PTEN Hamartoma Tumor Syndrome

Also called: PHTS, Cowden syndrome, Bannayan-Riley-Ruvalcaba 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 intellectual 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.

Type of Cancer	**Estimated Lifetime Risk**
Breast	85% (in women)
Thyroid	35% *(usually follicular, rarely papillary)*
Renal cell (kidney)	35%
Endometrium (lining of uterus)	28%
Colorectal	9%
Melanoma (skin cancer)	>5%

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

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

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 health care provider 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 health care provider 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.
- **Regular assessments of development and learning progress** as recommended by your health care provider.

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

- **Yearly physical exams** by a health care provider who knows this syndrome well.
- **Thyroid imaging** by ultrasound every year.
- **Skin exam** by a dermatologist may be indicated for some patients.
- ***For women*: Clinical breast exam** by a health care provider 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.
- ***For women*: Breast imaging every six months** alternating mammogram with breast MRI starting at age 30-35 years or 5–10 years before the earliest known breast cancer in the family, whichever is earlier. Consider risk-reducing mastectomy.
- ***For women*: Yearly random endometrial biopsy and/or ultrasound of the endometrium (uterus)** starting at age 30-35 years. 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. Consider risk-reducing hysterectomy after completion of childbearing.
- **Kidney imaging** by ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI) starting at age 40 years and repeated every 2 years. Note: ultrasound or MRI preferred.
- **Colonoscopy** starting at age 35 years (unless symptoms arise earlier or close relative with colon cancer under age 40 years). Colonoscopy should be done every 5 years or more frequently if patient is symptomatic or polyps 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. Health care providers 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 25-30 years.

It is possible that these recommendations may change over time as health care providers learn more about *PTEN* hamartoma tumor syndrome. Parents should discuss all screening options for their child with a health care provider who knows this syndrome well. Because *PTEN* hamartoma

tumor syndrome is a complex condition, it is very important that parents seek out an experienced health care provider for their child.

How is genetic testing for *PTEN* hamartoma tumor syndrome done?

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

The genetic counselor or health care provider 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. 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, 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 health care provider or genetic counselor will likely recommend genetic testing of the *PTEN* gene.

Diagnostic genetic testing

If the health care provider 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:
    - To help the family understand the cancer risks of *PTEN* hamartoma tumor syndrome
    - To find out if other family members should consider testing for the mutation
    - 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 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 *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 health care provider 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.

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 healthy 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 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 *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:

- *PTEN* Hamartoma Tumor Syndrome Foundation (www.ptenfoundation.org)
- *PTEN* World (www.ptenworld.com)
- *PTEN Study at the Cleveland Clinic (https://www.lerner.ccf.org/gmi/clinical/pten/)*
- *Genetics Home* Reference - *PTEN* (ghr.nlm.nih.gov/gene/PTEN)

Other resources:

- 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*)

Sources:

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