Cowden Syndrome

Cowden syndrome, also known as **Cowden disease** or **multiple hamartoma syndrome**, is a rare inherited condition with benign (non-cancerous) growths in different parts of the body, as well as an increased risk for some types of cancer. CS belongs to a family of syndromes called the **PTEN hamartoma tumor syndromes**.

What are the effects of Cowden syndrome?

People with Cowden syndrome can have different types of benign growths (many of which are hamartomas). These are most often found on the skin and in the lining of the mouth and nose, but they can appear in other parts of the body as well. Benign growths in people with Cowden syndrome can include:

- **Trichilemmomas:** benign, wart-like growths that start in hair follicles, most often on the face.
- **Oral papules** (raised bumps) **or fibromas** (hard, smooth growths that resemble scar tissue) inside the mouth or on the lips.
- **Keratoses** (rough, scaly skin growths) on the surfaces of the hands or feet.

People with Cowden syndrome also have an increased risk for certain types of cancer, including breast, thyroid, endometrial, colon, rectal, kidney, and skin cancers. They're also more likely to develop these cancers at a younger age, as well as to develop more than one cancer during their lifetime.

Some people might be described as having **Cowden-like syndrome** if they have some of the characteristic features of Cowden syndrome, such as developing cancers at a young age, but they don't meet the criteria for a diagnosis of Cowden syndrome (see below).

What causes Cowden syndrome?

Most often, Cowden syndrome is caused by an inherited change in the *PTEN* gene. The *PTEN* gene is a tumor suppressor gene[1]. It normally makes a protein that helps keep cell growth under control, which helps keep tumors from forming. When the *PTEN* gene is mutated, its tumor suppressing function is lost, allowing tumors to form.

Most people with Cowden syndrome inherit a mutated *PTEN* gene from either parent. If a person has Cowden syndrome, they have a 50/50 chance of passing the *PTEN* gene mutation on to each of their children. However, in some people with Cowden syndrome, the gene mutation isn't inherited from a parent. Instead, it's a random event that happens very early in life (possibly even before birth). It can then be passed down to that person's children.

Inherited changes in some other genes, such as the *KLLN* and *WWP1* genes, are also thought to cause Cowden syndrome in some families.

Options exist for people who carry a *PTEN* gene mutation and might want to have children. For more information, talk with an assisted reproduction specialist at a fertility clinic.

How common is Cowden syndrome?

Cowden syndrome is thought to be rare, although it is probably under-diagnosed. It is estimated that Cowden syndrome affects about 1 in every 200,000 to 250,000 people.

How is Cowden syndrome diagnosed?

People are diagnosed with Cowden syndrome based mainly on sets of major and minor diagnostic criteria. There are different sets of criteria. The criteria used by the National

Comprehensive Cancer Network (NCCN) is shown here:

A person with no family history of Cowden syndrome can be diagnosed with Cowden syndrome if they have:

- 3 or more major criteria (1 of which must be either macrocephaly, Lhermitte-Duclos disease (a rare, benign type of brain tumor), or gastrointestinal hamartomas)

OR

- At least 2 major and 3 minor criteria

Major criteria

- Breast cancer[2]
- Endometrial cancer[3] (epithelial)
- Thyroid cancer[4] (follicular)
- Gastrointestinal hamartomas or ganglioneuromas (more than one)
- Lhermitte-Duclos disease
- Macrocephaly (enlarged head size)
- Macular pigmentation (discolored area) of glans penis
- Mucocutaneous (skin or mucous membrane) lesions, such as trichilemmomas, acral keratoses, mucocutaneous neuromas, oral papillomas

Minor criteria

- Colon cancer[5]
- Esophageal glycogenic acanthoses (at least 3)
- Autism spectrum disorder
- Intellectual disability
- Thyroid cancer (papillary or follicular variant of papillary)
- Thyroid structural lesions (such as an adenoma or nodules)
- Renal cell carcinoma (kidney cancer[6])
- Vascular abnormalities, such as intracranial developmental venous anomalies
- Lipomas (benign fatty tumors)
- Testicular lipomatosis

People who meet these criteria are typically referred for genetic testing to determine if they carry a *PTEN* gene mutation.

What types of cancer are linked to Cowden syndrome?

The greatest cancer risk for people with Cowden syndrome is **female breast cancer**. The lifetime risk of breast cancer for a woman with Cowden syndrome is estimated to be in the range of 25% to 50%. Breast cancer may develop earlier in women with Cowden syndrome than in the general population.

The risk of **thyroid cancer** in people with Cowden syndrome is estimated to range from 3% to 38%. People with Cowden syndrome most commonly have the follicular type of thyroid cancer, but they may also have the papillary type.

- The risk of developing **kidney cancer** is in the range of 2% to 5%.
- The risk for **endometrial cancer** for females with Cowden syndrome is in the range of 13% to 30%.
- The risk for **colorectal cancer** is in the range of 5% to 10%, and it often occurs at a younger age than compared to the general population.

The risk for melanoma of the skin[7] for people with Cowden syndrome is thought to be about 6%. It is important to be aware of this risk because steps can be taken to lower risk as early as childhood by using sunscreen and protective clothing[8].

What are the cancer screening recommendations for people with Cowden syndrome?

Because people with Cowden syndrome have an increased risk for some types of cancer, medical experts typically recommend getting screened for these cancers, often starting at an early age. For example, experts from the NCCN recommend the following:

- Get screened for breast cancer (for females) with yearly mammograms[9] and breast MRI[10], starting at age 30, or 10 years before the earliest known breast cancer in the family (whichever comes first). Breast self-awareness and clinical breast exams should start even earlier.
- Get screened for colorectal cancer (with colonoscopy[11]) every 5 years, starting at age 35, or 5-10 years before the earliest known colorectal cancer in the family (whichever comes first).

- Consider screening for endometrial cancer (for females), starting at age 35.
- Consider screening for kidney cancer, starting at age 40.
- Get yearly skin exams.
- Get yearly thyroid ultrasound exams, starting at age 7.
- Get a yearly full physical exam, starting at age 18 or 5 years before the earliest known cancer in the family (whichever comes first).

Screening options may change over time as new technologies are developed and more is learned about Cowden syndrome. It's important to discuss the best cancer screening options for you with your health care team, as each person is different.

Questions to ask the health care team

If you are concerned about your risk of cancer, talk with your health care team. It can be helpful to bring someone along to your appointments to take notes. Consider asking your health care team the following questions:

- What is my risk of developing cancer?
- Is there anything I can do to lower my risk of cancer?
- What cancer screening tests should I get? When should I start getting screened?

If you're concerned about your family history and think your family may have Cowden syndrome, consider asking the following questions:

- Does my family history increase my risk of developing cancer?
- Could my family carry the gene for Cowden syndrome?
- Should I meet with a genetic counselor for a hereditary cancer risk assessment[12]? Can you refer me to one?

Hyperlinks

1. www.cancer.org/cancer/understanding-cancer/genes-and-cancer/oncogenes-tumor-suppressor-genes.html
2. www.cancer.org/cancer/types/breast-cancer.html
3. www.cancer.org/cancer/types/endometrial-cancer.html

4. www.cancer.org/cancer/types/thyroid-cancer.html
5. www.cancer.org/cancer/types/colon-rectal-cancer.html
6. www.cancer.org/cancer/types/kidney-cancer.html
7. www.cancer.org/cancer/types/melanoma-skin-cancer.html
8. www.cancer.org/cancer/risk-prevention/sun-and-uv/uv-protection.html
9. www.cancer.org/cancer/types/breast-cancer/screening-tests-and-early-detection/mammograms.html
10. www.cancer.org/cancer/types/breast-cancer/screening-tests-and-early-detection/breast-mri-scans.html
11. www.cancer.org/cancer/diagnosis-staging/tests/endoscopy/colonoscopy.html
12. www.cancer.org/cancer/risk-prevention/genetics/genetic-testing-for-cancer-risk.html

References

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):255-263.

MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US). Cowden syndrome. 2021. Accessed at https://medlineplus.gov/genetics/condition/cowden-syndrome on January 24, 2024.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 2.2024. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf on January 24, 2024.

Nelen MR, Kremer H, Konings IB, et al. Novel PTEN mutations in patients with Cowden disease: Absence of clear genotype-phenotype correlations.

Eur J Hum Genet. 1999;7(3):267-273.

Pilarski R, Burt R, Kohlman W, et al. Cowden syndrome and the PTEN hamartoma tumor syndrome: Systematic review and revised diagnostic criteria. *J Natl Cancer Inst*. 2013;105(21):1607-1616.

Pilarski R, Stephens JA, Noss R, Fisher JL, Prior TW. Predicting PTEN mutations: An evaluation of Cowden syndrome and Bannayan-Riley-Ruvalcaba syndrome clinical

features. *J Med Genet*. 2011;48(8):505-512.

Stanich PP, Roberts ME. PTEN hamartoma tumor syndromes, including Cowden syndrome. UpToDate. 2023. Accessed at https://www.uptodate.com/contents/pten-hamartoma-tumor-syndromes-including-cowden-syndrome on January 24, 2024.

Tan MH, Mester JL, Ngeow J, et al. Lifetime cancer risks in individuals with germline PTEN mutations. Clin Cancer Res. 2012;18(2):400-407.

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Written by

American Cancer Society medical and editorial content team
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