STK11 Mutations/Peutz-Jeghers Syndrome

Brought to you by the *National Society of Genetic Counselors, Cancer Special Interest Group*

What you should know about Peutz-Jeghers syndrome

Peutz-Jeghers syndrome (PJS) is a rare genetic condition that causes gastrointestinal (GI) polyps, increased cancer risks, and distinct freckling of the skin. These freckles are frequently seen around the mouth and on the lips, eyes, and fingers. The freckling is typically more pronounced in childhood, and begins to fade in puberty and adulthood. The polyps are a particular type called "Peutz-Jegher polyps." Polyps are most often found in the small intestine, but also in other areas of the gastrointestinal (GI) tract. Most individuals with PJS develop polyps by late childhood and may experience symptoms including rectal bleeding and anemia. PJS is caused by a mutation in the *STK11* gene.

Cancer Risks and Features Associated with Peutz-Jeghers syndrome

PJS is associated with an increased risk for a wide variety of cancer types (see below). Cancers in individuals with PJS often develop at relatively young ages. There is also an increased risk for benign and malignant tumors of the ovaries (sex cord tumors with annular tubules or SCTAT) and of the testicles (Sertoli cell tumors), which secrete estrogen and can lead to excess breast tissue development in males (gynecomastia).

Type of Cancer:	General Population Risk (SEER data)	PJS Risk by age 70
Breast	12%	32-54%
Colon	~5%	39%
Pancreas	1.5%	11-36%
Stomach	<1%	29%
Small Intestine	<1%	13%
Ovary	1-2%	18-21%
Lung	~6%	7-17%

Genetics and Inheritance of Peutz-Jeghers syndrome

Genes are our body's instructions. They provide our body with information about how to grow and develop. When there is a mutation in a gene, it can cause the gene to no longer function correctly. Each person has two copies of every gene. One copy is inherited from their mother and the other copy is inherited from their father.

PJS is due to a mutation in the *STK11* gene. Cancer risks associated with PJS are inherited in an autosomal dominant manner. This means that children, siblings and parents of individuals with a *STK11* mutation have a 50% (1 in 2) chance of having the mutation as well. Both males and females can inherit a *STK11* mutation and can pass it on to their children. Most people with PJS inherit the condition from one of their parents who has a mutation in the *STK11* gene. However, about 25% of the time, an individual with PJS is the first person in the family to have the condition.

When to Consider Evaluation for Peutz-Jeghers syndrome

Reviewing family history information with a genetic counselor can help determine the chance that a family has PJS or other genetic conditions that may predispose to cancer. Features in the family history that may suggest PJS include: two or more Peutz-Jeghers-type hamartomatous polyps of the GI tract; mucocutaneous hyperpigmentation of the mouth, lips, nose, eyes, genitalia, or fingers; and family history of PJS.

Managing Cancer Risks

The National Comprehensive Cancer Center Network (NCCN) provides regularly updated medical care guidelines for individuals with PJS. The most recent guidelines include:

Site	Screening Recommendations	
Breast	Mammogram and breast MRI annually Clinical breast exam every 6 months	Begin around age 25
Gastrointestinal	Small bowel visualization every 2-3 years Upper endoscopy every 2-3 years Colonoscopy every 2-3 years	Begin age 8-10 for small bowel Begin in late teens for endoscopy and colonoscopy
Pancreas	MR cholangiopancreatography and/or Endoscopic ultrasound	Begin age 30-35 or 10 years younger than the earliest pancreatic cancer diagnosis in the family
Ovary, Cervix and Uterus	Pelvic examination and Pap smear annually	Begin age 18-20
Testes	Annual testicular exam	Begin age 10

When possible, individuals with PJS should seek management with physicians or centers that are experienced with this condition. The NCCN Guidelines also provide information on how often to repeat these tests and further preventive interventions.

Genetic Counseling

In many families, the cancer history may be due to a combination of genetic and environmental factors. In addition, other genetic conditions (i.e. other gene mutations) may appear clinically similar to PJS. For this reason, a detailed review of the family history by a genetics professional is important before pursuing genetic testing. A genetic counselor can help determine which, if any, genetic tests may be helpful for a family and review the benefits, risks and limitations of genetic testing. Genetic testing is usually performed through a blood or saliva sample.

Genetic test results can be complicated and are most useful when interpreted by a genetics professional in the context of an individual's personal and family history. To locate a genetic counselor near you, please visit www.nsgc.org and click on the 'Find a Genetic Counselor' link.

Genetic Discrimination

The Genetic Information Nondiscrimination Act (GINA) was signed into federal law in 2008. GINA prohibits health insurers and most employers from discriminating against individuals based on genetic information (including the results of genetic tests and family history information). According to GINA, health insurance companies cannot consider genetic information to be a preexisting condition, nor can they use it to make decisions regarding coverage or rates. GINA also makes it illegal for most employers to use genetic information in making decisions about hiring, firing, promotion, or terms of employment. It is important to note that GINA does not offer protections for life insurance, disability insurance, or long-term care insurance. More information about GINA can be found by contacting a local genetic counselor or by visiting www.ginahelp.org.

Resources

- Hereditary Colon Cancer Foundation - www.hcctakesguts.org

References

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