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Multiple Endocrine Neoplasia Type 1 [1]

What is multiple endocrine neoplasia type 1?

Multiple endocrine neoplasia type 1 (MEN1) is a hereditary condition associated with tumors of the endocrine (hormone producing) glands. MEN1 was originally known as Wermer syndrome. The most common tumors seen in MEN1 involve the parathyroid gland [2], islet cells of the pancreas [3], and pituitary glands [4]. Other endocrine tumors seen in MEN1 include adrenal cortical tumors [5] and carcinoid tumors [6], as well as tumors in other parts of the digestive tract.

Non-endocrine tumors are also seen in MEN1. These tumors can include:

- facial angiofibromas, which are tumors of blood vessels and fibrous tissue
- collagenomas, which are flesh-colored tumors on the skin
- lipomas, which are fatty tumors
- leiomyomas, which are smooth muscle tumors
- meningiomas [7], which are tumors from nervous system tissue; uncommon
- ependymomas [8], which are tumors from nervous system tissue; uncommon
- Adrenal cortical tumors [5]

The majority of tumors in people with MEN1 are benign (noncancerous), however, approximately one-third of islet cell tumors [3] and mediastinal carcinoid tumors are malignant (cancerous, meaning it can spread to other parts of the body). However, all tumors can produce too much hormones. And, there is a broad spectrum of clinical syndromes associated with increased hormone production by these tumors. These include increased production of:

- Prolactin, which is the abnormal milk production by the breast and lack of menstruation in women)
- growth hormone, which is the excessive growth of the jaw and other soft tissues
- adrenocorticotropic hormone, which is the excessive cortisol production by pituitary tumors
- gastrin, which causes stomach ulcers
- glucagon causes diabetes mellitus and skin rash
- vasoactive intestinal peptide, called VIPoma, which causes intense watery diarrhea, by islet cell tumors of the pancreas
- parathyroid hormone, which causes high blood calcium and kidney stones, by parathyroid tumors

What causes MEN1?

MEN1 is a genetic condition. This means that the cancer risk and other features of MEN1 can be passed from generation to generation in a family. The gene associated with MEN1 is also called *MEN1*. A mutation (alteration) in the *MEN1* gene gives a person an increased risk of developing endocrine tumors and other symptoms of MEN1. More than 90% of individuals who inherit the MEN1 mutation will develop one or more symptoms of MEN1. A small percentage without *MEN1* genetic alterations have been found to have germline mutations (alterations in the body?s egg or sperm cells that become incorporated into the DNA of every cell in the body of the offspring) in a class of proteins called cyclin-dependent kinase inhibitors (CDKIs) that regulate cell growth and division. Research is ongoing to learn more about MEN1.

How is MEN1 inherited?

Normally, every cell has two copies of each gene: one inherited from the mother and one from the father. MEN1 follows an autosomal dominant inheritance pattern, in which a mutation happens in only one copy of the gene. 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. Therefore, any child from a parent with a mutation has a 50% chance of inheriting that mutation. A tumor develops in the affected individual when the normal copy of the gene (inherited from the unaffected parent) is lost or mutated (damaged) in a specific cell type during normal cell division.

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 MEN1?

It is estimated that about one in 30,000 people has MEN1. About 10% of people with MEN1 do not have a family history of the condition; they have a de novo (new) mutation in the *MEN1* gene.

How is MEN1 diagnosed?

MEN1 is suspected when a person has at least two of the most common tumors listed.

- Parathyroid [2]
- Pancreatic islet cell tumors [3]
- Pituitary [4]

If a person has a family history of MEN1, he or she is suspected of also having MEN1 if

diagnosed with a parathyroid, pancreatic, or pituitary tumor. Genetic testing for mutations in the *MEN1* gene is available for people suspected to have MEN1. A mutation in the *MEN1* gene is found in about 80% to 90% of families diagnosed with MEN1. Approximately 65% of people with two or more tumors associated with MEN1, but no family history, will have a mutation in the *MEN1* gene.

What are the estimated cancer risks associated with MEN1?

Approximately one-third of islet cell tumors of the pancreas are cancerous. If the cancer has spread, the most common site of spread is the liver. A small percentage of mediastinal carcinoid tumors are malignant and spread to local (nearby) lymph nodes or to the liver, lung, or other locations.

What are the screening options for MEN1?

Current suggested screening for people who are known or suspected to have MEN1 includes:

Genetic Testing

- Genetic testing [9] is available. It should be considered for children or young adults who are members of a family diagnosed with MEN1 and an identified mutation of the *MEN1* gene to determine which children/young adults should have the screening studies described below. In a family with an identified mutation of the *MEN1* gene, children with a genetic test showing no mutation (expected to be 50% of children born to an individual affected with MEN1) may not need the screening tests described below. Certified genetic testing laboratories for this condition can be found at www.genetests.org [10].

Diagnostic Studies

- Regular blood tests (every one to three years) for prolactin, insulin-like growth factor 1 (IGF-1), fasting glucose, insulin, and proinsulin, beginning at age 5 to 10 years.
- A yearly ionized or albumin-corrected calcium level test, beginning at age 8
- Regular blood tests for fasting gastrin and fasting and meal stimulated pancreatic polypeptide (PP), fasting VIP, and glucagon, beginning at age 20.
- Magnetic resonance imaging [11] (MRI) scan of the brain, every three to five years, beginning between ages 5 to 10, or at any time the results of the tests for serum prolactin or insulin-like growth factor is abnormal.
- MRI or computed tomography [12] (CT) scan of the chest and abdomen, every two to four years, beginning at age 20 or when the serum gastrin, PP, or VIP is noted to be abnormal.

Screening guidelines may change over time as new technologies are developed and more is learned about MEN1. It is important to talk with your doctor about appropriate screening tests.

What are the treatment options for the endocrine tumors?

Most of these tumors are treated with surgery or by taking a medicine that suppresses growth or function of the tumor. Parathyroid tumors, which are almost always benign, should be surgically removed when the albumin-corrected serum calcium level is greater than 12 mg/dl, there is

significant bone loss, or kidney damage or stones develop. The most challenging treatment issues relate to the pancreatic islet cell tumors [3]. In addition to its role in normal digestion, the pancreas regulates the level of blood glucose through insulin production. Removal of the pancreas will cause diabetes mellitus, a condition that can lead to significant health problems and it will be necessary to take pancreatic enzyme supplements to promote digestion. Doctors must balance the benefits of pancreatic removal in a person with MEN1 (such as the prevention of development of cancer spread) against the risks of diabetes mellitus. Patients with islet cell tumors that have spread to the liver may be treated with a somatostatin analogue or a drug that regulates signaling in the pancreatic islet cell, everolimus. Carcinoid tumors [6] are typically removed by surgery as soon as possible. Read more about the treatment for islet cell tumors [3] and carcinoid tumors [6].

Pituitary tumors producing prolactin (a hormone) are most commonly managed with dopamine agonists (drugs that imitate the action of dopamine, a naturally occurring substance produced in the brain); tumors that produce growth hormone or adrenocorticoptropin hormone or non-functioning tumors are most commonly treated with surgery [13]. Two hormonal therapies, a somatostatin analogue and a growth hormone antagonist, have been successfully used to treat growth hormone excess in patients who are not cured by surgery. Learn more about pituitary tumor treatment [14].

Learn more about what to expect when having common tests, procedures, and scans [15].

Questions to ask the doctor

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

- What is my risk of developing an islet cell tumor?
- What can I do to reduce my risk of other types of tumors?
- What are my options for screening?

If you are concerned about your family history and think you or other family members may have MEN1, consider asking the following questions:

- Does my family history increase my risk of developing cancer?
- Should I meet with a genetic counselor?
- Should I consider genetic testing [9]?

Additional resources

Guide to Endocrine Tumor[16]

Guide to Parathyroid Tumor[2]

Guide to Islet Cell Tumor[3]

Guide to Pituitary Tumor[4]

Guide to Carcinoid Tumor[6]

What to Expect When You Meet With a Genetic Counselor[17]

American Multiple Endocrine Neoplasia Support
http://www.amensupport.org/ [18]

[18]**Association for Multiple Endocrine Neoplasia Disorders (AMEND)**
www.amend.org.uk [19]

National Cancer Institute
www.cancer.gov [20]

American Cancer Society
www.cancer.org [21]

Cancer*Care*
www.cancercare.org [22]

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

National Society of Genetic Counselors
www.nsgc.org [23]

National Cancer Institute
www.cancer.gov/cancertopics/genetics/directory [24]

Links:
[1] http://www.cancer.net/cancer-types/multiple-endocrine-neoplasia-type-1
[2] http://www.cancer.net/node/19509
[3] http://www.cancer.net/node/18941
[4] http://www.cancer.net/node/19536
[5] http://www.cancer.net/node/18424
[6] http://www.cancer.net/node/18645
[7] http://www.cancer.net/node/19266
[8] http://www.cancer.net/node/18769
[9] http://www.cancer.net/node/24895
[10] http://www.genetests.org/
[11] http://www.cancer.net/node/24578
[12] http://www.cancer.net/node/24486
[13] http://www.cancer.net/node/24462
[14] http://www.cancer.net/node/19542
[15] http://www.cancer.net/node/24959
[16] http://www.cancer.net/node/18743
[17] http://www.cancer.net/node/24907
[18] http://www.amensupport.org/
[19] http://www.amend.org.uk/
[20] http://www.cancer.gov/
[21] http://www.cancer.org/
[22] http://www.cancercare.org/

[23] http://www.nsgc.org/
[24] http://www.cancer.gov/cancertopics/genetics/directory