Hereditary Polyposis Syndromes

Opportunities for early detection in individuals and families

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Colon polyps can be a clinical component of a variety of inherited polyposis syndromes. Evaluation begins by obtaining an accurate polyp history (histologic type, number, location, and age of onset), cancer history (location, type, and age of onset), and assessment for the presence of other features (desmoid tumors, congenital hypertrophy of the retinal pigment epithelium, and thyroid tumors). Referral to a credentialed genetics professional depends on the number and histology of polyps, as well as the presence of other clinical features (Basso, Bianchi, Malesci, & Laghi, 2017). The identification of families with polyposis syndromes is important because the appropriate use of aggressive surveillance and risk-reducing surgery can lead to the early detection and prevention of colorectal and other cancers (Valle, 2017). A summary of the clinical characteristics, cancer risks, screening guidelines, and indications for genetic evaluation for common polyposis syndromes is shown in Figure 1.

Adenomatous Polyposis Syndromes

Adenomatous polyposis often occurs because of mutations in the APC or MUTYH genes. Familial adenomatous polyposis (FAP) is characterized by cancer of the colon and rectum that is attributable to mutations in the APC gene. Testing for mutations in the APC gene has been available since the late 1980s (Basso et al., 2017). Individuals with classic FAP may begin to develop colorectal polyps in their teenage years, often resulting in hundreds to thousands of polyps. Some people have a variant called attenuated FAP (aFAP), in which polyp growth is delayed and not as numerous (Basso et al., 2017).

Individuals with FAP may have desmoid tumors, which are fibrous tumors usually found in the tissue covering the intestines and tend to recur after surgical resection (National Comprehensive Cancer Network [NCCN], 2017). Individuals who have colon polyps and tumors outside the colon (osteomas, dental abnormalities, epidermoid cysts, fibromas, lipomas) have a variant known as Gardner syndrome (NCCN, 2017).

Although most individuals with pathogenic APC mutations will develop colorectal cancer, the number of polyps and the time frame depend on the specific mutation (NCCN, 2017). Identification of individuals with FAP is important because annual colonoscopy screening for this population often begins at age 10 years; consequently, children should be tested for FAP at this age (Achatz et al., 2017). Screening continues until the polyp burden becomes too high. Total proctocolectomy with ileal pouch–anal anastomosis is the preferred risk-reducing surgery (Jasperson & Burt, 2015). As many as 20% of individuals with a mutation in

AT A GLANCE

- The identification of families with polyposis syndromes is important because aggressive surveillance and risk-reducing surgery can lead to the early detection and prevention of cancer.
- Identifying individuals at risk, referring them for genetic evaluation, and ensuring follow-up with prevention and early detection recommendations are responsibilities of oncology nurses.
- Oncology nurses can provide support and education to patients and families to help them medically and psychosocially manage their diagnoses.
FAMILIAL ADENOMATOUS POLYPOSIS (FAP)

Clinical features
- Hundreds to thousands of adenomatous colon polyps
- Polyps of the gastric fundus and duodenum
- Osteomas
- Dental anomalies
- Congenital hypertrophy of the retinal pigment epithelium
- Desmoid tumor
- Attenuated FAP (aFAP) is characterized by multiple colonic polyps (average of 30) and more proximally located polyps.

Risk for cancer
- Nearly 100% for colon cancer
- 4%–12% for small bowel cancer
- 1%–12% for thyroid cancer
- Risks for pancreas, bile duct, and stomach cancers are increased.

Average age of onset/cancer diagnosis
- The average age of onset is 16 years (range = 7–36 years).
- By age 35 years, 95% of individuals with FAP have polyps.
- The average age of colon cancer diagnosis in untreated individuals is 39 years (range = 34–43 years).
- The average age of colon cancer diagnosis in untreated individuals with aFAP is 55 years (range = 40–70 years).

Screening
- Annual colonoscopy should begin at age 10–12 years for FAP and in the late teenage years for aFAP.
- Esophagogastroduodenoscopy should begin by age 20–30 years and occur every 2–3 years.
- Regular physical examinations (thyroid palpation, neurologic examination, abdominal examination for desmoid tumors) should occur.
- Individuals should consider annual thyroid ultrasound imaging for increased risk for thyroid cancer, as well as hepatoblastoma screening by liver ultrasound.

Treatment
- Absolute indications for colectomy include colorectal cancer or symptoms such as bleeding or obstruction.
- Relative indications for colectomy include presence of multiple adenomas larger than 6 mm that cannot be removed endoscopically, a significant increase in adenoma number between examinations, adenomas with high-grade dysplasia, or inability to remove numerous adenomas.

Indications for genetic referral
- More than 10 adenomas in lifetime
- Known APC mutation in family

JUVENILE POLYPOSIS SYNDROME (JPS)

Clinical features
- Typically associated with 10 to a few hundred colon adenomatous polyps
- Duodenal adenomas are found in 17%–25% of individuals.
- Serrated adenomas, hyperplastic sessile serrated polyps, and mixed (hyperplastic and adenomatous) polyps can also occur.

Risk for cancer
- Lifetime risk of colorectal cancer is 43% to almost 100% in the absence of regular surveillance in homozygotes.
- 4% risk for duodenal cancer
- Increased risk for cancers of the ovary, bladder, skin, breast, and endometrium

Average age of onset/cancer diagnosis
- The average age of onset is 35–45 years.
- The average age of colon cancer diagnosis is 50 years.

Screening
- Colonoscopy should occur every 1–2 years beginning at age 25–30 years.
- Upper endoscopy and side-viewing duodenoscopy should begin at age 30–35 years, with follow-up based on initial findings.
- Individuals should consider screening for thyroid abnormalities with palpation and/or ultrasound.
- People with a heterozygous (monoallelic) germline MUTYH pathogenic mutation should have colorectal screening and other screening based on family history.

Treatment
- Suspicious polyps identified on colonoscopy should be removed until polypectomy alone cannot manage the large size and number of the polyps, at which point either subtotal colectomy or proctocolectomy is performed.

Indications for genetic referral
- More than 10 adenomas in lifetime
- Known MUTYH (recessive) mutation in family

PEUTZ–JEGHERS SYNDROME

Clinical features
- Hamartomas in stomach, small intestine, colon, and rectum

Risk for cancer
- The risk for gastrointestinal cancers in families with JPS is about 70%.

Average age of onset/cancer diagnosis
- Most have polyps by age 20 years.
- The colorectal cancer risk is 17%–22% by age 35 years and 68% by age 60 years; the median age of diagnosis is 42 years.
- The gastric cancer risk is 21% in those with gastric polyps.

Screening
- Colonoscopy should occur every 1–3 years, starting at age 12–15 years with endoscopic polypectomy.
- Screening for stomach cancers with gastroduodenal endoscopy should start at age 15 years and occur every 1–2 years.
- Small bowel surveillance with capsule endoscopy should start at age 15 years and occur every 1–2 years.

Treatment
- When a large number of polyps are present and complete removal is impractical or impossible, removal of all or part of the colon or stomach should be considered.

Indications for genetic referral
- At least 5 hamartomas in the colon
- Hamartomas anywhere else in the gastrointestinal tract
- Known SMAD4 or BMPR1A mutation in family
- Gastrointestinal polyps can result in chronic bleeding and anemia, as well as cause recurrent obstruction and intussusception, requiring repeated laparotomy and bowel resection.
- Mucocutaneous hyperpigmentation presents in childhood as dark blue to dark brown macules around the mouth, eyes, and nostrils; in the perianal area; and on the buccal mucosa.
- Hyperpigmented macules on the fingers are common. The macules may fade in puberty and adulthood.

**Risk for cancer**
- 5%–39% risk for colorectal cancer
- 1%–29% risk for stomach cancer
- Less than 1%–13% risk for small bowel cancer
- 32%–54% risk for breast cancer
- 1.6%–21% risk for ovarian cancer (mostly sex chord stromal tumors)
- 2%–10% risk for cervical cancer (adenoma malignum)
- 2.7%–9% risk for uterine cancer
- 11%–36% risk for pancreatic cancer
- 1%–9% risk for testicular cancer (Sertoli cell tumor)
- 7%–17% risk for lung cancer

**Average age of onset/cancer diagnosis**
- Some children develop symptoms in the first few years of life.
- 68% of affected individuals have undergone emergency laparotomy by age 18 years.
- Colorectal cancer diagnosis: age 42–46 years
- Stomach cancer diagnosis: age 30–40 years
- Small bowel cancer diagnosis: age 37–42 years
- Breast cancer diagnosis: age 37–59 years
- Ovarian cancer diagnosis: age 28–52 years
- Cervical cancer diagnosis: age 34–40 years
- Uterine cancer diagnosis: age 34–45 years
- Pancreatic cancer diagnosis: age 41–52 years
- Testicular cancer diagnosis: age 6–9 years
- Lung cancer diagnosis: age 47 years

**Screening**
- Routine endoscopic surveillance with polypectomy decreases the frequency of emergency laparotomy and bowel loss resulting from intussusception.
- Gastroduodenal endoscopy should start at age 8 years and occur every 2–3 years.
- Small bowel capsule endoscopy should start at age 8 years and occur every 2–3 years.
- Colonoscopy should start at age 8 years and occur every 1–3 years.
- Annual physical and gynecologic examinations should start at age 8 years.
- Annual physical examination, including testicular examination, should start at age 8 years.
- Annual breast examination, mammography, and/or breast magnetic resonance imaging should start at age 25–30 years.

**COWDEN SYNDROME**

**Clinical features**
- Skin lesions include trichilemmomas, acral keratoses, papillomas, and lipomas.
- Macrocephaly
- Gastrointestinal polyps (particularly hamartomas or ganglioneuromas)
- A child with macrocephaly, autism, developmental delay, lipomas, penile freckling, or vascular anomalies

**Risk for cancer**
- 25%–85% risk for breast cancer
- 5%–10% risk for thyroid cancer
- 17%–28% risk for endometrial cancer
- 9%–16% risk for colon cancer
- 35% risk for renal cell carcinoma

**Average age of onset/cancer diagnosis**
- More than 90% of individuals have at least one or two clinical criteria by their late 20s.
- 50% will be diagnosed with breast cancer by age 50 years.

**Note.** Based on information from Eng, 2016; Haidle & Howe, 2017; Jasperson et al., 2017; McGarrity et al., 2016; National Comprehensive Cancer Network, 2017; Nielsen et al., 2015.
the APC gene are de novo, meaning they are the first in the family to have the mutation (Basso et al., 2017). Nonsteroidal anti-inflammatory drugs have led to regression of adenomas in FAP and decreased the polyp burden; however, there are no U.S. Food and Drug Administration–approved chemoprevention agents for FAP (NCCN, 2017).

*MUTYH*-associated polyposis (MAP), first described in 2002, is an autosomal recessive syndrome (NCCN, 2017). Individuals who have two copies of the altered gene are homozygous (biallelic) and at increased risk for developing polyps, as well as colon and other cancers. Most individuals have from 20–100 adenomas, which makes it clinically difficult to differentiate between aFAP and MAP. Genetic testing is considered when an individual has 10 polyps (NCCN, 2017). People with one altered copy of the gene are heterozygous (monoallelic) and have a variable increased risk for colon and other cancers. An estimated 1%–2% of individuals of northern European ancestry are heterozygous for a pathogenic *MUTYH* variant; reproductive partners of *MUTYH* carriers should be offered testing to predict the risk of passing an altered copy of the gene to offspring (Nielsen, Lynch, Infante, & Brand, 2015).

**Hamartomatous Polyposis Syndromes**

Hamartomas are benign masses of normal tissue that accumulate in the intestines and other organs (Kanth, Grimmert, Champine, Burt, & Samadder, 2017). Although they are often referred to as juvenile polyps, hamartomas can occur at any age; it is a pathologic diagnosis (Ma et al., 2018).

Juvenile polyposis syndrome (JPS) is an autosomal dominant condition associated with multiple hamartomatous polyps, predominantly in the right colon, which often appear during childhood. The risk for gastrointestinal cancers may be close to 50% (NCCN, 2017). JPS is often because of mutations in the SMAD4 and BMPRIA genes. The primary symptom of JPS is gastrointestinal bleeding.

Identification of genetic risk is important because most carriers of SMAD4 mutations also develop hereditary hemorrhagic telangiectasia (HHT), which is a rare disease that leads to abnormal blood vessel formation in the skin, mucous membranes, lungs, liver, and brain. In HHT, some arterioles abnormally flow directly into veins rather than into capillaries. These abnormalities are arteriovenous malformations (AVMs) (Jackson et al., 2017). If there is a known SMAD4 mutation, genetic testing should occur at six months of age because of the risk for HHT and the need for monitoring and treatment of pulmonary and cerebral AVMs (Achatz et al., 2017).

Peutz–Jeghers syndrome (PJS) is an autosomal dominant polyposis syndrome with symptoms of hamartomas, mucocutaneous pigmentation (particularly in the mouth, lips, nose, and genitalia), and a variable increased predisposition toward developing multiple malignancies that require interprofessional management. Mutations in *STK11* predispose individuals to PJS (Daniell, Plazzer, Perera, & Macrae, 2017).

Cowden syndrome is a multisystem disease that is attributable to mutations in the *PTEN* gene and is associated with increased risks for breast, thyroid, and endometrial cancers, as well as benign hamartomas in the skin, colon, and thyroid (Eng, 2016). As many as 95% of patients with Cowden syndrome undergoing colonoscopy have multiple polyps of various histologic types. A scoring system is available to identify individuals who may benefit from genetic testing for Cowden syndrome (Tan et al., 2011), and an online risk calculator can be found at www.lerner.ccf.org/gmi/ccscore.

**Other Polyposis Syndromes**

Hereditary mixed polyposis syndrome (HMPS) is a rare condition characterized by multiple colorectal polyps including adenomatous, hamartomatous, and hyperplastic polyps that begin forming in the teenage years (Rohlin et al., 2016). Patients are usually asymptomatic, so screening is needed. The clinical features of HMPS are not yet well defined but are the result of mutations in the GREM1 gene, for which genetic testing is available. Colonoscopy is usually started in the teenage years and performed every 1–3 years, depending on the number of polyps (NCCN, 2017). If the polyp burden becomes too large to manage endoscopically, consideration for colectomy is indicated.

Serrated polyposis syndrome (SPS) is associated with multiple colorectal serrated polyps (Kalady, 2013). Although serrated polyps typically predominate, individuals with SPS frequently also have colorectal adenomas (Kalady, 2013). The clinical diagnosis of SPS is made based on the following findings: (a) presence of five serrated polyps proximal to the sigmoid colon, (b) two or more serrated polyps greater than 10 mm, or (c) 20 serrated polyps of any size (Basso et al., 2017). Risk of colorectal cancer may be as high as 25% (Kalady, 2013). Colonoscopy is recommended to be performed every 1–3 years. If there are too many polyps to remove endoscopically, consideration should be given to colectomy (NCCN, 2017). First-degree relatives should begin colonoscopy 10 years prior to the youngest colorectal

"Many of the polyposis syndromes begin to manifest in individuals aged as young as 10 years."
cancer diagnosis in the family or by age 40 years.

Mutations in the **POLE** and **POLD1** genes are associated with polyposis (Valle et al., 2014), and genetic testing is now available (Valle, 2017). Recommendations for management include colonoscopy starting at age 25 years and performed every 2–3 years if no polyps are detected and annually if polyps are detected (NCCN, 2017). Colectomy should be considered if poly burden cannot be managed with colonoscopy.

**Implications for Nursing**

Accurate and complete assessment of family and polyp history is the first step in identifying individuals who may be at risk for hereditary polyposis syndromes. Nurses need to inquire about polyp type and number of polyps detected at each colonoscopy. People with 10 or more adenomatous polyps detected on a single colonoscopy or when added together from multiple colonoscopies (lifetime poly burden) or with a history of hamartomas or serrated polyps should be offered the option of genetic evaluation.

Many of the polyposis syndromes begin to manifest in individuals aged as young as 10 years. Identification of families with hereditary risk is important because surveillance often begins before the teenage years (Ripperger et al., 2017). In addition, the identification of known mutation carriers enables aggressive surveillance in those likely to benefit and prevents unnecessary aggressive surveillance in those who do not have an inherited risk.

Genetic testing in children has an ethical dimension, and the best interests of the child should always be considered (Kesserwan, Friedman Ross, Bradbury, & Nichols, 2016). Other considerations include whether testing will guide surveillance decisions and the availability of evidence-based recommendations. Families with known **APC**, **SMAD4**, **BMPR1A**, **STK11**, and **PTEN** mutations can be at increased risk for developing pediatric malignancies. Because of the relative rarity of these syndromes, best management of these patients is referral and management by a genetics team with access to interprofessional care (Kesserwan et al., 2016).

Individuals with large poly burden often undergo colectomy at an early age. Changes in eating and increased toileting resulting from surgery can be a source of psychosocial distress (Eijzenga, Hahn, Aaronson, Klijt, & Bleiker, 2014). These changes can negatively affect employment, body image, and social activities. Because the individuals affected are often young adults forming relationships, stress can exist concerning when and how to tell a potential partner about their diagnosis (Mireskandari et al., 2009). Many known carriers also have concerns and dilemmas about reproduction and the possibility of passing a mutation to offspring. These individuals often require ongoing psychosocial support and interprofessional care to manage the consequences of their genetic predisposition. Oncology nurses can offer support to these individuals and families and refer them to resources (see Figure 2).

Hereditary polyposis syndromes may result in increased risk for multiple cancers, often at a very early age. Surveillance programs can be complex. Regular assessment to ensure that surveillance is comprehensive and current typically requires an interprofessional approach. Testing for some hereditary polyposis syndromes is relatively new, and management recommendations are likely to change (NCCN, 2017; Valle, 2017). Surveillance and prevention recommendations should be reviewed annually by the genetics team to verify that they are still current and evidence based. Nurses should encourage patients to re-contact the genetics professional annually to determine that the recommendations are appropriate (Otten et al., 2015).

**Conclusion**

Interprofessional management of individuals with hereditary polyposis syndromes demands accurate assessment of patients’ personal and family history, referral for genetic evaluation and testing, and implementation of complex surveillance and management plans to decrease the morbidity and mortality associated with these syndromes. Oncology nurses play an integral role in supporting these patients and families as they manage the complexities of their diagnoses.

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