BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority
Hereditary Cancer Program

Peutz-Jeghers Syndrome

Peutz-Jeghers syndrome (PJS) is an autosomal dominant condition characterized by hamartomatous gastrointestinal polyps, mucocutaneous pigmentation, and cancer predisposition. PJS polyps tend to be large and pedunculated, resulting in obstruction and bleeding. The characteristic mucocutaneous pigmentation/freckling (lips, buccal mucosa, vulva, fingers, toes) tends to fade during adulthood.

PJS is associated with increased risk for colorectal, gastric, pancreatic, breast, and ovarian cancers. Females are also at risk for sex cord tumors with annular tubules (a benign ovarian neoplasm) and adenoma malignum of the cervix (a rare aggressive cancer). Males may develop large calcifying Sertoli cell tumors of the testes, most often in childhood.

A clinical PJS diagnosis may be confirmed by the identification of a germline *STK11* gene mutation.

Referral Criteria

*Note: **close relatives** include children, brothers, sisters, parents, aunts, uncles, grandchildren & grandparents **on the same side of the family**. History of cancer in cousins and more distant relatives from the same side of the family may also be relevant.*

- family member with a confirmed *STK11* gene mutation – refer for carrier testing
- person with 2 or more histologically confirmed PJS-type hamartomatous polyps
- person with at least 1 PJS-type polyp and characteristic mucocutaneous pigmentation
- person with at least 1 PJS-type polyp and at least 1 close relative with PJS
- person with characteristic mucocutaneous pigmentation and at least 1 close relative with PJS
- person whose family history includes close relatives with features listed above

Referral of children is appropriate for this syndrome because it may inform their medical management.

Estimated Lifetime Cancer Risks (to age 70) for *STK11* mutation carriers

All cancers:	**76-85%** (compared with 18 % in the general population) 2% by age 20, 5% by 30, 17-20% by 40, 31-36% by 50, 58-60% by 60
Female breast cancer:	45-50% (8% by age 40, 13% by 50, 31% by 60)
Colorectal cancer:	39% (3% by 40, 5% by age 50, 15% by 60)
Stomach:	29% (to age 65)
Small bowel:	13% (to age 65)
Pancreas:	11-26% (2-3% by age 40, 4-5% by 50, 7-11% by 60)
Lung:	15-17%
Ovary:	18% (typically benign sex cord/Sertoli cell tumours, most common in the 40s-50s; can occur from infancy)
Cervix:	10%
Uterus	9%

Cancer Risk Management Recommendations for *STK11* mutation carriers

Note: There is limited data available regarding the efficacy of various screening modalities in PJS. The recommendations provided below are general in nature. Individualized recommendations based on personal and/or family medical histories may be provided through Hereditary Cancer Program assessment and/or by other specialists involved in a person's current care.

Gastrointestinal - surveillance reduces polyp burden and likelihood of complications such as intussusception. Begin the following surveillance at age 8 (or earlier if symptomatic):

- annual hemoglobin
- baseline video capsule endoscopy or magnetic resonance endoscopy, repeated every 3 years
- baseline gastroduodenoscopy and colonoscopy
    - If no polyps, recommence at 18 years and at least every 3 years
    - If polyps found, screening should occur at least every 3 years (or more frequently based on polyp load)
- Individuals with PJS are advised to present to a hospital emergency department with any symptoms suggestive of intussusception/bowel obstruction (e.g. acute onset of vomiting, severe abdominal pain with bloating)

Breast Cancer (women):

- women should be breast aware
- annual breast MRI from age 25-65
- annual mammograms beginning at age 30 (continue as long as clinically indicated)
- clinical examination of the breast and regional nodes by an experienced health professional (CBE) med every 12 months, in conjunction with appropriate breast imaging
- risk-reducing bilateral mastectomy may be considered by some women with *STK11* mutations, depending on family history. This decision requires discussion about the benefits and risks of surgery in the context of a woman's general health, life expectancy and personal health beliefs.

Pancreatic cancer

- screening MRI MRCP or endoscopic ultrasound and serum CA 19-9 every 1-2 years starting in the early 30s

Gynecological cancer

- pelvic exam and Pap smear annually starting at age 18

Testicular tumours

- annual examination and observation for feminizing changes from age 10

Lung cancer

- avoid cigarette smoking and/or encourage smoking cessation

Additional Information

A comprehensive review of this syndrome is available at Gene Reviews
https://www.ncbi.nlm.nih.gov/books/NBK1266/

References available on request.
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