

Peutz-Jeghers Syndrome [1]

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, pancreas, stomach, ovaries, and other types, listed below. The lifetime risk of cancer in people with PJS is around 93%. A hamartoma is a growth of normal-appearing tissue that builds up into a benign (noncancerous) tumor. However, the benign tumor can transform into cancer over time. Cancer begins when normal cells begin to change and grow uncontrollably. A tumor can be noncancerous or malignant (cancerous, meaning it can spread to other parts of the body).

Typically, signs of this condition 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.

The suggested criteria for a diagnosis of PJS are:

- Diagnosis of one or more hamartomatous polyps in the digestive tract, and at least **two** of the following:
 - Polyps in the small intestine
 - Characteristic freckling of the mouth, lips, fingers, or toes
 - At least one relative diagnosed with PJS

The diagnosis of PJS is also considered if someone has a family history of PJS and has the characteristic freckling. PJS may be a possible diagnosis if a person has the characteristic freckling and polyps even without a known family history.

What causes PJS?

PJS is a genetic condition that predisposes to increased risk to develop cancer. This means that the condition can be passed from generation to generation in a family. The *STK11* gene (also known as the *LKB1* gene) is the only gene that has been linked to PJS so far. A mutation

(alteration) in the *STK11* gene gives a person an increased lifetime risk of developing colorectal cancer [2] and other symptoms of PJS. It is possible that there may be other genes associated with PJS that have not yet been discovered

How is PJS inherited?

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. PJS is inherited in an autosomal dominant [3] manner from a parent who carries the *STK11* mutation. Each first-degree relative (parent, child, and/or sibling) of an individual with this condition has a 50% chance that he/she has inherited the same mutation that causes this disease.

However, approximately 45% of affected [4] individuals have no family history [5] of PJS. The exact proportion of cases caused by new (*de novo*) gene [6] mutations is unknown, as the frequency of subtle signs of the disorder in parents has not been thoroughly evaluated. However, 20% or more of individuals with PJS have a new (*de novo*) mutation that occurred at the time they were conceived. A person who has a new mutation has a 50% chance of passing on the *STK11* gene mutation to each biological child.

Options exist for couples interested in having a child when they know that one partner carries a gene mutation that increases the risk for hereditary cancer. Preimplantation Genetic Diagnosis (PGD) is a medical procedure done in conjunction with in-vitro fertilization (IVF). It allows people who carry a specific genetic mutation to have children who do not carry the mutation. A woman's eggs are removed and fertilized in a laboratory. When the embryos reach a certain size, one 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 a decade, and more recently has been used for several hereditary cancer predisposition syndromes. 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 one in 25,000 to one 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 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, people with a clinical diagnosis of PJS may not have a detectable mutation in *STK11*.

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

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- Breast cancer [7] 50%

- Colorectal cancer [2]

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

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

General cancer screening for anyone with PJS

- Pancreatic cancer [8] 35%
- Upper and lower endoscopy [17] (a thin, lighted, flexible tube with a small video camera is inserted into your mouth and down your esophagus to look for tumors or other abnormalities), beginning at age 10 and repeated every two years into adulthood
- Colonoscopy [18] (the doctor inserts a thin flexible tube with a small video camera into the anus to check for abnormalities within the colon and rectum), beginning at age 10 and repeated every two years
- Endoscopic ultrasound or abdominal ultrasound [19] to screen for pancreatic cancer [8], beginning at age 30 and repeated every one to two years

Cancer screening for women with PJS

- Small intestine cancer [12] 12%
- Monthly breast self-examination and yearly clinical breast examination (examination performed by a doctor or nurse), beginning at age 20
- Mammogram [20] every two to three years, beginning at age 20, and then a yearly mammogram, beginning at age 40
- Yearly gynecologic examination including Pap test [21], transvaginal ultrasound [19] (a test where a small ultrasound probe is inserted like a speculum for a pelvic examination in order to obtain better imaging of the uterus), and consideration of a uterine biopsy [22], beginning at age 20
- Uterine cancer [14] less than 10%
- Testicular cancer [15] less than 10%
- Females are at 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.
- Esophageal cancer [16] 2%

Cancer screening for men with PJS

- Yearly testicular examination and consideration of an ultrasound [19], beginning by age 20
- Males may develop 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 [23].

Questions to ask the doctor

If you are concerned about PJS and your risk of cancer, talk with your doctor. Consider asking the following questions of your doctor:

- What is my risk of developing colorectal cancer [2], breast cancer [7], or other types of cancer?
- How many colon polyps have I had in total?
- What type of colon polyps have I had? (The two 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?

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 [2], breast cancer [7], 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 [24]?

Additional resources

[2]

Guide to Colorectal Cancer [2]

Guide to Breast Cancer [7]

What to Expect When You Meet With a Genetic Counselor [25]

Colon Cancer Alliance

www.ccalliance.org [26]

Facing Our Risk of Cancer Empowered (FORCE)

www.facingourrisk.org [27]

National Cancer Institute

www.cancer.gov [28]

American Cancer Society

www.cancer.org [29]

CancerCare

www.cancercares.org [30]

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

National Society of Genetic Counselors

www.nsgc.org [31]

Links:

- [1] <http://www.cancer.net/cancer-types/peutz-jeghers-syndrome>
- [2] <http://www.cancer.net/node/18701>
- [3] <http://www.ncbi.nlm.nih.gov/books/n/gene/glossary/def-item/autosomal-dominant/>
- [4] <http://www.ncbi.nlm.nih.gov/books/n/gene/glossary/def-item/affected/>
- [5] <http://www.ncbi.nlm.nih.gov/books/n/gene/glossary/def-item/family-history/>
- [6] <http://www.ncbi.nlm.nih.gov/books/n/gene/glossary/def-item/gene/>
- [7] <http://www.cancer.net/node/18618>
- [8] <http://www.cancer.net/node/19495>
- [9] <http://www.cancer.net/node/19645>
- [10] <http://www.cancer.net/node/19481>
- [11] <http://www.cancer.net/node/19148>
- [12] <http://www.cancer.net/node/19632>
- [13] <http://www.cancer.net/node/18674>
- [14] <http://www.cancer.net/node/19308>
- [15] <http://www.cancer.net/node/19659>
- [16] <http://www.cancer.net/node/18783>
- [17] <http://www.cancer.net/node/24731>
- [18] <http://www.cancer.net/node/24481>
- [19] <http://www.cancer.net/node/24714>
- [20] <http://www.cancer.net/node/24584>
- [21] <http://www.cancer.net/node/24638>
- [22] <http://www.cancer.net/node/24406>
- [23] <http://www.cancer.net/node/24959>
- [24] <http://www.cancer.net/node/24895>
- [25] <http://www.cancer.net/node/24907>
- [26] <http://www.ccalliance.org/>
- [27] <http://www.facingourrisk.org>
- [28] <http://www.cancer.gov/>
- [29] <http://www.cancer.org/>
- [30] <http://www.cancercare.org/>
- [31] <http://www.nsgc.org/>
- [32] <http://www.cancer.gov/cancertopics/genetics/directory>