Dr Steven Lapere
MBChB, DA(SA), FCOphth, MMed (UCT)
Pr 0705853

Dr Hamzah Mustak
MBChB, FCOphth, MMed (UCT)
Pr 0685917

Dr Raoul Scholtz
MBChB (UCT), DCH (SA), FCS (SA)
Pr 2603721

Cape Town Ocular Oncology Service: 021 671 5154 • info@ocularoncology.co.za • www.ocularoncology.co.za

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Retinoblastoma

What is retinoblastoma?

The retina is the inner layer of cells in the back of the eye. It is made up of special nerve cells that are sensitive to light. These light-sensing cells are connected to the brain by the optic nerve.
Retinoblastoma is a cancer that arises from retinal cells. It is the most common type of eye cancer in children.

How does retinoblastoma develop?

The eyes develop very early as babies grow in the womb. During the early stages of development, the eyes have cells called retinoblasts that divide into new cells and fill the retina. At a certain point, these cells stop dividing and develop into mature retinal cells. Rarely, something goes wrong with this process. Instead of maturing into special cells that detect light, some retinoblasts continue to divide and grow out of control, forming a cancer known as retinoblastoma. The chain of events inside cells that leads to retinoblastoma is complex, but it almost always starts with a change (mutation) in a gene called the retinoblastoma (RB1) gene. The normal RB1 gene helps keep cells from growing out of control, but the change in the gene stops it from working like it should. Depending on when and where the change in the RB1 gene occurs, 2 different types of retinoblastoma can result.

Congenital (hereditary) retinoblastoma

In about 1 out of 3 children with retinoblastoma, the abnormality in the RB1 gene is congenital (present at birth) and is in all the cells of the body, including all of the cells of both retinas. This is known as a germline mutation. In most of these children, there is no family history of this cancer. Only about 25% of the children born with this gene change inherit it from a parent. In about 75% of children the gene change first occurs during early development in the womb. The reasons for this are not clear. Children born with a mutation in the RB1 gene usually develop retinoblastoma in both eyes (known as bilateral retinoblastoma), and there are often several tumors within the eye (known as multifocal retinoblastoma). Because all of the cells in the body have the changed RB1 gene, these children also have a higher risk of developing cancers in other areas as well. A small number of children with this form of retinoblastoma will develop another tumor in the brain, usually in the pineal gland at the base of the brain (a pineoblastoma). This is also known as trilateral retinoblastoma.

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Sporadic (non-hereditary) retinoblastoma
In about 2 out of 3 children with retinoblastoma, the abnormality in the RB1 gene develops on its own in only one cell in one eye. It is not known what causes this change. A child who has sporadic (non-hereditary) retinoblastoma develops only one tumor in one eye. This type of retinoblastoma is often found at a later age than the hereditary form.

Children with this type of retinoblastoma do not have the same increased risk of other cancers as children with congenital retinoblastoma.

How does retinoblastoma present?
Leukocoria (white pupil) and misaligned eyes (strabismus) are the most common signs of retinoblastoma. In other cases, the child may have developed neovascular glaucoma and may be in pain. Longstanding glaucoma can cause enlargement of the eye (buphthalmos).

How does retinoblastoma grow and spread?
If retinoblastoma tumors are not treated, they can grow and fill much of the eyeball. Cells might break away from the main tumor on the retina and float through the vitreous to reach other parts of the eye, where they can form more tumors. If these tumors block the channels that let fluid circulate within the eye, the pressure inside the eye can rise. This can cause glaucoma, which can lead to pain and loss of vision in the affected eye. Most retinoblastomas are found and treated before they have spread outside the eyeball. But retinoblastoma cells can occasionally spread to other parts of the body. The cells sometimes grow along the optic nerve and reach the brain. Retinoblastoma cells can also grow through the covering layers of the eyeball and into the eye socket, eyelids, and nearby tissues. Once the cancer reaches tissues outside the eyeball, it can then spread to lymph nodes (small bean-shaped collections of immune system cells) and to other organs such as the liver, bones, and bone marrow (the soft, inner part of many bones).

How is retinoblastoma treated?
Treatment of retinoblastoma should be co-ordinated by a team of specialists, which includes an ophthalmologist, oncologist, radiation services and vascular intervention surgeons. Treatment will depend on the size, number and location of the tumours and consists of localized therapy in the form of laser or cryotherapy, chemotherapy by various routes of administration and radiation treatment.

Local Treatment
Transpupillary Thermal Therapy (TTT)

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TTT is a form of diode laser, a specialized type of laser that heats the tumour cells slowly and causes damage to the cell structures. TTT is used for tumours that are less than 3mm in height.

Cryotherapy

Cryotherapy involves the use of a cold liquid such as liquid nitrogen that passes into a small probe. The probe is placed over the site of the tumour and causes cell damage by freezing the tumour cells.

Chemotherapy

Systemic chemotherapy

Chemo given into a vein (IV) is now commonly used to shrink tumors before local treatments such as cryotherapy or laser therapy. Doctors are now studying whether giving chemo after local treatments (known as adjuvant chemotherapy) might help prevent the recurrence of retinoblastoma, especially outside the eye. Doctors are also studying the use of different chemo drugs such as topotecan, as well as new ways of combining current drugs, to try to improve how well chemo works.

Localized chemotherapy

Chemo can help shrink most retinoblastomas, but when it's given into the bloodstream it can cause side effects in different parts of the body. This limits the doses that can be given. Newer techniques help keep the chemo concentrated in the areas around the tumors. This can help doctors get higher doses of chemo to the tumors while reducing some of these side effects.

Intra-arterial chemotherapy

In this approach, chemo is injected directly into the ophthalmic artery, the main artery feeding the eye, using a long, thin catheter. When intra-arterial chemotherapy is used, the dose of the chemo drug is much lower than when it is given by vein, and the side effects related to the chemo are minimal.

Intravitreal chemotherapy

Some doctors are studying injecting chemotherapy directly into the jelly-like fluid inside the eyeball (the vitreous humor) to treat tumors that are widespread within the eye and not helped by other treatments. The main concern with this technique is that placing the needle into the eye to give the chemo might open a small hole that could allow tumor cells to spread outside of the eye, so doctors are being very cautious with this approach. Some doctors are studying the use of cryotherapy (using very cold temperatures) at the site of injection to limit this risk. Intravitreal chemotherapy is still in the early stages of testing.

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Radiation treatment
In certain situations, radiation devices can be placed on the eye to treat the tumours inside. This form of radiation treatment is called brachytherapy.

How often do children with retinoblastoma need to be seen by the doctor?
Initially examinations under anaesthesia will need to be performed once a month until the tumours are regressed, and no new tumours seen. Once the tumours have regressed the intervals between examinations can be gradually increased. Children with retinoblastoma need to be followed-up for life to monitor for the development of secondary tumours. Once the child is old enough to co-operate then examination can be done in the doctors rooms.

What is the risk that the next baby we have will also have retinoblastoma?

	More than one affected person in family	The child has bilateral or multifocal retinoblastoma	The child has unilateral unifocal retinoblastoma
Siblings of Rb child	50%	5%	1%
Offspring of child who had Rb	50%	50%	5–10%
More distant relatives of child with Rb	Need to assess the family tree, may be at risk	Not at increased risk	Not at risk

High risk Low risk