NOONAN SYNDROME

GENETIC TESTING

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What is Noonan syndrome?

Noonan syndrome is a genetic disorder that typically causes affected children to be born with[1-3]:

- **Unusual facial features, such as widely spaced eyes, low-set ears that are rotated backward, and a deep indentation in the space between the nose and mouth.**
- **Heart defects, such as valve disorders (pulmonary valve stenosis) and thickening of the heart muscle (hypertrophic cardiomyopathy).**

Additionally, children with Noonan syndrome may develop the following[1-3]:

- Growth delays resulting in short stature
- Bleeding disorders (for example, frequent nosebleeds or easy bruising)
- A short or webbed neck
- An unusual chest shape (the nipples may be low-set and widely spaced, and the breastbone may appear unusually sunken or raised)
- Delayed puberty and undescended testicles (in males)
- Vision or hearing problems
- Fluid buildup in the hands and feet
- Developmental delays and mild learning disabilities
- Blood cancer (juvenile myelomonocytic leukemia)

The health problems caused by Noonan syndrome can be treated, but the disease itself cannot be cured.

What causes Noonan syndrome?

Noonan syndrome is caused by abnormal changes in certain genes. Genes are found in every cell in your body. They carry the instructions for making proteins that control how each of your cells work. Genes can undergo abnormal changes (called mutations) that may cause cells to stop working the way they should. Gene mutations may result in health problems, and they may be passed from parent to child (inherited).

Mutations in several different genes have been linked with the development of Noonan syndrome, as well as other, similar disorders that are called Noonan-like syndromes.

- These specific genes contain instructions for proteins that act like switches controlling the flow of information within cells so they know what kind of cells they should be, when they should grow and divide, when they should move, and when they should die.
- When one or more of these genes is altered, the resulting proteins don't work they way they should, and this disrupts the way information flows through cells. When this happens, the systems that control cell growth and division and cell death are disrupted, which leads to the problems seen in Noonan and Noonan-like syndromes.

How is Noonan syndrome inherited?

Normally, each of your cells carries 2 copies of all your genes. You inherit 1 copy of a gene from each of your parents. Noonan syndrome and Noonan-like syndromes are inherited in an autosomal dominant manner.[1-3] This means a child only needs to inherit 1 copy of a gene mutation (from 1 parent) to be affected with Noonan syndrome or a Noonan-like syndrome.

Thirty percent to 75% of people with Noonan syndrome have a parent who is affected with this disorder.[1] In the remaining cases, the gene mutation is *de novo*.[1] This means the mutation occurs for the first time in the affected child instead of being passed from parent to child.

How is Noonan syndrome diagnosed?

If your child has any of the health problems or physical features described earlier, his or her doctor may suspect Noonan syndrome. Specialized tests that may be used to diagnose health problems related to Noonan syndrome include the following[1,4]:

- Chest X-ray, electrocardiogram (EKG), or echocardiogram
- Platelet (blood cells that help cause clots) count
- Blood clotting factor test
- Hearing tests

If the results of these exams and tests lead your child's doctor to believe your child may have Noonan syndrome, the doctor may recommend a genetic test called gene sequencing to confirm the diagnosis.

What is Noonan syndrome gene sequencing?

Noonan syndrome gene sequencing is a procedure that reads the instructions (DNA) that make up the genes known to play a role in the development of Noonan syndrome and Noonan-like syndromes. This test, which is performed on a sample of blood, is a way to identify the presence of altered genes in a person's cells, which can help a doctor[1]:

- Confirm a diagnosis of Noonan syndrome.
- Identify close relatives of an affected child who may have previously undiagnosed Noonan syndrome or may be at risk of having children with the disorder.

What possible results of gene sequencing can be reported, and what might they mean?

- **Negative:** No mutations were found in the genes tested. A negative result may reduce the chance that a person has Noonan syndrome but cannot completely rule it out.
- **Positive:** A mutation was found in 1 or more f the genes tested, confirming the diagnosis of Noonan syndrome.
- **Variant of unknown significance:** A mutation was found in the genes tested that either has not been reported before, or previous reports about the mutation are conflicting. Therefore, it is unclear if the mutation is the cause of the person's signs and symptoms. Genetic testing of family members may provide more information. If all affected family members have the same mutation, then it is likely to be linked to the inherited disorder. If some affected family members do not have the mutation, it is less likely to be linked to the disorder.

Gene sequencing test results should be combined with clinical findings and reviewed by a heath professional who specializes in medical genetics.

Where can I find more information?

If you have questions or want more information about genetic testing for Noonan syndrome, ask your doctor or genetic counselor. You may search for a genetic counselor in your area using an online address book provided by the National Society of Genetic Counselors at **www.nsgc.org**.

Other information resources include:

- Genetics Home Reference
  Home page: **http://ghr.nlm.nih.gov**
- March of Dimes
  Telephone: 914-997-4488
  Home page: **www.marchofdimes.com**
- MedlinePlus®
  Home page: **http://www.nlm.nih.gov/medlineplus**
- National Human Genome Research Institute
  Telephone: 301- 402-0911
  Home page: **www.genome.gov**

Note: This material is provided for general information purposes only. It is not intended as a substitute for medical advice and/or consultation with a physician or technical expert.

References

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