndromes, including BRIC, LPAC, and ICP
- Evaluation of hyperbilirubinemia: Crigler-Najjar and Dubin-Johnson syndromes

Reference:


### Genes

- ABCB11, ABCB4, ABCG2, ABCG5, ABCG8, AKR1D1, ATP8B1, BAAT, CC2D2A, CFTR, CLDN1, CYP27A1, CYP7A1, CYP7B1, DGUOK, DHCR7, FAH, HNF1B, HSD3B7, INVS, JAG1, LIPA, MKS1, MPV17, NOTCH2, NPC1, NPC2, NPHP1, NPHP3, NPHP4, NPHP5, NPC10, PEX1, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PKHD1, POLG, SERPINA1, SLC25A13, SLC27A5, SMPD1, TJP2, TMEM216, TRMU, UGT1A1, VIPAS39, VPS33B

### Indications

This test is indicated for:

- Newborns with chronic liver disease.

### Methodology

#### Deletion/Duplication Analysis:

DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### Detection

#### Deletion/Duplication Analysis:

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

### Specimen Requirements

Submit only 1 of the following specimen types
Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml.

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

Type: Isolated DNA

Specimen Requirements:

In microtainer: 10 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

Related Tests

- Neonatal and Adult Cholestasis: Sequencing Panel