



The Genetics of Aniridia
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In terms of inheritance, there are 4 basic "types" of Aniridia. These are:

1) Familial Aniridia (Autosomal Dominant)

This is the most common form of Aniridia. It is inherited directly from a parent who has Aniridia themselves. It is the result of a mutation in a gene called the "PAX6" gene. Familial Aniridia is associated with many serious ocular (eye) conditions, including cataracts, glaucoma, and corneal pannus. Close follow-up by an experienced ophthalmologist is very important.

Each child of a person with familial Aniridia will have a 50% chance of inheriting the gene mutation.

2) Gillespie Syndrome (Autosomal Recessive)

This type of Aniridia is extremely rare. It may be inherited through parents who do not have Aniridia themselves, but who both have one normal copy of the PAX6 gene, and one mutated copy. This type of Aniridia is associated with a particular appearance of the iris remnant (described as having a "scalloped" border) mental retardation, and cerebellar ataxia, (muscle incoordination) There are reports of more than one case of Gillespie syndrome in a family. There have also been reports of people with Gillespie syndrome whose child(ren) also have the disorder.

3) Sporadic Aniridia (no deletion detected)

This type of Aniridia is the second most common form. Both parents have normal chromosomes. The affected person has a "new" mutation of the PAX6 gene (a mutation which occurred before or very soon after conception) It is not known what causes this mutation. People with sporadic Aniridia are at risk for the same eye complications as those with Familial Aniridia. Children with sporadic Aniridia should also be carefully followed for the development of Wilms tumor, regardless of the results of genetic testing. People with Sporadic Aniridia have a 50% chance of passing on this condition to their children.

4) WAGR Syndrome (Sporadic Aniridia, deletion of 11p13)

This type of Aniridia is rare. Both parents have normal chromosomes.

The affected person has a “new” mutation (as in Sporadic Aniridia, above) Unlike Sporadic Aniridia, however, this new mutation involves not only the PAX6 gene, but a large number of neighboring genes as well. This genetic abnormality is a “deletion,” or set of missing genes, which are located on the short arm of chromosome number 11. In addition to Aniridia, children with WAGR syndrome have a high risk for Wilms tumor (a type of cancer of the kidney) and other medical complications, such as genital abnormalities, and learning and behavior difficulties. Early diagnosis of the syndrome, along with close medical supervision and educational support will help the child to reach their best potential.

There has been a single report of two cases of WAGR syndrome within a family (this case involved an inherited translocation of genes. Genetic testing will help parents determine their own risk for having another child with WAGR syndrome) To date, there have been no reports of people with WAGR syndrome having children of their own.

Genetic Testing

In cases of Sporadic Aniridia, genetic testing is required to determine whether the individual has WAGR syndrome. Approximately 30% of people who are born with Sporadic Aniridia will also have WAGR syndrome.

Two genetic tests are required to check for WAGR syndrome. One is called the “Karyotype,” which is a basic examination of the chromosomes. The second test is called a “FISH” probe. The FISH probe is a very detailed examination of the WAGR-related portion of chromosome 11. Both tests are conducted on a small sample of blood.

There are currently three laboratories in the world which offer both a high-resolution Karyotype and the FISH probe test. These are the John F. Kennedy Institute in Denmark, the Kleburg Cytogenetics Laboratory in Houston, Texas, and the Wessex Regional Genetics Laboratory in Salisbury, UK. The Wessex Regional Genetics Lab offers research level clinical testing, which may be particularly helpful in unusual cases of Aniridia.

If the Karyotype and the FISH probe tests do not show the WAGR deletion, then the child most likely has Sporadic Aniridia only. However, since no genetic testing can be completely guaranteed, it is extremely important to monitor all children with Sporadic Aniridia for the development of Wilms tumor.

If genetic testing is positive for the WAGR deletion, then the child has WAGR syndrome. It is important to remember that while WAGR syndrome is associated with a variety of medical complications, few if any individuals will develop all of them. Each person with WAGR syndrome is a unique individual,

and will have their own set of symptoms, challenges, and potential for health and success in life.

For more information about WAGR syndrome, please see the website:
<http://www.wagr.org>