Multiple Endocrine Neoplasia Type 1
Also called: MEN1, MEN1 syndrome, Wermer Syndrome

What is multiple endocrine neoplasia type 1?

Multiple endocrine neoplasia type 1 is a genetic condition that increases the risk of developing cancerous and non-cancerous tumors. Some of these tumors may develop in the endocrine system, which is made up of different glands in the body that produce hormones. Hormones are chemicals that are important for sending messages in the body. The endocrine glands include the parathyroid gland, pituitary gland, adrenal gland, pancreas and others. Other tumors may develop in parts of the body, which are not in the endocrine system. These are known as non-endocrine tumors.

The main types of endocrine tumors seen in people with multiple endocrine neoplasia type 1 include the following:

- Parathyroid gland tumors – tumors in the small parathyroid glands located next to the thyroid gland in the neck
- Pituitary gland tumors – tumors in the pea-size pituitary gland located near the base of the brain
- Stomach, intestine or pancreas tumors – known as tumors of the “gastro-entero-pancreatic” or GEP tract
- Adrenal gland tumors – tumors in the glands that are on top of each kidney
- Carcinoid tumors – tumors of the cells that line the digestive system, lungs or the thymus gland, which is located in the chest

Non-endocrine tumors may include the following:

- Facial angiofibromas – acne-like bumps that form near the nose and mouth
- Collagenomas – skin-colored bumps on the trunk, neck and limbs
- Lipomas – tumors made of fatty tissue that grow just under the skin
- Meningiomas – tumors of the membranes that surround the brain and spinal cord
- Ependymomas – tumors of the fluid-producing cells in the brain or spinal cord
- Leiomyomas – smooth muscle tumors

How is multiple endocrine neoplasia type 1 diagnosed?

Genetic testing can be offered to people who have features that suggest multiple endocrine neoplasia type 1. Even so, it is possible to establish a clinical diagnosis without genetic testing. Multiple endocrine neoplasia type 1 is clinically diagnosed when a person develops any two of the following types of endocrine tumors:

- Parathyroid gland tumors
- Pituitary gland tumors
• Stomach, intestine or pancreas tumors (GEP tract tumors)

A person who develops only one of the tumors listed above may be diagnosed with multiple endocrine neoplasia type 1 if he or she has other family members with multiple endocrine neoplasia type 1.

**What is the tumor risk for people with multiple endocrine neoplasia type 1?**

People with multiple endocrine neoplasia type 1 have an increased risk of developing endocrine and non-endocrine tumors. These tumors are often non-cancerous, but sometimes they need to be removed or treated because they may press on nearby organs or may produce very high levels of hormones in the body.

Nearly all people with multiple endocrine neoplasia type 1 develop some type of endocrine tumor during their lifetime. The lifetime risks by tumor subtype are listed in the following table:

<table>
<thead>
<tr>
<th>Endocrine Tumors</th>
<th>Lifetime Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parathyroid gland tumors</td>
<td>100%</td>
</tr>
<tr>
<td>Pituitary gland tumors</td>
<td>10% to 60%</td>
</tr>
<tr>
<td>Stomach, intestine, or pancreas tumors (GEP tract tumors)</td>
<td>34% to 55%</td>
</tr>
<tr>
<td>Adrenal gland tumors</td>
<td>20% to 40%</td>
</tr>
<tr>
<td>Carcinoid tumors</td>
<td>10%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-Endocrine Tumors</th>
<th>Lifetime Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple facial angiofibromas</td>
<td>88%</td>
</tr>
<tr>
<td>Collagenomas</td>
<td>72%</td>
</tr>
<tr>
<td>Lipomas</td>
<td>34%</td>
</tr>
<tr>
<td>Meningiomas</td>
<td>8%</td>
</tr>
<tr>
<td>Ependymomas</td>
<td>1%</td>
</tr>
<tr>
<td>Leiomyomas</td>
<td>Rare, exact risk unknown</td>
</tr>
</tbody>
</table>

Sometimes, tumors that are non-cancerous undergo changes that make them act more like cancer. This is most likely to happen for carcinoid tumors or for stomach, intestine, or pancreas tumors (GEP tract tumors).

**What are other symptoms seen in people with multiple endocrine neoplasia type 1?**

Multiple endocrine neoplasia type 1 can affect many areas of the body. People with this condition may experience some or all of the following signs or symptoms. These are caused by the growth of tumors or by abnormal levels of hormones made by the tumors:

- Parathyroid gland tumors signs and symptoms
  - Altered mental status (tiredness, depression, decreased alertness, confusion)
  - Weight loss
  - Constipation
  - Nausea and vomiting
  - Producing too much urine
  - Dehydration (not enough fluids)
- Weak bones
- High blood pressure
- Heart rhythm problems

- Pituitary gland and adrenal gland tumors signs and symptoms
  - Lack of periods (amenorrhea) or abnormal production of milk in the breasts (galactorrhea) for women
  - Loss of sex drive in men
  - Cushing’s syndrome (obesity, diabetes, hypertension, bone loss and depression)
  - For pituitary gland tumors: Extremely tall stature (gigantism); overgrowth of the hands, feet, and face (acromegaly)

- Stomach, intestine or pancreas tumors (GEP tract tumors) signs and symptoms
  - Pain in the abdomen
  - Nausea and vomiting
  - Loss of appetite
  - Diarrhea
  - Heartburn (esophageal reflux)
  - Peptic ulcers

Not all people with multiple endocrine neoplasia type 1 will have all of these symptoms. Some people with the condition may have no symptoms, while others may have many symptoms.

What causes multiple endocrine neoplasia type 1?

Multiple endocrine neoplasia type 1 is caused by changes in a gene known as MEN1. Genes carry information telling cells within the body how to function. The MEN1 gene helps to control how and when cells grow and divide.

People without multiple endocrine neoplasia type 1 carry two working copies of the MEN1 gene in their cells. One copy of MEN1 is inherited from the mother and one from the father. Cells from people with multiple endocrine neoplasia type 1 carry one working copy of MEN1 and one copy that is changed. This change causes the gene to not work properly. It is called an MEN1 mutation.

About 90% (9 out of 10) children with multiple endocrine neoplasia type 1 inherit the MEN1 gene mutation from a parent who also has the syndrome. The other 10% of children with the condition have developed a new MEN1 mutation that did not come from a parent. These children have no history of the syndrome in their family. In these cases, the change either happened in an egg or sperm cell when the child was formed or in one of the child’s cells during pregnancy. These children are the first in their families to have multiple endocrine neoplasia type 1.

No matter how they acquired the MEN1 mutation, people with multiple endocrine neoplasia type 1 have a 50% (1 in 2) chance of passing it on to their children.

As people with multiple endocrine neoplasia type 1 get older, the remaining working copy of MEN1 often becomes changed within some of their cells. When both copies of the gene are
changed, tumors can develop. This is why people with multiple endocrine neoplasia type 1 have a higher risk of developing tumors than people who do not have multiple endocrine neoplasia type 1.

**How are people with multiple endocrine neoplasia type 1 screened for cancer?**

People with multiple endocrine neoplasia type 1 should be managed by a doctor who knows this condition well. The goal of screening is finding and treating tumors early to allow the best outcome for patients.

Recommended screenings for people with multiple endocrine neoplasia type 1:

- **Yearly physical exams** by a doctor who knows this condition well.
- **Blood tests** to screen for abnormally high levels of various hormones and calcium in the blood. These should be started at 5 years of age and repeated every year.
- **MRI of the head** starting at 5 years of age and repeated every 3 to 5 years.
- **MRI or CT scan of the abdomen** beginning at age 20 years and repeated every 3 to 5 years.

It is possible that recommended screenings may change over time as doctors learn more about multiple endocrine neoplasia type 1. Some physicians may order more tests and scans besides these. Parents should discuss all screening options for their child with a doctor who knows this condition well. Because multiple endocrine neoplasia type 1 is a complex condition, it is very important that parents seek out an experienced doctor for their child.

**How is genetic testing for multiple endocrine neoplasia type 1 done?**

The doctor may suspect multiple endocrine neoplasia type 1 after looking at a person’s medical or family history. In most cases, a doctor or genetic counselor will ask questions about a person’s health and the health of other family members.

The genetic counselor or doctor will record which family members have developed tumors, what types of tumors and at what ages tumors occurred. From this information they will create a family tree. Doctors and genetic counselors will look at the family tree to find out:

- If there are more tumors than normal,
- If tumors occurred at younger-than-expected ages, and
- If the types of tumors match up with what might be seen in those with multiple endocrine neoplasia type 1.

If multiple endocrine neoplasia type 1 is suspected in a child or other family members, the doctor or genetic counselor will likely recommend genetic testing of the *MEN1* gene.
**Diagnostic genetic testing**

If the doctor or genetic counselor suspects that a person has multiple endocrine neoplasia type 1, diagnostic testing may take place as follows:

- A blood sample is collected.
- DNA is isolated from the cells in the sample. A person’s genes are made of DNA.
- Both copies of the person’s MEN1 gene are checked for possible changes. A genetic specialist compares the two copies of the patient’s gene to a normal MEN1 gene. If there are differences, the specialist decides if these changes might cause multiple endocrine neoplasia type 1.
- If an MEN1 mutation is found, the genetic counselor will work with the family in the following ways:
  - To help the family understand the cancer risks of multiple endocrine neoplasia type 1
  - To find out if other family members should consider testing for the mutation
  - To help with decisions about prenatal genetic testing.

Even if genetic testing does not find a mutation in the MEN1 gene, a person can still have multiple endocrine neoplasia type 1. There may be other types of mutations that cause multiple endocrine neoplasia type 1 that doctors do not yet know about.

**Prenatal genetic testing**

Parents may undergo prenatal testing to find out if the pregnancy is affected with a known MEN1 mutation in the family. Testing may take place either before pregnancy occurs or during pregnancy.

People considering prenatal testing should work with a genetic counselor to review the pros and cons of the testing. The genetic counselor can also help parents consider how they wish to handle the results of the testing.

**Testing that occurs before pregnancy**—Testing that happens before pregnancy is called preimplantation genetic diagnosis (PGD). This special type of genetic testing is done along with in vitro fertilization (IVF). PGD offers a way to test embryos for a known MEN1 mutation before placing them into the uterus.

**Testing that occurs during pregnancy**—Testing can be used to see if a pregnancy is affected with a known MEN1 mutation. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)**—during the first trimester (first three months)
- **Amniocentesis**—during the second trimester or later (last six months)

Collected tissue can be checked for the presence of the MEN1 mutation identified in the family. Both of these tests carry minor risks and should be discussed with an experienced doctor or genetic counselor.
Special concerns

Genetic testing for multiple endocrine neoplasia type 1 is a complex process. Those thinking about testing should take time to consider the benefits and risks. They should discuss the process with a genetic counselor before testing is done. If they choose testing, they should review the test results with the doctor or genetic counselor to be sure they understand the meaning of the results.

Sometimes children or adults with multiple endocrine neoplasia type 1 can feel sad, anxious or angry. Parents who pass on an MEN1 mutation to one or more of their children can feel guilty. Some people with an MEN1 mutation could have trouble getting disability coverage, life insurance or long-term care insurance in some states. More information about genetic discrimination can be found at www.ginahelp.org.

Are there other special health care needs for children with multiple endocrine neoplasia type 1?

People of any age with multiple endocrine neoplasia type 1 have a higher risk of tumors. They should monitor their health and adopt healthful habits throughout life. It is important to continue to have regular physical checkups and screenings. That way, any tumor can be found early at the most treatable stage.

Other ideas to reduce the risk of tumors:

- Eat a healthful diet with lots of fruits and vegetables
- Get regular exercise
- Avoid smoking or using tobacco products
- Avoid secondhand smoke
- Avoid excess sun exposure and always wear sunscreen and a hat when out in the sun

People with multiple endocrine neoplasia type 1 should watch closely for general signs or symptoms that could signal a tumor:

- Unexplained weight loss
- Loss of appetite
- Pain in the abdomen
- Blood in the stool or changes in bowel habits
- Aches, pains, lumps, or swelling that cannot be explained
- Headaches or changes in vision or nerve function that do not go away

It is important to seek medical help if anything unusual appears.
What other information and resources are there for children with multiple endocrine neoplasia type 1 and their families?

Resources about multiple endocrine neoplasia type 1:

- American Multiple Endocrine Neoplasia Support (www.amensupport.org)
- Association for Multiple Endocrine Neoplasia Disorders (UK) (www.amend.org.uk)

Other resources:

- Gene Ed (geneed.nlm.nih.gov)

Sources:
1. Children’s Hospital of Philadelphia - Multiple endocrine neoplasia type 1  
   www.chop.edu/conditions-diseases/multiple-endocrine-neoplasia-type-1#.VcTyN2fb15s

2. Genetics Home Reference - Multiple endocrine neoplasia  
   ghr.nlm.nih.gov/condition/multiple-endocrine-neoplasia

3. Gene Reviews – Multiple endocrine neoplasia type 1  
   www.ncbi.nlm.nih.gov/books/NBK1538/