AGA Diagnosis and Management of Cancer Risk in the Gastrointestinal Hamartomatous Polyposis Syndromes: Recommendations From the US Multi-Society Task Force on Colorectal Cancer

By Cynthia Tran, MD

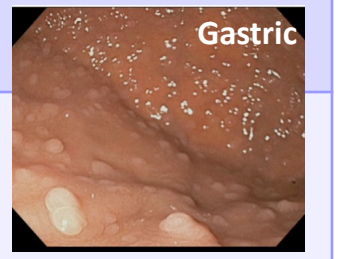
The Emoroid Digest
@EmoryGastroHep

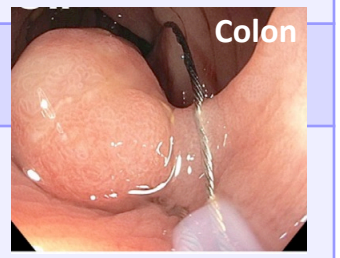
Gastrointestinal Hamartomatous Polyposis Syndromes

- **Hamartoma**: a non-neoplastic tumor with a markedly distorted architecture composed of an abnormal mixture of cells and tissue normally present in that particular area
- **Diagnosis**: based on the presence of a **pathogenic germline variant or meeting clinical criteria** for the syndrome

Peutz-Jeghers Syndrome

Clinical Features	• **Mucocutaneous freckling** around the mouth • Multiple **cerebriform-appearing polyps** due to smooth muscle bands coursing through the polyp • Autosomal dominant inheritance | Associated gene: STK11
Conditions Prompting Genetic Evaluation	• Presence of ≥ **2 histologically confirmed Peutz-Jeghers polyps** • First-degree relative with Peutz-Jeghers and any number of Peutz-Jeghers polyps • Family history of Peutz-Jeghers syndrome and presence of characteristic mucocutaneous pigmentation • Any number of Peutz-Jeghers polyps and the presence of characteristic mucocutaneous pigmentation
Organs for Cancer Surveillance	• GI: stomach, small bowel, colon, pancreas • Additional: lungs, breast, ovaries, cervix, uterus, testes
Surveillance of the Stomach, Duodenum, and Colon	• **Start at age 8-10 years**: baseline EGD and consider colonoscopy at the same time • If **(+)** Peutz-Jeghers Polyps: repeat **EGD and colonoscopy every 2-3 years** • If **(-)** Peutz-Jeghers Polyps: repeat at **age 18 years** (earlier if symptomatic) and then **every 3 years**
Small Bowel Surveillance: How and When	• **Start at age 8-10 years** (earlier if symptomatic): baseline surveillance with video capsule enteroscopy or magnetic resonance enterography • **Age 18 years: resume surveillance** if no polyps found on the initial examination • Adulthood: **surveillance every 2-3 years** due to risk of small bowel intussusception
Small Bowel Polypectomy	• Remove **symptomatic polyps** and **polyps ≥ 10 mm** to prevent intussusception and other complications, such as bleeding
Pancreatic Cancer Surveillance	• **Begin at age 35** and perform annually with either magnetic resonance cholangiopancreatography or endoscopic ultrasound

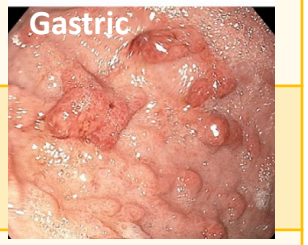


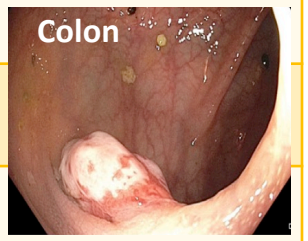


Boland CR, Idos GE, Durno C, Giardiello FM, Anderson JC, Burke CA, Dominitz JA, Gross S, Gupta S, Jacobson BC, Patel SG, Shaukat A, Syngal S, Robertson DJ. Diagnosis and Management of Cancer Risk in the Gastrointestinal Hamartomatous Polyposis Syndromes: Recommendations From the US Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol. 2022 Jun 1;117(6):846-864.

Juvenile Polyposis Syndrome

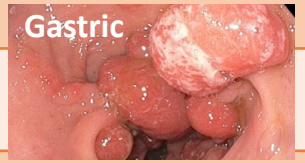
Clinical Features	• **Inflammatory polyps with a smooth red surface** • Autosomal dominant inheritance | Associated genes: SMAD4 or BMPR1A
Conditions Prompting Genetic Evaluation	• Presence of ≥ **5** juvenile polyps of the **colon or rectum** • Presence of ≥ **2** juvenile polyps in **other parts of the gastrointestinal tract** • Presence of any number of juvenile polyps and ≥ 1 first-degree relatives with juvenile polyposis syndrome
Organs for Cancer Surveillance	• Stomach and colon
Surveillance of the Stomach and Colon	• **Start at age 12-15 years** (earlier if symptomatic): baseline EGD and colonoscopy • **Repeat every 1-3 years** depending on polyp burden
Screening for Hereditary Hemorrhagic Telangiectasia (HHT)	• **Evaluate** those with **SMAD4** pathogenic variants for **HHT** at the time of diagnosis • Including screening for and appropriate management of cerebral and pulmonary AVMs

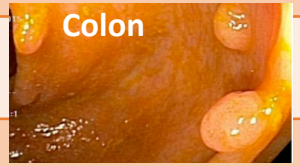




PTEN Hamartoma Tumor Syndrome

Clinical Features	• Phenotypic variations: Cowden Syndrome, Bannayan-Riley-Ruvalcaba syndrome, Proteus Syndrome • Hamartomas of the **skin and gastrointestinal tract**, mucocutaneous lesions, and macrocephaly • Autosomal dominant inheritance | Associated gene: PTEN (additionally WWP1 in Cowden-syndrome like Syndrome)
Conditions Prompting Genetic Evaluation	• Presence of **multiple gastrointestinal hamartomas or ganglioneuromas** should prompt evaluation for Cowden's syndrome and related conditions
Organs for Cancer Surveillance	• GI: colon • Additional: breast, thyroid, kidney, uterus, and skin
Surveillance of the Colon	• **Start at age 35 years** (or 10 years younger than age of any relative with colorectal cancer) • **Repeat at intervals ≤ 5 years** depending on polyp burden





Hereditary Mixed Polyposis Syndrome

Clinical Features	• Attenuated colonic polyposis of varying types and histologies • Autosomal dominant inheritance | Associated gene: GREM1 • **Start at age late 20s: colonoscopy** (onset of polyposis) • Not enough data to know optimal surveillance intervals or if there is extraintestinal neoplasia risk

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