



Cancer Predisposition Clinic

Li-Fraumeni syndrome

What is Li-Fraumeni syndrome?

Li-Fraumeni syndrome is a condition that makes a person more likely to develop one or more cancers in these areas of the body:

- Brain
- Breasts
- Bones
- Blood
- Adrenal gland (a tiny organ that is located on top of each kidney)
- Muscles or connective tissues

Less commonly, people with Li-Fraumeni syndrome develop other types of cancers, including those affecting these areas of the body:

- Skin
- Thyroid gland
- Lungs
- Digestive system (esophagus, stomach, pancreas or colon)
- Urinary system (kidney, bladder)
- Reproductive system (uterus, ovaries, prostate, gonads)

What causes Li-Fraumeni syndrome?

Li-Fraumeni syndrome is caused by changes in a gene known as *TP53*. Genes carry important information that tell our body's cells how to function.

The *TP53* gene controls how cells grow and divide. One of its main jobs is to prevent cancers from forming. Normally, your cells carry two working copies of *TP53*. One is inherited from your mother and one from your father.

Cells from people with Li-Fraumeni syndrome carry one working copy of *TP53* and one copy that is altered. This alteration causes the gene to not work properly and is called a mutation. When the remaining working copy of *TP53* becomes damaged within a cell, this can lead to a cancer.

What is the cancer risk for children with Li-Fraumeni syndrome?

- By age 30, it is estimated that half of all people with Li-Fraumeni syndrome will develop some kind of cancer.
- By age 60, the likelihood of cancer for people with Li-Fraumeni syndrome increases to about 80%–90%.
- People with Li-Fraumeni syndrome are more likely to develop multiple cancers and cancers caused by radiation.

Because of the wide range of cancer types that can affect children with Li-Fraumeni syndrome, it is hard to predict the kinds of cancer that will develop. It is also hard to know when these cancers will occur.

How are people with Li-Fraumeni syndrome screened for cancer?

It is not yet known whether monitoring for cancer in Li-Fraumeni syndrome patients is helpful. But, early evidence suggests that this is the case. As a result, children and adults with Li-Fraumeni syndrome should be watched closely for possible cancer. The goal is to detect cancer at the earliest and most treatable stage. The cancer screening tests should be discussed with a health care provider familiar with Li-Fraumeni syndrome. These tests may include the following:

- A yearly physical exam that includes a close check of skin health and neurological function
- Periodic blood tests that include a complete blood count (CBC)
- Tests that screen for hormone-producing cancers coming from the adrenal glands
- Yearly magnetic resonance imaging (MRI) of the brain and body
- Periodic ultrasound of the abdomen

Adults with Li-Fraumeni syndrome may also need to do some of the same tests, plus the following:

- A colonoscopy every two to five years starting in the early 20s
- Women should have a breast exam performed by a health care provider every six months. Starting in the early 20s, women should also have a mammogram and breast MRI exam at least once a year.

How do children get Li-Fraumeni syndrome?

Most children with Li-Fraumeni syndrome inherit the syndrome from a parent who also has the syndrome. But some children with Li-Fraumeni syndrome may have a new *TP53* mutation that did not come from a parent. In these cases, the *TP53* mutation either arose in an egg or sperm cell that formed the child or in one of the child's cells during pregnancy. These children are the first in their families to have Li-Fraumeni syndrome.

No matter how they acquired the altered gene, people with Li-Fraumeni syndrome have a 50% or 1 in 2 chance of passing it on to their children.

How is genetic testing for Li-Fraumeni syndrome done?

Hereditary cancer syndromes such as Li-Fraumeni syndrome may be suspected after looking at a person's medical or family history. In most cases, a health care provider or genetic counselor will ask questions about a person's health and the health of other family members.

The genetic counselor or health care provider will record which family members have developed cancers, and if so, the types of cancers and ages at which these cancers occurred. From this information, they will create a family tree. Health care providers and genetic counselors will examine the family tree to find out:

- If there are more cancers than normal,
- Whether cancers occurred at younger than expected ages, or
- If the types of cancers match up with what might be observed in those with Li-Fraumeni syndrome.

Health care providers or genetic counselors who suspect Li-Fraumeni syndrome in a child or other family members will likely recommend genetic testing of *TP53*.

Diagnostic testing

If health care providers or genetic counselors suspect a person has Li-Fraumeni syndrome, diagnostic testing may take place:

- A blood sample is collected.

- DNA is isolated from the cells in the sample, and the *TP53* gene is checked for possible mutations using a variety of methods such as DNA sequencing. DNA sequencing is when a genetic specialist checks the lettering (spelling) of the two copies of a gene to that of a normal sample. If there are differences, the specialist then decides if they might cause a specific disease, such as Li-Fraumeni syndrome. Please note that other methods may also be used, especially when the results of DNA sequencing are negative or unclear. These other tests look for changes that could affect the *TP53* gene but that may not be found by DNA sequencing.
- If a *TP53* mutation is found, a genetic counselor will work with the family to find out if other family members should consider testing for the mutation. The genetic counselor will help the family understand the cancer risks of those with Li-Fraumeni syndrome. The genetic counselor can also help with decisions about prenatal genetic testing.

Prenatal testing

Parents may undergo prenatal testing to find out whether a pregnancy is affected with a known *TP53* mutation in the family.

Testing may take place either before pregnancy occurs or after an embryo is formed. Those considering prenatal testing should work with a genetic counselor to review the pros and cons of the tests. The genetic counselor will also help parents consider how they wish to handle the results of the testing.

Testing that occurs before pregnancy: Testing that happens before pregnancy is called preimplantation genetic testing (PGT). This special type of genetic testing is done along with in vitro fertilization (IVF). PGT offers a way to test embryos for a known *TP53* mutation before placing them into the uterus.

Testing that occurs during pregnancy: Testing can be used to determine if a pregnancy is affected with a known *TP53* mutation. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)**—during first trimester
- **Amniocentesis**—during second trimester or later

Once these tissues are collected, DNA is isolated and checked for the presence of the *TP53* mutation identified in the family.

Both of these tests carry minor risks and should be discussed with an experienced doctor and/or genetic counselor.

Special concerns

Genetic testing for Li-Fraumeni syndrome is a complex process. Those thinking about testing should take time to consider the benefits and risks. They should discuss the process with a genetic counselor before undergoing the testing. If they choose testing, they should review the test results with the health care provider or genetic counselor to be sure that they understand the meaning of the results.

Sometimes, children or adults with Li-Fraumeni syndrome experience sadness, anxiety or anger. Parents who passed on an altered *TP53* gene to one or more of their children can feel guilty. It is also possible that a person who is found to have an altered *TP53* gene could have more trouble getting disability insurance or life insurance.

Are there other special health care needs for children with Li-Fraumeni syndrome?

People of any age with Li-Fraumeni syndrome have a higher risk of cancer. Steps should be taken to monitor their health and adopt healthy habits throughout life.

As children with Li-Fraumeni syndrome grow up, they should continue to have regular physical check-ups and screenings. That way, any cancer can be found early at the most treatable stage.

People with Li-Fraumeni syndrome should also watch closely for symptoms that could signal cancer, such as:

- Unexplained weight loss
- Loss of appetite
- Aches, pains, lumps or swellings that cannot be explained
- Headaches or changes in vision or nerve function that do not go away
- New moles or changes in moles that are already present

Parents of children with Li-Fraumeni syndrome should watch for signs and symptoms of illness and seek medical help if anything unusual appears.

To prevent cancer, children and adults with Li-Fraumeni syndrome should do the following:

- Eat a healthy diet with lots of fruits and vegetables
- Get regular exercise
- Avoid excess sun exposure and always wear sunscreen, hat and protective clothing when out in the sun
- Avoid unnecessary radiation exposure
- Avoid smoking or the use of tobacco products
- Avoid being around secondhand smoke

What other information and resources are there for children with Li-Fraumeni syndrome and their families?

Other resources about Li-Fraumeni syndrome include:

- Genetics Home Reference: Li-Fraumeni syndrome (<http://ghr.nlm.nih.gov/condition/li-fraumeni-syndrome>)
- Li-Fraumeni syndrome Association (www.lfsassociation.org)
- Living LFS (<http://www.livinglfs.org/>)
- Making Sense of Your Genes: A Guide to Genetic Counseling (www.ncbi.nlm.nih.gov/books/NBK115508/)
- Young People with Cancer: A Parent's Guide (www.cancer.gov/publications/patient-education/young-people)

Sources:

1. Genetics Home Reference: Li-Fraumeni Syndrome
ghr.nlm.nih.gov/condition/li-fraumeni-syndrome
2. National Cancer Institute: Genetic Testing for Hereditary Cancer Syndromes
www.cancer.gov/cancertopics/factsheet/Risk/genetic-testing
3. GeneReviews
www.ncbi.nlm.nih.gov/books/NBK1311/

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