PTEN

The *PTEN* gene is a tumor suppressor gene. Tumor suppressor genes slow down cell division, repair DNA mistakes, or tell cells when to die. When they don't work properly, cells can grow out of control, which can lead to cancer. *PTEN* has many important roles, including regulating cell movement and interaction, sending signals that prevent cell growth and survival, and instructing abnormal cells to die by a process known as apoptosis. The death of cells with significant DNA damage helps to prevent these cells from growing out of control and becoming a tumor.

Like most genes, each person has two copies of the *PTEN* gene: one inherited from each parent. A mutation in a single *PTEN* gene inherited from either parent can cause Cowden syndrome, which is associated with an increased risk of developing certain cancers over a lifetime, including breast, kidney, thyroid, uterine, and others. Individuals with Cowden syndrome often have many non-cancerous findings, including non-cancerous skin bumps (called trichilemmomas and papillomatous papules), very large head circumference (macrocephaly), uterine fibroids, multinodular goiter of the thyroid, learning disabilities, and autism spectrum disorders.

Mutations in the *PTEN* gene can also cause other hereditary syndromes, such as Bannayan-Riley-Ruvalcaba syndrome (BRRS) and Proteus syndrome (PS). BRRS and PS are associated with increased tumor and cancer risks as well as specific physical and intellectual disabilities that occur in childhood. The entire spectrum of genetic syndromes related to mutations in the *PTEN* gene are collectively referred to as *PTEN* Hamartoma Tumor syndrome (PHTS). Rarely, individuals have been reported who have deletions of the *PTEN* gene as well as the *BMPR1A* gene. This causes a condition called Juvenile Polyposis of Infancy (JPI), which is typically diagnosed prior to age six.

How common are mutations in the *PTEN* gene?

Mutations in the *PTEN* gene are rare—the exact frequency is not yet known. Studies to establish the frequency of *PTEN* mutations are ongoing.

How mutations in this gene impact risk

Women

If a woman has a mutation in the *PTEN* gene, her chances of developing breast, kidney, thyroid, uterine, colorectal cancer and melanoma are greater than that of the average US woman. This does not mean that she has a diagnosis of cancer or that she will definitely develop cancer in her lifetime.

Cancer by age 70	Average US woman[1]	With *PTEN* mutation
Breast	7.1%	77-80%[2,3]
Kidney	<1%	34%[2,3]
Thyroid	1.4%	35-38%[2,3]
Uterine	1.7%	28%[2]
Colorectal	1.6%	9%[2]
Melanoma	<1%	6%[2]

Elevated: Risk is increased, but further research may clarify the exact risk figure.

Men

If a man has a mutation in the *PTEN* gene, his chances of developing kidney, thyroid, colorectal cancer and melanoma are greater than that of the average US man. This does not mean that he has a diagnosis of cancer or that he will definitely develop cancer in his lifetime.

Cancer by age 70	Average US man[1]	With *PTEN* mutation
Kidney	1%	34%[2,3]
Thyroid	<1%	35-38%[2,3]
Colorectal	2%	9%[2]
Melanoma	1.2%	6%[2]

Elevated: Risk is increased, but further research may clarify the exact risk figure.

[1] Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute. 2010-2012. DevCan software (http://surveillance.cancer.gov/devcan) V 6.7.0, Accessed June 2015.
[2] Tan MH, Mester JL, Ngeow J, Rybicki LA, Orloff MS, Eng C. Lifetime cancer risks in individuals with germline PTEN mutations. *Clin Cancer Res*. 2012;18(2):400-7.
[3] Bubien V, Bonnet F, Brouste V, et al. High cumulative risks of cancer in patients with PTEN hamartoma tumour syndrome. *J Med Genet*. 2013;50(4):255-63.

Additional information

Cowden syndrome is often diagnosed based on a physical exam for specific clinical features, both cancerous and non-cancerous. Approximately 25% of individuals who meet the clinical criteria for Cowden syndrome will have a mutation in the *PTEN* gene.[4]

Screening guidelines

Below is a summary of screening guidelines from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) established by experts at the National Comprehensive Cancer Network (NCCN).[5] They are for individuals who have a mutation in the *PTEN* gene that causes Cowden syndrome. If you have a mutation in this gene, your healthcare provider may use these NCCN Guidelines® to help create a customized screening plan for you.

Women

Breast cancer[6]

- **Starting at age 18:** Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Performing regular breast self exams may help increase breast awareness, especially when checked at the end of the menstrual cycle.
- **Starting at age 25 or 5-10 years before the earliest known breast cancer in the family:** Breast exam by your provider every 6-12 months.
- **Starting at age 30-35 or 5-10 years before the earliest known breast cancer in the family:** Mammogram and breast MRI screening with contrast every year. Your provider may wish to alternate between these two screenings every 6 months.
- **After age 75:** Your provider may discuss an individualized management plan with you.
- Your provider may discuss the option of having a risk-reducing bilateral mastectomy (the surgical removal of both breasts).

Uterine cancer[6]

- **Starting at age 30-35:** Your healthcare provider may discuss the benefits and limitations of a transvaginal ultrasound along with endometrial biopsies (sampling) every year.
- Report any vaginal bleeding that is not typical to your provider.
- Your provider may discuss the option of having a risk-reducing hysterectomy (the surgical removal of the uterus).

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[4] Tan MH, Mester J, Peterson C, et al. A clinical scoring system for selection of patients for PTEN mutation testing is proposed on the basis of a prospective study of 3042 probands. Am J Hum Genet. 2011;88(1):42-56.

[5] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast and Ovarian V.1.2017 © National Comprehensive Cancer Network, Inc 2016. All rights reserved. Accessed September 20, 2016. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

[6] National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian. *NCCN Guidelines Version 1.2017.* Available at www.nccn.org. Published September 2016.

Thyroid cancer[6]

- **Starting at age 18 or 5 years before the earliest age of diagnosis of cancer in the family:** Comprehensive physical exam by your provider every year, with particular attention to examining the thyroid.
- Thyroid ultrasound every year.

Kidney cancer[6]

- **Starting at age 40:** Your healthcare provider may discuss a renal (kidney) ultrasound every 1-2 years.

Colorectal cancer[6]

- **Starting at age 35, or 5-10 years younger than the earliest diagnosed colorectal cancer in the family, if under age 40:** Colonoscopy every five years, or more frequently if polyps are found or symptoms of colorectal cancer arise.

Melanoma[6,7]

- Your provider may discuss a skin exam every year.
- To reduce the chance of developing melanoma, the American Cancer Society recommends limiting exposure to UV light by avoiding excess sun exposure, wearing a hat, sunglasses and long protective clothing, applying sunscreen with SPF of 30 or higher and avoiding tanning beds and sun lamps.
- Any new, unusual, or changing moles should be reported to your provider or dermatologist.

Men

Thyroid cancer[6]

- **Starting at age 18 or 5 years before the earliest age of diagnosis of cancer in the family:** Comprehensive physical exam by your provider every year, with particular attention to examining the thyroid.
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Kidney cancer[6]

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- **Starting at age 35, or 5-10 years younger than the earliest diagnosed colorectal cancer in the family, if under age 40:** Colonoscopy every five years, or more frequently if polyps are found or symptoms of colorectal cancer arise.

[7] Skin Cancer Prevention and Early Detection. The American Cancer Society. Available at www.cancer.org. Updated 3/20/2015. Accessed April 2015.

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Useful resources

FORCE
Providing support, education, research, and resources for survivors and people at increased risk of cancer due to an inherited mutation or family history of cancer.
www.facingourrisk.org

PTEN Foundation
Founded with a mission to educate about PTEN syndromes, provide financial support to patients, support research, and to promote awareness.
www.ptenfoundation.org

Hereditary Colon Cancer Foundation
A nonprofit organization serving the hereditary colorectal cancer community.
www.hcctakesguts.org

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