Ataxia-Telangiectasia

Also called: A-T, ataxia-telangiectasia syndrome, ATM, cerebello-oculocutaneous telangiectasia, Louis-Bar syndrome

What is ataxia-telangiectasia?

Ataxia-telangiectasia is a rare genetic condition that affects the nervous system, immune system and other body systems. Children with this condition have ataxia, or trouble coordinating their movements. They also have small clusters of enlarged blood vessels called telangiectasias, which occur in the eyes and on the surface of the skin. Compared to people who do not have ataxia-telangiectasia, they are at higher risk for developing certain types of blood cancers and immune system cancers.

In people with ataxia-telangiectasia, the ataxia often begins in early childhood, typically before age 5 years, and gets worse over time. Most children with ataxia-telangiectasia will eventually find it hard to walk and will have problems with balance and hand coordination. They may have other nervous system problems as well, including the following:

- Slurred speech
- Oculomotor apraxia (trouble moving the eyes from side-to-side)
- Chorea (involuntary jerking movements)
- Myoclonus (muscle twitches)
- Neuropathy (disturbances in nerve function).

By adolescence, many people with ataxia-telangiectasia will require a wheelchair.

What causes ataxia-telangiectasia?

Ataxia-telangiectasia is caused by changes in a gene known as *ATM*. Genes carry information telling cells within the body how to function. The *ATM* gene is needed for cells to repair damaged genetic material (DNA).

Most people without ataxia-telangiectasia carry two working copies of the *ATM* gene in their cells. One copy is inherited from the mother and one from the father. Cells from people with ataxia-telangiectasia carry two changed copies of the *ATM* gene in their cells. One changed copy was inherited from the mother, and another changed copy was inherited from the father. The changes cause the *ATM* gene to not work properly. They are called mutations.

When both copies of the *ATM* gene have mutations, cells cannot repair damage to their DNA as well as someone without ataxia-telangiectasia. The cells become unstable and sometimes die or grow to form a tumor. That is why people with ataxia-telangiectasia are at higher risk of developing some kinds of cancer.

People with only one mutated copy of the *ATM* gene do not have ataxia-telangiectasia and do not show the signs and symptoms of the condition. These people are called “carriers”. Female carriers (women with one mutated copy of the *ATM* gene) have a slightly higher risk of developing breast cancer than the general population.

The parents of a child with ataxia-telangiectasia have a 25% (1 in 4) chance of having another child with the condition. They have a 50% (1 in 2) chance of having a child who carries just one copy of an *ATM* mutation. That child would be a carrier. Carriers do not have ataxia-telangiectasia but could pass on the mutated *ATM* gene to their own children. There is a 25% (1 in 4) chance of having another child with two normal copies of the *ATM* gene. That child would not have ataxia-telangiectasia and would not be a carrier. Children with two normal copies of the ATM gene would pass on only normal copies of the *ATM* gene to their own children.

A person with ataxia-telangiectasia has different risks of having a child with ataxia-telangiectasia. Specifically, a person with ataxia-telangiectasia will pass one *ATM* mutation to each of his or her children. This person’s chance of having a child with ataxia-telangiectasia depends on whether or not his or her partner also carries an *ATM* mutation. If the partner carries an *ATM* mutation, the chance of having a child with the condition is 50% (1 in 2). The chance of having a child who carries just one copy of an *ATM* mutation is 50% (1 in 2). If the partner does not carry an *ATM* mutation, no children will have ataxia-telangiectasia, but all of the children will be carriers.

What is the cancer risk for people with ataxia-telangiectasia?

People with ataxia-telangiectasia have about a 40% chance of developing cancer. Of those that develop cancer, most will develop leukemia (blood cell cancer) or lymphoma (immune cell cancer). Other types of cancer that may develop include the following:

- Ovarian cancer
- Breast cancer
- Thyroid cancer
- Parotid (salivary) gland tumors
- Gastric (stomach) cancer
- Melanoma (skin cancer)
- Leiomyomas (smooth muscle tumors)

Female carriers (women with one mutated copy of the *ATM* gene) have a slightly higher risk of developing breast cancer than those who are not carriers. The risk is relatively low (about 2–4 times greater than the general population). Given this risk, some health care providers may recommend that female *ATM* mutation carriers consider breast cancer screening at an earlier age than people who are not carriers. Currently, *ATM* mutation carriers are not thought to be at an increased risk for other types of cancer besides breast cancer.

What are other physical findings seen in people with ataxia-telangiectasia?

People with ataxia-telangiectasia may have other medical concerns. Not all people with ataxia-telangiectasia will have all the physical findings listed below. These physical findings vary from person to person.

- Weakened immune system resulting in infections more often
- Sensitive to ionizing radiation (such as the radiation used for CT scans and medical X-rays)
- Premature aging with graying of the hair
- Abnormal endocrine (hormone) system, including type 2 diabetes, short stature and delayed puberty
- Mild learning problems or mild intellectual disability
- Smaller-than-normal cerebellum (a part of the brain), which can be seen on an MRI exam after the age of about 7 or 8 years
- Shortened life span (most patients live into their 20s; some patients live into their 40s or 50s)

How severe the signs and symptoms of ataxia- telangiectasia are may vary between families. However, people with ataxia-telangiectasia who are in the same family often have a disease course that is similar.

How are people with ataxia-telangiectasia screened for tumors?

People with ataxia-telangiectasia should be managed by a doctor who knows the condition well. Children with ataxia-telangiectasia should have regular screenings to detect cancer as early as possible. The goal of screening is finding and treating cancer early to allow the best outcome for patients.

At this time, there are no established guidelines for cancer screening in children with ataxia-telangiectasia. The following are generally recommended:

- **Yearly lab work** (complete blood count, complete metabolic panel, and lactate dehydrogenase) to screen for lymphoma and leukemia.
- **Yearly physical exams** by a doctor who knows this condition well, giving special attention to any signs of leukemia or lymphoma (weight loss, bruising and localized pain or swelling).
- **Yearly check-ups** with the child's regular pediatrician.

For carriers of one copy of a mutated *ATM* gene, early breast cancer screening may be advisable. This should be decided by a doctor who manages patients who have an increased risk for breast cancer.

If cancer is detected, it is very important to seek out a doctor who is experienced in treating cancer in people who have ataxia-telangiectasia. Standard doses of some types of chemotherapy and radiation therapy may be more harmful to patients with ataxia-telangiectasia. Lower doses of chemotherapy or radiation therapy may be needed.

It is possible that recommended screenings may change over time as doctors learn more about ataxia-telangiectasia. Parents should discuss all screening options for their child with a doctor who knows this condition well. Because ataxia-telangiectasia is a complex condition, it is very important that parents seek out an experienced doctor for their child.

How is ataxia-telangiectasia diagnosed?

A doctor may suspect ataxia-telangiectasia based on signs and symptoms of the condition. Several lab tests can be used to support a clinical diagnosis of ataxia-telangiectasia:

- Specialized tests to measure the amount of ATM protein in cells. The *ATM* gene makes a protein that is also called ATM. If a person has a mutated copy of the *ATM* gene, that person usually will have ATM protein levels in their cells that are much lower than normal.

- Blood tests to measure the level of a protein called alpha-fetoprotein. More than 95% of people with ataxia-telangiectasia have high levels of alpha-fetoprotein, but levels are very low in most people without the condition. Doctors do not know why the level of alpha-fetoprotein is so high in people with this condition.

- Radiosensitivity test to measure how well a cell can repair damaged DNA. Normal cells that contain working ATM protein should be able to repair themselves after being exposed to radiation. The cells from people with ataxia-telangiectasia do not survive normally after exposure to radiation because they do not repair DNA as well.

- Chromosome analysis to look for a translocation that can occur in cells treated with a certain chemical. Chromosomes are the part of the cell that contains the genetic material (DNA). A translocation occurs when chromosomes break and the fragments reattach improperly to other chromosomes.

How is genetic testing for ataxia-telangiectasia done?

The doctor may suspect ataxia-telangiectasia after looking at a person's medical or family history and after conducting some of the lab tests listed above. In most cases, a doctor or genetic counselor will ask questions about the person's health and the health of other family members.

The genetic counselor or doctor will record which family members have developed signs and symptoms of ataxia-telangiectasia, including cancer, and at what ages these occurred. From this information they will create a family tree. Doctors and genetic counselors will look at the family tree to find out if the patterns match what might be seen with ataxia-telangiectasia. If the condition is suspected in a child or other family members, the doctor or genetic counselor will likely recommend genetic testing of the *ATM* gene.

Diagnostic genetic testing

If the doctor or genetic counselor suspects that a person has ataxia-telangiectasia, diagnostic testing may take place as follows:

- A blood sample is collected.
- DNA is isolated from the cells in the sample. A person's genes are made of DNA.
- Both copies of the person's *ATM* gene are checked for possible changes. A genetic specialist compares the two copies of the person's *ATM* gene to normal copies of the gene. If there are differences, the specialist decides if they might cause a certain condition such as ataxia-telangiectasia.
- If a mutation is found in the *ATM* gene, the genetic counselor will work with the family in the following ways:
    - To help the family understand the risks of ataxia-telangiectasia
    - To find out if other family members should consider testing for the mutation
    - To help with decisions about prenatal genetic testing

It is important to remember that genetic testing does not always find mutations in the *ATM* gene for all people with ataxia-telangiectasia. A person can still have ataxia-telangiectasia even if no *ATM* mutation is found. There may be other genes that are related to the condition that doctors do not yet know about, or there may be mutations that the test did not discover.

Prenatal genetic testing

Parents may undergo prenatal testing to find out if the pregnancy is affected with known *ATM* mutations in the family. Testing may take place either before pregnancy occurs or during pregnancy.

People considering prenatal testing should work with a genetic counselor to review the pros and cons of the testing. The genetic counselor can also help parents consider how they wish to handle the results of the testing.

Testing that occurs before pregnancy—Testing that happens before pregnancy is called preimplantation genetic testing (PGT). This special type of genetic testing is done along with in vitro fertilization (IVF). PGT offers a way to test embryos for known *ATM* mutations before placing them into the uterus.

Testing that occurs during pregnancy—Testing can be used to see if a pregnancy is affected with known *ATM* mutations. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)—**during the first trimester (first three months)
- **Amniocentesis—**during the second trimester or later (last six months)

Collected tissue can be checked for the presence of *ATM* mutations identified in the family. Both of these tests carry minor risks and should be discussed with an experienced doctor or genetic counselor.

Special concerns

Genetic testing for ataxia-telangiectasia is a complex process. Those thinking about testing should take time to consider the benefits and risks. They should discuss the process with a genetic counselor before testing is done. If they choose testing, they should review the test results with the doctor or genetic counselor to be sure they understand the meaning of the results.

Sometimes children or adults with ataxia-telangiectasia can feel sad, anxious or angry. Parents who pass on an *ATM* mutation to one or more of their children can feel guilty. Some people with an *ATM* mutation or mutations could have trouble getting disability coverage, life insurance or long-term care insurance in some states. More information about genetic discrimination can be found at www.ginahelp.org.

Are there other special health care needs for children with ataxia-telangiectasia?

Because of the other medical concerns related to ataxia-telangiectasia, other specialists should assess the patient:

- Neurology
- Immunology

- Supportive therapy (such as physical, occupational and speech therapies)
- Regular checks of development and school progress, as doctors believe are needed for the child.

People of any age with ataxia-telangiectasia have a higher risk of cancer. They should monitor their health and adopt healthful habits throughout life. It is important to continue to have regular physical checkups and screenings. That way, any cancer can be found early at the most treatable stage.

Both people with ataxia-telangiectasia and carriers are more sensitive to the effects of radiation. It may increase their risk of developing cancer. Therefore, medical tests that use radiation, such as CT scans, X-rays and mammograms, should be avoided when possible. A doctor may at times decide that these tests are needed if the benefit of the test outweighs the risk of developing cancer as the result of the test. Also, people with ataxia-telangiectasia require special care when anesthesia is needed.

Other ideas to reduce the risk of cancer:

- Eat a healthful diet with lots of fruits and vegetables
- Get regular exercise
- Avoid smoking or using tobacco products
- Avoid secondhand smoke

Avoid excess sun exposure and always wear sunscreen, hat and protective clothing when out in the sun
People with ataxia-telangiectasia should watch closely for general signs or symptoms that could signal cancer:

- Unexplained weight loss
- Loss of appetite
- Easy bruising
- Blood in the stool or changes in bowel habits
- Aches, pains, lumps or swelling that cannot be explained
- Headaches or changes in vision or nerve function that do not go away

It is important to seek medical help if anything unusual appears.

What other information and resources are there for children with ataxia-telangiectasia and their families?

Resources about ataxia-telangiectasia:

- A-T Children's Project
  (www.atcp.org)

- National Ataxia Foundation
  (www.ataxia.org)

- National Organization for Rare Disorders – Ataxia-Telangiectasia
  (rarediseases.org/rare-diseases/ataxia-telangiectasia/)

More resources about genetic testing and hereditary cancer:

- Making Sense of Your Genes: A Guide to Genetic Counseling (www.ncbi.nlm.nih.gov/books/NBK115508/)

- Young People with Cancer: A Parent's Guide (www.cancer.gov/publications/patient-education/young-people)

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