Ataxia-Telangiectasia [1]

What is ataxia-telangiectasia?

Ataxia-telangiectasia (A-T) is a hereditary condition characterized by progressive neurologic problems that lead to difficulty walking and an increased risk of developing various types of cancer. Signs of A-T often develop in childhood. Children with A-T may begin staggering and appear unsteady (called ataxia) shortly after learning to walk. Most people with A-T will eventually need to use a wheelchair.

People with A-T have normal intelligence, but over time, they will develop slurred speech and have difficulty with writing and other tasks. Red marks called telangiectasias are caused by dilated capillaries (tiny blood vessels) and may appear on the skin and eyes as people get older. People with A-T also have a weakened immune system and are prone to infections. In addition, they appear to be particularly sensitive to ionizing radiation, such as x-rays, and have an increased risk of cancer.

What causes A-T?

A-T is a genetic condition. This means that the risk for A-T can be passed from generation to generation in a family. The gene associated with A-T is *ATM*, meaning ataxia telangiectasia mutated. Mutations (changes) in the *ATM* gene cause A-T.

How is A-T inherited?

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. A-T follows an autosomal recessive inheritance pattern. In autosomal recessive inheritance, a mutation must be present in both copies of the gene in order for a person to be affected. This means that each parent must pass on a gene mutation for a child to be affected. A person who has only one copy of the gene mutation is called a carrier. When both parents are carriers of a recessive gene mutation, there is a 25% chance that a child will inherit two mutations and be affected with A-T. First-degree relatives, such as parents, brothers, sisters, and children of a person with A-T, have a 50% chance of inheriting the single gene mutation and becoming a carrier.

Options exist for couples interested in having a child when they know that one of them carries a

gene mutation that increases the risk for this hereditary cancer syndrome. Preimplantation genetic diagnosis (PGD) is a medical procedure done in conjunction with in-vitro fertilization (IVF). It allows people who carry a specific known genetic mutation to have children who do not carry the mutation. A woman?s eggs are removed and fertilized in a laboratory. When the embryos reach a certain size, one cell is removed and is tested for the hereditary condition in question. The parents can then choose to transfer embryos which do not have the mutation. PGD has been in use for over a decade, and more recently has been used for several hereditary cancer predisposition syndromes. However, this is a complex procedure with financial, physical, and emotional factors for couples to consider before starting. For more information, talk with an assisted reproduction specialist at a fertility clinic.

How common is A-T?

A-T is rare. It is estimated that A-T affects one in 40,000 to one in 100,000 people. The chance that a person is a carrier of a single *ATM* gene mutation is about 1%, or one in 100.

How is A-T diagnosed?

A-T is suspected whenever a child develops signs of ataxia, meaning unsteady walking. Testing of the *ATM* gene is available and genetic mutations can be identified in about 90% of people with A-T. The following tests may be more helpful in determining if someone has A-T or another type of ataxia:

Immunoblotting (*ATM* protein testing). This is the best test to diagnose A-T. Nearly all individuals with A-T will have very low or no amounts of the protein made by the *ATM* gene.

Radiosensitivity assay. Since people with A-T have an increased sensitivity to radiation, removing some cells and treating the sample with radiation therapy can help make the diagnosis. It can take up to three months to get a result from this test.

***ATM* kinase activity.** This test looks at the activity level of the protein made by the *ATM* gene. Little to no activity means that there is likely a mutation in the *ATM* gene.

What are the estimated cancer risks associated with A-T?

People with A-T also have about a 40% risk of developing cancer. The most common types of cancer seen in people with A-T are leukemia and lymphoma. These two types of cancers can appear in childhood and account for 85% of all cancers in people with A-T. As people with A-T live longer, there appears to be an increased risk of other cancer types, including breast cancer [2], ovarian cancer [3], stomach cancer [4], melanoma [5], and sarcoma [6].

What are the estimated cancer risks associated with being a carrier or heterozygote for an A-T gene mutation?

Carriers, meaning people with one *ATM* gene mutation, also seem to have an increased risk of developing breast cancer. Some studies have shown a five to nine times higher lifetime risk for breast cancer for women who are carriers, while other studies have shown two times the lifetime risk of developing breast cancer compared to the general population. There is some data

suggesting that these individuals may also be at an increased risk for colon and/or stomach cancer but this isn?t entirely clear.

Additional research is needed to clarify the cancer risk for *ATM* mutation carriers. Studies also show that carriers may have an increased risk of heart disease.

As testing for hereditary cancer expands to include multi-gene panels, the classical definition of syndromes such as A-T may change. Some individuals may have a mutation in the *ATM* gene but do not meet any of the criteria listed above for A-T. It is not known if these people will have the same risks for developing cancer.

What are the screening options for A-T?

Children and adults with A-T should see their doctor regularly and be monitored for signs of cancer. Individuals with A-T who frequently develop infections are encouraged to have their immune status checked regularly.

There are no specific cancer screening or prevention recommendations for individuals with A-T or gene mutation carriers. However, women who are carriers are encouraged to talk with their doctor about breast cancer screening options.

Screening options may change over time as new technologies are developed and more is learned about A-T. It is important to talk with your doctor about appropriate screening tests [7].

Learn more about what to expect when having common tests, procedures, and scans [8].

Questions to ask the doctor

If you are concerned about your risk of cancer, talk with your doctor. Consider asking the following questions of your doctor:

- What is my risk of developing cancer?
- What can I do to reduce my risk of cancer?
- What are my options for cancer screening?

If you are concerned about your family history and think your family may have A-T, consider asking the following questions:

- Does my family history increase my risk of developing cancer?
- Could my family have A-T?
- Should I consider genetic testing [9]?
- Should I meet with a genetic counselor?

More Information

The Genetics of Cancer [10]

Genetic Testing [9]

What to Expect When You Meet With a Genetic Counselor [11]

Collecting Your Family Cancer History [12]

Sharing Genetic Test Results with Your Family [13]

Additional resources

A-T Children?s Project
www.atcp.org [14]

National Ataxia Foundation
www.ataxia.org [15]

Facing Our Risk of Cancer Empowered (FORCE)
Information for women who are at a high risk of developing ovarian cancer or breast cancer.
www.facingourrisk.org [16]

National Cancer Institute
www.cancer.gov [17]

American Cancer Society
www.cancer.org [18]

To find a genetic counselor in your area, ask your doctor or visit these websites:

National Society of Genetic Counselors
www.nsgc.org [19]

National Cancer Institute: Cancer Genetics Services Directory
www.cancer.gov/cancertopics/genetics/directory [20]

Links:
[1] http://www.cancer.net/cancer-types/ataxia-telangiectasia
[2] http://www.cancer.net/node/31322
[3] http://www.cancer.net/node/31343
[4] http://www.cancer.net/node/31376
[5] http://www.cancer.net/node/31265
[6] http://www.cancer.net/node/31379
[7] http://www.cancer.net/node/18621
[8] http://www.cancer.net/node/24959
[9] http://www.cancer.net/node/24895
[10] http://www.cancer.net/node/24897
[11] http://www.cancer.net/node/24907
[12] http://www.cancer.net/node/30761
[13] http://www.cancer.net/node/24906
[14] http://www.atcp.org/
[15] http://www.ataxia.org/
[16] http://www.facingourrisk.org/
[17] http://www.cancer.gov/

[18] http://www.cancer.org/
[19] http://www.nsgc.org/
[20] http://www.cancer.gov/cancertopics/genetics/directory