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Peutz-Jeghers Syndrome

Approved by the Cancer.Net Editorial Board (http://www.cancer.net/about-us/cancernet-editorial-board) **, 09/2021**

What is Peutz-Jeghers syndrome?

Peutz-Jeghers syndrome (PJS) is an inherited condition that puts people at an increased risk for developing hamartomatous polyps in the digestive tract, as well as cancers of the breast, colon and rectum, pancreas, stomach, testicles, ovaries, lung, cervix, and other types listed below. Without appropriate medical surveillance, the lifetime risk of cancer in people with PJS may be as high as 93%. A hamartoma is a growth of normal-appearing tissue that builds up into a benign (noncancerous) tumor. In PJS, hamartomatous polyps often develop in the small and large intestine, and they can cause **bleeding** (http://www.cancer.net/node/25243) or other problems, such as an **intestinal blockage** (http://www.cancer.net/node/25244) .

Some signs of PJS can appear in childhood with the development of pigmented areas on the skin and in the mouth, called mucocutaneous hyperpigmentation. People with PJS tend to develop dark blue or dark brown freckling, especially around the mouth and on the lips, fingers, or toes. Freckles generally appear in childhood and often fade with age, so that they often are not visible in an adult with PJS newly diagnosed with cancer. Another sign of PJS is the development of hamartomatous polyps of the gastrointestinal tract that can cause bleeding and blockages. The average age when gastrointestinal symptoms appear is 10 years old.

Individuals with at least 2 of the following characteristics may be considered to have PJS:

- At least 2 Peutz-Jeghers type hamartomatous polyps in the small intestine
- Characteristic freckling of the mouth, lips, fingers, or toes
- At least 1 relative diagnosed with PJS

Individuals who meet these criteria are recommended to have genetic testing to look for an inherited mutation, also called an alteration, in the *STK11* gene. More information is below.

What causes PJS?

PJS is a genetic condition that causes a person to have an increased risk of developing cancer and polyps. This means that the condition can be passed from generation to generation in a family. PJS is caused by inheriting a mutation in the *STK11* gene, also known as the *LKB1* gene. It is possible that there are other genes that could cause PJS that have not yet been discovered.

How is PJS inherited?

Normally, every cell has 2 copies of each gene: 1 inherited from the mother and 1 inherited from the father. PJS is inherited in an **autosomal dominant** (http://www.ncbi.nlm.nih.gov/books/n/gene/glossary/def-item/autosomal-dominant/) manner from a parent who carries the *STK11* mutation. Each first-degree

relative of a person with PJS has a 50% chance that they inherited the same mutation that causes this disease. First-degree relatives include parents, children, and siblings.

Some individuals with PJS have no **family history** (http://www.ncbi.nlm.nih.gov/books/n/gene/glossary/def-item/family-history/) of PJS or PJS-like symptoms or cancers. It is estimated that approximately 25% of individuals with PJS have a new (*de novo*) *STK11* gene mutation that was not inherited. Family members of someone with a suspected *de novo STK11* mutation should still have genetic testing to confirm that this was indeed a new mutation that happened to the *STK11* gene after the person was born. A person who has a *de novo STK11* mutation has a 50% chance of passing this mutation on to each of their biological children.

Options exist for people interested in having a child when a prospective parent carries a gene mutation that increases the risk for this hereditary cancer syndrome. Preimplantation genetic diagnosis (PGD) is a medical procedure done in conjunction with in-vitro fertilization (IVF). It allows people who carry a specific known genetic mutation to reduce the likelihood that their children will inherit the condition. A person's eggs are removed and fertilized in a laboratory. When the embryos reach a certain size, 1 cell is removed and is tested for the hereditary condition in question. The parents can then choose to transfer embryos that do not have the mutation. PGD has been in use for over 2 decades and has been used for several hereditary cancer predisposition syndromes. However, this is a complex procedure with financial, physical, and emotional factors to consider before starting. For more information, talk with an assisted reproduction specialist at a fertility clinic.

How common is PJS?

PJS is considered to be rare. It is estimated that between 1 in 50,000 to 1 in 200,000 people will have PJS. The syndrome may be underdiagnosed because the skin features like freckles or pigmented spots are often not visible in adulthood.

How is PJS diagnosed?

The diagnosis of PJS is assumed if someone meets the diagnostic criteria listed above. People who may possibly have PJS can have **genetic counseling** (http://www.cancer.net/node/24907) followed by genetic testing that includes a blood test to look for a mutation in the *STK11* gene. If an *STK11* gene mutation is found, other family members may also be diagnosed with PJS if they are tested and have the same gene mutation. However, some people with a clinical diagnosis of PJS will not have a detectable mutation in *STK11*. It is recommended that individuals with known or suspected PJS be evaluated by a specialist to confirm the diagnosis and assist with appropriate medical management.

What are the estimated cancer risks associated with PJS, by each type?

- **Breast cancer** (http://www.cancer.net/node/31322) 30% to 50%
- **Colorectal cancer** (http://www.cancer.net/node/31317) 40%
- **Pancreatic cancer** (http://www.cancer.net/node/31388) 10% to 35%
- **Stomach cancer** (http://www.cancer.net/node/31376) 30%
- **Ovarian cancer** (http://www.cancer.net/node/31343) 20%
- **Lung cancer** (http://www.cancer.net/node/31273) 15%
- **Small intestine cancer** (http://www.cancer.net/node/31377) 13%
- **Cervical adenoma malignum cancer** (http://www.cancer.net/node/31319) 10%

- **Uterine cancer** (http://www.cancer.net/node/31260) less than 10%
- **Testicular cancer** (http://www.cancer.net/node/31375) less than 10%
- **Esophageal cancer** (http://www.cancer.net/node/31310) 2%

What are the screening options for PJS or people at risk for PJS?

It is important to discuss with your health care team the following screening options, as each individual is different:

General cancer screening for anyone with PJS

- Upper **endoscopy** (http://www.cancer.net/node/24731) and video capsule endoscopy, beginning at age 8. If polyps are seen, this should be repeated every 2 to 3 years. If no polyps are seen at age 8, these should be repeated by age 18, and then every 2 to 3 years afterwards. An endoscopy uses a thin, lighted, flexible tube with a small video camera that is inserted into your mouth and down your esophagus to look for tumors or other problems.
- **Colonoscopy** (http://www.cancer.net/node/24481), beginning at age 8. If polyps are seen, this should be repeated every 2 to 3 years. If no polyps are seen at age 8, this should be repeated by age 18, and then every 2 to 3 years afterwards. During a colonoscopy, doctor inserts a thin flexible tube with a small video camera into the anus to check for problems within the colon and rectum.
- Annual endoscopic ultrasound and/or pancreatic MRI to screen for pancreatic cancer, beginning at age 30 to 35, or 10 years younger than the youngest pancreatic cancer diagnosis in the family, whichever is earlier.
- Specific lung cancer screening is not currently recommended, but individuals with PJS should avoid smoking, due to the link with both lung and pancreatic cancers.

Cancer screening for girls and women with PJS

- Monthly breast self-examination and yearly clinical breast examination performed by a doctor or nurse, beginning at age 20
- **Mammogram** (http://www.cancer.net/node/24584) every 2 to 3 years, beginning at age 20, and then a yearly mammogram, beginning at age 40
- Yearly gynecologic examination including a **Pap test** (http://www.cancer.net/node/24638), transvaginal **ultrasound** (http://www.cancer.net/node/24714), and consideration of a uterine **biopsy** (http://www.cancer.net/node/24406), beginning at age 25
- PJS brings a higher risk for sex cord tumors with annular tubules (SCTAT), a benign neoplasm of the ovaries, and adenoma malignum of the cervix, a rare aggressive cancer often characterized by a heavy mucous-like vaginal discharge.

Cancer screening for boys and men with PJS

- Yearly testicular examination beginning in childhood. Testicular **ultrasound** (http://www.cancer.net/node/24714) should be performed to look for anything abnormal, or to investigate any signs of possible hormone problems.
  - PJS brings a risk of large calcium-containing Sertoli cell tumors (LCST) of the testicles, which secrete estrogen and can lead to enlarged breasts (gynecomastia), advanced skeletal age, and ultimately short stature, if untreated.

Screening options may change over time as new technologies are developed and more is learned about PJS. It is important to talk with your doctor about appropriate screening tests.

Learn more about **what to expect when having common tests, procedures, and scans** (http://www.cancer.net/node/24959) .

Questions to ask the health care team

If you are concerned about PJS and your risk of cancer, talk with your health care team. It can be helpful to bring someone along to your appointments to take notes. Consider asking your health care team the following questions:

- What is my risk of developing colorectal cancer, breast cancer, or other types of cancer?
- How many colon polyps have I had in total?
- What type of colon polyps have I had? The 2 most common kinds are hyperplastic and adenomatous.
- What can I do to reduce my risk of cancer?
- What are my options for getting a cancer risk assessment, genetic counseling, and possible genetic testing?
- What are my options for cancer screening and prevention?

If you are concerned about your family history and think your family may have PJS, consider asking the following questions:

- Does my family history increase my risk of colorectal cancer, breast cancer, or other types of cancer?
- Does it suggest the need for a cancer risk assessment?
- Will you refer me to a genetic counselor or other genetics specialist?
- Should I consider **genetic testing** (http://www.cancer.net/node/24895) ?

Related Resources

The Genetics of Cancer (http://www.cancer.net/node/24897)

Genetic Testing (http://www.cancer.net/node/24895)

What to Expect When You Meet With a Genetic Counselor (http://www.cancer.net/node/24907) (http://www.cancer.net/node/24895)

Collecting Your Family Cancer History (http://www.cancer.net/node/30761)

Sharing Genetic Test Results with Your Family (http://www.cancer.net/node/36141)

Family Genetic Testing Q & A (http://www.cancer.net/node/39036)

More Information

Facing Our Risk of Cancer Empowered (FORCE) (https://www.facingourrisk.org)

Pancreatic Cancer Action Network (https://www.pancan.org)

National Cancer Institute (https://www.cancer.gov)

To find a genetic counselor in your area, ask your doctor or visit the following website:

National Society of Genetic Counselors (https://findageneticcounselor.nsgc.org/?reload=timezonee)