

Ataxia Telangiectasia: Fact Sheet

Key Points

- **What is ataxia telangiectasia?** Ataxia telangiectasia (A-T) is a primary immunodeficiency disease which affects a number of different organs in the body. An immunodeficiency disease is one that causes the immune system to break down, making the body susceptible to diseases. (Question 1)
- **Is the disorder curable?** It is a rare, recessive genetic disorder of childhood that occurs in between 1 out of 40,000 and 1 out of 100,000 persons worldwide. The ailment is progressive. Patients with A-T are frequently wheelchair-bound by their teens, and the disease is generally fatal to patients by the time they reach their twenties. (Question 1)
- **What are the signs of ataxia telangiectasia?** The first signs of the disease, which include delayed development of motor skills, poor balance, and slurred speech, usually occur during the first decade of life. Telangiectasias (tiny, red “spider” veins), which appear in the corners of the eyes or on the surface of the ears and cheeks, are characteristic of the disease, but are not always present and generally do not appear in the first years of life. (Question 2)
- **How many A-T carriers are there in the United States?** An estimated one percent of the U.S. population, or about 2.5 million people, may be carriers of A-T. A-T has no racial, economic, geographic or education barriers. Both males and females are equally affected. (Question 6)

1. What is ataxia telangiectasia?

Ataxia telangiectasia (A-T) is a primary immunodeficiency disease which affects a number of different organs in the body. An immunodeficiency disease is one that causes the immune system to break down, making the body susceptible to diseases. It is a rare, recessive genetic disorder of childhood that occurs in between 1 out of 40,000 and 1 out of 100,000 persons worldwide. The ailment is progressive. Patients with A-T are frequently wheelchair-bound by their teens, and the disease is generally fatal to patients by the time they reach their twenties.

A-T is characterized by neurological problems, particularly abnormalities of balance, recurrent sinus and respiratory infections, and dilated blood vessels in the eyes and on the surface of the skin. Patients usually have immune system abnormalities and are very sensitive to the effects of radiation treatments.

In the United States, where recurrent infections typical of the disorder are usually controlled by antibiotics, patients are at high risk of developing and dying of cancer, particularly leukemias and lymphomas.

2. What are the signs of ataxia telangiectasia?

The first signs of the disease, which include delayed development of motor skills, poor balance, and slurred speech, usually occur during the first decade of life. Telangiectasias (tiny, red “spider” veins), which appear in the corners of the eyes or on the surface of the ears and cheeks, are characteristic of the disease, but are not always present and generally do not appear in the first years of life. About 20% of those with A-T develop cancer, most frequently acute lymphocytic leukemia or lymphoma. Many individuals with A-T have a weakened immune system, making them susceptible to recurrent respiratory infections. Other features of the disease may include mild diabetes mellitus, premature



graying of the hair, difficulty swallowing, and delayed physical and sexual development. Children with A-T usually have normal or above normal intelligence.

3. Is the disorder curable?

There is no cure for A-T at this time. The cloning and sequencing of the gene (named ATM, for ataxia telangiectasia, mutated) has opened several avenues of research to develop better treatment, including: (1) gene therapy; (2) the design of drugs to correct the function of the altered protein; and (3) direct replacement of the functional protein. Physical, occupational and speech therapy are used to help maintain flexibility, gamma-globulin injections help supplement the immune systems of A-T patients and high-dose vitamin regimens are being researched with some moderate results.

Research shows that a protein kinase called ATM reacts to DNA damage by chemically modifying and triggering accumulation of a molecular or tumor suppressor called p53. This tumor suppressor is defective in about half of all human cancers and is the master control switch for a process that normally prevents cells from dividing. In A-T patients, the ATM protein is missing or defective. This delays the accumulation of p53, allowing cells to replicate without repair of their DNA and thereby increasing the risk of cancer. This research was reported by two separate groups of researchers in the September 1998 issue of Science.

4. What does it mean that the disorder is recessive?

A recessive disorder requires two copies of the predisposing gene—one from each parent—for the child to have the disease.

5. What is a carrier?

A carrier is a person with one normal and one altered copy of a gene that is linked to a particular disease. These individuals usually do not realize they are carriers because the disease is not present or its signs and symptoms are very mild.

A person with one normal copy and one altered copy of the ATM gene is an A-T carrier.

6. How many A-T carriers are there in the United States?

An estimated one percent of the U.S. population, or about 2.5 million people, may be carriers of A-T. A-T has no racial, economic, geographic or education barriers. Both males and females are equally affected. It is believed that many children with A-T, particularly those who die at a young age, are never properly diagnosed. Therefore, this disease may actually be much more common than projected.

7. How do I know if I'm a carrier?

In the past, carriers were identified mainly because they were parents of a child with A-T. With the cloning of the ATM gene, however, physicians or cancer genetics professionals can now conduct genetic testing, analyzing patients' DNA to look for A-T mutations in the ATM gene. The genetic testing is complex and difficult, however; definitive results may not be possible. One of the most helpful laboratory tests used to assist in the diagnosis of A-T is the measurement of "fetal proteins," or serum alpha-fetoprotein, in the blood. These are proteins that are usually produced during fetal development but may persist at high levels in some conditions (such as A-T) after birth. The vast majority of A-T patients (more than 95%) have elevated levels of serum alpha-fetoprotein. When other causes of elevations of alpha-fetoprotein are eliminated, elevated alpha-fetoprotein in the blood, in association with the characteristic signs and symptoms, makes the diagnosis of A-T a virtual certainty.

8. Do A-T patients have an increased risk of developing cancer? If so, what cancers?

Yes. Overall, the risk of an A-T patient developing any cancer is 37-fold higher than individuals in the general population. The risk of developing lymphoid tumors, however, the most frequently diagnosed cancers in A-T patients, is 100-fold higher than in the general population; A-T patients have about a 10 percent risk of developing lymphoma or leukemia. Cancers also occur in the stomach, brain, ovary, skin, liver, larynx, parotid gland, and breast.

9. Do A-T carriers have an increased risk of developing cancer? If so, what cancers?

Definitive information does not yet exist to answer this question, but some scientists believe that A-T carriers, compared with the general population, might have a higher risk of certain cancers. In population-based studies, the most consistent elevations are for breast cancer, and possibly stomach cancer. These elevations, when seen, are small.

Animal models have not supported the theory of increased cancer risk in A-T carriers. In animal studies of ATM, virtually all mice with the disease died of cancer, while no A-T carrier mice have yet to show tumors.

Case-control studies have suggested a link between the ATM gene and increased breast cancer risk, but findings have been inconsistent. The National Cancer Institute (NCI) is currently funding two large, international studies to further examine the risk of cancer in A-T families.

10. Are A-T patients sensitive to radiation?

Yes. A-T patients have an increased sensitivity to ionizing radiation, the type found in X-rays. When cultured in the laboratory, the blood and skin cells of these patients have markedly reduced ability to replicate and to form cell colonies after X-ray exposure.

11. Are A-T carriers sensitive to the effects of radiation?

This is a question that needs further research. When cultured in the laboratory, blood and skin cells of known ATM gene carriers are less sensitive to X-rays than cells from A-T patients, and more sensitive than cells from the general public. There are not yet data from clinical studies to definitively answer the question about sensitivity of carriers. The NCI is currently funding a large, multi-institutional study to better understand the interaction between radiation exposure and the ATM gene.

12. Are X-rays harmful to A-T patients?

A-T patients are sensitive to the effects of radiation and should be monitored for adverse effects. However, they do receive diagnostic X-rays when necessary.

The information about radiation sensitivity in A-T comes largely from observations of A-T patients who undergo radiation treatments, especially for cancer, and also from laboratory studies on skin and blood cells. Physicians who treat A-T patients limit X-ray exposures by using the most modern equipment and techniques available, but they do recommend these diagnostic tests when needed.

13. Is it dangerous for carriers to have diagnostic X-rays, given their possible increased sensitivity to radiation compared to the general public?

At this point, the evidence overall does not show a documented risk to A-T carriers. However, diagnostic X-rays should be limited because of the theoretical risk that the X-ray may cause a chromosomal break, which could result in the development of a malignancy. In general, X-rays should only be done if the result will influence therapy and there is no other way to obtain the information that the X-ray will provide.

14. Suppose I learn I am an A-T carrier. Will mammography increase my chances of getting breast cancer?

There is not yet definitive evidence that A-T carriers of any age have increased sensitivity to X-rays from mammograms or other diagnostic tests.

Clinical breast examination and breast ultrasound are approaches to screening that avoid radiation exposure. When exposure to radiation is required, doctors who treat A-T carriers should use the most modern equipment and technology available, in order to minimize radiation exposure.

15. What about environmental sources of radiation, such as cellular phones? Should A-T carriers avoid these exposures?

In NCI studies to date, no link has been found between non-ionizing radiation—such as that from cellular phones and power lines—and cancer.

16. What studies does NCI have under way to answer these questions more definitively?

NCI is sponsoring a wide variety of research on A-T, DNA mutations and repair, and the interaction between ATM and mutations in BRCA1 and 2 (breast cancer susceptibility genes). Clinical scientists at NCI have over 30 years of experience with A-T, and are continuing research to develop better diagnostic tests, immune dysfunction analyses, and treatments.

In addition, NCI is supporting three large, multi-national studies investigating A-T. One population-based study, a collaboration of investigators from the United States, Canada, Costa Rica, Germany, Israel, Italy, Poland, and Turkey, is examining the risk of cancer in A-T patients and their relatives. NCI is conducting another analysis of cancer risk in A-T families in collaboration with registries in Norway, Sweden, Denmark, and Finland. Another large, multi-site study, taking place in the United States and Denmark, is investigating whether women who are ATM carriers who have received radiation therapy as part of breast cancer treatment are at high risk of developing a second breast cancer in the other breast (second primary contralateral breast cancer).

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Related NCI materials and Web pages:

- National Cancer Institute Fact Sheet 5.28, *Mammograms* (<http://www.cancer.gov/cancertopics/factsheet/Detection/mammograms>)
- Hodgkin Lymphoma Home Page (<http://www.cancer.gov/cancertopics/types/hodgkin>)
- Leukemia Home Page (<http://www.cancer.gov/cancertopics/types/leukemia>)
- Non-Hodgkin Lymphoma Home Page (<http://www.cancer.gov/cancertopics/types/non-hodgkin>)

How can we help?

We offer comprehensive research-based information for patients and their families, health professionals, cancer researchers, advocates, and the public.

- **Call** NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237)
- **Visit** us at <http://www.cancer.gov> or <http://www.cancer.gov/espanol>
- **Chat** using LiveHelp, NCI's instant messaging service, at <http://www.cancer.gov/livehelp>
- **E-mail** us at cancergovstaff@mail.nih.gov
- **Order** publications at <http://www.cancer.gov/publications> or by calling 1-800-4-CANCER
- **Get help** with quitting smoking at 1-877-44U-QUIT (1-877-448-7848)

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