ASHKENAZI JEWISH SCREENING PANEL 36+2

- **Cystic fibrosis (1 in 26):** Causes severe pulmonary and gastrointestinal disease and affects fertility. Intelligence is normal.

- **Canavan disease (1 in 57):** Presents with severe neurological insufficiencies in infancy, seizures, and failure to reach milestones.

- **Familial dysautonomia (1 in 30):** Characterized by abnormal functioning of the nervous system causing decreased sensitivity to pain, abnormal regulation of body temperature, unstable blood pressure, and gastrointestinal abnormalities.

- **Tay-Sachs disease (1 in 30):** Causes progressive deterioration in brain function, leading to mental retardation, blindness, seizures, and paralysis.

- **Bloom syndrome (1 in 100):** Causes poor growth, immune dysfunction, characteristic facial rash, and high risk for developing various cancers. Intellect is usually normal.

- **Fanconi Anemia Group C (1 in 89):** Causes poor growth, immune dysfunction, characteristic facial rash, and high risk for developing various cancers. Intellect is usually normal.

- **Gaucher disease (1 in 15):** Variable presentation of symptoms, including fatigue, enlarged liver and spleen, bone pain and fractures, and easy bruising. Onset may not be until age 45, or may not be detected at all. Enzyme replacement therapy is available for treatment.

- **Mucolipidosis type IV (1 in 122):** Presents with profound mental retardation and blindness.

- **Niemann-Pick disease, type A (1 in 90):** Causes poor growth, liver enlargement, and mental retardation.

- **Glycogen storage disease, type 1A (1 in 71):** Leads to severe low blood sugar, which can result in irreversible neurological damage if untreated. Dietary intervention is necessary to avoid symptoms.

- **Maple syrup urine disease (1 in 81):** Causes mental retardation, seizures, and characteristic odor in urine if not treated properly. Dietary intervention is important to avoid symptoms.

- **Familial hyperinsulinism (1 in 66):** Causes dangerously low blood sugar levels, starting any time between neonatal period and 5 years of age. If untreated, causes irreversible brain damage.

- **Lipoamide dehydrogenase deficiency (1 in 96):** Presents with persistent lactic acidosis, with episodes of vomiting and abdominal pain, neurological impairment, cortical blindness, and coma.

- **Nemaline myopathy (1 in 149):** Leads to progressive weakness and poor muscle tone in face, neck, and limbs. Interferes with normal breathing, mobility, and feeding.

- **Usher syndrome, type 1F (1 in 141):** Causes profound hearing loss at birth, progressive vision problems, and loss of balance.

- **Usher syndrome, type III (1 in 107):** Causes progressive hearing and vision loss, but balance is not usually affected.

- **Joubert syndrome (1 in 92):** Causes hypotonia, abnormal rapid breathing, rotary nystagmus, variable developmental delay.

- **Walker-Warburg syndrome (1 in 149):** Presents with congenital muscular dystrophy, brain and eye malformations, seizures, and blindness.

- **Smith-Lemli-Opitz syndrome (1 in 36):** Presents with distinctive facial features, small head size, intellectual disability, behavioral problems, and other birth defects.

- **Carnitine Palmityltransferase II Deficiency (1 in 51):** Characterized by recurrent attacks of muscle pain accompanied by muscle destruction precipitated by prolonged exercise, infection, fasting, cold exposure, or stress.

- **Congenital Amegakaryocytic Thrombocytopenia (1 in 55):** Presents in the newborn period with low platelets and megakaryocytes, which could result in abnormal bruising and bleeding. Bone marrow failure and pancytopenia develop later in life.

- **Congenital Disorder of Glycosylation 1a (1 in 57):** Presents with low tone, cerebellar hypoplasia, distinct facial features, psychomotor retardation, and abnormal fat distribution. Adolescents and adults may have cognitive impairment, poor coordination and strokes.

- **Wilson disease (1 in 70):** Presents with liver dysfunction, abnormal movement patterns, and psychiatric disturbances.

- **Bardet-Biedl syndrome (1 in 107):** Characterized by eye abnormalities causing vision loss, obesity, cognitive impairment, malformations of the genitourinary organs, polydactyly, and renal abnormalities.

- **Polycystic kidney disease, autosomal recessive (1 in 107):** Causes renal diseases such as nephromegaly, hypertension, and varying degrees of renal dysfunction. More than 50% of children with this condition progress to end-stage renal disease within the first decade of life and may require kidney transplantation.

See page 2 for remainder of panel
• **Retinitis pigmentosa 59 (1 in 118):** Affected individuals first experience night blindness, followed by constriction of peripheral visual fields and, eventually, loss of central vision.

• **Tyrosinemia type 1 (1 in 150):** Untreated, this condition results in severe liver dysfunction and significant renal involvement, growth failure, neurological crises, and a tendency to bleed.

• **Galactosemia (1 in 152):** Without a lactose-restricted diet, this condition can result in feeding problems, failure to thrive, hepatocellular damage, bleeding, and sepsis, developmental delays, speech problems, and motor dysfunction.

• **Zellweger syndrome (1 in 172):** Causes hypotonia, poor feeding, distinctive facial features, seizures, and liver dysfunction. Also involves skeletal, kidney and heart problems. Infants typically die during the first year of life.

• **Abetalipoproteinemia (1 in 180):** Leads to failure to thrive, abnormal star-shaped red blood cells, and fatty, foul-smelling stools. Later in life, poor balance and coordination, and sometimes retinitis pigmentosa are noted.

• **Alport syndrome, autosomal recessive (1 in 188):** Characterized by severe kidney problems that result in end stage renal disease, progressive hearing loss, and eye abnormalities (which seldom cause loss of vision).

• **Dyskeratosis congenita, autosomal recessive (1 in 203):** Causes bone marrow failure, pulmonary fibrosis, aplastic anemia, and increased risk for leukemia and other cancers. Physical traits include abnormally growing nails and pigmentary changes on neck and chest.

• **Ehlers-Danlos VIIC (1 in 248):** Connective-tissue disorder, characterized by extreme skin fragility and bruising, characteristic facial features, joint laxity, droopy skin, umbilical hernia, and blue sclera.

• **3-Phosphoglycerate dehydrogenase deficiency (1 in 280):** Causes congenital microcephaly, psychomotor retardation and intractable seizures in the infantile form. Absence seizures, moderate developmental delay and behavioral disorders are seen in the juvenile form.

• **Multiple sulfatase deficiency (1 in 320):** Causes neurologic deterioration with mental retardation, deafness, skeletal anomalies, enlarged organs, and dry and scaly skin.

• **Arthrogryposis, Mental Retardation, and Seizures (1 in 373):** Causes severe skeletal problems and joint contractures, microcephaly, mental retardation, autism-like behavior, and epilepsy.

Aside from conditions which are common in the Ashkenazi Jewish population, there are additional conditions which may warrant testing due to their high carrier frequency in all populations:

• **Spinal muscular atrophy:** Causes progressive muscle weakness and atrophy, poor weight gain, spinal curvature and joint contractures. Presentation varies and lifespan may be limited. Inherited in an autosomal recessive manner. The carrier frequency is 1 in 41.

• **Fragile X syndrome:** Most common cause of mental retardation in boys. Approximately 1 in 250 women are carriers of the fragile X premutation. Unlike all the other conditions mentioned, fragile X is inherited in an X-linked manner. This means that if a female is a carrier, each of her sons has a ½ chance of being affected and each of her daughters has a ½ chance of being a carrier. Traditionally, carriers of genetic diseases show no effects of having a mutation. However, female premutation carriers are at risk for primary ovarian insufficiency, and males with premutations are at risk for fragile X associated tremor/ataxia syndrome.

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