



Cancer Predisposition Clinic

Juvenile Polyposis Syndrome

Also called: JPS, familial juvenile polyposis, generalized juvenile polyposis, juvenile polyposis of infancy

What is juvenile polyposis syndrome?

Juvenile polyposis syndrome (JPS) is a hereditary condition in which individuals have a higher risk for benign (non-cancerous) polyps in the gastrointestinal (GI) tract, most commonly in the colon. Polyps can also be found in the stomach, small intestine, and rectum. “Juvenile” refers to the type of polyp that is seen in this condition. If these polyps are not removed, they can develop into cancer.

Individuals who meet any of the following criteria are considered to have a clinical diagnosis of JPS:

- 1.) More than five juvenile polyps in the colorectum
- 2.) Multiple juvenile polyps throughout the GI tract
- 3.) Any number of juvenile polyps and a family history of juvenile polyposis

Most individuals with JPS will develop polyps by the age of 20 years. Some people only have a few polyps over the course of their life, but others may have more than 100 polyps.

What is the cancer risk for people with juvenile polyposis syndrome?

While the polyps themselves are not cancerous, they can develop into cancer. The lifetime risk for gastrointestinal cancers in individuals with JPS is thought to be 40-50%. People with JPS are also at an increased lifetime risk for stomach cancer (21% if multiple polyps are present) as well as small intestine and pancreatic cancers (rare but increased).

What are other health conditions that can be seen in people with juvenile polyposis syndrome?

Some people with JPS have a combined syndrome called JPS and hereditary hemorrhagic telangiectasia (JPS/HHT). Individuals with this condition can have juvenile polyps, nosebleeds, telangiectasias (widened thread-like tiny blood vessels near the surface of the skin), and arteriovenous malformations (abnormal connection between arteries and veins, sometimes in the brain or spine).

What causes juvenile polyposis syndrome?

JPS are caused by changes in the genes *BMPRIA* and *SMAD4*. Genes carry information telling cells within the body how to function. Most individuals with changes in the *SMAD4* gene have JPS/HHT.

Most people without JPS carry two working copies of the *BMPRIA* and *SMAD4* genes in their cells. One copy of each gene is inherited from the mother and one from the father. Cells from people with JPS carry one working copy of *BMPRIA* or *SMAD4* and one copy of *BMPRIA* or *SMAD4* that is changed. This change causes the gene to not work properly. It is called a *BMPRIA* or *SMAD4* mutation.

Mutations in *BMPRIA* are found in about 28% of cases of JPS and mutations in *SMAD4* are found in about 27% of cases of JPS. For the remaining 45% of people with the condition who do not have mutations in any of these genes, doctors do not yet know what other genes are related to JPS.

About a third (33%) of people with JPS have a parent who is also affected with the condition. About two-thirds (67%) of people with JPS do not have an affected parent or family history of polyps. In these cases, the change either happened in an egg or sperm cell when the person was formed or in one of the child's cells during pregnancy. These children are the first in their families to have JPS. No matter how they acquired the *BMPRIA* or *SMAD4* mutation, people with JPS who are able to have biological children have a 50% or 1 in 2 chance of passing it on to their children.

How are people with juvenile polyposis syndrome screened for tumors?

People with JPS should be managed by a medical provider who knows this condition well. Children with JPS should have regular screenings to detect juvenile polyps. The goal of screening is finding and removing polyps early to allow the best outcome for patients.

Recommended screenings for children with JPS include the following:

- **Annual evaluation** by a healthcare provider familiar with JPS
- **Monitoring** for rectal bleeding, anemia, abdominal pain, constipation, diarrhea, or changes in the stool. These symptoms should prompt additional evaluation
- **Complete blood count** beginning in the mid-teenage years to monitor for anemia
- **Colonoscopy and upper endoscopy** beginning in the mid-teenage years or at the time of initial symptoms
 - If negative, screening should be repeated in three years or as per GI provider's recommendations
 - If only one or a few polyps are identified, they should be removed and subsequent screening should be done annually or as per GI provider's recommendations
 - If many polyps are identified, removal of part or most of the colon or stomach may be necessary

What other screening is recommended for people with JPS/HHT?

In addition to the screening recommendations listed above, recommended screenings for children with JPS/HHT include the following:

- **Annual evaluation** by a healthcare provider familiar with HHT, with close attention to history of nosebleeds or other bleeding, shortness of breath or getting overly tired during exercise, and headache or other neurological symptoms
- **Periodic blood counts and ferritin determination** with appropriate treatment for iron deficiency
- **Evaluation for pulmonary arteriovenous malformations** about every 5 years by performing contrast echocardiogram if available
 - **Chest CT with contrast** should be used if previous contrast echocardiogram revealed evidence of a right to left shunt
- **Evaluation for cerebral arteriovenous malformations** via brain MRI performed in childhood and again after puberty if the initial childhood brain MRI was normal

Because of the complex care that individuals with JPS/HHT require, it is recommended that patients consider being treated at a Hereditary Hemorrhagic Telangiectasia Treatment Center. A list of North American and international centers can be found at: <http://curehht.org/resources/hht-treatment-centers>.

How is genetic testing for juvenile polyposis syndrome done?

Hereditary cancer syndromes such as JPS may be suspected after looking at a person's medical or family history. In most cases, a health care providers or genetic counselor will ask questions about a person's health and the health of other family members.

The genetic counselor or health care providers will record which family members have developed tumors, what types of tumors and at what ages the tumors occurred. From this information they will create a family tree. Health care providers and genetic counselors will look at the family tree to find out:

- If there are more cancers than normal,
- If cancers occurred at younger-than-expected ages,
- If the types of tumors match up with what might be seen in those with JPS, and
- If the people with cancer had other physical or health features related to JPS syndrome.

If JPS is suspected in a child or other family members, the health care providers or genetic counselor will likely recommend genetic testing of *BMPRIA* and *SMAD4*.

Diagnostic genetic testing

If the health care providers or genetic counselor suspects that a person has JPS or JPS/HHT, diagnostic testing may take place as follows:

- A blood sample is collected
- DNA is isolated from the cells in the sample. A person's genes are made of DNA
- Both copies of the person's *BMPRIA* and *SMAD4* genes are checked for possible changes. A genetic specialist compares the two copies of the person's *BMPRIA* and *SMAD4* genes to a normal *BMPRIA* and *SMAD4* gene. If there are differences noted, the specialist decides if these differences might cause a condition such as JPS or JPS/HHT
- If a *BMPRIA* or *SMAD4* mutation is found, the genetic counselor will work with the family in the following ways:
 - To help the family understand the cancer risks of JPS or JPS/HHT
 - To find out if other family members should consider testing
 - To help with decisions about prenatal genetic testing

Prenatal genetic testing

Parents may undergo prenatal testing to find out if a pregnancy is affected with a known *BMPRIA* and *SMAD4* mutation in the family.

Testing may take place either before pregnancy occurs or during pregnancy. People considering prenatal testing should work with a genetic counselor to review the pros and cons of the tests. The genetic counselor can also help parents consider how they wish to handle the results of the testing.

Testing that occurs before pregnancy—Testing that happens before pregnancy is called preimplantation genetic testing (PGT). This special type of genetic testing is done along with in vitro fertilization (IVF). PGT offers a way to test embryos for a known *BMPRIA* and *SMAD4* mutation before placing them into the uterus.

Testing that occurs during pregnancy—Testing can be used to see if a pregnancy is affected with a known *BMPRIA* or *SMAD4* mutation. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)**—during the first trimester of the pregnancy
- **Amniocentesis**—during the second trimester of the pregnancy or later

Once the tissue is collected, DNA is isolated and examined for the presence of the *BMPRIA* or *SMAD4* mutation in the family.

Both of these tests carry minor risks and should be discussed with an experienced doctor and/or genetic counselor.

Special concerns

Genetic testing for JPS is a complex process. Those thinking about testing should take time to consider the benefits and risks. They should discuss the process with a genetic counselor before testing is done. If they choose testing, they should review the test results with the health care providers or genetic counselor to be sure they understand the meaning of the results.

Sometimes children or adults with JPS can feel sad, anxious or angry. Parents who passed on a *BMPRIA* or *SMAD4* mutation to one or more of their children may feel guilty. Some people with a *BMPRIA* or *SMAD4* mutation may have trouble getting disability coverage, life insurance or long-term care insurance. More information about genetic discrimination can be found at www.ginahelp.org.

Are there other special health care needs for children with juvenile polyposis syndrome?

People of any age with JPS or JPS/HHT have a higher risk of cancer. They should monitor their health and adopt healthy habits throughout life. It is important to continue to have regular physical checkups and screenings. That way, any polyp or cancer can be found early at the most treatable stage.

Other ideas to reduce the risk of cancer include the following:

- Eat a healthy diet with lots of fruits and vegetables
- Get regular exercise
- Avoid smoking or using tobacco products
- Avoid secondhand smoke
- Avoid excess sun exposure and always wear sunscreen, hat and protective clothing when out in the sun

People with juvenile polyposis syndrome should watch closely for general signs or symptoms that could signal polyps or cancer:

- Unexplained weight loss
- Loss of appetite
- Pain in the abdomen
- Blood in the stool or changes in bowel habits
- Aches, pains, lumps, or swelling that cannot be explained
- Headaches or changes in vision or nerve function that do not go away

It is important to seek medical help if anything unusual appears.

What other information and resources are there for children with juvenile polyposis syndrome and their families?

Resources for juvenile polyposis syndrome:

- Hereditary Colon Cancer Takes Guts (<http://www.hcctakesguts.org>)
- Peutz-Jeghers Syndrome and Juvenile Polyposis Syndrome Online Support Group (<http://www.acor.org/listservs/join/114>)
- National Organization for Rare Disorders – Juvenile Polyposis Online Support Group (<https://rarediseases.org/organizations/juvenile-polyposis-syndrome-online-support-group>)

Resources about genetic testing and hereditary cancer:

- Making Sense of Your Genes: A Guide to Genetic Counseling (www.ncbi.nlm.nih.gov/books/NBK115508/)
- Young People with Cancer: A Parent's Guide (www.cancer.gov/publications/patient-education/young-people)
- Gene Ed (geneed.nlm.nih.gov)

Sources:

1. GeneReviews – Juvenile Polyposis Syndrome <https://www.ncbi.nlm.nih.gov/books/NBK1469>
2. GeneReviews – Hereditary Hemorrhagic Telangiectasia <https://www.ncbi.nlm.nih.gov/books/NBK1351>
3. Genetics Home Reference – <https://ghr.nlm.nih.gov/condition/juvenile-polyposis-syndrome>
4. National Comprehensive Cancer Network. Genetic/Familial High Risk Assessment: Colorectal. https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf

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