

Li-Fraumeni Syndrome

What is Li-Fraumeni Syndrome?

Li-Fraumeni syndrome (LFS) is a rare genetic condition that increases the risk of developing several types of cancer. It is hereditary, meaning that it can be passed to an individual from their parents. The cancers that happen in someone with LFS may be diagnosed during childhood, adolescence or adulthood. The most common types of cancers associated with LFS are:

- Breast cancer, often before the age of 50
- Soft tissue sarcomas – These tumors can start anywhere in the body. Typically they begin in fat, muscle, nerves, joints, blood vessels or deep skin tissue.
- Osteosarcoma – These tumors occur in the bone, most often in the long bones during adolescence
- Brain tumors (cancer)

Three rare early childhood tumors often happen in patients with LFS. These are embryonal rhabdomyosarcoma (rab-do-my-o-sar-coma), adrenal cortical tumor, and choroid plexus tumors.

Other cancers that happen less often in patients with LFS include colon cancer and other GI cancers, lung cancer and leukemia (cancer of the bone marrow). People with LFS often develop cancer at a younger age than the general population. The lifetime risk of cancer for a person with LFS may be as high as 85-90 percent, and cancer often happens before age 50. However, even within the same family, the age when cancer occurs can vary widely, from infancy through old age.

What causes LFS?

LFS is caused by a genetic change, called a mutation, in the gene TP53. Genes are the set of instructions that tell all of the cells in our bodies what to do. We have two copies of most genes, one from our mother and one from our father. Sometimes, a change or mutation happens in a gene that causes the gene to stop working properly. When it is working properly, the TP53 gene controls cell growth and prevents tumors (cancer) from forming. In the case of LFS, a mutation in the TP53 gene causes the gene to stop working properly. This genetic change can be passed from a parent to child.

Although most people with LFS have a mutation passed down to them from one of their parents, a new mutation can happen in TP53 so that a person will be the first in the family to have it. In this case, a person may have LFS even if they have little to no family history of cancer. Once

there is a new mutation, it can be passed on to future generations as described in the next section.

What are the chances of inheriting LFS?

Every person has two copies of the TP53 gene. One copy is inherited from their mother and one from their father. If a person inherits one TP53 gene mutation from either his or her mother or father, it will cause LFS. Each child of a parent with LFS has a 50 percent (1 in 2) chance to inherit LFS. LFS does not skip generations.

Why is it important to diagnose LFS?

People who have LFS are at an increased risk of developing several types of cancers. People with LFS who have been diagnosed with cancer have an increased risk of developing another type of cancer in a different part of the body, called a second primary cancer. Because of this increased cancer risk, it is important for people with LFS to see their doctors for regular exams, which may include screening tests to detect cancer as early as possible. Patients with LFS need additional screening for cancer that may begin at earlier ages than people in the general population.

Because LFS is an inherited condition, relatives of the person with LFS may also have this condition. If the specific TP53 mutation causing LFS in the family can be identified through genetic testing, then other family members can be tested to determine those who will need screening and those who will not.

How is LFS diagnosed?

Family History

The first step in diagnosing LFS is to review medical and family history. This includes making a multi-generation family tree, or pedigree, that indicates which relatives have had and have not had cancer. A genetic counselor or doctor will use this medical and family history to assess the family's risk of LFS. Some signs that suggest LFS may run in families include:

- cancer diagnosed at a younger age than is typical for that cancer;
- cancer in multiple family members and in two or more generations;
- family members who have had two or more cancers; and
- family members who have had rare forms of cancer.

Genetic Testing for LFS

Genetic testing, which is done with a blood sample, can identify a mutation in the TP53 gene. If a mutation is found, then the LFS diagnosis is confirmed. Next, other family members may have the same test to learn whether or not they carry the same TP53 mutation and have LFS.

How is LFS managed?

Because persons with LFS can develop several types of cancer often at younger ages than normally expected, it is important to have regular check-ups and cancer screening tests. Cancer

screening examinations are medical tests performed when a person has no symptoms. These tests help ensure that cancers are detected at their earliest, most treatable stages. General screening guidelines for LFS include:

Breast Cancer Screening (women)

- Monthly breast self-examination beginning at age 18
- Clinical breast examination every six months, beginning at age 20-25 or five to 10 years before the youngest breast cancer in the family (whichever is earlier)
- Annual mammogram and breast MRI, beginning at age 20-25 or five to 10 years before the youngest breast cancer in the family (whichever is earlier)
- Women with LFS may also consider preventive mastectomy (a surgery to remove the breasts before cancer develops)

Other Cancer Screening (men and women)

- Annual comprehensive physical exam by a doctor who is informed about LFS, including careful skin and neurological exams.
- Anyone who has LFS should learn the signs and symptoms of cancer and should quickly tell their doctor about any symptoms they have.
- Pediatricians caring for children with LFS should be aware of the risk of childhood cancers.
- Consider colonoscopy every two to five years starting at age 25 or younger.
- Discuss options to participate in novel screening approaches using technologies within clinical trials when possible, such as whole body MRI, abdominal ultrasound and brain MRI.
- There are no established screening tests for many of the cancers associated with LFS. Screening may be targeted based on the cancers in the family. Your doctor will discuss specific screening exams with you.

Radiation Therapy and LFS

Radiation therapy can be an important treatment of many cancers. However, radiation therapy can increase cancer risk somewhat in the general population. People with LFS may be more likely to develop new cancers in parts of the body where radiation therapy was used. In some cases, cancer could be treated with radiation therapy or with a different method. When there is a choice, it may be preferable to avoid radiation therapy. However, there are other situations where radiation therapy is the best way to treat the cancer, and in those cases the benefits of the radiation therapy may outweigh the risks for the person with LFS. Anyone with LFS who is considering radiation therapy should discuss the risks and benefits with their doctor. It is important for LFS patients treated with radiation and their doctor to know about the increased cancer risk and to pay special attention to symptoms in the area of the body treated.

Li-Fraumeni syndrome Resources

LFS Association

www.lfsassociation.org

LFS Association provides a wide range of information, advocacy, and support services for individuals and families with Li Fraumeni Syndrome. They also support researchers, medical providers and caregivers to further research and promote care for the LFS community.

General Cancer and Genetics Resources

National Cancer Institute

<http://www.cancer.gov>

This site has valuable cancer related health information on more than 200 cancer types, clinical trials, cancer statistics, prevention, screening, risk factors, genetics and support resources. Information is available in Spanish.

American Cancer Society (ACS)

<http://www.cancer.org>

The ACS is a voluntary national health organization with local offices around the country. The ACS supports research, provides information about cancer and offers many programs and services to patients and their families. Information is available in Spanish.