



Cancer Predisposition Clinic

Peutz-Jeghers Syndrome

Also called: *PJS, Peutz-Jeghers polyposis, Hutchinson Weber-Peutz syndrome*

What is Peutz-Jeghers syndrome?

Peutz-Jeghers syndrome is a genetic condition that causes non-cancerous growths to develop in the digestive system. The growths, called hamartomatous polyps, usually grow in the small intestine. They can also grow in the stomach or large intestine. Sometimes they grow outside the digestive system and may appear in the kidneys, lungs, gall bladder, nasal passages, bladder or the tubes that connect the kidneys to the bladder (ureters).

People with Peutz-Jeghers syndrome often also have small, dark-colored spots that look like freckles on some parts of their skin. The spots usually appear during childhood and often fade as the person gets older. Most spots are on the lips, around and inside the mouth, near the eyes and nostrils, and around the anus. The spots may also occur on the hands and feet.

Having Peutz-Jeghers syndrome increases a person's risk of developing the following types of cancers:

- Digestive system cancer (stomach, esophagus, small intestine, pancreas, colon, or rectum)
- Breast cancer (females)
- Uterine cancer (females)
- A rare type of cervical cancer (females)
- Lung cancer
- Tumors of the ovaries and testicles (can be cancerous or non-cancerous)

Because Peutz-Jeghers syndrome is hereditary, the condition can be passed from parents to children in a family. Peutz-Jeghers syndrome often varies in how severe it is, even among people in the same family. Some people may have many polyps and may develop cancer at a young age, while others may only develop a few polyps and may not develop cancer.

What causes Peutz-Jeghers syndrome?

Peutz-Jeghers syndrome is caused by changes in a gene known as *STK11*. Genes carry information telling cells within the body how to function. The *STK11* gene is needed for cells to grow and divide properly.

Most people without Peutz-Jeghers syndrome carry two working copies of the *STK11* gene in their cells. One copy is inherited from the mother and one from the father. Cells from people with Peutz-Jeghers syndrome carry one working copy of the *STK11* gene in their cells and one copy that is changed. This change causes the *STK11* gene to not work properly. It is called a mutation.

About half of children with Peutz-Jeghers syndrome have inherited the *STK11* gene mutation from a parent. The other half of the children with Peutz-Jeghers syndrome are the first people in

their families to have a *STK11* gene mutation. These children have no history of the condition in their families. In these cases, the change either happened in an egg or sperm cell when the child was formed or in one of the child's cells during pregnancy. These children are the first in their families to have Peutz-Jeghers syndrome.

No matter how they acquired the mutation, people with Peutz-Jeghers syndrome have a 50% (1 in 2) chance of passing it on to their children.

What is the cancer risk for people with Peutz-Jeghers syndrome?

People with Peutz-Jeghers syndrome have an 85% risk of developing cancer by 70 years of age. The risks for each type of cancer are shown in the table below:

Type of Cancer	Lifetime Risk
Breast (female)	32-54%
Colorectal cancer	39%
Pancreatic cancer	11-36%
Stomach cancer	29%
Ovarian	21%
Lung cancer	7-17%
Cervical cancer (adenoma malignum)	10%

Other types of cancers have been reported in individuals with Peutz-Jeghers syndrome.

What are other symptoms or physical findings seen in people with Peutz-Jeghers syndrome?

People with Peutz-Jeghers syndrome may have other medical issues. Not all people with Peutz-Jeghers syndrome will have all the symptoms or physical findings listed below.

The growth of polyps in the digestive system may cause the following:

- Bowel obstruction (blockage in the large or small intestine)
- Rectal prolapse (the wall of the rectum slides out of place, sometimes sticking out of the anus)
- Severe bleeding in the digestive system
- Anemia (too little oxygen in the blood), causing the person to feel tired

Tumors of the ovaries and testicles may cause the following:

- Puberty that happens at an unusually young age
- Irregular or heavy menstrual periods in women

- Growth of breasts in boys
- Unusually short height in boys

How are people with Peutz-Jeghers syndrome screened for tumors?

People with Peutz-Jeghers syndrome should be managed by a health care provider who knows this condition well. Children with Peutz-Jeghers syndrome should have regular screenings to detect cancer as early as possible. The goal of screening is finding and treating cancer early to allow the best outcome for patients. Cancer screening should only be performed in a center with experience in taking care of people with Peutz-Jeghers syndrome. People with Peutz-Jeghers syndrome should carefully talk about the benefits and risks of cancer screening with a health care provider who knows the condition well.

The following guidelines for cancer screening in children and young adults with Peutz-Jeghers syndrome are recommended:

- **Yearly physical exams** by a health care provider who knows Peutz-Jeghers syndrome well.
- **Stomach and intestinal cancer screening:**
 - **Upper endoscopy plus small bowel examination (MR enterography or wireless capsule endoscopy)** beginning at age 8 years. The health care provider will determine how often this should be repeated based on what is seen. If polyps are found, repeat imaging in 3 years. If no polyps are found, repeat at age 18 years.
 - **Colonoscopy** (using a small camera to see the inside lining of the colon) beginning at age 8 years. The health care provider will determine how often this should be repeated based on what is seen. If polyps are found, repeat imaging in 3 years. If no polyps are found, repeat at age 18 years.
- **Breast cancer screening (women only)** (starting at age 25 years or 5-10 years before the earliest diagnosis of breast cancer in the family, whichever is earlier):
 - **Breast self-exam** monthly
 - **Breast exam by a health care provider** every 6 months
 - **MRI imaging of the breasts and mammogram** annually
- **Pancreatic cancer screening:**
 - **MR imaging of the pancreas and bile ducts (MR cholangiopancreatography)** beginning at age 30 years and repeated every 1–2 years. An endoscopic ultrasound (combining endoscopy and ultrasound to let the health care provider see the digestive tract) may be done instead of MR imaging.
- **Uterus, ovary and cervix cancer screening (women only)**
 - **Exam by a gynecologist and Pap smear test** beginning at age 18–20 years and repeated every year.
 - **Consider transvaginal ultrasound** (a test where a health care provider uses ultrasound to see the uterus, cervix and ovaries) and serum CA-125 lab work
- **Testicle cancer screening (boys and men only)**

- **Testicular exam** to observe enlargement, masses, and/or evidence of feminizing changes, beginning at age of diagnosis
- **Yearly checkups** with the person's regular primary care health care provider.

It is possible that recommended screenings may change over time as health care providers learn more about Peutz-Jeghers syndrome. Parents should discuss all screening options for their child with a health care provider who knows this syndrome well. Because it is a complex condition, it is very important that parents seek out an experienced health care provider for their child.

How is genetic testing for Peutz-Jeghers syndrome done?

The health care provider may suspect Peutz-Jeghers syndrome 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 tumors, what types of tumors and at what ages the tumors occurred. From this information they will create a family tree. Health care providers and genetic counselors will look at the family tree to find out:

- If there are more tumors than normal,
- If tumors occurred at younger-than-expected ages, and
- If the types of tumors match up with what might be seen in those with Peutz-Jeghers syndrome.

If Peutz-Jeghers syndrome is suspected in a child or other family members, the health care provider or genetic counselor will likely recommend genetic testing of the *STK11* gene.

Diagnostic genetic testing

If the health care provider or genetic counselor suspects that a person has Peutz-Jeghers syndrome, diagnostic testing may take place as follows:

- A blood sample is collected.
- DNA is isolated from the cells in the sample. A person's genes are made of DNA.
- Both copies of the person's *STK11* gene are checked for possible changes. A genetic specialist compares the two copies of the person's *STK11* gene to normal copies of those genes. If there are differences, the specialist decides if they might cause a certain condition such as Peutz-Jeghers syndrome.
- If a mutation is found in the *STK11* gene, the genetic counselor will work with the family in the following ways:
 - To help the family understand the cancer risks of Peutz-Jeghers syndrome
 - To find out if other family members should consider testing for the mutation
 - To help with decisions about prenatal genetic testing

It is important to remember that genetic testing does not always find mutations in the *STK11* genes for all people with Peutz-Jeghers syndrome. A person can still have Peutz-Jeghers syndrome even if no mutations are found in these genes. There may be other genes that are related to the condition that health care providers do not yet know about.

Prenatal genetic testing

Parents may undergo prenatal testing to find out if the pregnancy is affected with a known *STK11* gene mutation in the family. Testing may take place either before pregnancy occurs or during pregnancy.

People considering prenatal testing should work with a genetic counselor to review the pros and cons of the testing. The genetic counselor can 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 *STK11* gene mutation before placing them into the uterus.

Testing that occurs during pregnancy—Testing can be used to see if a pregnancy is affected with a known *STK11* gene mutation. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)**—during the first trimester (first three months)
- **Amniocentesis**—during the second trimester or later (last six months)

Collected tissue can be checked for the presence of the *STK11* gene mutation identified in the family. Both of these tests carry minor risks and should be discussed with an experienced doctor or genetic counselor.

Special concerns

Genetic testing for Peutz-Jeghers 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 testing is done. If they choose testing, they should review the test results with the health care provider or genetic counselor to be sure they understand the meaning of the results.

Sometimes children or adults with Peutz-Jeghers syndrome can feel sad, anxious or angry. Parents who pass on an *STK11* gene mutation to one or more of their children can feel guilty. Some people with an *STK11* gene mutation could have trouble getting disability coverage, life insurance or long-term care insurance in some states. More information about genetic discrimination can be found at www.ginahelp.org

Are there other special health care needs for children with Peutz-Jeghers syndrome?

People of any age with Peutz-Jeghers syndrome have a higher risk of cancer. They should monitor their health and adopt healthy habits throughout life. It is important to continue to have regular physical checkups and screenings. That way, any cancer can be found early at the most treatable stage.

Other ideas to reduce the risk of cancer:

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

People with Peutz-Jeghers syndrome should watch for signs or symptoms that could signal cancer:

- Unexplained weight loss
- Loss of appetite
- Pain in abdomen
- Blood in the stool or changes in bowel habits
- Aches, pains, lumps or swelling that cannot be explained
- Headaches or changes in vision or nerve function that do not go away

It is important to seek medical help if anything unusual appears.

What other information and resources are there for children with Peutz-Jeghers syndrome and their families?

Resources about Peutz-Jeghers syndrome:

- Hereditary Colon Cancer Take Guts (www.hcctakesguts.org/)
- National Organization for Rare Disorders – Peutz-Jeghers Syndrome (<https://rarediseases.org/rare-diseases/peutz-jeghers-syndrome/>)

More resources about genetic testing and hereditary cancer:

- 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 – Peutz-Jeghers Syndrome <https://ghr.nlm.nih.gov/condition/peutz-jeghers-syndrome>

2. GeneReviews – Peutz-Jeghers Syndrome www.ncbi.nlm.nih.gov/books/NBK1266/
3. Hearle N, Schumacher V, Menko FH, et al. Frequency and spectrum of cancers in the Peutz-Jeghers syndrome. *Clin Cancer Res.* 2006;12:3209-3215.
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Colorectal. NCCN.org

Developed by:

St. Jude Division of Cancer Predisposition

Updated 5/2020

