Juvenile polyposis syndrome (JPS) is a polyp predisposition syndrome, where there is a higher risk to develop polyps in your digestive tract running in the family. The name juvenile describes the specific types of polyps that develop, not the age when you develop them. This type starts with many small growths, or polyps, in your colon that can cause bleeding and anemia and may eventually develop into cancer if not removed. A specialized doctor called a gastroenterologist can go in and remove these growths before they turn into cancer.

Pathogenic (or harmful) variants in one of two genes cause JPS: *BMPR1A* and *SMAD4*. It is inherited in an autosomal dominant pattern, meaning that children of someone who carries a pathogenic variant each have a 50% risk to inherit the variant and associated cancer risks. Notably, women and men both have the *BMPR1A* and *SMAD4* genes and have the same chances to inherit and pass down variants in these genes. Therefore, both sides of the family are important when assessing inherited risk. About 33% (or 1 in 3 people) with this condition will have a parent with polyps. The other 2 in 3 (or 67%) of people have no family history and will be the first ones in their family with this condition.

JPS is suspected in a person with any of the following:

- More than 5 juvenile polyps in the colon
- Multiple juvenile polyps anywhere else in the GI tract (such as stomach or small intestine)
- Juvenile polyps with a family history of someone else with juvenile polyps

Genetic Testing for JPS

Genetic testing is available for this condition. There are different ways to complete this testing. This can include:

- *Single site analysis*: Testing specific to a known pathogenic variant in the family
- *Full gene sequencing and rearrangement analysis*: Comprehensive testing to search for all currently detectable variants in the genes.
- *Gene panels*: Newer, more broadly based gene tests that would include not only the *BMPR1A* and *SMAD4* genes, but other genes known or suspected to be associated with increased cancer risks.

Risks for cancer with JPS include:

The risk that someone with JPS will get cancer over their lifetime is between 9 and 50%, including cancer of the colon, rectum, small intestine, and pancreas. The chance of stomach

cancer is 21% in those who have gastric polyps. One study showed the risk for colon cancer may be as high as 68%.

There is also a risk for an increased number of polyps, from 4 or 5 to more than 100. These are not cancerous and many of them will stay benign, but they have the potential to develop into cancer. They can be anywhere in your digestive tract: stomach, small intestine, colon, or rectum.

The chance to develop colon cancer partly depends on if you get regular colonoscopies. A colonoscopy can reduce the risk of colon cancer by removing the polyps before they have a chance to develop into cancer.

Screening and Management information for JPS

- Routine colonoscopy (every 1 year if polyps are found, every 2-3 years if no polyps are found) starting at around age 15.
- Screening by complete blood count (CBC) and upper endoscopy starting at around age 15, or earlier if symptoms occur. Repeat every 1 year if polyps are found, and every 2-3 years if no polyps are found)
- When a large number of polyps are present, removal of all or part of the colon or stomach may be necessary.
- Treatment as needed for manifestations of HHT (see below).

JPS and HHT

Another thing to know about JPS is that people with a *SMAD4* pathogenic gene variant have a higher chance of also having another condition called hereditary hemorrhagic telangiectasia (HHT). Our genes are very complex, and sometimes different changes in the same gene can cause different health issues. Some variants in the *SMAD4* gene **only** cause JPS, while different variants in the same *SMAD4* gene can cause JPS **and** HHT. This result may come up while doing testing for another, unrelated condition as part of general genetic screening. HHT can cause nose bleeds and an increased risk for aneurysms and arteriovenous malformations (groups of abnormal blood vessels connecting arteries and veins in the brain and lungs). There is treatment available for people with HHT.

Click here to learn more about scheduling a genetic counseling appointment for questions about hereditary cancer predisposition.