What Causes Retinoblastoma?

There are very few known risk factors for retinoblastoma, but the main gene changes inside cells that can lead to retinoblastoma are now fairly well known.

Early in fetal development, well before birth, cells in the retina of the eye divide to make new cells to fill the retina. At a certain point, these cells normally stop dividing and become mature retinal cells. But sometimes something goes wrong with this process. Instead of maturing, some retinal cells continue to grow out of control, which can lead to retinoblastoma.

Certain changes in a person's DNA can cause cells of the retina to grow out of control. DNA is the chemical in each of our cells that makes up our **genes**, which control how our cells function. We usually look like our parents because they are the source of our DNA. But DNA affects much more than how we look.

Some genes control when our cells grow, divide into new cells, and die at the right time:

- Genes that help cells grow, divide, or stay alive are called **oncogenes**.
- Genes that help keep cell division under control or cause cells to die at the right time are called **tumor suppressor genes**.

Cancers can be caused by DNA changes (mutations) that keep oncogenes turned on, or that turn off tumor suppressor genes.

The most important gene in retinoblastoma is the *RB1* tumor suppressor gene. This gene makes a protein (pRb) that helps stop cells from growing too quickly. Each cell normally has two *RB1* genes. As long as a retinal cell has at least one *RB1* gene that works as it should, it will not form a retinoblastoma. But when both of the *RB1* genes are mutated or missing, a cell can grow unchecked. This can lead to further gene changes, which in turn may cause cells to become cancerous.

Heritable or bilateral retinoblastoma

About 1 out of 3 children with retinoblastoma have a **germline mutation** in one *RB1* gene; that is, the *RB1* gene mutation is in all the cells in the body. In most of these children (75%), this mutation occurs very early in development, while still in the womb. The other 25% of children inherit the gene mutation from one of their parents.

About 9 of 10 children who are born with this *RB1* germline mutation develop retinoblastoma. This happens when the second *RB1* gene is lost or mutated. Most often the retinoblastoma is **bilateral** (in both eyes), but sometimes it is found early enough that it is still only in one eye.

These children have heritable retinoblastoma (also called hereditary or congenital retinoblastoma). All bilateral retinoblastomas are considered heritable, although not all heritable retinoblastomas are bilateral when they are found.

Everybody has two *RB1* genes but passes only one on to each of their children. (The child gets the other *RB1* gene from the other parent.) Therefore there is a 1 in 2 chance that a parent who had heritable retinoblastoma will pass the mutated gene on to his or her child.

Most children with heritable retinoblastoma don't have an affected parent. But these children can still pass their *RB1* gene mutation on to their children. This is why this form of retinoblastoma is called "heritable" (even though neither of the child's parents may have been affected).

Because children with this form of retinoblastoma have *RB1* gene changes in all the cells in their body, they are also at higher risk for developing some other types of cancer. For more on this, see After Treatment for Retinoblastoma.

Non-heritable (sporadic) retinoblastoma

Most of the remaining 2 out of 3 children with retinoblastoma do not have the *RB1* gene mutation in all the cells of their body. Instead, the *RB1* mutation happens early in life and first occurs only in one cell in one eye. These children are not at risk for passing the gene mutation on to their offspring.

(In a very small portion of non-heritable retinoblastomas, there is no *RB1* gene mutation. Some of these retinoblastomas seem to be caused by changes in another gene, known as *MYCN*.)

Whether the changes in the *RB1* gene are heritable or sporadic, it's not clear what causes these changes. They may result from random gene errors that sometimes occur when cells divide to make new cells. There are no known lifestyle-related or environmental causes of retinoblastoma, so it's important to remember that there is nothing these children or their parents could have done to prevent these cancers.

Last Medical Review: December 3, 2018 | Last Revised: December 3, 2018