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# Peutz-Jeghers syndrome: Clinical manifestations, diagnosis, and management

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## INTRODUCTION

Peutz-Jeghers syndrome (PJS) is an autosomal dominant syndrome characterized by multiple hamartomatous polyps in the gastrointestinal tract, mucocutaneous pigmentation, and an increased risk of gastrointestinal and nongastrointestinal cancer [1-3].

This topic will review the genetic basis, clinical manifestations, and diagnosis of PJS. The management of PJS and other familial hamartomatous polyposis syndromes of the gastrointestinal tract (eg, juvenile polyposis, Cowden syndrome, and Bannayan-Riley Ruvalcaba syndrome) are discussed in detail, separately [4]. (See "Overview of colon polyps" and "Juvenile polyposis syndrome".)

## EPIDEMIOLOGY AND GENETICS

Peutz-Jeghers syndrome (PJS) is rare with an estimated prevalence of 1:8000 to 1:200,000 births [5]. Males and females are equally affected.

PJS is an autosomal dominant disorder that is most often due to germline mutations in the *STK11* (*LKB1)* gene encoding a serine threonine kinase mapped to chromosome 19p13.3 [6-8]. Germline mutations in *STK11,* a designated tumor suppressor gene in combination with an acquired genetic defect of the second *STK11* allele in somatic cells, are responsible for the

clinical manifestations of PJS [7-10]. PJS has a high penetrance of over 90 percent by the age of 30 years, but 10 to 20 percent of individuals with PJS have no family history and are presumed to have PJS due to *de novo* mutations [11].

*STK11* is a tumor suppressor that regulates the activity of AMP-activated protein kinase (AMPK) family members to control multiple cellular processes including cell polarity, metabolism, and apoptosis [12]. In addition, deletion of *STK11* specifically in T-cells has been shown to promote the development of gastrointestinal polyps in an animal model, indicating a provocative role for the immune system in tumor formation [13].

Mutations in *STK11* are detected in only 50 to 80 percent of families with PJS, suggesting that there is a second PJS gene locus [9,14-17].

## CLINICAL MANIFESTATIONS

The two characteristic manifestations of Peutz-Jeghers syndrome (PJS) are pigmented mucocutaneous macules and multiple hamartomatous gastrointestinal polyps. Individuals with PJS are also at an increased risk for both gastrointestinal and extra-intestinal cancers.

**Mucocutaneous pigmentation** — Mucocutaneous pigmented macules (melanin spots) are present in more than 95 percent of individuals with PJS and are caused by pigment-laden macrophages in the dermis. They are typically flat, blue-gray to brown spots 1 to 5 mm in size. These pigmented macules most commonly occur on the lips and perioral region (94 percent), palms of the hands (74 percent), buccal mucosa (66 percent), and soles of the feet (62 percent) ( picture 1) [18]. They may also be seen on the nose, perianal area, and genitals, and rarely in the intestines. Mucocutaneous pigmentation usually occurs during the first one to two years of life, increases in size and number over the ensuing years, and finally fades after puberty with the exception of those on the buccal mucosa. Malignant transformation is extremely rare.

Mucocutaneous pigmented macules in individuals with PJS may be confused for ephelides (freckles). However, ephelides are typically sparse near the nostrils and mouth, are absent at birth, and never appear on the buccal mucosa. The mucocutaneous pigmented macules, although sensitive for PJS, are not specific and may be associated with other syndromes. (See 'Differential diagnosis' below.)

**Hamartomatous polyps** — Gastrointestinal hamartomatous polyps are present in most patients with PJS. Although polyps most commonly occur in the small bowel (60 to 90 percent) and more specifically in the jejunum, they can be found throughout the gastrointestinal tract including the stomach (15 to 30 percent) and colon (50 to 64 percent) [18].

Gastrointestinal polyps develop in the first decade of life and most patients become symptomatic between the ages of 10 and 30. Hamartomatous polyps may also occur outside the gastrointestinal tract, including the renal pelvis, urinary bladder, lungs, and nasopharynx.

Although 50 percent of patients are asymptomatic at the time of diagnosis, individuals with PJS can present with obstruction caused by intussusception or occlusion of the gastrointestinal lumen by the polyp, abdominal pain caused by infarction, anemia from acute or chronic bleeding, or extrusion of the polyp through the rectum. Up to 69 percent of patients experience an intussusception during their lifetime, most often in the small intestine [18-22].

On gastrointestinal endoscopy, the Peutz-Jeghers (PJ) polyps have no major distinguishing features, and may be sessile, pedunculated, or lobulated. The number of polyps ranges from 1 to more than 20 per segment of bowel, although some patients have solitary lesions. The size of the polyps ranges from 0.1 to more than 5 cm in diameter ( picture 2). On histology, PJ polyps are hamartomas that characteristically contain a proliferation of smooth muscle extending into the lamina propria in an arborization-like fashion; the overlying epithelium is normal ( picture 3A-B) [23]. Epithelial misplacement involving all the layers of the bowel has been reported in approximately 10 percent of small intestinal polyps in PJS. Epithelial misplacement, possibly due to mechanical forces, may extend into the serosa and be misdiagnosed as a well-differentiated adenocarcinoma.

**Cancer risk** — PJS is associated with an increased risk of gastrointestinal and extra-intestinal malignancies [24-27]. In a systematic review of 20 observational studies which included 1644 patients with PJS, the reported lifetime risk for any cancer varied between 37 and 93 percent [24]. The average age of developing a malignancy was 42 years. The most common sites for malignancy were colorectal, followed by breast, stomach, small bowel, and pancreas.

In a subsequent report of 133 patients with PJS, the cumulative cancer risk at age 40 and 70 years was 20 and 76 percent, respectively, with a cumulative risk of gastrointestinal cancer of 12 and 51 percent, respectively [26]. The risk of cancer was higher in women as compared with men (hazard ratio 4.8, 95% CI 2.8-8.0). During 5004 person-years of follow-up there were 42 deaths, occurring at a mean age of 45 years. Two-thirds of the deaths were cancer-related. An Italian collaborative study of 119 patients with PJS reported similar rates of cancer [27].

**Gastrointestinal cancers** — Individuals with PJS have an estimated lifetime risk of gastrointestinal cancer of 38 to 66 percent [24]. The lifetime cancer risk by organ site is as follows:

- Colorectal – 39 percent
- Stomach – 29 percent

- Small bowel – 13 percent
- Pancreas – 11 to 36 percent

Other gastrointestinal tumors that have been associated with PJS include cancers of the biliary tree, gallbladder, and esophagus [26,28,29].

The distribution of gastrointestinal cancers in PJS is similar to that of the hamartomatous polyps and carcinoma arising in hamartomas has been clearly documented [30-33]. The reason for the increased risk of gastrointestinal cancer is uncertain, but does not appear to be due to increased oncogene expression, known to be involved in the adenoma-carcinoma sequence in colorectal cancer [34]. (See 'Epidemiology and genetics' above and "Molecular genetics of colorectal cancer".)

**Extra-intestinal cancers** — The risk of extra-intestinal cancers is also increased in individuals with PJS [35,36]. In a meta-analysis of six studies that included 210 individuals with PJS, extracolonic cancers accounted for 55 of the 66 malignancies (83 percent) between the ages of 15 and 64 years [29]. As compared with population-based controls, the risk was increased for cancers of the lung, breast, uterus, and ovary.

- Women with PJS have an increased lifetime risk for cancers of the breast (32 to 54 percent), ovary (21 percent), and cervix (10 percent). Cervical tumors include cervical adenoma malignum, a highly differentiated mucinous adenocarcinoma with a highly aggressive behavior [37]. In addition, small, asymptomatic, benign ovarian tumors known as "sex-cord" tumors with annular tubules (SCTAT tumors) occur commonly in women with PJS [38,39]. These tumors are often associated with signs of hyperestrogenism, which can lead to sexual precocity [38,39]. (See "Sex cord-stromal tumors of the ovary: Epidemiology, clinical features, and diagnosis in adults".)

- Men with PJS have an increased lifetime risk of Sertoli cell testicular tumors (9 percent) [24,36,40]. While these tumors are often hormonally active, some present with gynecomastia, rapid growth, and advanced bone age with markedly elevated levels of estradiol [41]. (See "Anatomy and pathology of testicular tumors", section on 'Sertoli cell tumors'.)

## DIAGNOSIS

A clinical diagnosis of PJS can be made by the presence of any of the following [42]:

- Two or more Peutz-Jeghers-type hamartomatous polyps of the gastrointestinal tract

- Characteristic mucocutaneous hyperpigmentation of the mouth, lips, nose, eyes, genitalia, or fingers in a person with a family history of PJS
- Any number of Peutz-Jeghers polyps in an individual with a family history of PJS in a first-degree relative

- Any number of Peutz-Jeghers polyps in a person with the characteristic mucocutaneous pigmentation of PJS

Individuals who meet clinical criteria for PJS should undergo genetic testing for a germline mutation in the *STK11* gene. Genetic testing in an individual who meets clinical criteria for PJS serves to confirm the diagnosis of PJS and counsel at-risk family members. However, not all mutations associated with PJS have been identified [9]. Thus, if no pathogenic *STK11* mutation is found in an individual who meets clinical criteria for PJS and there is no known mutation of PJS in the family, this does not exclude the diagnosis of PJS. Such individuals and their at-risk relatives still require frequent endoscopic surveillance for removal of polyps throughout the gastrointestinal tract and screening for extraintestinal cancers. (See 'Epidemiology and genetics' above and "Juvenile polyposis syndrome", section on 'Screening and management'.)

If genetic testing is performed and a mutation is found in an affected individual, then genetic testing of at-risk relatives will provide true positive or negative test results. At-risk members who receive true negative test results have a risk of cancer similar to that of the general population. At-risk relatives who test positive should follow the surveillance guidelines for individuals with PJS. A detailed list of laboratories performing genetic testing can be obtained through the web site www.genetest.org.

## DIFFERENTIAL DIAGNOSIS

Peutz-Jeghers syndrome (PJS) can be differentiated from other disorders that may present with pigmented mucocutaneous macules or multiple hamartomatous gastrointestinal polyps based on the clinical presentation and/or genetic testing.

- Hamartomatous polyps of the small intestine can be associated with Cowden syndrome, Bannayan-Riley Ruvalcaba syndrome (BRRS), and juvenile polyposis syndrome (JPS). BRRS is characterized by macrocephaly, lipomas, vascular abnormalities, and developmental delay. Cowden syndrome has characteristic skin and oral findings including trichilemmomas, acral keratoses, and facial papules/oral papillomas. Pigmented spots in BRRS and Cowden syndrome characteristically occur on the glans penis in males and not on the lips as seen in PJS. Unlike PJS, which is associated with germline mutations in the

*STK11* gene, Cowden syndrome and BRRS are associated with germline mutations in *PTEN1*.

JPS is characterized by multiple gastrointestinal juvenile polyps (hamartomas) but is not associated with mucocutaneous pigmentation, which is associated with PJS. JPS is associated with germline mutations in *SMAD4, BMPR1A*, and *ENG* genes and not *STK11* as seen in patients with PJS. (See "PTEN hamartoma tumor syndromes, including Cowden syndrome", section on 'Cowden syndrome' and "PTEN hamartoma tumor syndromes, including Cowden syndrome", section on 'Bannayan-Riley-Ruvalcaba syndrome' and "Juvenile polyposis syndrome".)

- Mucocutaneous pigmentation may be associated with Laugier-Hunziker syndrome (LHS). LHS is an acquired, sporadic, benign disorder that is characterized by intraoral hyperpigmentation on the lips, hard and soft palate, and buccal mucosa. Approximately 60 percent of patients with LHS also have longitudinal hyperpigmented bands on the fingernails and toenails without associated nail dystrophy [43]. Unlike pigmentation in PJS, which occurs in the first few years of life, LHS lesions are progressively acquired in young or middle-age adults. In addition, LHS is not associated with hamartomatous gastrointestinal polyps or a pathogenic mutation in the *STK11* gene. (See "Congenital and inherited hyperpigmentation disorders", section on 'Peutz-Jeghers syndrome'.)

## MANAGEMENT

Guidelines for cancer screening in individuals with Peutz-Jeghers syndrome (PJS) have been proposed by several groups and are largely based on expert opinion and limited observational data [24,36,42,44]. Our recommendations are largely consistent with the guidelines issued by the US Multi-Society Task Force on Colorectal Cancer and the National Comprehensive Cancer Network (NCCN) [44-46].

**Routine management** — Individuals with PJS should undergo an annual physical examination with a complete blood count to detect iron deficiency anemia due to occult bleeding from gastrointestinal tract polyps or cancer. (See 'Hamartomatous polyps' above and "Causes and diagnosis of iron deficiency and iron deficiency anemia in adults", section on 'Causes and risk factors for iron deficiency'.)

**Cancer screening** — Individuals with PJS are at an increased risk of gastrointestinal and extraintestinal cancer. The lifetime risk of cancer ranges between 37 and 93 percent, with an average age of 42 years at cancer diagnosis [24]. The most common sites of gastrointestinal

tract malignancy are the colon and pancreas, and the most common site of extraintestinal tract cancer is the breast. (See 'Clinical manifestations' above.)

**Gastrointestinal cancer** — Due to the increased risk for gastric, small bowel, and colorectal polyps and cancer in individuals with PJS, baseline endoscopic screening of the gastrointestinal tract should include upper gastrointestinal endoscopy (esophagogastroduodenoscopy), video capsule endoscopy (VCE), and colonoscopy, beginning between the ages of eight and ten years [46]. The subsequent screening interval should be based on the findings at baseline examination:

- If polyps are detected on baseline screening, an upper endoscopy, VCE, and colonoscopy should be repeated every two to three years.
- If no polyps are detected on baseline screening, an upper endoscopy, VCE, and colonoscopy should be repeated at age 18 years, or sooner if symptoms arise, and then every two to three years.

Magnetic resonance enterography (MRE) is an alternative imaging modality for individuals with PJS in whom capsule endoscopy cannot be performed [47]. While neither methodology is associated with ionizing radiation, magnetic resonance imaging (MRI) may be more accurate in identifying and localizing clinically relevant PJS polyps [48]. The use of barium follow-through and computed tomography enterography is limited by radiation exposure and should be avoided in children. (See "Wireless video capsule endoscopy", section on 'Contraindications' and "Radiation-related risks of imaging", section on 'Children and adolescents'.)

**Management of gastrointestinal tract polyps** — Endoscopic polypectomy should be performed for polyps >0.5 cm that are detected during upper endoscopy and colonoscopy [46]. All other small bowel polyps that are symptomatic or >1 cm in size should be resected in order to reduce the risk of polyp-related complications (eg, anemia, bleeding, obstruction, malignancy, and need for urgent surgery) [42,44]. Advances in small bowel endoscopy have improved the ability to treat small bowel polyps without surgery. Successful small bowel polypectomy using balloon-assisted enteroscopy has been described with both single and double balloon enteroscopies [48,49]. Endoscopists should be aware of possible challenges in performing double balloon enteroscopy in patients who have had previous abdominal surgery and may have peritoneal adhesions and altered anatomy. Patients with PJS may also be at increased risk for perforation with polypectomy due to serosal invagination within the polyp stalk [49].

Indications for surgery include the inability to achieve endoscopic polyp control either due to polyp size or number and the presence of neoplasia. Surgery may also be required in patients

with small bowel obstruction or intussusception. Patients with PJS undergoing laparotomy should undergo intraoperative enteroscopy to identify and resect small bowel polyps [19]. (See "Intussusception in children", section on 'Treatment' and "Evaluation of suspected small bowel bleeding (formerly obscure gastrointestinal bleeding)", section on 'Intraoperative enteroscopy'.)

**Chemoprevention** — Chemopreventive approaches to decrease polyp burden in PJS have been studied, but there are insufficient data to recommend their use [50]. Polyps in PJS overexpress cyclooxygenase-2 (COX-2), suggesting that COX-2 inhibitors may be useful in reducing polyp burden [51]. In addition, inhibition of mammalian target of rapamycin (MTOR) in a PJS mouse model has also been demonstrated to decrease polyp burden [52].

### Genital tract cancers

**Testicular tumors** — Patients with PJS are at increased risk for Sertoli cell tumors [53,54]. Annual examinations of the testicles should be performed starting around age 10 years. If abnormalities are detected on testicular examination or if patients have signs of feminization (eg, gynecomastia), additional evaluation (eg, testicular ultrasound) is warranted [42]. (See 'Extra-intestinal cancers' above and "The pediatric physical examination: The perineum", section on 'Male genitourinary system'.)

**Cervical cancer** — Women with PJS are at increased risk for adenoma malignum, a well-differentiated adenocarcinoma of the uterine cervix. We therefore advise women with PJS to undergo annual screening for cervical cancer (including Pap smear) starting at age 18 to 20 years [44,45]. (See 'Extra-intestinal cancers' above and "Screening for cervical cancer in resource-rich settings".)

**Ovarian and endometrial cancer** — Annual physical examination for observation of precocious puberty should be performed starting at age eight years. We screen women with PJS for endometrial and ovarian cancer with an annual pelvic exam and pap smear starting at age 18 to 20 years [24,42,44]. However, screening for endometrial and ovarian cancer in women with PJS is controversial, and guidelines differ in their recommendations. The NCCN recommends screening with pelvic exam annually between the ages of 18 and 20 years, but other societies also include pelvic ultrasound [44,45]. Other expert guidelines do not recommend screening for endometrial cancer, given that most cases of sporadic endometrial cancer are detected at an early stage, the low risk of endometrial cancer in PJS, and the lack of evidence to support screening [42]. (See 'Extra-intestinal cancers' above.)

**Breast cancer** — The risk for breast cancer in PJS patients approaches that of *BRCA* mutation carriers [42]. We therefore suggest clinical breast examinations for women with PJS every six months and annual breast MRI and mammography starting at age 30 years [44,45]. (See

"Screening for breast cancer: Evidence for effectiveness and harms", section on 'Effectiveness of imaging studies in breast cancer screening' and 'Extra-intestinal cancers' above.)

**Pancreatic cancer** — Screening for pancreatic cancer in individuals with PJS should be performed in experienced centers, preferably within an Institutional Review Board (IRB)-approved clinical research study [42,55]. Screening for pancreatic cancer should be performed with MRI/magnetic resonance cholangiopancreatography or endoscopic ultrasound of the pancreas every one to two years, beginning at age 35 years [44-46,56,57]. (See 'Gastrointestinal cancers' above and "Familial risk factors for pancreatic cancer and screening of high-risk patients", section on 'Pancreatic cancer screening'.)

**Other malignancies** — Individuals with PJS are also at an increased risk for thyroid and lung cancer. However, evidence to support routine screening for these cancers in the absence of other risk factors is lacking. Patients should seek medical attention for evaluation of new symptoms and should be strongly counselled to quit smoking [36,42,44]. (See "Radiation-induced thyroid disease" and "Screening for lung cancer".)

**Other issues**

**Cutaneous hyperpigmentation** — Approximately 95 percent of PJS patients develop mucocutaneous pigmented macules. While most cutaneous lesions fade with age, lesions that are disfiguring or associated with psychological morbidity may require treatment [42,58-61]. The management of cutaneous hyperpigmentation is discussed in detail, separately. (See "Acquired hyperpigmentation disorders", section on 'General principles of treatment' and "Congenital and inherited hyperpigmentation disorders", section on 'Peutz-Jeghers syndrome'.)

**Genetic counseling** — PJS is an autosomal dominant disorder, and a child of a PJS parent has a 50 percent chance of inheriting the disease. Individuals with an *STK11* mutation should be offered the option of a pre-implantation genetic diagnosis during preconception counseling [62-64]. However, patients should also be made aware of the limitations and the risks for misdiagnosis. (See "Preimplantation genetic testing", section on 'Genetic analysis'.)

First-degree relatives of patients with PJS should be screened annually, beginning at birth, for clinical features of PJS. Screening consists of a history and a physical examination that includes evaluation for mucocutaneous pigmentation and signs of precocious puberty. In addition, male patients should be examined for signs of feminization (eg, gynecomastia) and for testicular tumors with testicular palpation. Predictive genetic testing should be offered to at-risk individuals in whom the diagnosis is not already clinically apparent by eight years of age, provided a pathogenic *STK11* mutation has been identified in an affected family member. The results of genetic testing can then guide future screening recommendations. (See "Definition,

etiology, and evaluation of precocious puberty", section on 'Definition' and "Genetic testing", section on 'Testing children' and "The pediatric physical examination: The perineum", section on 'Male genitourinary system'.)

## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Hereditary colorectal cancer syndromes".)

## SUMMARY AND RECOMMENDATIONS

- **Epidemiology and genetics** – Peutz-Jeghers syndrome (PJS) is an autosomal dominant syndrome characterized by multiple hamartomatous polyps in the gastrointestinal tract, mucocutaneous pigmentation, and an increased risk of gastrointestinal and extra-intestinal cancer.

  PJS is associated with germline mutations in t*he STK11 (LKB1)* g*e*ne encoding a serine threonine kinase mapped to chromosome 19p13.3. PJS is rare, with prevalence estimates ranging between 1:8000 and 1:200,000 births. (See 'Epidemiology and genetics' above.)

- **Clinical manifestations** – There are two main clinical manifestations of PJS: pigmented mucocutaneous macules and multiple gastrointestinal polyps. (See 'Clinical manifestations' above.)

  - The characteristic mucocutaneous pigmentations (melanin spots) of PJS are present in more than 95 percent of patients, occurring most commonly on the lips and perioral region, palms of the hands, buccal mucosa, and soles of the feet.

  - Gastrointestinal hamartomatous polyps are present in most patients with PJS and can occur anywhere in the gastrointestinal tract. Polyps develop in the first decade of life and most patients become symptomatic between the age of 10 and 30 years. The number of polyps ranges from 1 to more than 20 per segment of bowel.

- **Cancer risk** – PJS is associated with an increased risk of gastrointestinal and extra-intestinal cancers. The lifetime risk of cancer ranges between 37 and 93 percent, with an average age of 42 years at cancer diagnosis. The most common sites of gastrointestinal tract malignancy are the colon and pancreas, and the most common site of extraintestinal

tract cancer is the breast. Women are also at increased risk for cervical tumors including cervical adenoma malignum and benign ovarian tumors known as "sex-cord" tumors with annular tubules (SCTAT tumors). Men with PJS have an increased lifetime risk of Sertoli cell testicular tumors. (See 'Cancer risk' above.)

- **Diagnosis** – A clinical diagnosis of PJS can be made by the presence of any of the following:
  - Two or more Peutz-Jeghers-type hamartomatous polyps of the gastrointestinal tract
  - Characteristic mucocutaneous hyperpigmentation of the mouth, lips, nose, eyes, genitalia, or fingers in a person with a family history of PJS
  - Any number of Peutz-Jeghers polyps in an individual with a family history of PJS in a first-degree relative
- Any number of Peutz-Jeghers polyps in a person with the characteristic mucocutaneous pigmentation of PJS

  Individuals who meet clinical criteria for PJS should undergo genetic testing for a mutation in t*he STK11* gene. Genetic testing in an individual who meets clinical criteria for PJS serves to confirm the diagnosis of PJS. However, the absence of a pathogen*ic STK11* mutation in an individual who meets clinical criteria for PJS does not exclude the diagnosis of PJS. (See 'Diagnosis' above.)

  PJS can be differentiated from other disorders with pigmented mucocutaneous macules or multiple hamartomatous gastrointestinal polyps based on the clinical manifestations and/or genetic testing. (See 'Differential diagnosis' above.)

- **Management** – Our approach to cancer screening in individuals with PJS is as follows (see 'Routine management' above and 'Cancer screening' above):
  - Annual physical examination with a complete blood count to detect iron deficiency anemia due to occult bleeding from gastrointestinal tract polyps or cancer.
  - Baseline screening of the stomach and colon with upper endoscopy and colonoscopy every two to three years beginning in the late teens.
  - Baseline endoscopic screening of the small intestine with video capsule endoscopy (VCE) between age eight and ten years. The interval for follow-up is based on the findings. However, in the absence of polyps, follow-up screening is recommended at 18 years and then repeated every two to three years. Computed tomography enterography (CTE) or magnetic resonance enterography (MRE) are alternative imaging modalities for individuals with PJS in whom capsule endoscopy cannot be performed.

- Annual examination of the testicles from age 10 years. If abnormalities are detected on testicular examination or if patients have signs of feminization (eg, gynecomastia), a testicular ultrasound should be obtained.
- Annual pelvic examination and Pap smear starting at age 18 to 20 years in women.
- Monthly breast self-examinations and clinical breast exams every six months for women and annual breast magnetic resonance imaging (MRI) and mammography starting at age 30 years.
- MRI/magnetic resonance cholangiopancreatography or endoscopic ultrasound of the pancreas every one to two years, beginning at age 35 years, to screen for pancreatic cancer. Screening for pancreatic cancer should be performed at centers of expertise in the setting of a research protocol.

- Individuals with an *STK11* mutation should be offered the option of a pre-implantation genetic diagnosis during preconception counseling. First-degree relatives of patients with PJS should be screened beginning at birth for clinical features of PJS. Screening consists of an annual history, a physical examination that includes evaluation for mucocutaneous pigmentation, and signs of precocious puberty. In addition, male patients should be examined for signs of feminization (eg, gynecomastia) and for testicular tumors with testicular palpation. Predictive genetic testing should be offered to at-risk individuals in whom the diagnosis is not already clinically apparent by age eight years, provided a pathogenic *STK11* mutation has been identified in an affected family member. (See 'Genetic counseling' above.)

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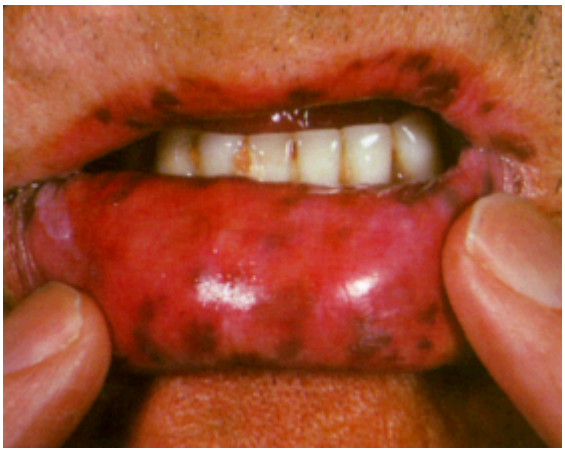
Topic 2533 Version 35.0

## GRAPHICS

### Oral lesions in Peutz-Jeghers syndrome



Photograph shows the characteristic circumoral pigmentation in a patient with the Peutz-Jeghers syndrome. The pigmentation may not be obvious as in this patient, and it should always be sought carefully in young patients presenting with unexplained gastrointestinal bleeding, particularly if there is a family history of such bleeding.

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*Reprinted with permission from Pounder RE, Allison MC, Dhillon AP. A Colour Atlas of the Digestive System, Wolfe, London 1989 p. 118.*

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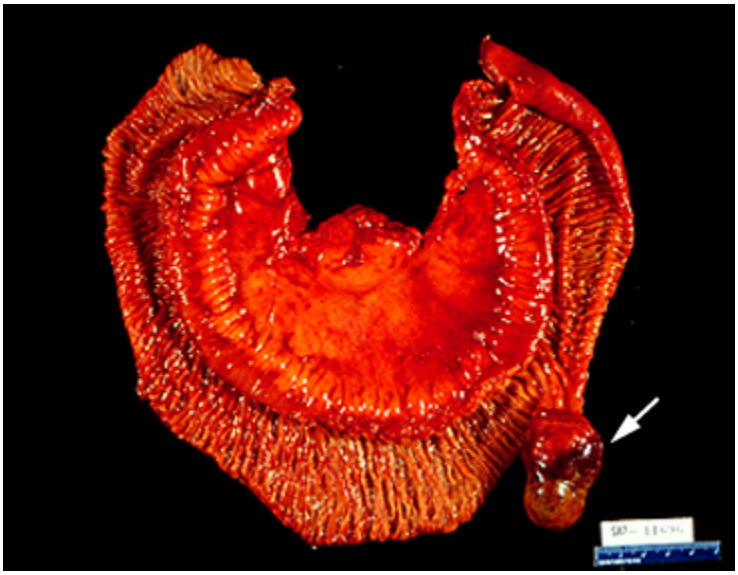
Graphic 80815 Version 4.0

## Peutz-Jeghers polyp



Gross picture of an intestinal polyp (arrow) removed from a patient with the Peutz-Jeghers syndrome.

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*Courtesy of Robert Odze, MD.*

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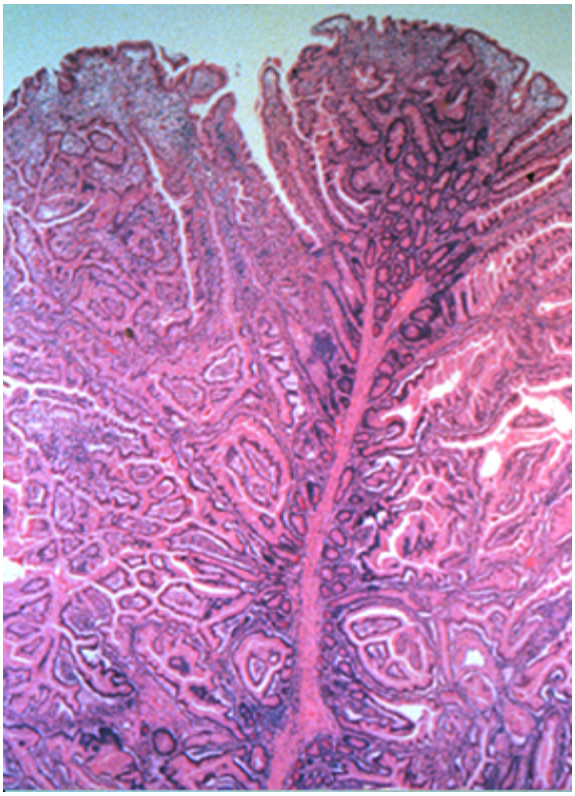
Graphic 67988 Version 3.0

## Duodenal Peutz-Jeghers polyp

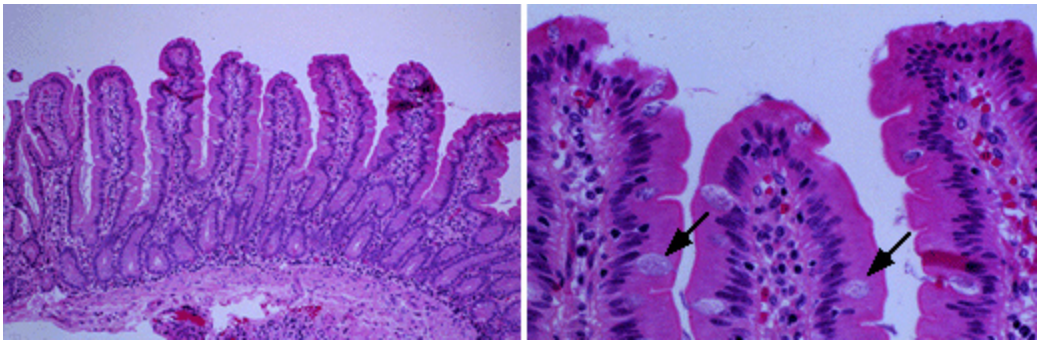


Low power view of a duodenal Peutz-Jeghers polyp shows a tree-like proliferation of smooth muscle lined by normal small intestinal epithelium; the overlying epithelium is normal.

*Courtesy of Robert Odze, MD.*

Graphic 81889 Version 1.0

## Normal small intestine



Low-power (left) and high-power (right) views of the normal villous architecture of the small intestine. The high-power view shows the enterocytes and interspersed goblet cells (arrows).

*Courtesy of Robert Odze, MD.*

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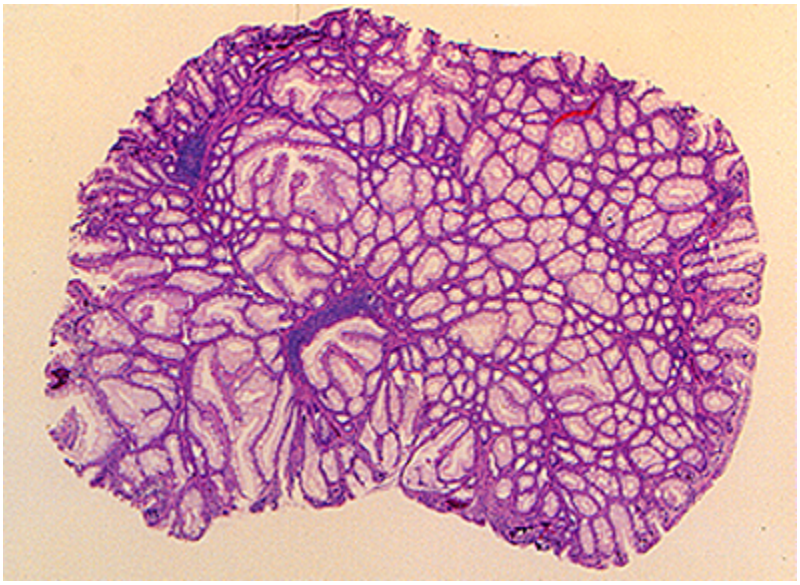
Graphic 63225 Version 2.0

## Colonic Peutz-Jeghers polyp

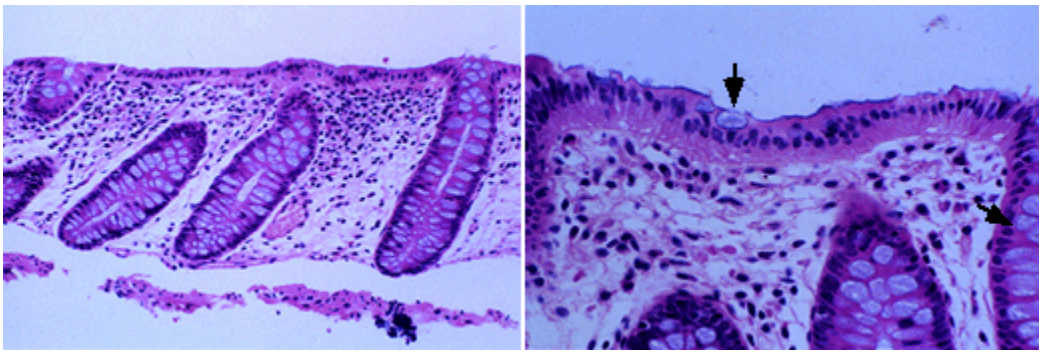


Low power view of a colonic Peutz-Jeghers polyp shows a tree-like proliferation of smooth muscle lined by normal colonic cell types.

*Courtesy of Robert Odze, MD.*

Graphic 69268 Version 1.0

## Normal colon



Low (left) and high (right) power views of a biopsy of a normal colon. Low power reveals straight crypts and mild lamina propria mononuclear cell infiltration. High power shows the surface enterocytes with interspersed goblet cells (arrows).

*Courtesy of Robert Odze, MD*

Graphic 81083 Version 6.0

## Contributor Disclosures

**Daniel C Chung, MD** Grant/Research/Clinical Trial Support: Janssen [Clinical trial support - FAP syndrome]. All of the relevant financial relationships listed have been mitigated. **J Thomas Lamont, MD** Equity Ownership/Stock Options: Allurion [Weight loss]. Consultant/Advisory Boards: Teledoc [Gastrointestinal diseases]. All of the relevant financial relationships listed have been mitigated. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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