What is Cowden syndrome?
Cowden syndrome (CS), also known as PTEN hamartoma syndrome (PHTS) or multiple hamartoma syndrome, is a condition that increases a person’s risk for benign (non-cancerous) tumors and certain types of cancer.

People with CS are more likely to develop benign tumors of the breast, thyroid, uterus and colon, as well as the skin and mucous membranes (lining of the mouth and nose). The specific skin findings found in people with CS are called trichilemmomas (growths involving the hair follicle) and papillomatous papules (raised growths on the face). People with CS often have a larger than average head size (macrocephaly). A small number of people with CS may have developmental delay or autism. People with CS can also develop a hamartoma (benign tumor) of the brain, a condition called Lhermitte-Duclos disease.

Cowden syndrome is often due to changes in a gene called PTEN. The table below shows the risks of cancer for people with CS compared to people in the general population. These percentages are lifetime risks of cancer. This means that these are the risks of cancer totaled up over a lifetime. The risk estimates may change as more research is done. Families with CS who do not have a PTEN gene mutation may have different risks than those shown here but are still followed closely.

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Cowden Syndrome Risk</th>
<th>General Population Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast (Women)</td>
<td>25-50% (but may be higher)</td>
<td>11-12%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>10-35%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Uterine (Endometrial)</td>
<td>5-28%</td>
<td>2-3%</td>
</tr>
<tr>
<td>Colorectal</td>
<td>up to 9%</td>
<td>5-6%</td>
</tr>
<tr>
<td>Skin Cancer (Melanoma)</td>
<td>up to 5%</td>
<td>2%</td>
</tr>
<tr>
<td>Kidney (Renal Cell)</td>
<td>increased</td>
<td>2%</td>
</tr>
<tr>
<td>Breast (Men)</td>
<td>slightly increased</td>
<td>&lt;0.1%</td>
</tr>
</tbody>
</table>

What causes Cowden syndrome?
About 80% of people with CS have an alteration in the PTEN gene. Some individuals with CS do not have a PTEN gene mutation. Their diagnosis of CS may be based on clinical features and family history. It is likely that alterations in other genes can also cause CS. The role of other genes in CS is less well understood and for that reason genetic testing may not be available at this time.

All of us have about 22,000 genes in almost every cell in our body. We have two copies of almost every gene (one from each parent). Each gene has a specific job in the body. Genes are made up of a series of four chemical letters (our DNA) in a set pattern. If there is an error (alteration) in the DNA pattern of a gene, then it will not be able to do its job. The PTEN gene helps to fix DNA damage in our cells and keeps our cells growing normally.
Most people with CS are born with one altered PTEN gene that does not work and one normal PTEN gene that does work. As long as the one working PTEN gene is doing its job, then cancer is unlikely to occur. This is why some people with PTEN alterations never develop cancer. But over time, there is a chance that the working PTEN gene will get damaged in a single cell. This happens because of chance or because of exposures to cancer-causing agents. Then the cell has no PTEN gene to protect its DNA. Cancer can eventually develop when this happens.

Most people with CS have one altered PTEN gene in almost every cell of their body, but they are only at risk for developing certain types of cancer. This is because the PTEN is most active in certain organs and cell types.

**How is Cowden syndrome inherited?**
Cowden syndrome is inherited in a “dominant” manner. Dominant means that it takes only one altered copy of a gene in order to cause CS. People with CS do not always inherit a PTEN alteration from one of their parents. About 11-47% of people with CS have a PTEN gene alteration that occurs as a brand new change in them.

Here are the chances that your relatives might have the altered gene:
- **Your Children** — 50% risk for each child.
- **Your Mother or Father** — almost a 50% risk. In most cases, one of your parents will be found to have the altered gene. Less often, neither of your parents will have the altered gene, because it has occurred as a new genetic event in you.
- **Your Brothers and Sisters** — 50% risk if one of your parents had the alteration. If neither of your parents had the alteration, then your siblings have a very low risk of having the alteration.
- **Your aunts, uncles, cousins, nieces, and nephews** — their chances of having an altered gene depend on where they are in the family tree. Remember that only one side of your family will be at risk of having the altered gene.

**What are the recommendations for cancer screening and risk reduction?**
Screening refers to medical tests that try to find cancer at an early stage of disease. Risk reduction strategies are used to try to prevent a specific type of cancer.

**Screening:**
For both men and women:
- physical exam every year with attention to thyroid, skin, and breast
- thyroid ultrasound every year beginning in childhood
- colonoscopies every 5 to 10 years or more often (if polyps or symptoms found) beginning at age 35
- skin examinations by a dermatologist every year beginning in childhood

For certain families:
- imaging of the kidneys (MRI) every 2 years beginning at 40 may be considered
For women:

- clinical breast examinations every year beginning at age 25
- mammograms every year beginning at age 30-35 (or 5 to 10 years before the youngest breast cancer diagnosis in the family)
- breast MRIs every year beginning at age 30 to 35 (or 5 to 10 years before the youngest breast cancer diagnosis in the family)
- transvaginal ultrasound and endometrial biopsies may be considered beginning at age 30

**Risk Reduction:**

- Preventive surgery to remove breast tissue – This surgery is called prophylactic mastectomy. This surgery can reduce breast cancer risk by over 90%. Issues to consider about mastectomy: the timing of the procedure, the type of surgery, options for breast reconstruction, and the benefits and risks of this surgery. We would be happy to refer you to a breast surgeon and a plastic surgeon to talk more about these issues.
- Some medications can reduce the risk of breast cancer - We do not have specific data on medications such as tamoxifen, raloxifene, and exemestane, to reduce breast cancer risk in women with CS. Women with CS should discuss the use of these medications with their physicians.
- Preventive surgery to remove the uterus- This surgery is called a hysterectomy. Screening for uterine cancer has not been proven to be very effective at detecting early cancer. Some women with CS may consider removal of the uterus (and sometimes the ovaries) after they have completed their families.

**Where can I find more information?**
Dana Farber Cancer Institute, Cancer Genetics & Prevention
[www.dana-farber.org/cancergenetics](http://www.dana-farber.org/cancergenetics)

American Cancer Society
[www.cancer.org](http://www.cancer.org)

Cancer Information Service
[www.cancer.gov](http://www.cancer.gov)

Genetic Alliance
[www.geneticalliance.org](http://www.geneticalliance.org)

Susan G. Komen Breast Cancer Foundation
[www.breastcancerinfo.com](http://www.breastcancerinfo.com)

**References**

- NCCN Guidelines Version 3.2013 Cowden Syndrome