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 a son or daughter from his or her parent. 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 cancers are common in patients with LFS and are listed below.

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

Although the above cancers are most common in people with LFS, many types of cancer can occur and these can include, but are not limited to:

- Colon cancer and other cancers in the gastrointestinal tract
- Cancers in women (uterine, ovarian)
- Cancers in men (prostate, testicular)
- Thyroid cancer
- Kidney cancer
- Lung cancer
- Leukemia (cancer of the bone marrow)

People with LFS often develop cancer at a younger age than the general population and they usually develop multiple types of cancer. The lifetime risk of cancer for a person with LFS may be as high as 90-95%, and cancer typically 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 our 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 to sons and daughters from mothers or fathers.

Although most people with LFS have a *TP53* gene mutation passed down to them from one of their parents, sometimes an individual has a new mutation in the *TP53* gene that neither parent has. 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. Cancer patients with LFS 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 yearly 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.

Additionally, it may be important to know whether or not someone has LFS when considering the best treatment for certain cancers. Persons with LFS are at higher risk to develop cancers after radiation therapy compared to those without LFS. In some cases, the 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. If this is the case, 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 patients with LFS treated with radiation and their doctors to know about this increased cancer risk and to pay close attention to areas of the body treated with radiation.

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 cancer 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
- Family members who have had rare forms of cancer

Genetic Testing for LFS

Genetic testing, which is often done with a blood sample, is very important to help diagnose LFS. If a mutation in the *TP53* gene is found, then the LFS diagnosis is confirmed. Next, other family members may have the same genetic test to learn whether or not they carry the same *TP53* mutation and have LFS. This helps identify who in the family needs annual screening for LFS and who does not.

How is LFS managed?

Because persons with LFS can develop several types of cancer often at younger ages than those without LFS, it is important to have yearly check-ups and cancer screening tests. Cancer screening exams are medical tests performed when a person has no symptoms. These tests help ensure that cancers are detected at their earliest, most treatable stages. If you are identified to have LFS, the specific screening that will be recommended depends on your age, previous cancer history and sex. Most person will be recommended to have annual blood tests and imaging tests done, and others may be recommended to consider surgeries to prevent cancer.

The National Comprehensive Cancer Network (NCCN) has general screening guidelines for LFS. These guidelines are on the NCCN website and are updated annually. MD Anderson's comprehensive screening program is based on published medical literature and expert opinion. Our program, called the Li-Fraumeni syndrome Education and early Detection (LEAD) Program, is specific to children and adults. LEAD helps individuals with LFS stay up to date with all recommended screenings.

Resource

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.