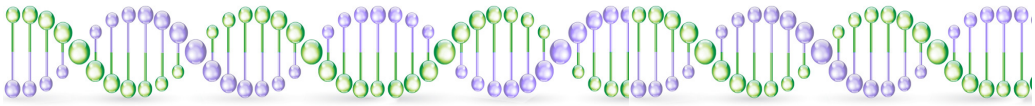
Information Sheet



Peutz Jeghers syndrome and the STK11

Peutz Jeghers syndrome (pronounced (pootz-JAY-gerz) is a hereditary cancer syndrome caused by germline mutations in the STK11 gene (pronounced: S T K eleven). It is a rare syndrome, affecting 1 in 50,000 to 1 to 200,000 people.

Peutz Jeghers syndrome is characterised by polyps called hamartoma which occur in the digestive tract, especially the small and large intestines, and freckling (hypermelanotic spots) around the mouth as well as inside the mouth.

Individuals with Peutz Jeghers syndrome are at increased risk of cancer, particularly of the large and small intestine, stomach, pancreas, breast and ovary. These cancers can occur at a young age. Tumours which secrete oestrogen, involving the ovary or testes, can also occur.

How is Peutz Jeghers syndrome diagnosed?

An individual has a 90% chance of carrying an STK11 germline mutation if they meet the clinical diagnosis of Peutz Jeghers syndrome:

- 2 or more PJS-related hamartomatous polyps.
- any number of PJS-related hamartomatous polyps AND mucocutaneous pigmentation.
- either a hamartomatous polyp or mucocutaneous pigmentation AND a family history of Peutz Jeghers syndrome.

Note: Peutz Jeghers syndrome related polyps have characteristic histopathology of smooth muscle bundles with arborising (branching tree) appearance.

Most people with an STK11 mutation and Peutz Jeghers syndrome have freckling (actually dark blue to dark brown macules referred to as mucocutaneous pigmentation) on the lips and inside the mouth. While freckles are very common, it is very unusual to have many on the lips or inside the mouth. These dark macules appear in childhood but may fade as a person gets older. They also occur around the nostrils and the finger nails. They don't become cancerous.

Not all individuals with dark spots on the lips and in the mouth have Peutz Jeghers syndrome. Laugier–Hunziker syndrome is an example of acquired pigmentation. It is not associated with polyps or increased cancer risk.

How is Peutz Jeghers syndrome managed?

Because the hamartomatous polyps can grow large and bleed and may cause bowel blockages (intussusception) in children, screening in Peutz Jeghers syndrome starts at age 8 and includes:

- Annual blood test to check for anaemia
- endoscopy and colonoscopy to screen the stomach, duodenum and colon
- video capsule endoscopy (VCE) or magnetic resonance endoscopy (MRE) to screen the small intestines
- If no polyps are found, the screening restarts at age 18, occurring every 3 years or as determined by polyp load.

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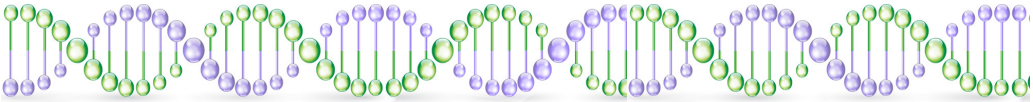
Peutz Jeghers syndrome and the STK11 gene



Management of cancer risk in Peutz Jeghers syndrome
Men and women with Peutz Jeghers syndrome are at increased risk for pancreatic cancer. This risk may be 10% over a lifetime. It is not yet known whether screening for pancreatic cancer is helpful (by finding the cancers early) or harmful (due to investigations and even surgery for things that turn out not to be cancer). Patients are encouraged to enrol in research studies.

For women with Peutz Jeghers syndrome
Women with Peutz Jeghers syndrome have a high risk of breast cancer (~45% lifetime risk). Breast screening, with annual breast MRIs, should start at age 30. Some women choose to have the breast tissue removed (bilateral mastectomies), reducing the risk to less than 1%.

There is an increased risk of cervical cancer. It is a rare but aggressive form that is NOT caused by the Human Papilloma Virus (HPV). Guidelines recommend review by a gynaecologist with an endocervical smear annually from 18 years of age.

Women and girls with Peutz Jeghers syndrome can develop a benign growth of the ovaries (a sex cord tumour with annular tubules or SCTAT). These growths can secrete oestrogen and can cause early puberty or menstrual problems.

For men with Peutz Jeghers syndrome
Men also develop oestrogen secreting tumours. These are large calcifying Sertoli cell tumours (LCST) of the testes. If untreated, the excess oestrogen can result in gynecomastia (breast tissue development), feminisation and if LCST occurs before puberty, advanced skeletal age and short stature. LCST usually present as a lump in the testicle.

Is Peutz Jeghers syndrome inherited?
Yes. Peutz Jeghers syndrome is a hereditary cancer syndrome caused by a mutation in the STK11 gene. There is a 50% chance of a person who carries a germline STK11 mutation, whether male or female, passing the mutation to their son or daughter. If a mutation is identified, then predictive testing is available for blood relatives.

What are de novo STK11 mutations?
Many people with Peutz Jeghers syndrome do not have parents or siblings with hamartomatous polyps or mucocutaneous pigmentation. This is because 30% to 50% of the time, they are the first person in their family to carry an STK11 mutation. This is called a “de novo” mutation, meaning "from new". That is, the mutation occurred either in the making of that particular sperm or egg or the first few cell divisions after fertilisation. In this situation, the parents are not affected but the mutation can be passed on to the next generation.

Does this sound like you or your family?
Do you have mucocutaneous pigmentation or do you meet the clinical criteria for Peutz Jeghers syndrome? Has an STK11 mutation been detected in you or a blood relative? Genetic testing is available
Make an appointment with Dr Hilda High at Sydney Cancer Genetics. It is a confidential opportunity to discuss your personal and family history of cancer and genetic testing can be organised, if needed.

More information is available on our website, including links to the following:

- The Peutz-Jeghers Syndrome Online Support Group is a support group for individuals and families affected by Peutz-Jeghers syndrome. It is based in the USA but has members worldwide.
- The Cancer Genetics section of the Cancer Institute's eviQ website provides up-to-date Australian-based management guidelines

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