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What is Nijmegen Breakage Syndrome?
Nijmegen breakage syndrome (NBS) is an inherited disease characterized by significant small head circumference from birth (or shortly after), short stature, distinct facial features, recurrent respiratory infections, progressive intellectual disability, decreased fertility in females, and increased cancer risk.[1] The symptoms of NBS are caused by defects in a protein called Nibrin that is involved in repairing damaged DNA as well as in regulating cell creation and growth. NBS is also known as ataxia-telangiectasia variant 1, Berlin breakage syndrome, and Seemanova syndrome.[2]

What are the symptoms of Nijmegen Breakage Syndrome and what treatment is available?
Some features of Nijmegen breakage syndrome may be present at birth, while other features develop over time. The symptoms of NBS may include: [1]

- Microcephaly (small head size)
- Short stature
- Distinct facial features
- Recurrent respiratory infections
- Developmental and motor delays with borderline to moderate intellectual disability
- Cancer (about 50% develop cancer by age 15)
- Premature ovarian insufficiency and infertility in females
- Irregular skin pigmentation

Treatment for NBS is supportive and can include IV immunoglobulin infusion and vitamin E and folic acid supplementation. Due to the inability of the body to repair damaged DNA, reduced doses of radiation may be considered for cancer treatment as normal doses could be lethal.[1]

How is Nijmegen Breakage Syndrome inherited?
NBS is an autosomal recessive disease caused by mutations in the *NBN* gene.[2] An individual who inherits one copy of an *NBN* gene mutation is a "carrier" and is not expected to have related health problems. An individual who inherits two mutations in this gene, one from each parent, is expected to be affected with NBS.

If both members of a couple are carriers, the risk for an affected child is 25% for each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for Nijmegen Breakage Syndrome?
NBS can occur in individuals of all races and ethnicities, but it appears to be most common in Eastern European Slavic populations in which the carrier frequency is estimated at 1 in 177, corresponding to an approximate incidence of 1 in 125,000.[3]

Having a relative who is a carrier or is affected can increase an individual's risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?
If a gene mutation is identified, an individual should speak to a genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

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What does a negative test result mean?
A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?
- Genetics Home Reference: www.ncbi.nlm.nih.gov/books/NBK1176

References

1. Concannon P, Gatti R. Nijmegen Breakage Syndrome. *GeneReviews*. Available at http://www.ncbi.nlm.nih.gov/books/NBK1176. Accessed: Feb 8, 2012
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3. Varon, R et al. Clinical ascertainment of Nijmegen breakage syndrome (NBS) and prevalence of the major mutation, 657del5, in three Slav populations. *Eur J Hum Genet* 2000; 8: 900-902.

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