**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.

 Currently, there are no guidelines for screening people with **DICER1** syndrome, but some experts recommend annual exams and selected imaging in these patients. Many questions remain about when screening should begin, how long screening should continue, and the best methods to use for screening. People with **DICER1** syndrome should discuss the benefits and risks of screening with a doctor familiar with the condition. Screening recommendations are likely to evolve over time as we learn more about **DICER1** syndrome and the tumor risks it poses.

**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 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, and if so, the types of tumors and ages at which these tumors occurred. From this information, they will create a family tree. Doctors 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.

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

**Diagnostic testing**

If doctors 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. DNA sequencing is when a genetic specialist checks the lettering (spelling) of the two copies of a gene to that of a normal 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 whether a pregnancy is affected with a known DICER1 mutation in the family.

Testing may take place either before pregnancy occurs or after an embryo is formed. Those considering prenatal testing should work with a genetic counselor to review the pros and cons of the tests. The genetic counselor will 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
• Amniocentesis—during second trimester or later

Once these tissues are collected, DNA is isolated and checked for the presence of the DICER1 mutation in the family.

Both of these tests carry minor risks and should be discussed with an experienced doctor 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 doctor 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 \textit{DICER1} gene could have more trouble getting disability insurance or life insurance.

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

Other resources about the \textit{DICER1} syndrome include the following:

- International Pleuropulmonary Blastoma Registry (http://www.ppbregistry.org/)
- Ovarian and Testicular Stromal Tumor Registry (http://www.otstregistry.org/)
- Pleuropulmonary Blastoma: Childhood Treatment Options (www.cancer.net/cancer-types/pleuropulmonary-blastoma-childhood/treatment-options)
- GeneReviews: \textit{DICER1}-Related Disorders (www.ncbi.nlm.nih.gov/books/NBK196157/)
- RareConnect: Connecting Rare Disease Patients Globally (www.rareconnect.org/en)

**Keywords:**

Primary: \textit{DICER1}, pleuropulmonary blastoma, PPB
Secondary: Cancer predisposition syndrome, Sertoli-Leydig tumor, cystic nephroma, multinodular goiter, pineoblastoma, ovarian stromal sex-cord tumor

**Sources:**

1. Children’s Hospital of Philadelphia: \textit{DICER1} Syndrome (www.chop.edu/conditions-diseases/DICER1-syndrome#.VIkh-vldWzY)