

Cowden Syndrome

What is Cowden syndrome?

Cowden syndrome (CS) is a genetic condition, meaning that it can be passed to a child from their mom or dad. A person with CS has an increased risk of developing a variety of benign (non-cancerous) and cancerous tumors. People with CS are at increased risk to develop thyroid cancer. Women with CS also have an increased risk of developing breast and uterine cancer. Many different benign tumors are also common in people with CS.

Cowden syndrome is sometimes called PTEN Hamartoma Tumor Syndrome or PHTS. There is also a rare type of CS that is called Bannayan-Ruvalcaba-Riley syndrome.

What are the signs and symptoms of CS?

Many signs and symptoms **can** be associated with CS. However, CS affects each person differently and most people with CS have some of these symptoms, but not all. Symptoms include the following.

- Learning disabilities, autism and/or intellectual disability
- Large head size
- Certain types of lesions or papules (bumps) on the skin. A dermatologist can recognize the most common, including:
 - Trichilemmomas on the face
 - Papillomatous lesions, particularly if they are on the face and/or mucous membranes (such as gums). A “cobblestone” appearance on the tongue or gums may happen.
 - Keratoses (hard growths on the skin) found on the palms of the hands or soles of the feet
- High risk of developing tumors, both benign and cancerous. For more information see the next section.

What are the cancer risks with CS?

CS is a rare condition. Because it is rare, researchers are still learning about the specific cancer risks caused by CS. If you have CS, it is important that you stay in contact with your genetics clinic so that you can stay informed about new developments. The estimated cancer risks with CS are listed below.

Women:

- Have a 25-50% lifetime risk to develop breast cancer. More recent studies suggest the lifetime risk can be as high as 85% to develop breast cancer. This is higher than the average woman’s lifetime risk of about 12%. Women with CS are also more likely to develop breast cancer at a younger age (38-50 years of age) than average.
- Have an increased chance of developing endometrial (uterine) cancer.

Men and Women:

- Have about a 10-35% lifetime risk to develop thyroid cancer, compared to less than 1% in the general population. The thyroid is a gland in the base of the throat that helps to make hormones. There are different types of thyroid cancer. Follicular thyroid cancer is the most common type associated with CS. Medullary thyroid cancer is never associated with CS.
- May be at increased risk for other types of cancers, such as kidney and colon cancer.
- Rarely, a type of brain tumor called Lhermitte-Duclos disease occurs in adults with CS.

What are the benign tumor risks with CS?

People with CS may have an increased chance to develop the following benign tumors, which are also common in the general population.

- A goiter (enlarged thyroid) or a benign tumor in the thyroid
- Polyps in the stomach, small intestine or colon
- Uterine fibroids (growths in the uterus)
- Fibrocystic breast changes (a feeling of lumps and or tenderness in the breasts)
- Lipomas (benign fatty tumors) and fibromas (benign tumors of connective tissue)

What causes CS?

Genetic conditions are caused by changes in a person's genes. These gene changes are called mutations. Genes are the body's instruction manual that tell the body how to grow and develop. Every person has thousands of genes. If a person is born with a mutation in one of their genes, then this gene may not work correctly and can cause medical problems.

The gene that causes CS is called *PTEN*. Every person has two copies of this gene. When both copies of *PTEN* work correctly, they help the body prevent tumors from forming. However, when a person is born with a mutation in one of their *PTEN* genes, they are at high risk to develop tumors. These tumors may be cancerous or benign. A mutation in *PTEN* can also cause the other signs and symptoms of CS.

What are the chances of inheriting CS?

The parents of a person with CS may or may not have CS. It is possible for a person to be born with CS and to be the first person in their family with the *PTEN* mutation (this happens in more than half of cases). However, a person with CS has a 50% (1 out of 2) chance of passing CS onto each of his or her children. Although CS cannot skip generations, each person is affected differently by CS. In addition, both men and women are equally likely to inherit CS from a parent.

Why is it important to diagnose CS?

A person with CS is at increased risk to develop cancer. Even if a person with CS already has cancer, there is a risk that a second cancer may develop. A more aggressive cancer screening schedule can help to prevent or detect cancer at an earlier stage.

CS is a genetic condition, so other family members of the person with CS are also at risk. Therefore, family members may also benefit from screening. Sometimes genetic testing can identify the *PTEN* mutation that caused CS. In this case, genetic testing can identify family members who will need screening and those who will not.

How is CS diagnosed?

Usually, the first steps in figuring out if someone has CS are:

- A physical exam – including a skin check by a dermatologist who is familiar with CS.
- Family history – a genetic counselor will ask the person for a detailed family history in order to find signs of CS in the family.

If the evaluations show signs of CS, then *PTEN* genetic testing is usually the next step. The test, which requires a blood sample, examines the *PTEN* gene and may detect a mutation. If a *PTEN* mutation is found, then the person has CS. But the genetic test is not perfect, so if a *PTEN* mutation is not found, the person could still have CS. A doctor who is familiar with genetics or a genetic counselor can best understand and explain the test results.

If a *PTEN* mutation is found, then family members of a person with CS may request predictive testing. Predictive testing helps determine which family members are at risk for developing tumors associated with CS and which ones have the same risk as the general population. Healthy family members who are found to have a *PTEN* mutation can take advantage of cancer screenings and other cancer prevention measures.

How is CS managed?

There is no cure for CS. Because cancer is the major health risk associated with CS, it is important to follow cancer prevention and early detection screening guidelines. Cancer screening exams are medical tests performed when a person has no symptoms. These tests help detect cancer at the earliest, most treatable stage. Screening for people with CS is outlined below.

Breast Cancer Screening (Women)

- Monthly self-breast exams (patient checks herself)
- Breast exam by a medical provider every 6 months, beginning at age 25 years
- Yearly mammogram and yearly breast MRI (imaging tests) beginning at age 30-35 years
- Women with CS may consider having preventive surgery (removing the breasts before cancer develops).

Thyroid Cancer Screening (Men and Women)

Yearly thyroid ultrasound (imaging test) once an individual is diagnosed with CS.

Other Screenings

- Yearly comprehensive physical exam starting at age 18
- Consider a yearly skin exam by a dermatologist
- Women with CS should consult a gynecologist or gynecologic oncologist about their uterine

cancer risk. A doctor can explain options for screening or preventive surgery (removing the uterus before cancer develops).

- Colonoscopy, an exam of the inner lining of the large intestine (colon and rectum), every 5 years, beginning at the age of 35 (may be more frequent if polyps are found on colonoscopy)
- Consider a kidney ultrasound (imaging test), every 1-2 years, beginning at age 40 years
- Consider cognitive and motor assessment in children at time of diagnosis.

Where can I find more information?

Genetic Alliance

202-966-5557

<http://www.geneticalliance.org>

This organization provides support to individuals and families with genetic conditions. A helpline is available to answer questions.

American Cancer Society

800-ACS-2345 (800-227-2345)

www.cancer.org

The American Cancer Society (ACS) is a voluntary national health organization with local offices around the country. The ACS supports research, provides information about cancer, and offers many programs and services to patients and their families.

Cancer Information Service

800-4-CANCER (800-422-6237)

www.cancer.gov

The Cancer Information Service (CIS) is a program of the National Cancer Institute. People who call the CIS speak with highly trained information specialists who can answer questions about cancer screening tests, risks, symptoms, how cancer is diagnosed and the latest treatments.

Susan G. Komen Breast Cancer Foundation

800-462-9273

www.breastcancerinfo.com

The Komen Foundation answers questions from recently diagnosed breast cancer patients and provides emotional support. Information is available in Spanish.

National Society of Genetic Counselors, Inc. (NSGC)

312-321-6834

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www.nsgc.org

This professional organization helps consumers find local genetic counseling services.