DICER1 syndrome

Also called: *DICER1-related pleuropulmonary blastoma cancer predisposition syndrome, pleuropulmonary blastoma familial tumor and dysplasia syndrome, pleuropulmonary blastoma family tumor susceptibility syndrome, pleuropulmonary blastoma (PPB)*

What is *DICER1* syndrome?

DICER1 syndrome is a rare disorder that makes a person more likely to develop certain types of tumors, both benign (non-cancerous) and malignant (cancerous). Children with this syndrome can develop one or more tumors in these areas of the body:

- Lungs
- Ovaries
- Thyroid gland
- Kidneys
- Brain (pineal and pituitary glands)
- Other

In babies and young children with *DICER1* syndrome, the most common type of tumor appears in the lung, and is known as pleuropulmonary blastoma (PPB).

What causes *DICER1* syndrome?

DICER1 syndrome is caused by changes in a gene known as *DICER1*. Genes carry important information that tells our body's cells how to function. In ways that are not well understood, *DICER1* aids in preventing tumors.

Most cells of the body carry two working copies of the *DICER1* gene. One is inherited from the mother and one from the father. Cells from people with *DICER1* syndrome carry one working *DICER1* gene copy and one copy that is altered. This alteration causes the gene to not work properly and is called a mutation.

What is the cancer risk for children with *DICER1* syndrome?

Children and young people with *DICER1* syndrome have an increased risk of developing the following:

- PPB, a rare type of lung tumor usually occurring before 6 years of age
- Ovarian sex-cord stromal tumors, such as Sertoli-Leydig cell tumor
- A rare and non-cancerous kidney tumor known as cystic nephroma
- An enlarged thyroid gland that contains growths known as nodules
- A type of eye tumor known as ciliary body medulloepithelioma
- A type of muscle cancer known as rhabdomyosarcoma (specifically, botryoid-type embryonal)
- A type of nose tumor known as nasal chondromesenchymal hamartoma
- Types of brain tumors known as pineoblastoma and pituitary blastoma

The exact risks for developing these tumors are not known at this time. Other tumor types have been described.

How are children with *DICER1* syndrome 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
- Chest imaging
- Renal (kidney) ultrasound
- Thyroid exam
- Eye exam
- Brain MRI
- Pelvic ultrasound (for females)
- Gynecological exam (for females)

How do children get *DICER1* syndrome?

Most people with *DICER1* syndrome inherit it from a parent who also has the syndrome. But some people with *DICER1* syndrome may have a new *DICER1* mutation (alteration) that did not come from a parent. In these cases, the *DICER1* mutation is new in these people and they are the first in their families to have *DICER1* syndrome.

No matter how they acquired the mutation, all people with *DICER1* syndrome have a 50% or 1 in 2 chance of passing it on to their children.

How is genetic testing for *DICER1* syndrome done?

Hereditary cancer syndromes such as *DICER1* syndrome 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 *DICER1* syndrome.

Health care providers or genetic counselors who suspect *DICER1* syndrome in a child or other family members will likely recommend genetic testing of *DICER1*.

Diagnostic testing
If health care providers or genetic counselors suspect a person has *DICER1* syndrome, diagnostic testing may take place:

- A blood sample is collected.
- DNA is isolated from the cells in the sample. The *DICER1* gene is 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 a gene to a typical sample. If there are differences, the specialist then decides if those differences might cause a specific disease, such as *DICER1* syndrome. 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 *DICER1* gene but that may not be found by DNA sequencing.
- If a *DICER1* 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 *DICER1* syndrome. 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 *DICER1* 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 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 *DICER1* 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 *DICER1* 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

Once the tissue is collected, DNA is isolated and examined for the presence of the *DICER1* mutation found 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 *DICER1* syndrome 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 *DICER1* syndrome experience sadness, anxiety or anger. Parents who passed on an altered *DICER1* 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 *DICER1* 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 *DICER1* syndrome?

Children with *DICER1* syndrome 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 *DICER1* syndrome should watch closely for general signs or symptoms that could signal cancer. It is important to seek medical help if anything unusual appears.

What other information and resources are there for children with *DICER1* syndrome and their families?

Other resources about the *DICER1* syndrome include the following:

- Genetics Home Reference: (http://ghr.nlm.nih.gov/condition/dicer1-syndrome)
- International Pleuropulmonary Blastoma Registry (http://www.ppbregistry.org/)
- Ovarian and Testicular Stromal Tumor Registry (http://www.otstregistry.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*)
- Young People with Cancer: A Parent's Guide (*www.cancer.gov/publications/patient-education/young-people*)

Sources:
Genetics Home Reference: *DICER1* Syndrome
ghr.nlm.nih.gov/condition/DICER1-syndrome

GeneReviews: *DICER1*-Related Disorders
www.ncbi.nlm.nih.gov/books/NBK196157/

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