# Cowden Syndrome [1]

**What is Cowden syndrome?**

Cowden syndrome (CS) is part of the PTEN hamartoma tumor syndrome. Hamartomas are benign (noncancerous) tumor-like growths. Other clinical syndromes that are part of the PTEN hamartoma tumor syndrome are Bannayan-Riley-Ruvalcaba syndrome (diagnosed in children), Proteus syndrome, and Proteus-like syndrome. CS is characterized by a high risk of both benign (noncancerous) and cancerous tumors of the breast [2], thyroid [3], endometrium [4] (uterus), colorectal [5], kidney [6], and skin (melanoma [7]).

Other key features of CS are skin changes (such as trichilemmomas [skin tags] and papillomatous papules) and macrocephaly (larger than average head size).

**How is CS diagnosed?**

The diagnostic criteria for CS are complex and reviewed by geneticists (health professionals with specialized training in medical genetics) frequently as new information becomes available. Sometimes CS is difficult to diagnosis. That?s why teams of hereditary cancer risk specialists including oncologists (cancer doctors), geneticists, genetic counselors, and nurses certified in hereditary cancer have worked together to create diagnostic categories (termed major and minor criteria) summarized in the National Comprehensive Cancer Network (NCCN) guidelines.

Below are the current major and minor criteria as well as the testing criteria for Cowden syndrome:

**Major criteria:**

Breast cancer [2]

Endometrial cancer [4]

Follicular thyroid cancer [3]

Multiple gastrointestinal hamartomas or ganglioneuromas

Macrocephaly

Macular pigmentation of glans penis (a discolored area on the skin)

Mucocutaneous lesions

One biopsy proven trichilemmoma

Multiple palmoplantar keratosis (abnormal thickening of the hands and feet)

Multifocal or extensive oral mucosal papillomatosis

Multiple cutaneous facial papules (often verrucous)

**Minor Criteria:**

Colon cancer [5]

Esophageal glycogenic acanthosis (3)

Autism spectrum disorder

Mental retardation

Papillary or follicular variant of papillary thyroid cancer [3]

Thyroid structural lesions (such as, adenoma, nodule(s), goiter)

Renal cell kidney carcinoma [6]

Vascular anomalies (including multiple intracranial developmental venous anomalies)

Lipomas (benign soft tissue tumor)

Single gastrointestinal hamartoma or ganglioneuroma

Testicular lipomatosis

**Cowden Syndrome PTEN Gene Testing Criteria**

Individuals with a personal history of:

A family with a known PTEN gene mutation

Meeting clinical diagnostic criteria for CS

Bannayan-Riley-Ruvalcaba syndrome (BRR)

Adult Lhermitte-Duclos disease (cerebellar tumors)

Autism spectrum disorder and macrocephaly

Two or more biopsy-proben trichilemmomas

Two or more major criteria (one must be macrocephaly)

*Source: Eng C. Will the real Cowden syndrome please stand up: revised diagnostic criteria. Med Genet 2000;37:828-830.*

CS is suspected if a person has either three major criteria without macrocephaly, one major and three minor criteria, four minor criteria, or a relative with a clinical diagnosis of CS or BRR.

Research is ongoing to better understand CS. Approximately 80% of the people who meet the current clinical diagnosis of CS will have a mutation in the *PTEN* gene. A blood test can determine if someone has a mutation in the *PTEN* gene. If a person has a mutation in the *PTEN* gene, he or she has CS.

**How is CS inherited?**

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. CS follows an autosomal dominant inheritance pattern in which a mutation in only one copy of the gene can cause the Cowden syndrome. This means that a parent with a gene mutation may pass along a copy of their normal gene or a copy of the gene with the mutation. It takes only one copy of the gene with the mutation to have the disease. Therefore, a parent with a mutation in the PTEN gene has a 50% chance of passing the mutation to their child with each pregnancy. A brother, sister, or parent of a person who has a mutation also has a 50% chance of having inherited the same gene mutation. Learn more about genetics. [8]

Options exist for couples interested in having a child when they know that one of them carries a gene mutation that increases the risk for this hereditary cancer syndrome. Preimplantation Genetic Diagnosis (PGD) is a medical procedure done in conjunction with in-vitro fertilization (IVF). It allows people who carry a specific known genetic mutation to have children who do not carry the mutation. A woman?s eggs are removed and fertilized in a laboratory. When the embryos reach a certain size, one cell is removed and is tested for the hereditary condition in question. The parents can then choose to transfer embryos which do not have the mutation. PGD has been in use for over a decade, and more recently has been used for several hereditary cancer predisposition syndromes. For more information, talk with an assisted reproduction specialist at a fertility clinic.

**How common is CS?**

CS is thought to be rare, although it is probably under-diagnosed. It is estimated that CS affects about one in every 200,000 individuals.

**What are the estimated cancer risks associated with CS?**

- The greatest cancer risk for a woman with CS is breast cancer [2]. The lifetime risk for a woman with CS to develop breast cancer is estimated to be 85%. Breast cancer may develop earlier in women with CS than the general population. There is also an increased risk for a

second breast cancer in the opposite breast and some increased risk of breast cancer in men [9] with CS, but the specific risk is not known.

- The risk of thyroid cancer [3] in men and women with CS is estimated to be 35%. Thyroid cancer in CS is most commonly the follicular type but may also be the papillary type.
- The risk to develop kidney cancer [6] is 33% and it is one of the highest cancer risks for those with a PTEN mutation.
- The risk of endometrial cancer [4] in women with CS is 28%.
- The risk for colorectal cancer [5] is 9% and often occurs at a younger age than compared to the general population.
- The risk for melanoma [7] is 6%. It is important to be aware of this risk because prevention can begin in childhood by using sunscreen and protective clothing [10] to reduce the number of blistering burns before age 20. Melanoma is a cancer that is influenced by multiple factors including skin color, and eye and hair color, as well as sun exposure and in some cases, inherited gene mutations. If a person tests negative for a PTEN gene mutation that has previously been identified in their family, they may still have risk factors that increase their risk of melanoma.
- Many other types of cancer have been seen in people with CS. It is not yet known if the risk of these cancers is increased in people with CS. The list reported includes liver cancer [11], pancreatic cancer [12], ovarian cancer [13], bladder cancer [14], basal cell and squamous cell skin cancers [15], Merkel cell skin cancer, brain cancer [16], liposarcoma [17], and non-small cell lung cancer [18].

**What are the screening options for CS?**

It is important to discuss with your doctor the following screening options, as each individual is different:

| | | | |
|---|---|---|---|
| **From diagnosis:** | • Annual thyroid ultrasound<br>• Annual skin exam | • Annual thyroid ultrasound<br>• Annual skin exam | • Annual thyroid ultra<br>• Annual skin exam |
| **From age 30** | • N/A | • N/A | • Annual mammogra<br>• Consider annual b dense breasts<br>• Annual endometria transvaginal ultras 5 years before age uterine cancer in th |
| **From age 40** | • N/A | • Colonoscopy every 2 years<br>• Kidney ultrasound or MRI every 2 years | • Colonoscopy every<br>• Kidney ultrasound 2 years |

| | | | |
|---|---|---|---|
| **Preventive surgery** | • N/A | • N/A | • Individual discussi preventive mastec hysterectomy |

*Source: Min-Han Tan, Jessica L. Mester, Joanne Ngeow, et al. ?Lifetime Cancer Risks in Individuals with Germline PTEN Muataions [19]? Clin Cancer Res. 2012 January 15; 18(2) : 400?407.*

Surveillance may begin five years earlier than the youngest person diagnosed with a specific cancer in the family, but no later than noted above. And, the frequency of scheduled colonoscopies may increase due to how many polyps are found.

Screening options may change over time as new technologies are developed and more is learned about CS. It is important to talk with your doctor about appropriate screening tests.

Learn more about what to expect when having common tests, procedures, and scans [20].

**Questions to ask the doctor**

If you are concerned about your risk of cancer, talk with your doctor. Consider asking the following questions:

- What is my risk of developing cancer?
- Where can I be referred to for a hereditary cancer risk assessment?
- What can I do to reduce my risk of cancer?
- What are my options for cancer screening?

If you are concerned about your family history and think your family may have CS, consider asking the following questions:

- Does my family history increase my risk of cancer?
- Could my family have CS?
- Will you refer me to a genetic counselor for a cancer risk assessment?
- Should I meet with a genetic counselor [21]?

**Additional resources**

**Guide to Breast Cancer[2]**

**Guide to Thyroid Cancer[3]**

**Guide to Kidney Cancer[6]**

**Guide to Uterine Cancer[4]**

**Guide to Colorectal Cancer[5]**

**Guide to Melanoma[7]**

**What to Expect When You Meet With a Genetic Counselor[21]**

**Facing Our Risk of Cancer Empowered (FORCE)**
Information for women who are at a high risk of developing ovarian cancer or breast cancer.
www.facingourrisk.org [22]

**National Comprehensive Cancer Network (NCCN)**
http://www.nccn.org/members/network.asp [23]

**National Cancer Institute**
www.cancer.gov [24]

**American Cancer Society**
www.cancer.org [25]

**To find a genetic counselor in your area, ask your doctor or visit these websites:**

National Society of Genetic Counselors
www.nsgc.org [26]

National Cancer Institute: Cancer Genetics Services Directory
www.cancer.gov/cancertopics/genetics/directory [27]

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**Links:**
[1] http://www.cancer.net/cancer-types/cowden-syndrome
[2] http://www.cancer.net/node/18618
[3] http://www.cancer.net/node/19293
[4] http://www.cancer.net/node/19308
[5] http://www.cancer.net/node/18701
[6] http://www.cancer.net/node/18969
[7] http://www.cancer.net/node/19251
[8] http://www.cancer.net/node/24897
[9] http://www.cancer.net/node/18590
[10] http://www.cancer.net/node/24659
[11] http://www.cancer.net/node/19134
[12] http://www.cancer.net/node/19495
[13] http://www.cancer.net/node/19481
[14] http://www.cancer.net/node/18520
[15] http://www.cancer.net/node/19618
[16] http://www.cancer.net/node/18562
[17] http://www.cancer.net/node/19604
[18] http://www.cancer.net/node/19148
[19] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3261579/
[20] http://www.cancer.net/node/24959

[21] http://www.cancer.net/node/24907
[22] http://www.genetests.org/servlet/access?db=genestar&id=8888891&fcn=e&fcn2=refer&refer=http%3A%2F%
[23] http://www.nccn.org/members/network.asp
[24] http://www.genetests.org/servlet/access?db=genestar&id=8888891&fcn=e&fcn2=refer&refer=http%3A%2F%
[25] http://www.genetests.org/servlet/access?db=genestar&id=8888891&fcn=e&fcn2=refer&refer=http%3A%2F%
[26] http://www.nsgc.org/
[27] http://www.cancer.gov/search/geneticsservices