

# Cowden Syndrome

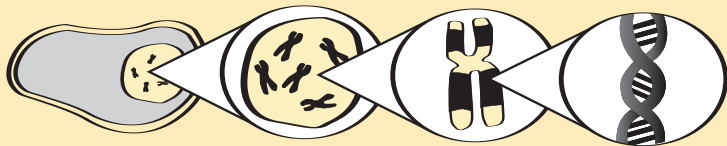
## What is Cowden Syndrome?

Cowden syndrome is a rare genetic condition, affecting around one out of every 200,000 people. Cowden syndrome can cause a variety of non-cancerous growths, such as fibrocystic breasts, thyroid nodules and goiters, uterine fibroids and polyps in the intestines (a type called a hamartoma). Cowden syndrome also causes skin growths that occur on the face, tongue, mouth and hands. These include papillomatous papules (skin-colored bumps), trichilemmomas (benign tumors of the hair root), and lipomas (fatty growths under the skin). In addition, many people with Cowden syndrome have pitting and/or keratoses (dark flat spots) on their hands and feet. Other signs of Cowden syndrome include a large head size.

Cancers of the breast and thyroid can be caused by Cowden syndrome. Other cancers that may be seen more frequently in people with Cowden syndrome are uterine (endometrial) cancer, kidney cancer (a type called renal cell carcinoma) and melanoma skin cancer.

## How is Cowden Syndrome inherited?

Inherited information is contained in every cell in our body, in structures called chromosomes. We have 46 chromosomes, which come in pairs; 23 from our mother and 23 from our father. Each chromosome is made up of thousands of genes. Genes, like chromosomes, come in pairs. They are packages of genetic information (DNA) that act as instructions for making the substances that help our bodies function properly. An alteration in this genetic information can interfere with proper body functions by causing the gene to no longer work. These gene alterations are called mutations.



Cowden syndrome is caused by mutations in the *PTEN* gene which controls cell growth and division. If there is a mutation in the *PTEN* gene, it can no longer control cell growth and division. For this reason, people with mutations in the *PTEN* gene tend to develop the characteristic benign growths, as well as having an increased risk for certain cancers.

## What are the chances of inheriting an altered *PTEN* gene?

The *PTEN* gene is inherited in an “autosomal dominant” pattern. Autosomal means that both men and women can inherit a *PTEN* gene mutation. Dominant means that it takes only one *PTEN* gene mutation to have Cowden syndrome. All people have two copies of the *PTEN* gene, one from each parent. A person who has a parent with a Cowden syndrome mutation may inherit either the parent’s *PTEN* gene with the mutation or the parent’s working *PTEN* gene. Therefore, that individual has a 50 percent chance of inheriting the *PTEN* gene mutation and would then have Cowden syndrome and the increased likelihood for developing certain cancers. That person also has a 50 percent chance of not inheriting the *PTEN* gene mutation and would not have Cowden syndrome or any increased risk for developing cancer.

## How are *PTEN* gene mutations detected?

It is possible to test for *PTEN* mutations using a blood sample. Once a mutation has been found in the *PTEN* gene, the laboratory can look for that same mutation in other family members. Research and clinical genetic testing for the *PTEN* gene are available.

## Is it possible to receive an unclear *PTEN* test result?

About 5-10 percent of people who have *PTEN* testing are found to have an unclear result. This means that the person is found to have a gene alteration, but it is not clear if it causes Cowden syndrome or not. In many cases, it may take years, if ever, before we know the meaning of this type of result.

Please feel free to contact the  
Clinical Cancer Genetics Program at  
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if you have any additional questions.  
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## What if testing does not detect an altered *PTEN* gene?

Negative results (meaning a *PTEN* mutation is not found) can mean several things. First, it might mean that there is a *PTEN* gene mutation that cannot be located by current testing methods. Twenty percent of people with a diagnosis of Cowden syndrome will *not* have a mutation detected in the *PTEN* gene when genetic testing is done. This is a limitation of many genetic tests. It could also mean that a different gene is responsible for the cancers or medical problems in the family. For this reason, families who test negative for the *PTEN* gene may be interested in pursuing testing for other genes as they are discovered in the future. It is also possible that the cancers or medical problems in the family are not hereditary. On the other hand, if one member of a family has already been found to have a *PTEN* gene mutation, a negative result in another relative means that relative does not have Cowden syndrome.

## What if testing reveals that a person has inherited an altered *PTEN* gene?

People with a *PTEN* gene mutation are at risk for the non-cancerous growths discussed above. Women with Cowden syndrome have a 25 to 50 percent lifetime risk for developing breast cancer, with an average age of diagnosis between ages 38 and 46. Men with Cowden syndrome may have a slightly increased risk for breast cancer, too. The lifetime risk for thyroid cancer for men and women with Cowden syndrome is around 10 percent. The third most common cancer in Cowden syndrome is endometrial (uterine) cancer. Although, the exact lifetime risk for endometrial cancer among women with Cowden syndrome is less well known, it may be about 5 percent.

## If a person has an altered *PTEN* gene, what are the options for cancer screening and prevention?

Women with Cowden syndrome should have increased breast cancer screening, including monthly breast self-examination beginning at age 18, clinical breast exams every 6–12 months beginning at age 25, and annual mammography and breast MRI beginning at age 30. We recommend that men with Cowden syndrome perform monthly breast self-examination as well.

Women who may have Cowden syndrome should also receive endometrial cancer screenings. This consists of annual random endometrial biopsies beginning around age 35. After menopause, endometrial cancer screening should consist of annual transvaginal ultrasound with biopsy of suspicious areas.

People with Cowden syndrome should have a baseline thyroid ultrasound at age 18, followed by an annual thyroid examination by an endocrinologist. It is likely that some nodules will be seen on ultrasound because they are common in Cowden syndrome, but an expert will be able to determine whether or not they are benign.

Although kidney cancer is rare in Cowden syndrome, we recommend that people at risk for Cowden syndrome receive an annual urinalysis (to test for blood in the urine) and consider renal (kidney) ultrasounds. We also recommend an annual dermatology examination to detect any skin cancers at an early stage.

## What are the possible risks and benefits of *PTEN* testing?

The only physical risks of testing are those of a routine blood draw. However, other risks and benefits should be considered before undergoing testing. The process of genetic testing may be emotionally difficult, regardless of whether a *PTEN* mutation is found. Finding a gene mutation may indirectly provide information about other family members, who may have chosen not to be tested. In addition, costs for the cancer screening and prevention options for a person with Cowden syndrome may or may not be covered by their health insurance. Another issue with genetic testing is the possibility that the results could be used by an employer or insurance company to discriminate against a person. Health insurance companies in Ohio are not permitted to use pre-symptomatic genetic test results, such as *PTEN* gene testing, to affect health insurance coverage for people with group or self-insurance. Specifically, under the Ohio law, health insurance companies are not permitted to request the results of genetic testing or use that information in determining whether to insure a person, renew or cancel a policy, or limit benefits. However, the law does not prohibit insurers from raising the insurance premiums of people with self-insurance, or of the whole group for a group plan, on the basis of genetic test results. The Ohio law is in effect until 2014. A national law also specifies that pre-symptomatic genetic conditions cannot be considered a “pre-existing” condition by group health insurers (this law does not apply to self-insurers). While a single individual in a group plan cannot have their premiums raised, the federal law does not prohibit group insurers from raising the premiums of an entire group. Additionally, the ability to obtain life and disability insurance are not protected by any laws.

## What are the possible benefits of *PTEN* testing?

One of the major advantages of learning *PTEN* gene test results is reduced uncertainty about the risks of cancer and other Cowden syndrome-related problems for people and their families. In addition, the testing may allow doctors to modify medical care to decrease the risk of cancer. Likewise, if *PTEN* testing is negative, it may allow doctors to decrease the frequency of cancer screening.

The decision to have *PTEN* testing is a complicated one. People and families must not only weigh the risks and benefits of testing, they must also consider their unique situations. Ultimately, people must make their own decisions.