SickKids | Genome Diagnostics

Duchenne/Becker Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is one of the most common inherited diseases, occurring once in every 3,500 males. It is characterized by progressive muscle weakness, inability to walk after age 12, serious respiratory infections by age 14 to 18, and respiratory failure in the 20s to 30s.

Becker muscular dystrophy (BMD) has a similar disease course to DMD, but with slower onset and progression. BMD is also less common, occurring once in every 35,000 males. Both DMD and BMD are caused by mutations in the *dystrophin* gene on the X chromosome.

Genetics

Males normally have one X chromosome in each cell. If it carries the mutation in the *dystrophin* gene, he will have muscular dystrophy. Females normally have two X chromosomes in each cell. If one carries the mutation and the other one does not, the girl will be a carrier of muscular dystrophy. In some cases, a female carrier will show some symptoms of the disease (a manifesting carrier), however most do not have and will not develop muscular dystrophy.

If a female is a carrier, her sons have a 50% chance of inheriting the mutation and being affected with D/BMD. Her daughters are unlikely to be affected but have a 50% chance of inheriting the mutation and being carriers themselves.

Who Should Be Tested?

- Individuals clinically suspected of being affected with D/BMD
- Women with a family history of D/BMD, to determine carrier status
- Pregnancies at risk due to a family history of D/BMD.

Test Methods

- Quantitative testing of all 79 exons of the *dystrophin* gene to detect larger deletions or duplications, using MLPA (Multiplex Ligation-dependent Probe Amplification)
- Complete sequencing of the coding region and flanking exon/intron boundaries of the *dystrophin* gene to detect point mutations may be used when strong clinical evidence suggests D/BMD, however no deletion/duplication is detected
- Linkage analysis may also be used when a deletion or duplication is not detected, but there is strong clinical evidence for D/BMD in the family.

Test Sensitivity

Deletions or duplications in the *dystrophin* gene are found in 70% of D/BMD cases; these mutations will be detected. The remaining 30% caused by other types of mutations will be detected by sequence analysis.

Potential Outcomes & Interpretation of Test Results

Sex of Patient	*Dystrophin* Gene Mutation	Explanation
Male	None detected	This result does not support a diagnosis of D/BMD
Male	Mutation detected	This result confirms a diagnosis of D/BMD
Female	None detected / none detected	It is unlikely that this person is affected with, or is a carrier of D/BMD. Family history is used to determine the likelihood this person is a carrier due to causes other than deletion or duplication
Female	Mutation detected / none detected	This individual is a carrier of D/BMD and may transmit a mutation to offspring

For More Information

Online Mendelian Inheritance in Man http://www.ncbi.nlm.nih.gov/omim/ Item # 310200

GeneReviews online clinical information resource http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part= dbmd

To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca or the National Society of Genetic Counsellors website at www.nsgc.org

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1. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the possibility of D/BMD, or the possibility the individual is a carrier.

2. It is helpful to first identify the mutation(s) in an affected family member or parent of the affected family member. If the familial mutation can be identified, only the familial mutation will be tested for.

3. The clinical course or severity of symptoms cannot be predicted by molecular analysis.

4. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.

5. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.