PTEN Hamartoma Tumor syndrome (PHTS) is a rare genetic condition that can affect children and adults. Over the years, many different names have been used to describe what we now consider the variability of features we see in PHTS. Other names for PHTS have included Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba syndrome (BRRS), *PTEN*-related Proteus syndrome (PS), and Proteus-like syndrome.

Individuals with PHTS syndrome have an increased chance to develop benign growths, neurodevelopmental differences such as autism or intellectual disability and certain cancers in adulthood.

PHTS is caused by a harmful change (called a mutation or pathogenic variant) in the *PTEN* gene. *PTEN* gene variants are inherited in an autosomal dominant pattern, meaning that children someone who carries a variant each have a 50% risk to inherit the variant and associated risks. This also means women and men both have the *PTEN* gene and have the same chance to inherit and pass down variants in this gene. Therefore, both sides of the family are important when assessing inherited risk. However, the associated cancers and screening recommendations are different between men and women.

Cancers commonly associated with PHTS include:

- Breast cancer
- Endometrial (uterine) cancer
- Thyroid cancer
- Kidney cancer
- Colon cancer

Cancer Type	**General Population Risk**	**PTHS Risk**
Breast Cancer	12%	30-50%
Male Breast	0.1%	unknown
Thyroid (non-medullary)	0.9%	5-10%
Endometrial (Uterine)	2.6%	5-10%
Some data suggests there may be a slight increased risk for other types of cancer, such as renal, glioblastoma, melanoma, lung, pancreatic, ovarian, and bladder cancers.		

Some of the other characteristic signs of PTHS include:

- Larger than average head size (macrocephaly)
- Colon polyps (called hamartomas or ganglioneuromas)
- Benign skin growths (including trichilemmomas, keratoses, neuromas, papillomas, and lipomas)
- Pigmented spots (freckles) on the penis
- Thyroid goiters, adenomas, or nodules
- Lhermitte-Duclos (non-cancerous growth in the cerebellum)
- Autism
- Intellectual delay

Genetic testing for PTEN

Genetic testing for pathogenic variants in PTEN are currently available, but there are a few different ways to approach testing:

- *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 gene
- Gene panels: Newer, more broadly based gene tests that would include not only the PTEN gene, but other genes known or suspected to be associated with increased cancer risks

Determining whether an individual meets criteria for genetic testing for PTHS is very complex, and would likely be best left to a genetic counselor or other healthcare provider. PTHS can be diagnosed by a clinical exam performed by a physician familiar with PTHS, or by genetic testing for pathogenic variants in the *PTEN* gene.

Cancer Screening & Management for PTEN

If you are tested and found to have a pathogenic variant in the PTEN gene, it is recommended to discuss your management plan with your healthcare team, and if available, to seek consultation through a specialized high-risk clinic. General recommendations are included here based on updated guidelines of the NCCN, but may be tailored to your

specific medical and family history.

Childhood (below age 18):

- Yearly thyroid ultrasound starting at the time of diagnosis
- Yearly skin check with physical examination
- Consider neurodevelopmental evaluation

For Women:

- Breast awareness starting at age 18
- Clinical breast exam every 6-12 months starting at age 25, or 5-10 years before the earliest known breast cancer in the family (whichever comes first)
- Breast screening
  - Annual mammogram and breast MRI screening with contrast starting at age 30-35, or 5-10 years before the earliest known breast cancer in the family (whichever comes first)
  - For women over age 75, management should be considered on an individual basis
  - Women who have been treated for breast cancer should still have screening of remaining breast tissue with annual mammogram and breast MRI.
- Encourage patient education and prompt response to symptoms of endometrial (uterine) cancer, such as abnormal bleeding. Consider annual random uterine biopsies and/or ultrasound beginning at age 30-35.
- Discussion of the option of a hysterectomy upon completion of childbearing; discuss degree of protection, extent of cancer risk, and psychosocial, social, and quality-of-life aspects.
- Discuss option of risk-reducing mastectomy, including degree of protection, extent of cancer risk, reconstruction options and psychosocial, social, and quality-of-life aspects.

For Men and Women:

- Annual comprehensive physical exam starting at age 18, or 5 years before the youngest age of diagnosis of cancer in the family (whichever comes first), with particular attention to the thyroid.

- Annual thyroid ultrasound starting at the time of diagnosis
- Colonoscopy starting at age 35 unless symptomatic, or if close relative with colon cancer before age 40, then start 5-10 years before the earliest known colon cancer in the family. Colonoscopy should be done every 5 years or more frequently if patient is symptomatic or polyps are found.
- Consider renal ultrasound starting at age 40, then every 1-2 years.
- Visits and procedures for skin lesions may necessitate visits with a dermatologist.
- Consider psychomotor assessment in children at diagnosis and brain MRI if there are symptoms.
- Education regarding the signs and symptoms of cancer.

Resources

PTEN Foundation: PTEN Hamartoma Tumor Syndrome Foundation

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