Hereditary Multiple Osteochondromas

Also called: *Hereditary multiple extoses, multiple cartilaginous extoses, diaphyseal aclasis*

What is hereditary multiple osteochondromas?

Hereditary multiple osteochondromas is a rare genetic condition. People with hereditary multiple osteochondromas are more likely to develop certain types of tumors. These tumors can be benign (non-cancerous) and malignant (cancerous).

Children with this condition can develop one or more tumors in their bones. These tumors are called osteochondromas. They are typically located near the metaphyses (growth plates or ends) of the bone. Osteochondromas are benign, but they may become malignant over time. People with hereditary multiple osteochondromas have a 95% chance of developing non-cancerous osteochondromas by age 12 years. The malignant form of osteochondroma is called osteochondrosarcoma. Individuals with hereditary multiple osteochondromas have a 2-5% lifetime risk of developing osteochondrosarcoma.

Individuals with hereditary multiple osteochondromas may have other symptoms that result from the development of osteochondromas. These symptoms may vary from person to person, even within the same family. These symptoms include:

- Reduced skeletal growth
- Restricted joint motion
- Short stature
- Premature osteoarthritis
- Nerve compression
- Bowing of forearm or ankle
- Abnormal development of hip joints
- Difficulty walking and/or discomfort when walking

What causes hereditary multiple osteochondromas?

Hereditary multiple osteochondromas is caused by changes in one of two genes: *EXT1* or *EXT2*. Genes carry information telling cells within the body how to function. The role of *EXT1* and *EXT2* in tumor development is not understood. It is thought the normal functions of *EXT1* and *EXT2* help prevent tumors.

Most cells of the body carry two working copies of the *EXT1* and *EXT2* genes. One copy of each gene is passed down from each parent. People with hereditary multiple osteochondromas carry one working copy of the *EXT1* or *EXT2* gene and one non-working copy. This non-working copy is also called a mutation. When the remaining copy of the *EXT1* or *EXT2* gene becomes damaged, it can lead to osteochondromas.

How do children get hereditary multiple osteochondromas?

Most people with hereditary multiple osteochondromas inherit it from a parent who also has the syndrome. But some people with hereditary multiple osteochondromas may have a new *EXT1* or *EXT2* mutation that was not passed down from a parent. In these cases, the *EXT1* or *EXT2* mutation is new in these people, and they are the first in their families to have hereditary multiple osteochondromas.

Individuals who have hereditary multiple osteochondromas have a 50% (1 in 2) chance of passing on the condition with each of their pregnancies.

How are children with hereditary multiple osteochondromas screened for cancer?

In general, tumor screening involves undergoing certain tests to check for tumors before symptoms occur. The goal is to detect tumors at the earliest and most treatable stage. The tumor screening tests should be discussed with a health care provider who knows this syndrome well.

Screening test may include the following:

- Full physical exams
- MRI, X-Ray, or CT scan

How is genetic testing for hereditary multiple osteochondromas done?

Hereditary cancer syndromes such as hereditary multiple osteochondromas 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 the tumors occurred. From this information, they will create a family tree. Health care providers and genetic counselors will examine the family tree to find out:

- If there are more tumors than normal,
- Whether tumors occurred at younger than expected ages, or
- If the types of tumors match up with what might be observed in those with hereditary multiple osteochondromas, including osteochondromas and osteochondrosarcoma

Health care providers or genetic counselors who suspect hereditary multiple osteochondromas in a child or other family members will likely recommend genetic testing of *EXT1* and *EXT2*. Sometimes *EXT1* and *EXT2* are included in genetic testing, even if hereditary multiple osteochondromas is not suspected.

Diagnostic testing

If health care providers or genetic counselors suspect a person has hereditary multiple osteochondromas, diagnostic testing may take place:

- Usually a blood sample is collected; however, saliva can also sometimes be used.

- In the lab, DNA is isolated from the cells in the sample. The *EXT1* and *EXT2* genes are checked for possible mutations using a variety of methods, such as DNA sequencing. To perform DNA sequencing, a genetic specialist compares the lettering (spelling) of the two copies of the genes to a normal reference sample. If there are differences, the specialist then decides if those differences might cause hereditary multiple osteochondromas. Please note that other methods may also be used, especially when the results of DNA sequencing are negative or unclear. These other tests look for changes that could affect the *EXT1* or *EXT2* gene but that may not be found by DNA sequencing.
- If an *EXT1* or *EXT2* mutation is found, a genetic counselor will work with the family to find out if other family members should consider testing for the mutation. The genetic counselor will help the family understand the tumor risks for those with hereditary multiple osteochondromas. The genetic counselor can also help with decisions about prenatal genetic testing.

Prenatal testing
Parents may undergo prenatal testing to find out if a pregnancy is affected with a known *EXT1* or *EXT2* mutation in the family.

Testing may take place either before pregnancy occurs or during pregnancy. Those considering prenatal testing should work with a genetic counselor to review the pros and cons of the tests. 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 *EXT1* or *EXT2* 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 *EXT1* or *EXT2* mutation. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)—**during first trimester of the pregnancy
- **Amniocentesis—**during second trimester of the pregnancy or later

Collected cells from the pregnancy can then be checked for the presence of *EXT1* or *EXT2* mutations that have already been identified in the family.

Both of these tests carry minor risks and should be discussed with an experienced health care provider and/or genetic counselor.

Special concerns
Genetic testing for hereditary multiple osteochondromas 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 undergoing the testing. If they choose testing, they should review the test results with the health care provider or genetic counselor to be sure that they understand the meaning of the results.

Sometimes, children or adults with hereditary multiple osteochondromas experience sadness, anxiety, or anger. Parents who passed on an altered *EXT1* or *EXT2* gene to one or more of their children can feel guilty. It is also possible that a person who is found to have an altered *EXT1* or *EXT2* gene could have more trouble getting disability insurance or life insurance. More information about genetic discrimination can be found at www.ginahelp.org.

Are there other special health care needs for children with hereditary multiple osteochondromas?

Children with hereditary multiple osteochondromas have a higher risk of cancer. They should monitor their health and adopt healthy habits. It is important to continue to have regular physical checkups and screenings. That way, any cancer can be found early at the most treatable stage.

Other ideas to reduce the risk of cancer include the following:

- 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 hereditary multiple osteochondromas should watch closely for general signs or symptoms that could signal cancer:

- Unexplained weight loss or fever
- Lack of appetite
- Aches, pains, lumps, swelling that cannot be explained

It is important to seek medical help if anything unusual appears.

What other information and resources are there for children with hereditary multiple osteochondromas and their families?

Other resources about hereditary multiple osteochondromas include the following:

- MHE Coalition (https://www.mhecoalition.org/)
- The MHE Research Foundation (https://www.mherf.org/)
- Making Sense of Your Genes: A Guide to Genetic Counseling (www.ncbi.nlm.nih.gov/books/NBK115508/)
- RareConnect: Connecting Rare Disease Patients Globally (www.rareconnect.org/en)

Sources:

- GeneReviews—Hereditary Multiple Osteochondromas https://www.ncbi.nlm.nih.gov/books/NBK1235/
- MedlinePlus—Hereditary Multiple Osteochondromas https://medlineplus.gov/genetics/condition/hereditary-multiple-osteochondromas/
- OMIM—EXT1 https://www.omim.org/entry/133700
- OMIM—EXT2 https://www.omim.org/entry/608210

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