Disease	Disease Description	AJ Carrier Frequency
Phosphoglycerate Dehydrogenase Deficiency	Phosphoglycerate dehydrogenase deficiency is a metabolic disorder that is associated with growth retardation, microcephaly, hypogonadism, and hypertonia. Affected individuals develop intellectual disabilities and seizures.	1 in 280
Polycystic Kidney Disease, Autosomal Recessive (ARPKD)	Primary Ciliary Dyskinesia, DNAI1-Associated is characterized by the development of multiple renal cysts and liver dysfunction. Kidney and/or liver transplantation may be necessary for survival. There is significant clinical variability.	1 in 108
Retinitis Pigmentosa 59	Retinitis pigmentosa is characterized by the deterioration on light detecting retinal cells, which results in a loss of night and peripheral vision. Vision loss associated with retinitis pigmentosa 59 is progressive.	1 in 120
Smith-Lemli-Opitz Syndrome	Smith-Lemi-Opitz is characterized by growth impairment in both the pre and postnatal periods, intellectual disability, microcephaly, and congenital abnormalities due to a defect in cholesterol metabolism. There is significant variability of symptoms in affected individuals.	1 in 37
Spastic Tetraplegia, Thin Corpus Callosum & Progressive Microcephaly	Developmental Delay, Microcephaly, and Hypomyelination is characterized by global developmental delay, progressive postnatal microcephaly, and brain abnormalities. As a result of the developmental delay, speech is absent or minimal and walking is sometimes achieved. Affected individuals frequently also experience seizures.	1 in 118
Spinal Muscular Atrophy (SMA)	SMA leads to progressive muscle weakness and atrophy; especially in the muscles of the torso, upper legs and upper arms. Symptoms can begin prior to six months of age, in childhood and, more rarely, in adulthood. In the most common form of the disease, lifespan is often less than two years of age.	1 in 41
Tay-Sachs Disease	Tay-Sachs disease is a neurological disorder that causes motor weakness, seizures, vision loss, and paralysis. An acute, or classic, form of Tay-Sachs presents with loss of developmental skills between 6 and 10 months of age, with a rapid progression of neurological symptoms leading to death in early childhood. Other variant forms differ in age of onset and severity.	1 in 28
Tyrosinemia, Type 1	The clinical spectrum of this disorder is highly variable even within the same family. The acute form presents with acute liver failure. A sub-acute form presents with liver disease, low blood sugar, failure to thrive, an enlarged liver and spleen and kidney disease. A chronic form presents with chronic liver disease, kidney disease, rickets, and heart disease. Life-threatening neurologic crises, include symptoms such as alterations in mental state, irritability, abdominal pain, nerve problems, and respiratory failure. All patients have a high risk of developing liver cancer, even at a young age. If untreated, death often occurs in early childhood.	1 in 100
Usher Syndrome, Type 1F	Usher syndrome, type 1F is one of several types of Usher Syndrome, which are characterized by hearing and vision loss. In Usher Syndrome Type 1F, hearing loss is typically congenital, with progressive vision loss presenting in adolescence.	1/140
Usher Syndrome, Type 3	Usher syndrome, type 3 is one of several types of Usher Syndrome, which are characterized by hearing and vision loss. Usher Syndrome Type 3 is associated with progressive hearing loss that occurs after a child develops language skills and late onset progressive vision loss.	1/140
Walker-Warburg Syndrome	Walker-Warburg syndrome is a neuromuscular disorder characterized by muscle weakness, low muscle tone, feeding difficulties, seizures, eye abnormalities and a characteristic brain malformation associated with severe developmental delay. Life expectancy is up to three years of age.	1 in 144
Wilson Disease	Wilson disease is associated with liver, neurologic, and psychiatric problems. The severity of the condition is variable and onset ranges from three years of age to over 50 years of age.	1 in 100

Reference:

1. Carrier screening in Individuals of Ashkenazi Jewish Descent. ACMG Practice Guidelines. American College of Medical Genetics, and Genomics. Genet Med 2008 10:1:54-56.

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EXPANDED ASHKENAZI JEWISH PROFILE

Disease Descriptions

Ashkenazi Jewish carrier testing helps to identify carriers for inherited genetic conditions that occur frequently in individuals with Eastern European (Ashkenazi) Jewish ancestry.

According to ACMG, **1 in 4 Ashkenazi Jews is a carrier** of a genetic disorder.[1]

GenPath's Ashkenazi Jewish carrier panel screens for 47 disorders. The clinical presentations of the disorders on the panel are mostly severe, often with childhood onset. For some, clinically managed treatment can significantly improve quality of life.

Reasons for testing

- Patients in the US represent increasingly diverse ethnic backgrounds
- Testing will identify carriers of a genetic disorder, who are typically healthy individuals who show no sign of disease
- Carriers, although healthy, can have children with the disease and its symptoms
- Some diseases cause physical and mental impairment, have a shortened lifespan, or require lifelong treatment and management

Disease	Disease Description	AJ Carrier Frequency
Abetalipoproteinemia	Abetalipoproteinemia is associated with abnormal absorption of fats, cholesterol and fat-soluble vitamins, such as vitamins A, D, E and K. Symptoms include failure to thrive, abnormally shaped red blood cells, diarrhea and fatty stools, and impaired nervous system function. Vitamin deficiencies can also lead to vision loss.	1 in 131
Alport Syndrome	Alport syndrome affects the ears, eyes, and kidneys. Alport syndrome causes progressive sensorineural hearing loss. Ocular changes in Alport syndrome include anterior lenticonus, maculopathy, posterior polymorphous dystrophy, and recurrent erosion of the cornea. Renal disease associated with Alport syndrome is progressive.	1 in 183
Arthrogryposis, Mental Retardation, and Seizures	Arthrogryposis, mental retardation, and seizures is associated with contractures of the fingers and other joints. Affected individuals have autism spectrum disorders with delayed speech development. Seizures typically develop in early to mid-childhood.	1 in 373

Disease	Disease Description	AJ Carrier Frequency
Bardet-Biedl Syndrome 2	Bardet-Biedl syndrome is a multisystem disorder resulting in progressive vision loss, obesity, polydactyly, cognitive impairment, genitourinary malformations, and renal abnormalities. Affected individuals may also have facial differences, eye and cardiovascular abnormalities, and hepatic disease.	1 in 136
Bloom Syndrome	Affected individuals have growth deficiency, feeding difficulties and increased susceptibilities to infectious diseases, diabetes, and various types of cancer. Most individuals have a red, sun-sensitive rash across the nose and cheeks. Intelligence is usually normal, but may be limited. Males are infertile and females have reduced fertility.	1 in 107
Canavan Disease	Canavan disease is a progressive and degenerative neurological disorder that causes developmental delay, muscle weakness, and an enlarged head. Disease severity is variable and although most cases of Canavan disease begin in early infancy and are severe, there are cases where symptoms begin later in life. Lifespan typically ranges from early childhood through the teenage years.	1 in 55
Carnitine Palmitoyltransferase Deficiency, Type 2	There are three forms of Carnitine Palmitoyltransferase Deficiency, Type 2: the lethal neonatal form, severe infantile hepatocardiomuscular form, and myopathic form. The lethal neonatal and severe infantile hepatocardiomuscular forms are multisystem diseases associated with early death. Affected individuals experience seizures, liver failure, and cardiomyopathy. Individuals affected with the myopathic form experience attacks of myalgia induced by exercise, cold exposure, or stress.	1 in 43
Ciliary Dyskinesia, Primary 1	DNAI1 associated primary ciliary dyskinesia is characterized by abnormal cilia that results in recurrent respiratory, sinus, and ear infections. Additionally, males are infertile. Respiratory infections can be life threatening.	1 in 357
Coenzyme Q10 Deficiency, Primary, 7	Coenzyme Q10 deficiency, primary, 7 is characterized by neonatal encephalopathy, respiratory distress, small cerebellum, cardiomyopathy, hypotonia, neonatal seizures and lactic acidosis. Most patients present in the neonatal period with neonatal encephalopathic epilepsy, heart failure secondary to cardiomyopathy or a combination of both.	1/151
Congenital Amegakaryocytic Thrombocytopenia (CAMT)	CAMT is characterized by severe thrombocytopenia (low platelet count) at birth. Affected individuals develop bone marrow failure and are at increased risk for leukemias.	1 in 55
Cystic Fibrosis (CF) Expanded	Cystic fibrosis affects the lungs, pancreas, gastrointestinal tract and reproductive systems. Symptoms vary among affected individuals, but most frequently includes chronic lung infections that can progress to end stage lung disease as well as pancreatic insufficiency.	1 in 24
Deafness, Autosomal Recessive 1A (GJB2)	Deafness, Autosomal Recessive 1A (GJB2) results in non-syndromic, profound, prelingual sensorineural deafness. It is also associated with vertigo.	1/21
Dihydrolipoamide Dehydrogenase Deficiency	Dihydrolipoamide dehydrogenase deficiency results in recurrent vomiting, frequent episodes of abdominal pain, and an enlarged liver. Neurological features include episodes of brain swelling (leading to blindness), disorientation, confusion, and possible coma. Other symptoms include: delays in mental and physical development, ADHD, gait imbalances, motor incoordination, and muscle weakness.	<1 in 80
Dyskeratosis Congenita, Autosomal Recessive 5	Dyskeratosis Congenita, Autosomal Recessive 5 is classically associated with a triad of symptoms: underdeveloped nails, lacy pigmentation of the neck and/or upper chest, and white patches of the oral mucosa. Individuals are also at increased risk for progressive bone marrow failure, certain cancers, and pulmonary fibrosis. Varying degrees of developmental delay are present in some affected individuals.	1 in 204
Ehlers-Danlos Syndrome, Type VIIC	Ehlers-Danlos syndrome, type VIIC results in tearing of the skin (dermatosparaxis) and joint and skin laxity. Other symptoms of Ehlers-Danlos syndrome, type VIIC include umbilical hernia, bruising easily, and characteristic facial features.	1 in 501
Factor XI Deficiency (Hemophilia C)	Factor XI deficiency is characterized by excessive bleeding in homozygotes and some heterozygotes. Bleeding incidents can include: excessive post-surgical bleeding, frequent bleeding of the nose and gums, and easy bruisability.	1 in 11
Familial Dysautonomia	Familial dysautonomia presents with general weakness, insensitivity to pain and temperature differences, imbalance, decreased reflexes, and feeding difficulties. Gastrointestinal dysfunction, vomiting crises, and cardiovascular instability are common. Children with familial dysautonomia are frequently hospitalized and have a shortened life span and risk of sudden death.	<1 in 52
Familial Hypercholesterolemia, LDLRAP1 Associated	Familial hypercholesterolemia is characterized by a severe increase in blood cholesterol levels in childhood or early adulthood. This can then result in premature atherosclerosis (hardening of the arteries) and the development of abnormal lipid deposits, called xanthomas, in the tendons and beneath the skin.	1 in 130
Familial Hyperinsulinism	Familial hyperinsulinism is characterized by persistent elevated levels of insulin in the blood resulting in severe episodes of low blood sugar (hypoglycemia). Hypoglycemic episodes can cause lethargy, irritability, difficulty feeding, and difficulty breathing. If left untreated, the repeated incidence of hypoglycemia can cause seizures, possible irreversible brain damage, and in the most severe cases, coma and death.	1 in 67

Disease	Disease Description	AJ Carrier Frequency
Familial Mediterranean Fever	Familial Mediterranean fever is characterized by recurrent episodes of fever and inflammation causing pain. Inflammation most frequently impacts the joints, abdomen, and chest. Affected individuals are at risk to develop amyloidosis, which can result in renal failure.	1 in 5
Fanconi Anemia, Type C	Fanconi anemia, type C is associated with bone marrow failure, an increased risk of leukemia and other cancers, and characteristic physical anomalies including limb defects. Additional features include problems with the heart, kidneys and gastrointestinal tract, development delay and short stature.	1 in 127
Galactosemia	Classic galactosemia presents during the neonatal period with poor feeding, vomiting, failure to thrive, tendency towards bleeding, jaundice, low blood sugar, elevated ammonia levels, liver and renal failure, low muscle tone, and cataracts. Without treatment, intellectual disability, sepsis and neonatal death can occur; however, with early and lifelong dietary restriction of galactose, individuals can expect to have a normal lifespan.	1 in 127
Gaucher Disease	Gaucher disease is characterized by bone disease, an enlarged liver and spleen, low blood cell and platelet counts, and lung disease. Gaucher disease is divided into subtypes based on clinical symptoms, including types 1, 2, and 3. Types 2 and 3 are more severe and usually involve progressive neurodegenerative disease.	1 in 15
Glycogen Storage Disease, Type IA (GSDIA)	Glycogen storage disease-type 1A is associated with short stature, liver enlargement, kidney disease, osteoporosis, gout, pancreatitis, and seizure disorders. If diagnosed early, adherence to a specific diet may improve prognosis and lifespan. When not treated, survival to adulthood is rare.	1 in 71
Hermansky-Pudlak Sydrome 3	Hermansky-Pudlak syndrome is associated with oculo-cutaneous albinism (abnormally light color eyes, hair and skin), bleeding and bruising problems, severe vision loss, involuntary eye movements, pulmonary fibrosis (scarring or thickening of the lungs) and colitis.	1 in 235
Joubert Syndrome	Joubert syndrome 2 is characterized by a distinctive brain malformation, low muscle tone, an abnormal breathing pattern, and developmental delay. Additional features may include abnormal eye movements, abnormal gait, mental retardation, vision problems, extra fingers and/or toes, and kidney disease. The condition is associated with shortened life expectancy; however, the severity of various symptoms is variable and can influence life expectancy.	1 in 92
Maple Syrup Urine Disease, (Type 1A & 1B)	MSUD1B presents with a characteristic maple syrup odor of the ear wax and urine. If left untreated, infants experience irritability and lethargy, poor feeding, episodes of apnea, and abnormal and repetitive eye movements and can lead to coma, respiratory failure and death. Currently there is no cure, however early identification and dietary management can dramatically improve prognosis.	1 in 80
Mitochondrial Complex I Deficiency	Mitochondrial complex I deficiency presents with Leigh syndrome, a progressive neurological disorder resulting in progressive deterioration of intellectual and motor function and early death, in some affected individuals. The symptoms of Mitochondria Complex 1 Deficiency varies significantly among affected individuals. Other associated features may include: intrauterine growth restriction, adrenal insufficiency, and brain abnormalities.	1 in 291
Mucolipidosis, Type IV	Mucolipidosis, type IV is an autosomal recessive progressive disorder characterized by severe develop-mental and motor delay, as well as vision problems. Symptoms usually become apparent within the first year of life and individuals with this condition usually live into adulthood, but may have a shorter lifespan.	1 in 96
Multiple Sulfatase Deficiency	Multiple sulfatase deficiency is characterized by progressive deterioration of neurological function, including intellectual disability, skeletal abnormalities, enlarged organs, and ichthyosis. Age of onset varies but is typically within the first two years of life.	1 in 320
Nemaline Myopathy 2	Nemaline myopathy 2 is characterized by muscle weakness, especially in the face, neck and limbs, low muscle tone, depressed or absent tendon reflexes, and usually presents in infancy.	<1/108
Niemann-Pick Disease, (Type A & B)	Niemann-Pick disease, type A presents in infancy with progressive enlargement of the liver and spleen, followed by feeding difficulties, poor growth, severe developmental delays and respiratory complications. The average life expectancy is 3 years.	1 in 90
Osteopetrosis, Autosomal Recessive 1	Autosomal recessive osteopetrosis I is characterized by macrocephaly, progressive deafness and blindness, and enlargement of the liver and spleen resulting from abnormal bone formation. Affected individuals may also experience anemia due to bone marrow failure.	1 in 350
Peroxisome Biogenesis Disorder 5A (Zellweger)	Affected individuals with peroxisome biogenesis disorder 5A typically present in the newborn period with failure to thrive due to hypotonia (low muscle tone), seizures, characteristic facial features, liver dysfunction, and bone abnormalities. Death usually occurs in the first year of life.	1 in 123
Phenylketonuria (PKU)	Untreated Phenylketonuria (PKU) results in intellectual disability, behavioral problems, and skin conditions. Treatment involves strict adherence to a modified diet. Treated individuals do not develop intellectual disabilities but may develop attention deficiencies and psychological disorders.	1 in 225