Carrier Screening and Diagnostic Testing for the Ashkenazi Jewish Population

Genetic Testing

FOR DISEASES OF INCREASED FREQUENCY IN THE ASHKENAZI JEWISH POPULATION

Our Science. Your Care.

An extensive carrier screening and diagnostic menu to provide a range of options for you and your patients.

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Genzyme Genetics Ashkenazi Jewish Carrier Screening and Diagnostic Testing

The options. The science. Your care.

The options

Extensive testing menu for diseases of increased frequency in the Ashkenazi Jewish population.

Our science

More than twenty years of expertise in genetic testing, result interpretation and clinical support set us apart in this rapidly advancing field of health care.

Your care

Patient education tools to assist you in obtaining informed consent.

Genetic prenatal screening in the Ashkenazi Jewish population:

The diseases included in this brochure differ from one another in severity, carrier frequency and availability of treatment. We provide this information to assist physicians and patients in making informed decisions regarding carrier screening.

It is standard of care to offer carrier screening for cystic fibrosis, Tay-Sachs disease, Canavan disease and familial dysautonomia to individuals of Ashkenazi Jewish descent.[1-4]

Facts About the Diseases

Cystic fibrosis (CF)

A disorder of mucus production, primarily affecting the pulmonary, gastrointestinal and reproductive systems. Although there is some variability of clinical expression, most individuals with CF require lifelong medical care and experience reduced life expectancy. Intelligence is normal.
Carrier frequency: 1 in 26
Number of mutations: 86
Detection rate: 97%

Tay-Sachs disease

A lysosomal storage disorder caused by a deficiency of the enzyme hexosaminidase A. The resulting build-up of lipids causes untreatable neurological degeneration. In the common infantile form, death occurs by 5 years of age.
Carrier frequency: 1 in 30
Number of mutations: 8 (6 disease-causing mutations and 2 pseudodeficiency alleles)
Detection rate: 97-98% (enzymes), 94% (DNA)

Canavan disease

A demyelinating disorder affecting the central nervous system. Symptoms usually occur within the first few months of life and the disease is fatal in early childhood.
Carrier frequency: 1 in 57*
Number of mutations: 4
Detection rate: 98%

Familial dysautonomia (FD)

A nervous system disorder that commonly includes pain insensitivity, vomiting and sweating episodes, inability to produce overflow tears and unstable blood pressure or temperature. Intelligence is often normal, but learning disabilities are common. Symptom management improves quality of life, but only 50% will reach 30 years of age.
Carrier frequency: 1 in 30
Number of mutations: 2
Detection rate: 99%

Bloom syndrome

A disorder of DNA repair, characterized by poor growth, immune deficiency, sun sensitivity and high susceptibility to cancer. Death from cancer usually occurs before 30 years of age. Intelligence is normal.
Carrier frequency: 1 in 100
Number of mutations: 1
Detection rate: 97%

Fanconi anemia group C

An inherited anemia sometimes accompanied by short stature, radial ray defects and cardiac and urogenital abnormalities. Learning disabilities or mental retardation sometimes occur. The risk of early childhood cancer, especially leukemia, is increased.
Carrier frequency: 1 in 89
Number of mutations: 1
Detection rate: 99%

* Recently changed from 1 in 40 due to our laboratory experience and other published data[5]

Gaucher disease

A lysosomal storage disorder with variable severity. Children or adults may have anemia, hepatosplenomegaly, nosebleeds and fractures. Effective treatment is available for Gaucher disease type 1. In the more severe and rare form, the brain and nervous system are involved.
Carrier frequency: 1 in 15
Number of mutations: 5
Detection rate: 95%

Glycogen storage disease type 1a (GSD1a)

A metabolic disorder that, if untreated, results in severe hypoglycemia, hepatomegaly, growth retardation and bleeding disorders. Treatment consists of a strict diet and continuous feedings of glucose.
Carrier frequency: Approximately 1 in 71*
Number of mutations: 2
Detection rate: 99%

Maple syrup urine disease (MSUD)

A metabolic disorder that leads to the accumulation of branched-chain amino acids in the blood. Without treatment, classic MSUD results in mental retardation, physical disabilities, coma and death. Treatment requires dietary restriction of branched-chain amino acids through a special medical formula and intensive monitoring.
Carrier frequency: 1 in 81[6]
Number of mutations: 4
Detection rate: 99%

Mucolipidosis type IV (MLIV)

A lysosomal storage disorder characterized by psychomotor retardation, corneal clouding, strabismus and retinal degeneration. Onset is usually within the first year of life, and affected individuals reach the developmental age of 1 to 2 years. There is currently no treatment.
Carrier frequency: 1 in 122
Number of mutations: 2
Detection rate: 96%

Niemann-Pick disease type A

A lysosomal storage disorder resulting in poor growth, hepatosplenomegaly and progressive mental and physical deterioration. There is no treatment, and death occurs by 4 years of age.
Carrier frequency: 1 in 90
Number of mutations: 3
Detection rate: 95%

* We are currently evaluating GSD1a mutation frequency in our population. However, published data indicate a frequency of 1 in 71 for individuals of Ashkenazi Jewish descent.[7]

Why use Genzyme Genetics for Ashkenazi Jewish carrier screening and diagnostic testing?

- Extensive menu – 11 tests, including the ACOG recommended tests, to provide the most choices for you and your patients.
- 10 to 14 day turnaround time – Rapid turnaround time is essential if further genetic counseling or testing is indicated.
- Easy-to-read reports – Ashkenazi Jewish carrier test results are consolidated, allowing you easy review.
- Access to genetic experts – Board-certified geneticists or genetic counselors telephone abnormal test results immediately.
- Mouthwash samples accepted – For patients who have already had Tay-Sachs enzyme testing, one mouthwash sample can be sent for all carrier tests in this brochure.

Indications for testing

Carrier screening

- Ashkenazi Jewish individuals and their partners
- Ashkenazi Jewish gamete donors
- Individuals with a family history of any of the disorders

Prenatal diagnosis

- Disease-specific testing for at-risk couples

Diagnosis

- Mutation analysis for affected children or adults

Carrier Screening and Diagnostic Testing for the Ashkenazi Jewish Population

1 in 6 individuals of Ashkenazi Jewish descent is a carrier for cystic fibrosis, Canavan disease, Tay-Sachs disease or Gaucher disease[8]

Disease	Carrier Frequency	Number of Mutations Analyzed	Detection Rate
Cystic fibrosis	1 in 26	86	97%
Tay-Sachs disease	1 in 30	8	97-98% (enzymes), 94% (DNA)
Canavan disease	1 in 57	4	98%
Familial dysautonomia	1 in 30	2	99%
Bloom syndrome	1 in 100	1	97%
Fanconi anemia group C	1 in 89	1	99%
Gaucher disease	1 in 15	5	95%
Glycogen storage disease type 1a	1 in 71	2	99%
Maple syrup urine disease	1 in 81	4	99%
Mucolipidosis type IV	1 in 122	2	96%
Niemann-Pick disease type A	1 in 90	3	95%

References: 1. ACOG Committee Opinion #162, November 1995. 2. ACOG Committee Opinion #212, November 1998. 3. ACOG Preconception and Prenatal Carrier Screening for Cystic Fibrosis: Clinical and Laboratory Guidelines, October 2001. 4. ACOG Committee Opinion #298, August 2004. 5. Feigenbaum A, et al, Canavan Disease: Carrier-Frequency Determination in the Ashkenazi Jewish Population and Development of a Novel Molecular Diagnostic Assay. *Am J Med Genet*, 2004;124A(2):142-147. 6. Kornreich, R et al., High frequency of carriers for maple syrup urine disease in the Ashkenazi Jewish population (abstract). Annual Meeting of the ASHG; Oct. 2004; http://www.ashg.org/cgi-bin/ashg04s/ashg04. 7. Ekstein J, et al, Mutation frequencies for glycogen storage disease 1a in the Ashkenazi Jewish population. *Am J Med Genet*, 2004;129A(2):162-164. 8. Kronn, D,et al., Carrier Screening for Cystic Fibrosis, Gaucher Disease, and Tay-Sachs Disease in the Ashkenazi Jewish Population. *Arch Intern Med*, 1998; 158:777-781.

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