**PTEN Hamartoma Tumor Syndrome**

*Also called: PHTS, Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, Proteus syndrome, Proteus-like syndrome, PTEN-related Proteus syndrome*

**What is PTEN hamartoma tumor syndrome?**

**PTEN** hamartoma tumor syndrome is a genetic condition in which non-cancerous growths, called hamartomas, develop in different areas of the body. In addition to hamartomas, patients can have other physical findings, including larger-than-average head size, abnormal skin growths, and learning disabilities.

People with **PTEN** hamartoma tumor syndrome are at higher risk of developing breast, thyroid, kidney, uterus, colorectal, and skin cancer.

**PTEN** hamartoma tumor syndrome is hereditary, which means it can be passed from parents to their children.

**What is the cancer risk for people with PTEN hamartoma tumor syndrome?**

People with **PTEN** hamartoma tumor syndrome are at high risk for certain cancers. These cancers generally occur in adults, not children, with the condition. The average age of cancer diagnosis is about 30 to 50 years of age. The exception is thyroid cancer, which sometimes occurs in children with **PTEN** hamartoma tumor syndrome.

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Estimated Lifetime Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>77%–85% (in women)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>35%–38%</td>
</tr>
<tr>
<td>Renal cell (kidney)</td>
<td>33%</td>
</tr>
<tr>
<td>Endometrium (lining of uterus)</td>
<td>28%</td>
</tr>
<tr>
<td>Colorectal</td>
<td>9%</td>
</tr>
<tr>
<td>Melanoma (skin cancer)</td>
<td>6%</td>
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</tbody>
</table>

Rarely, people with **PTEN** hamartoma tumor syndrome develop a type of brain tumor called cerebellar dysplastic gangliocytoma (also called adult-onset Lhermitte-Duclos disease). The exact risk of developing this type of tumor is unknown because it is so rare.

**What are other physical findings seen in people with PTEN hamartoma tumor syndrome?**

People with **PTEN** hamartoma tumor syndrome may have other physical findings. Not all people with **PTEN** hamartoma tumor syndrome will have all of these physical findings.
### Physical Findings

<table>
<thead>
<tr>
<th></th>
<th>Estimated Risk</th>
</tr>
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<tbody>
<tr>
<td>Larger-than-average head (macrocephaly)</td>
<td>94%</td>
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<tr>
<td>Skin growths or coloring:</td>
<td></td>
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<tr>
<td>• Smooth, white skin growths on the face (trichilemmomas)</td>
<td>greater than 90%</td>
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<tr>
<td>• Smooth, flesh-colored skin growths on the hands or feet (acral or plantar keratosis)</td>
<td>90%</td>
</tr>
<tr>
<td>• Smooth skin growths in the mouth (oral papillomas)</td>
<td>75%</td>
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<tr>
<td>• Freckling of the skin of the penis in boys and men</td>
<td>67%</td>
</tr>
<tr>
<td>Non-cancerous growths (polyps) in the digestive system</td>
<td>greater than 90%</td>
</tr>
<tr>
<td>Non-cancerous growths (nodules, goiter, adenoma) in the thyroid gland</td>
<td>75%</td>
</tr>
<tr>
<td>Non-cancerous growths (fibrocystic disease) in the breast</td>
<td>67%</td>
</tr>
<tr>
<td>Intellectual disability/learning disability/autism spectrum disorder</td>
<td>47%–89%</td>
</tr>
</tbody>
</table>

Other physical findings may include non-cancerous growths in the uterus (fibroids), non-cancerous growths of fatty cells under the skin (lipomas), muscle weakness, or an abnormally curved spine (scoliosis).

### What causes PTEN hamartoma tumor syndrome?

PTEN hamartoma tumor syndrome is caused by changes in a gene known as PTEN. Genes carry information telling cells within the body how to function. The PTEN gene helps to control how and when cells grow, divide, and die.

Most people carry two working copies of the PTEN gene in their cells. One copy is inherited from the mother and one from the father. Cells from people with PTEN hamartoma tumor syndrome carry one working copy of PTEN and one copy that is changed. This change causes the gene to not work properly. It is called a PTEN mutation.

Between 10% and 50% of children with PTEN hamartoma tumor syndrome inherit the PTEN gene mutation from a parent who also has the syndrome. The rest have a new PTEN mutation that did not come from a parent. These children have no history of the syndrome in their family. In these cases, the change either happened in an egg or sperm cell when the child was formed or in one of the child’s cells during pregnancy. These children are the first in their families to have PTEN hamartoma tumor syndrome. No matter how they acquired their PTEN mutation, people with PTEN hamartoma tumor syndrome have a 50% or 1 in 2 chance of passing it on to their children.

As people with PTEN hamartoma tumor syndrome get older, the working copy of PTEN often becomes changed within some of their cells. When both copies of the gene are changed, cancer can develop. That is why people with PTEN hamartoma tumor syndrome have a higher risk of developing cancer than people who do not.
How are people with *PTEN* hamartoma tumor syndrome screened for tumors?

People with *PTEN* hamartoma tumor syndrome should be managed by a doctor who knows this condition well. Screening is recommended for all people with this condition. The goal of screening is finding and treating tumors early to allow the best outcome for patients.

**Recommended screenings for children with *PTEN* hamartoma tumor syndrome:**

- **Yearly physical exams** by a doctor who knows this syndrome well.
- **Thyroid exam** by ultrasound starting at diagnosis and repeated every year. An ultrasound exam uses sound waves to make images of the inside of the body.
- **Skin exam** by a dermatologist (skin specialist) starting at diagnosis and repeated every year.
- **Regular assessments of development and learning progress** as recommended by your doctor.

**Recommended screenings for adults with *PTEN* hamartoma tumor syndrome:**

- **Yearly physical exams** by a doctor who knows this syndrome well.
- **Thyroid imaging** by ultrasound every year or 5–10 years before the earliest known thyroid cancer in the family, whichever is earlier.
- **Skin exam** by a dermatologist (skin specialist) every year.
- **Breast exam** by a doctor starting at age 25 years or 5–10 years before the earliest known breast cancer in the family, whichever is earlier, and repeated every 6 to 12 months.
- **Breast imaging** by mammogram or breast MRI starting at age 30 years or 5–10 years before the earliest known breast cancer in the family, whichever is earlier, and repeated every year.
- **Consider biopsy of the endometrium** starting at age 30 years (for women) or ultrasound. A biopsy is performed by suctioning a small amount of tissue out through the vagina and sending it to the laboratory to be tested for cancer cells. After menopause, yearly ultrasound imaging of the endometrium is recommended. A biopsy can be taken if suspicious areas are seen.
- **Consider kidney imaging** by ultrasound or magnetic resonance imaging (MRI) starting at age 40 years and repeated every 1–2 years.
- **Colonoscopy** starting at age 35 years (unless symptoms arise earlier) and repeated every 5–10 years. Colonoscopy may be done more often if the person has symptoms or if growths are found.

If a family member with *PTEN* hamartoma tumor syndrome was diagnosed with a certain type of cancer, then screening for other family members will likely happen sooner than described above. Doctors usually start screening for that type of cancer at least 5 years before the earliest known diagnosis in the family. For example, if a family member with *PTEN* hamartoma tumor syndrome developed breast cancer at age 35 years, it is recommended that other family members with the syndrome start breast cancer screening at age 30 years.

It is possible that these recommendations may change over time as doctors learn more about *PTEN* hamartoma tumor syndrome. Parents should discuss all screening options for their child with a doctor who knows this syndrome well. Because *PTEN* hamartoma tumor syndrome is a complex condition, it is very important that parents seek out an experienced doctor for their child.
How is genetic testing for PTEN hamartoma tumor syndrome done?

The doctor may suspect PTEN hamartoma tumor syndrome after looking at a person’s medical or family history. In most cases, a doctor or genetic counselor will ask questions about a person’s health and the health of other family members.

The genetic counselor or doctor will record which family members have developed tumors, what types of tumors, and at what ages tumors occurred. From this information they will create a family tree. Doctors 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, and
• If the types of tumors match up with what might be seen in those with PTEN hamartoma tumor syndrome.

If PTEN hamartoma tumor syndrome is suspected in a child or other family members, the doctor or genetic counselor will likely recommend genetic testing of the PTEN gene.

Diagnostic genetic testing

If the doctor or genetic counselor suspects that a person has PTEN hamartoma tumor syndrome, 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 PTEN gene are checked for possible changes. A genetic specialist compares the two copies of the patient’s gene to a normal PTEN gene. If there are differences, the specialist decides if they might cause a condition such as PTEN hamartoma tumor syndrome.
• If a PTEN mutation is found, the genetic counselor will work with the family in the following ways:
  o To help the family understand the cancer risks of PTEN hamartoma tumor syndrome
  o To find out if other family members should consider testing for the mutation
  o To help with decisions about prenatal genetic testing.

It is important to remember that genetic testing does not always find a mutation in the PTEN gene for all people with PTEN hamartoma tumor syndrome. A person can still have PTEN hamartoma tumor syndrome even if no PTEN mutation is found.

Prenatal genetic testing

Parents may undergo prenatal testing to find out if the pregnancy is affected with a known PTEN 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 testing. 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 diagnosis (PGD). This special type of genetic testing is done along with in vitro fertilization (IVF). PGD offers a way to test embryos for a known $PTEN$ 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 $PTEN$ mutation. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)**—during the first trimester (first three months)
- **Amniocentesis**—during the second trimester or later (last six months)

Collected tissue can be checked for the presence of the $PTEN$ mutation identified in the family.

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

**Special concerns**

Genetic testing for $PTEN$ hamartoma tumor syndrome 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 doctor or genetic counselor to be sure they understand the meaning of the results.

Sometimes children or adults with $PTEN$ hamartoma tumor syndrome can feel sad, anxious or angry. Parents who pass on a $PTEN$ mutation to one or more of their children can feel guilty. Some people with a $PTEN$ mutation could have trouble getting disability coverage, life insurance, or long-term care insurance in some states. More information about genetic discrimination can be found at [www.ginahelp.org](http://www.ginahelp.org).

**Are there other health care needs for children with $PTEN$ hamartoma tumor syndrome?**

People of any age with $PTEN$ hamartoma tumor syndrome have a higher risk of cancer. They should monitor their health and adopt healthful habits throughout life. It is important to continue to have regular physical checkups and screenings. That way, any cancer can be found early at the most treatable stage.

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

- Eat a healthful diet with lots of fruits and vegetables
- Get regular exercise
- Avoid smoking or using tobacco products
- Avoid secondhand smoke
People with PTEN hamartoma tumor syndrome should watch closely for general signs or symptoms that could signal cancer:

- Unexplained weight loss
- Loss of appetite
- Pain in 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

**What other information and resources are there for children with PTEN hamartoma tumor syndrome and their families?**

Resources about PTEN hamartoma tumor syndrome:

- Genetics Home Reference - PTEN (ghr.nlm.nih.gov/gene/PTEN)
- PTEN Hamartoma Tumor Syndrome Foundation (www.ptenfoundation.org)
- PTEN World (www.ptenworld.com)
- PTEN Study at the Cleveland Clinic (www.lerner.ccf.org/gmi/research/documents/pten_info_prospects.pdf)

Other resources:

- Gene Ed (geneed.nlm.nih.gov)

**Sources:**

1. Children’s Hospital of Philadelphia - PTEN hamartoma tumor syndrome
   www.chop.edu/conditions-diseases/pten-hamartoma-tumor-syndrome#.VSKnEGd0ytU
2. Genetics Home Reference - PTEN
   ghr.nlm.nih.gov/gene/PTEN
   www.ncbi.nlm.nih.gov/books/NBK1488/