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 (non-endocrine tumors).

The main types of endocrine tumors seen in people with multiple endocrine neoplasia type 1 are:

- Parathyroid gland tumors (tumors in the small parathyroid glands that 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:

- 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)

People with multiple endocrine neoplasia type 1 may develop tumors that are cancerous (the tumor cells spread to other parts of the body) or non-cancerous (the tumor cells do not spread).

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; however, 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 that 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 are cancerous. Even non-cancerous tumors may 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 over the course of their lifetime. The lifetime risks by subtype are listed in the following table:

Endocrine Tumors	**Lifetime Risk**
Parathyroid gland tumors	100%
Pituitary gland tumors	10% to 60%
Stomach, intestine, or pancreas tumors (GEP tract tumors)	34% to 55%
Adrenal gland tumors	20% to 40%
Carcinoid tumors	10%
Non-Endocrine Tumors	**Lifetime Risk**
Multiple facial angiofibromas	88%
Collagenomas	72%
Lipomas	34%
Meningiomas	8%
Ependymomas	1%
Leiomyomas	Rare, exact risk unknown

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 symptoms, which are caused by the growth of tumors or by abnormal levels of hormones made by the tumors:

- Parathyroid gland tumors signs/symptoms
    - Altered mental status (lethargy, depression, decreased alertness, confusion)
    - Weight loss
    - Constipation
    - Nausea and vomiting
    - Excessive urine production
    - Dehydration
    - Weak bones
    - High blood pressure
    - Heart rhythm problems
- Pituitary gland or adrenal gland tumors signs/symptoms

    - Lack of periods (amenorrhea) and/or abnormal production of milk in the breasts (galactorrhea) for women
    - Loss of sex drive or impotence in men
    - Cushing's syndrome (obesity, diabetes, hypertension, bone loss, and depression)
    - For pituitary gland tumors: Extremely tall stature (gigantism) and/or overgrowth of the hands, feet, and face (acromegaly)
- Stomach, intestine, or pancreas tumors (GEP tract tumors) signs/symptoms
    - Abdominal pain
    - 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 health care provider who is familiar with the condition. The goal of screening is to find and treat tumors early to allow the best outcome for patients.

Recommended screenings for individuals with multiple endocrine neoplasia type 1 include:

- **Yearly physical exams** by a health care provider who is familiar with multiple endocrine neoplasia type 1.
- **Blood tests** to screen for abnormally high levels of various hormones and calcium in the blood. These should be started at age 5 years and repeated yearly.
- **MRI of the head** starting at age 5 years and repeated every 3 to 5 years.
- **MRI or CT scan of the abdomen** beginning at age 10 years.

It is possible that recommendations may change over time as health care providers learn more about multiple endocrine neoplasia type 1. Some physicians may order additional tests and/or scans besides these. Parents should discuss all screening options for their child with a health care provider who is familiar with multiple endocrine neoplasia type 1. Because multiple endocrine neoplasia type 1 is a complex condition, it is very important that parents seek out an experienced health care provider for their child.

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

Multiple endocrine neoplasia type 1 may be suspected after looking at a person's medical or family history. In most cases, a health care provider or genetic counselor will ask questions about a person's health and the health of other family members.

The genetic counselor or health care provider 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. Health care providers 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
- 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 health care provider or genetic counselor will likely recommend genetic testing of the *MEN1* gene.

Diagnostic genetic testing

If the health care provider 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 are consistent with multiple endocrine neoplasia type 1.
- If an *MEN1* mutation is found, the genetic counselor will work with the family to:
    - Help the family understand the cancer risks of multiple endocrine neoplasia type 1
    - Find out if other family members should consider testing for the mutation
    - Help with decisions about prenatal genetic testing.

MEN1 mutations are found in:

- About 80% to 90% people who have one of the three main types of endocrine tumors and who have a family history multiple endocrine neoplasia type 1.
- About 65% of patients who are the first in their family to have multiple endocrine neoplasia type 1.

Therefore, 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 health care providers 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 testing (PGT). This special type of genetic testing is done along with in vitro fertilization (IVF). PGT 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 determine 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
- **Amniocentesis—**during the second trimester or later

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 health care provider or genetic counselor to be sure they understand the meaning of the results.

Sometimes children or adults with multiple endocrine neoplasia type 1 experience sadness, anxiety, or anger. 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 http://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 healthy habits throughout life. It is important to continue to have regular physical check-ups and screenings. That way, any tumor can be found early at the most treatable stage.

Other recommendations to reduce the risk of malignant tumors include:

- Eat a healthy 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, hat and protective clothing 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, such as:

- Unexplained weight loss
- Loss of appetite
- Abdominal pain
- Blood in the stool or changes in bowel habits
- Aches, pains, lumps, or swelling that can’t be explained
- Headaches or changes in vision or nerve function that don’t 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 (http://www.amensupport.org/)
- Association for Multiple Endocrine Neoplasia Disorders (UK) (http://www.amend.org.uk/)

- Genetics Home Reference (http://ghr.nlm.nih.gov/condition/multiple-endocrine-neoplasia)
- National Organization for Rare Disorders (https://rarediseases.org/rare-diseases/multiple-endocrine-neoplasia-type-1/)

Additional resources:

- Making Sense of Your Genes: A Guide to Genetic Counseling (www.ncbi.nlm.nih.gov/books/NBK115508/)
- Young People with Cancer: A Parent's Guide (www.cancer.gov/publications/patient-education/young-people)

Sources:

1. Genetics Home Reference - Multiple endocrine neoplasia
http://ghr.nlm.nih.gov/condition/multiple-endocrine-neoplasia

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

3. NIH/NIDDK– Multiple endocrine neoplasia type 1
https://www.niddk.nih.gov/health-information/endocrine-diseases/multiple-endocrine-neoplasia-type-1

Developed by:

St. Jude Division of Cancer Predisposition

Updated: 06-2020