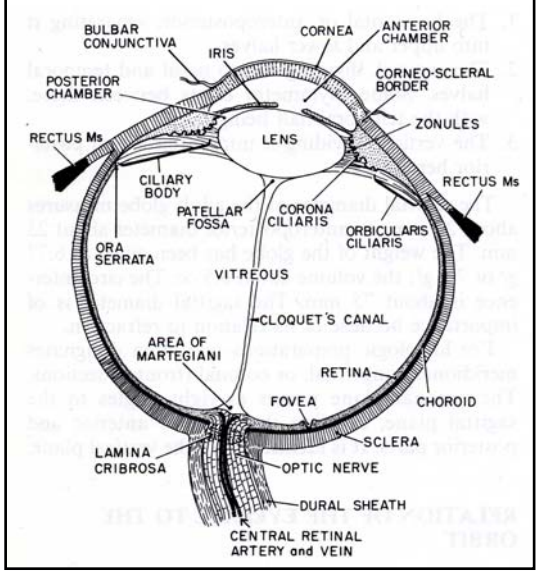
What You Should Know About Retinoblastoma

By David J. Browning, MD, PhD

Retinoblastoma is a cancer arising from a cell or several cells in the retina, the neural lining of the back of the eye that converts light into a nerve signal traveling to the brain. Figure 1 shows the location of the retina in the eye. Retinoblastoma occurs in infants and young children. Approximately one child in every 20,000 births will develop retinoblastoma. Retinoblastoma comprises 12% of all cancers developing in infants and small children. In the United States, between 350-400 new cases of retinoblastoma develop per year. Without treatment this cancer is fatal in 99% of cases. With treatment, over 90% of patients survive into adulthood.

Figure 1. Anatomy of the Eye



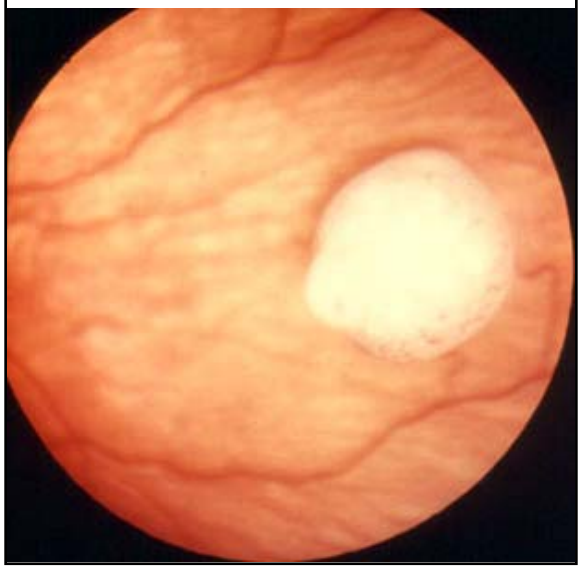
Two Types of Retinoblastoma

To understand this topic, one must first know that each cell of the body has 2 copies of each gene, or piece of DNA coding for a protein. One copy comes from the mother and one copy comes from the father. There are two types of retinoblastoma – heritable and nonheritable. In both types, a cell that becomes cancerous must develop two mutations – one for each copy of the retinoblastoma tumor suppressor gene (RB) found on chromosome 13. In the nonheritable type of retinoblastoma, a single retina cell is unfortunate enough to develop two independent random mutations – something akin to a single person being struck by lightning twice. In the heritable type of retinoblastoma, the affected person has an inherited mutation in RB in every cell in the body. Then, by chance, a second mutation occurs in the second RB gene. When both RB genes are mutated, the cell becomes cancerous. Because there are millions of retina cells in each eye, the odds of more than one cell developing a second RB gene mutation are sufficiently high that several heritable retinoblastomas may develop in the affected person – both eyes may have tumors, and each eye may develop more than one tumor. Nonheritable cases of retinoblastoma, also called sporadic cases, comprise 60% of cases of retinoblastoma. Heritable cases comprise the remaining 40%.

In the days before genetic testing, this was one way doctors determined that a retinoblastoma was heritable or not. If a person had a retinoblastoma in both eyes, or developed more than one tumor in a single eye, then the doctor could conclude that the case was heritable. If a single retinoblastoma developed in only one eye, then the doctor could not tell for sure whether the case was heritable or not. In such a case, the chances are 92% that the retinoblastoma is not heritable, and 8% that it is heritable.

Naturally, inquiries about a family history of retinoblastoma could clarify the situation as well. In 2006, analysis of DNA from white blood cells can make the diagnosis of heritable retinoblastoma in a direct way, but the test is not easily available and there is the obstacle to overcome of test cost, estimated in 2004 to be $3,000 to test a 4-member family with a time to report of approximately one month.

Figure 2. Retinoblastoma



Treatment of Retinoblastoma

Small retinoblastomas, usually <4mm in diameter and <3mm thick, can be treated with local therapies such as a form of laser therapy called transpupillary thermotherapy (TTT), cryotherapy (freezing), and radioactive plaque therapy (brachytherapy).

Larger retinoblastomas are treated first with chemotherapy to make them smaller (so-called chemoreduction), and then are treated with TTT, cryo, or brachytherapy. Some tumors are treated with external beam radiation therapy, but a drawback of this therapy is a higher incidence of secondary cancers in the field of radiation.

The largest retinoblastomas sometimes require that the entire eye be surgically removed (enucleation). This is generally only done if the ophthalmologist thinks that the tumor is too advanced to allow preservation of useful vision with more conservative treatment. Extensive vitreal seeding is one such indication.

The general trend in treatment of retinoblastoma in the past 20 years has been toward fewer enucleations, lesser use of external beam irradiation, and greater use of local therapies, chemoreduction, and combination approaches.

Recurrence of Retinoblastoma After Treatment

Recurrent retinoblastoma can occur after any form of treatment. In bilateral retinoblastoma, recurrence is seen in 24-50% of cases. In unilateral retinoblastoma, recurrence is seen in 6% of cases. Thus, lifelong regular follow-up and ophthalmic examination is necessary in the management of retinoblastoma. Certain factors make recurrence more likely. For example, eyes with tumors in the front half of the retina have recurrences after radiation therapy more often than eyes with tumors in the back half of the retina.

Frequency of Examination Under Anesthesia

In heritable retinoblastoma cases, children must be examined under anesthesia at frequent intervals to detect whether new tumors are developing, and to look for

recurrences of previously treated tumors. In the first two years of life, as many as 12 examinations under anesthesia may be needed. Past 2 years of age, the frequency of examination decreases. Children who need to be examined in this way include those at risk for having heritable retinoblastoma:

1.) All children of a parent with a bilateral or multiple retinoblastoma.
2.) All children of a parent with a unilateral, single retinoblastoma in whom genetic testing has not verified that a germline mutation in the parent is absent.

Pinealblastomas in Patients with Hereditary Retinoblastoma

Patients with hereditary retinoblastoma have a higher risk of developing a tumor of the pineal gland, found in the brain. Approximately 8% develop this brain tumor. Periodic MRI examinations are required to investigate this possibility. Some patients who have a specific syndrome associated with an extensive deletion of part of chromosome 13 (13Q deletion syndrome) have other medical problems requiring attention, such as hip dislocation, facial bone deformities, and mental retardation.

Other Testing

In addition to examination under anesthesia, it is typical for patients to undergo CT scan of the orbits to look for the presence of intralesional calcification, a common, but not invariable, sign of retinoblastoma.

Final Comments

The management of retinoblastoma has evolved considerably in the past 20 years. Fewer eyes are enucleated now. A commitment to lifelong follow-up is necessary for a favorable outcome.

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