

Cowden Syndrome

What is Cowden Syndrome?

Cowden syndrome (CS) is a genetic condition, meaning that it can be passed to an individual through their blood relatives. A person with CS has an increased risk to develop a variety of tumors. These tumors may or may not be cancerous. Individuals with CS are at increased risk to develop thyroid cancer and women with CS are also at increased risk to develop breast or uterine cancer. Many different benign (non-cancerous) tumors are also common in individuals with CS.

What are the signs and symptoms of Cowden syndrome?

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

- High risk of developing tumors, both benign and cancerous (see section below)
- Large head size
- Cobblestone appearance of the tongue
- Keratoses (hard growths on the skin) found on the arms, legs, palms of the hands, or soles of the feet
- Mental retardation

What are the cancer risks with Cowden syndrome?

- Women with CS:
 - Have a 25 to 50% lifetime risk to develop breast cancer, compared to 12% in the general population. (See Figure 1 on page 2.) On average, women are diagnosed between the ages of 38 and 46. Although the risk is low, men with Cowden syndrome occasionally develop breast cancer.
 - Have a 5 to 10% lifetime risk to develop uterine (endometrial) cancer, compared to 2 to 3% in the general population.
- Individuals with CS have approximately a 10% 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.
- Other cancers that occur less commonly in individuals with CS include skin cancer and kidney cancer.

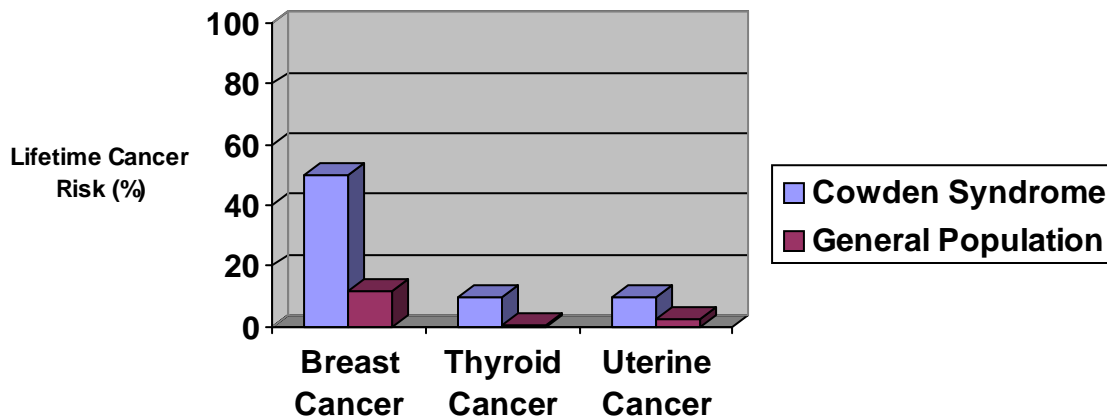


Figure 1

What are the benign tumor risks with Cowden Syndrome?

- Women have up to a 67% risk to develop benign breast disease (fibrocystic breast disease).
- Individuals with CS may develop:
 - A goiter (enlarged thyroid) or a benign tumor in the thyroid (75% risk)
 - Polyps in the stomach, small intestine, or colon (60% risk)
 - Uterine fibroids
 - Trichilemmomas and papillomas (small growths) are often found on the face or in the mouth
 - Lipomas (benign fatty tumors) and hemangiomas (benign tumor in a blood vessel)
 - Other benign tumors that occur less commonly in CS include tumors of the central nervous system, including brain tumors. Lhermitte-Duclos disease sometimes occurs and involves tumors in the nerve cells of the cerebellum, a region in the brain. This may lead to seizures, tremors, or poor coordination.

What causes Cowden syndrome?

Genetic conditions are caused by changes in a person's genes. These gene changes are called mutations. Genes are the body's instruction manuals 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 PTEN. 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 Cowden syndrome?

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 to have the PTEN mutation (this happens more than 50% of the time). However, a person with CS has a 50% (1 out of 2) chance of passing CS onto each of their children. Cowden syndrome cannot skip generations. In addition, both men and women are equally likely to be affected.

Why is it important to diagnose Cowden syndrome?

An individual with CS is at increased risk to develop tumors, some of which are cancerous. Even if an individual with CS already has cancer, there is a risk that they may develop a second cancer. A more aggressive cancer screening schedule can help a person with CS prevent cancer or to detect it at an early stage.

Because CS is a genetic condition, other family members of the person with CS are also at risk. Therefore, his or her 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 Cowden syndrome diagnosed?

CS is diagnosed two ways. Most people are diagnosed clinically, which is a diagnosis based upon their signs and symptoms. Factors influencing a clinical diagnosis include: the type, number, and location of different lesions on the skin and in the mouth and the combination of cancerous and benign tumors. A clinical diagnosis may also take into account the person's family history. Individuals with CS are each affected differently. Therefore, an individual who may have CS needs careful evaluation to determine if his or her symptoms meet the clinical criteria.

The second way to diagnose CS is through PTEN genetic testing. The genetic test, which requires a blood sample, examines the PTEN gene and may detect a mutation. Approximately 80% of individuals who have a clinical diagnosis are found to have a PTEN mutation. This means that if the test is unable to identify a genetic mutation, a person may still have CS. Negative test results are best interpreted by a physician who is familiar with genetics or by a genetic counselor.

A person is diagnosed with CS if a mutation in the PTEN gene is identified. Family members of person with CS can have predictive testing. Predictive testing helps determine which family members are at risk to develop the tumors associated with CS and which ones have the same risk

as the general population. Healthy family members who have a PTEN mutation can take advantage of cancer screenings and other cancer prevention measures.

How is Cowden syndrome managed?

There is no cure for CS. Because cancer is the major health risk associated with CS, it is important to screen for cancer by following cancer prevention and early detection guidelines. Cancer screening examinations are medical tests performed when a person has no symptoms. These tests help ensure that cancers are detected at their earliest, most treatable stages. Screening options include:

Breast Cancer Screening

- Men and women: Monthly self breast examinations
- Women: Yearly clinical breast examinations beginning at age 25 years
- Women: Yearly mammography beginning at age 30 to 35 years (or 5 to 10 years before the youngest breast cancer diagnosis in the family)

Thyroid Cancer Screening

- Men and women: Baseline thyroid ultrasound beginning at age 18; yearly thyroid ultrasound may be considered thereafter

Uterine Cancer Screening

- Women: Yearly uterine biopsies starting at age 35 to 40
- Women: Yearly endometrial ultrasound after menopause with biopsy of any suspicious lesions

Kidney Cancer Screening

- Men and women: If there is a family history of kidney cancer, yearly urine analysis, urine cytology, and kidney ultrasound is recommended

Where can I find more information?

Cowden Syndrome Foundation

The CS Foundation provides communication between patients and family members affected by CS. Provides information about CS and available clinical trials.

<http://groups.msn.com/cowdenssyndrome/welcome.msnw>
(734) 944-8313

Genetic Alliance

An organization that provides support to individuals and families with genetic conditions. A helpline is available for people with genetic questions.

(202) 966-5557

<http://www.geneticalliance.org>

American Cancer Society

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.

(800) ACS-2345 (1-800-22702345)

www.cancer.org

Cancer Information Service

The Cancer Information Service (CIS) is a program of the National Cancer Institute (NCI). 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.

(800) 4-CANCER (1-800-422-6237)

www.cancer.gov

Susan G. Komen Breast Cancer Foundation

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

(800) 462-9273

www.breastcancerinfo.com

National Society of Genetic Counselors, Inc. (NSGC)

This professional organization has developed a resource that enables consumers to locate local genetic counseling services.

(610) 872-7608

FYI@nsgc.org

www.nsgc.org