PEUTZ-JEGHERS SYNDROME (PJS)

PATIENT INFORMATION

What is Peutz-Jeghers syndrome?
PJS is a condition that increases one’s risk to develop polyps (small growths) in the gastrointestinal tract and certain cancers (see chart below). Individuals who have PJS may have freckling on their lips, inside their mouth and/or on their hands. Often, these freckles fade with age. Someone may be diagnosed with PJS based on their personal medical history with or without a family history of certain polyps or cancers, or because of a genetic test result.

Gastrointestinal polyps occur along the inside wall of the stomach, small bowel, or large bowel. The most common type of polyp seen in individuals with PJS is a hamartomatous polyp. This is a benign (non-cancer causing) polyp that can grow very large and can cause a blockage in the bowel, bleeding or anemia. Another type of polyp that can be seen in PJS is an adenomatous polyp. This is considered a pre-cancerous polyp that, if not removed, can potentially turn into a cancer. Polyps often begin forming in childhood. Although most commonly seen in the gastrointestinal tract, polyps can grow elsewhere in the body.

People with PJS have an increased risk to develop cancer. Below are the lifetime risks of cancer in people who have PJS without screening or follow-up, as compared to the general population.

<table>
<thead>
<tr>
<th>Cancer</th>
<th>PJS Risk</th>
<th>General Population Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>45-50%</td>
<td>12%</td>
</tr>
<tr>
<td>Colorectal</td>
<td>39%</td>
<td>5-6%</td>
</tr>
<tr>
<td>Stomach</td>
<td>29%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>11-36%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>13%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Lung</td>
<td>15-17%</td>
<td>7%</td>
</tr>
<tr>
<td>Ovary-sex cord tumors (women)</td>
<td>18-21%</td>
<td>1-2%</td>
</tr>
<tr>
<td>Cervix (women)</td>
<td>10%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Uterus (women)</td>
<td>9%</td>
<td>2-3%</td>
</tr>
<tr>
<td>Testes (men)</td>
<td>Low, but increased</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>


PJS may affect different individuals in very different ways, even within a family. Some people with PJS may only have lip freckling while others may have multiple features of PJS.

What causes Peutz-Jeghers syndrome?
About 90% of people with PJS carry a change or alteration in the STK11 gene. There are some people who have PJS who carry a gene alteration that cannot be found by today’s technology.

If a person is born with a harmful alteration (a mutation) in one copy of the STK11 gene, then they are at risk for developing the cancers seen in PJS. Genes are the units of hereditary information that tell our bodies how to grow and develop. We all have two copies of almost every gene (one from
each parent). STK11 is important for controlling cell growth. If a person has a harmful alteration in one copy of the STK11 gene, the other one can work normally. However, if the second copy of the gene is damaged by chance, the cell no longer has a working copy of the gene to help protect it from uncontrolled cell growth. This uncontrolled growth over time can cause cancer.

How is Peutz-Jeghers syndrome inherited?
Peutz-Jeghers syndrome is inherited in an “autosomal dominant” manner. Autosomal means that both men and women can have PJS and pass it on to their children. Dominant means that it takes only one altered copy of a gene in order to cause PJS. An alteration in STK11 can be inherited from a parent like other family traits. About 50% (1 out of 2) of people with PJS do not have a family history of the condition. In some of these people, the STK11 mutation may not have been inherited from a parent, but instead occurred as a brand new change in that person.

If you have an altered STK11 gene, here are the chances that other relatives might have inherited it:
- Your Children – 50% risk for each child.
- Your Mother or Father – In about 50% of cases you will have inherited the altered STK11 gene from either your mother or your father.
- Your Brothers and Sisters – 50% risk if one of your parents had the STK11 alteration. If neither of your parents had the STK11 alteration, then your siblings have a very low risk of having the STK11 alteration.
- More distant relatives like your aunts, uncles, cousins, nieces, and nephews may have inherited this gene alteration depending on where they are in the family tree. Please talk to your health care team about risks for specific relatives.

How is Peutz-Jeghers syndrome managed?
There are a number of medical recommendations to help manage these increased risks that should be considered. Although we do not currently have any perfect strategies for reducing cancer risks, we do know that by close monitoring, some cancers can be detected in their earliest stages when they are most amenable to treatment. A screening test is one that is done in an effort to identify cancer (or pre-cancerous changes) early. Risk reduction strategies are used to try to prevent cancer.

Recommendations marked with an * require careful consideration as there is extremely limited data on how well they work and they can be invasive, time-consuming, costly, and can prompt further evaluations.

Screening:
For both men and women:
- annual physical exam
- colonoscopies every 2-3 years (beginning in late teens)
- upper endoscopies every 2-3 years (beginning in late teens)
- small bowel visualization with CT enterography (baseline at age 8-10), continue every 2-3 years
• magnetic resonance cholangiopancreatography (MRCP) and/or endoscopic ultrasound (EUS) every 1-2 years (beginning at age 25-30)

For women:
• mammogram and breast MRI each once a year (beginning at age 25)
• clinical breast exam every 6 months (beginning at age 25)
• pelvic exams with Pap smear once a year (beginning at age 18-20), transvaginal ultrasound consideration

For men:
• testicular exam and observation for feminizing changes once a year (beginning at age 10)

**Risk Reduction:**
• avoid smoking and speak with your doctor about smoking cessation if you do smoke

**Where can I find more information?**
Dana Farber Cancer Institute, Cancer Genetics & Prevention
www.dana-farber.org/cancergenetics

Cancer Institute NSW

PJS patient information page
http://www.peutz-jeghers.com/

**References:**
• NCCN Guidelines Version 02.2013 Peutz-Jeghers Syndrome