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 down in families from a parent to a child. Cancers related to LFS can occur at any age.

Cancer Risks

People with LFS have a very high risk of developing cancer. As many as 95 out of 100 people with LFS will develop at least one cancer in their life.

- People with LFS often develop cancer before age 50.
- People with LFS often develop multiple types of cancer.
- Patients with cancer and LFS have an increased risk of developing another type of cancer in a different part of the body, called a second primary cancer.
- The age when cancer occurs can vary widely, even in the same family.

The most common types of cancers for people with LFS are:

- Breast cancer, often before the age of 50
- Soft tissue sarcomas – These tumors can start anywhere in the body. Most often, they start in fat, muscle, nerves, joints, blood vessels or deep skin tissue.
- Osteosarcoma – These tumors grow in bone. They most often develop during adolescence, in the long bones in the arms and legs.
- Brain tumors

There are 3 rare early childhood cancers that are common with LFS:

- Embryonal rhabdomyosarcoma (rab-do-my-o-sar-coma)
- Adrenal cortical cancer
- Choroid plexus cancers

Other types of cancer may occur with LFS. These cancers can include, but are not limited to:

- Leukemia (cancer of blood cells, including bone marrow)
- Colon cancer and other cancers in the gastrointestinal tract
- Uterine and ovarian cancers
- Prostate and testicular cancers
- Thyroid cancer
- Kidney cancer
- Lung cancer

TP53 Gene Mutation

LFS is caused by a genetic change, called a mutation, in the *TP53* gene. Genes are the set of instructions that tell all cells in your body what to do. A mutation can cause a gene to stop

working properly. The *TP53* gene normally works to control cell growth and prevent cancer. When the gene stops working properly, it causes increased risk of cancer.

In most cases of LFS, a parent passes the *TP53* gene mutation to a child. You have 2 copies of the *TP53* gene. One copy is from your mother and one copy is from your father.

- A gene mutation in one of your *TP53* genes will cause LFS.
- Each child of a parent with LFS has a 1 in 2 chance to inherit LFS.
- LFS does not skip generations.

In some cases, the *TP53* gene mutation can be present even if neither parent has the mutation. When a child's *TP53* gene mutation is not passed down from a parent, it is a new gene mutation. A new mutation that occurs in a family can be passed to children.

Diagnosis

The first step in diagnosing LFS is to review medical and family history. This includes making a pedigree (a drawing of your family tree) to record which family members have and have not had cancer. A genetic counselor or doctor will use this information to assess your family's risk of LFS.

Some signs that cancer may run your family include:

- Cancer that is diagnosed at a younger age in your family than in the general population
- Cancer in multiple family members and in 2 or more generations
- Family members who have had 2 or more cancers
- Family members who have had rare forms of cancer

Genetic Testing

If your medical or family history show signs of LFS, *TP53* genetic testing may be the next step. Genetic testing uses a blood sample to look for mutations in the *TP53* gene. If the test finds a *TP53* mutation, the LFS diagnosis is confirmed.

Family Members

LFS is a genetic condition, so your family members are also at risk. If your family's specific *TP53* gene mutation can be identified through genetic testing, other family members may benefit from genetic testing. This can help doctors decide which family members need additional cancer screenings and preventive care.

Screening and Prevention

Cancer screening exams are medical tests performed when a person has no symptoms. Screening helps find cancer as early as possible when it may be easier to treat. Because you are at an increased risk of cancer, it is important to follow cancer prevention and early detection screening guidelines.

- You should start screenings earlier and may need to have more screenings than the general population.

- Screening recommendations depend on the your age, sex and medical history.
- Yearly blood tests and imaging tests are recommended for most people with LFS. Your doctor may recommend that you consider surgeries to prevent cancer.

Li-Fraumeni Syndrome Screening Clinic

MD Anderson's Li-Fraumeni Screening Clinic (LFS Screening Clinic) is a complete screening program for children and adults. The LFS Screening Clinic provides screening guidelines and helps patients stay up-to-date with all recommended screenings.

Radiation Therapy

People with LFS are at higher risk than patients without LFS to develop cancers after radiation therapy. When there are other treatment options, it may be preferred for you to avoid radiation therapy.

The benefits of radiation therapy may be greater than the risks. In these cases, radiation therapy may be the best way to treat cancer. Talk with your doctor about your medical history and the risks and benefits of your treatment options.

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 care givers to further research and promote care for the LFS community.