

# Importance of the red reflex test in the diagnosis of eye cancer

## Abstract

Retinoblastoma is the most common malignant tumour of the eye in children and accounts for 3% of all childhood cancers. It can occur either unilaterally or bilaterally and generally develops before the first five years of life. A red reflex test must be performed if a child presents with any of the following: a white reflex (leukocoria) or an abnormal reflex in flash photographs; a recently onset squint (strabismus); a change in colour to the iris; deterioration in vision; a red, sore or swollen eye without infection. The presentation of any of these signs or symptoms in isolation can indicate retinoblastoma. However, it is vital to note that a child with retinoblastoma may appear well, apart from one or more of these signs.

This article gives detailed instruction on how to carry out a red reflex test and appropriate referral information for suspected cases. A swift referral pathway is vital to reduce loss of vision and the risk of mortality.

cells undergo a malignant transformation and grow to invade the vitreous or subretinal space, or both. Tumours can then infiltrate the brain and spinal cord via the optic nerve and subarachnoid space, as well as penetrating the blood supply into the bone and bone marrow (Chintagumpala et al, 2007).

Vital prognosis is promising and has improved as a result of earlier detection and diagnosis, speedy referral and prompt treatment. Greater than 90% retinoblastoma-free survival is generally achievable (Aerts et al, 2006; Sundaram et al, 2009; Kanski and Bowling, 2011) but preservation of visual function is dependent on treatment success and whether the eye can be saved. However, some treatments, while saving the eye (and life), can affect visual function.

## The red reflex test

Leukocoria can be detected by viewing a child at a working distance of approximately 50 cm with a direct ophthalmoscope set to a prescription of +2.00D (*Figure 1*). This should be carried out in a darkened room. In order to put the child at ease, it is useful to focus the light on the parent's eyes first. This demonstrates that the test is non-invasive and painless. This also provides the opportunity to determine what the red reflex should be like in the child's particular ethnic group as it can often vary with the degree of ocular pigmentation (melanin) and may be a cause for misdiagnosis (Muen et al, 2010). For thorough examination, the reflex should be observed in all positions of gaze to confirm that the colour is even. In general, the red reflex should be symmetrical in colour and intensity in both eyes (Tamura and Teixeira, 2009).

Additionally, it is important to remember that abnormal or asymmetric red reflexes can be observed as a result of anisometropia or strabismus. In patients who have been diagnosed with strabismus, the reflex is noticed to be darker in the fixating eye due to darker pigmentation from the macula. This is known as Brückner's phenomenon (Roe and Guyton, 1984).

Although leukocoria is the first presenting sign in 60% of retinoblastoma cases, the intraocular tumour can also present as:

- A recently onset squint (strabismus)
- A change in colour to the iris
- Deterioration in vision
- A red, sore or swollen eye without infection.

A normal red retinal reflex can be observed by shining a beam of light from an ophthalmoscope or retinoscope through the pupil. The reflex observed is from a partial reflection of light from the highly vascularised retina (Tamura and Teixeira, 2009). Any parent or clinician taking action on observing a white reflex (leukocoria) instead of the typical 'red-eye' effect as seen in photographs may be vital in the detection of retinoblastoma or other serious eye conditions. This article will discuss how to carry out a red reflex test and what to do if an absent or abnormal red reflex is suspected. This article is aimed at ophthalmic nurses, orthoptists, optometrists and other allied professions in ophthalmology who may be the first point of contact with any such child.

## Retinoblastoma

Although very rare, retinoblastoma is still the most common malignant primary intraocular tumour of childhood and the second most common of all ages. It is responsible for half of all cases of leukocoria, with an incidence of 1/15 000–1/20 000 live births (Aerts et al, 2006). The condition is non-gender-specific and onset is usually within the first five years of life. The cause of retinoblastoma is varied. It can occur in one or both eyes, and there may or may not be a family history. It occurs as a result of a genetic mutation of both alleles of the retinoblastoma tumour-suppressor (Rb1) gene (Aerts et al, 2006). Histopathology shows that fast-growing

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A red reflex test must be carried out for any of these presenting symptoms in order to rule out retinoblastoma. In particular, children with strabismus often wait far too long to be seen by an ophthalmologist; this must not be the case if eye cancer is suspected as a delay of a few months often means treatment needs to be unnecessarily aggressive.

Table 1 and Figure 2 summarise the presenting signs and symptoms of retinoblastoma, how they may be described by the family, and the investigations necessary to support clinical diagnosis.

## What to do next

If it is not possible to confidently rule out retinoblastoma with a red reflex test, an urgent referral must be made for children with (National Institute for Health and Care Excellence, 2009):

- A white pupillary reflex, which may be identified in photographs (Figure 3) or found on examination. The health professional should pay careful attention to the report by a parent of noticing an odd appearance in their child's eye
- A new squint or change in visual acuity if cancer is suspected
- A family history of retinoblastoma and visual problems. Offspring of a parent who has had retinoblastoma, or siblings of an affected child, should undergo screening soon after birth.

Depending on local referral protocol, urgent referrals should be made to the local ophthalmology department, Accident and Emergency Department or GP, stating 'suspected retinoblastoma'. It is important to be aware that the child may be able to see (using the other eye) and will not appear unwell, despite having a life-threatening cancer in the eye.

The speed of referral is vital as a swift referral can reduce the long-term impact of the disease and treatment of the baby or child. It is recommended that the health professional calls through to alert the relevant department and to find out the speed with which urgent referrals are seen (in some cases it can be longer than two weeks). In the UK, if the local ophthalmology department identifies or suspects retinoblastoma, an urgent referral is then made to one of two NHS specialist retinoblastoma treatment centres—Birmingham Children's Hospital or the Royal London Hospital—for diagnosis and treatment. Although this cancer has a very high survival rate, many children live with the consequences of a delayed diagnosis. Late diagnosis for a child with retinoblastoma can mean loss of one or both eyes, life with an artificial eye, a visual impairment or, in some cases, complete blindness. In unilateral cases, 70% of children will need their eye removed to save their life.

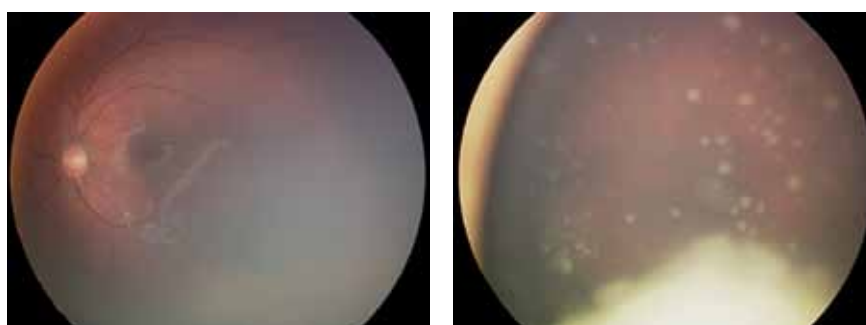


Figure 1. A healthy retina (left) and retinoblastoma tumour with vitreous seeding (right)

Table 1. Retinoblastoma: presenting symptoms and investigations

Presenting symptom	Description by family	Investigation
Leukocoria Intermittently present or seen in flash photographs	'Flashes like a cat's eye' 'Looks like a jelly' 'Sometimes I can see into the back of the eye'	Red reflex test
Strabismus	'Lazy eye' 'The eye is turned in' 'One eye moves independently'	Red reflex test
Poor vision A child with retinoblastoma may have always had poor vision or it may have deteriorated	'Their eyes won't fix or follow' 'One eye moves independently'	Red reflex test
Red or inflamed eye This may look like orbital cellulitis	–	Red reflex test
Family history	There is a 50% chance a parent will pass on the heritable form of retinoblastoma to their child. However, not every adult who had retinoblastoma as a child will be aware of the risks to their children, or may not have been told by their parents what condition(s) they had as a baby	Red reflex test Referral to a retinoblastoma centre

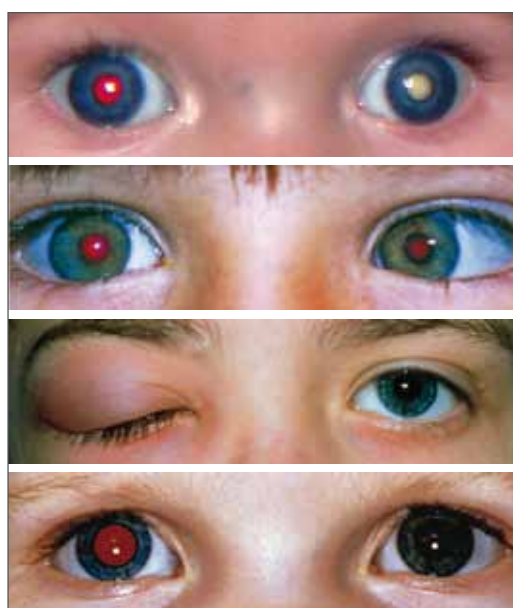


Figure 2. Signs and symptoms of retinoblastoma (from top to bottom): leukocoria; strabismus; red or inflamed eye; absent red reflex



**Figure 3. Retinoblastoma is commonly first noticed by parents as a white 'glow' in the eye in a photograph**

### Breaking the news to parents

If a patient is referred to an ophthalmologist, it is appropriate to inform the patient about concerns and suspicions, even though a full diagnosis cannot be made until the child is seen under anaesthetic by a specialist ophthalmologist. This can be done by telling a child and his/her parents that a specialist eye examination is taken for many reasons and that it is important to rule out anything serious. It is not necessary to tell the families of all patients that eye cancer is suspected, but some families will already be aware of and/or know about eye cancer as there have been articles in the mass media alerting people to the warning signs. If parents have such concerns, the health professional should reassure them that eye cancer is very rare and that the signs and symptoms may sometimes be indicative of something less severe. Most importantly, inform parents that retinoblastoma is treatable and survival rates are extremely high; childhood cancers are different from adult cancers with which they may be more familiar.

### Optician's protocol on suspected retinoblastoma

Although most optometrists are good at recognising and referring children with retinoblastoma, anecdotally the Childhood Eye Cancer Trust (CHECT) is aware of problems where non-medical staff in optometry practices can unwittingly cause delays. This stems from a lack of awareness and understanding of the signs and symptoms of retinoblastoma and the need for urgent examination to rule out its presence. As a result, staff may either give the family a non-urgent appointment or turn

them away, saying their practice does not examine small children, without stressing to the family the importance of ensuring the child is examined urgently elsewhere.

In response to this issue, the CHECT developed an opticians' protocol on suspected retinoblastoma to be distributed to optical stores. This ensures that all practice staff, including receptionists and dispensing opticians, are aware of:

- 1 The most common signs of retinoblastoma (i.e. a white or abnormal pupil reflex in a photograph or a recently onset squint)
- 2 The need for any suspected case to have an urgent assessment by a GP or an optometrist.

The opticians' protocol on suspected retinoblastoma is a one-page summary that describes in lay language the key signs and symptoms of retinoblastoma and the appropriate action required. It is approved by the Royal College of Ophthalmologists and the College of Optometrists, and has been adopted by Vision Express and Boots Opticians, along with a number of independent optical stores.

### Differential diagnosis

Although retinoblastoma is one of the most common causes of leukocoria, it is important to be aware of the possible differential diagnoses:

- Congenital cataract
- Coats' disease
- Retinopathy of prematurity
- Optic disc coloboma
- Myelinated nerve fibres
- Toxocariasis
- Persistent hyperplastic primary vitreous.

On rare occasions, leukocoria may be from an observation of the normal optic disc, but a pathological cause should always be actively ruled out.

### Conclusions

Children with retinoblastoma usually show no other signs of illness and a red reflex test should be carried out in every case of parental concern regarding the eyes. If an abnormal red reflex is confirmed or there is an inconclusive examination, a prompt and appropriate referral should be made.

*Acknowledgement: All images are reproduced with kind permission from the Childhood Eye Cancer Trust.*

*Conflict of interest: none declared.*

### Further reading and resources

- For more information on the Childhood Eye Cancer Trust and the opticians' protocol on suspected retinoblastoma, please visit: [www.checht.org.uk](http://www.checht.org.uk)

- The National Cancer Institute provides information about managing the physical and emotional effects of retinoblastoma and its treatment: [www.cancer.gov/cancertopics/types/retinoblastoma](http://www.cancer.gov/cancertopics/types/retinoblastoma)
- The American Cancer Society website is a resource that can be used to help patients find out more about retinoblastoma, including risk factors, symptoms, how it is found and how it is treated: [www.cancer.org/cancer/retinoblastoma](http://www.cancer.org/cancer/retinoblastoma)
- The Canadian Retinoblastoma Society provides support to ensure families impacted by retinoblastoma have equal access to support, information and medical care: [www.rbsociety.ca](http://www.rbsociety.ca)

## References

- Aerts I, Lumbroso-Le Rouic L, Gauthiers-Villars M, Brisse H, Doz F, Desjardins L (2006) Retinoblastoma. *Orphanet J Rare Dis* 1: 31. doi: 10.1186/1750-1172-1-31
- Chintagumpala M, Chevez-Barrios P, Paysse EA, Plon SE, Hurwitz R (2007) Retinoblastoma: review of current management. *Oncologist* 12(10): 1237–46
- Kanski JJ, Bowling B (2011) *Clinical Ophthalmology: A Systemic Approach*. 7th edn. Elsevier Saunders, Edinburgh
- Muen WJ, Hindocha M, Reddy MA (2010) The role of education in the promotion of red reflex assessments. *JRSM Short Rep* 1(5): 46. doi: 10.1258/shorts.2010.010036
- National Institute for Health and Care Excellence (2009) *Children's Tumours–Suspected*. <http://cks.nice.org.uk/childrens-tumours-suspected#!scenario recommendation:8> (accessed 10 December 2014)
- Roe LD, Guyton DL (1984) The light that leaks: Brückner and the red reflex. *Surv Ophthalmol* 28(6): 665–70
- Sundaram V, Barsam A, Alwitry A, Khaw P, eds (2009) *Training in Ophthalmology: The Essential Curriculum*. Oxford University Press, Clarendon
- Tamura MYY, Teixeira LF (2009) *Leukocoria and the Red Reflex Test*. <http://apps.einstein.br/revista/arquivos/PDF/1403-Einstein%20v7n3p376-82.pdf> (accessed 5 December 2014)

## Key points

- A red reflex test should be carried out in every case of parental concern regarding the eyes
- White pupillary reflex (leukocoria) or a recent onset squint (strabismus) are the most common signs of retinoblastoma
- An urgent referral is crucial in any case of suspected retinoblastoma to preserve the patient's sight, eyes and life.

• Retinoblastoma • Ophthalmoscopy • Pupillary reflex • Leukocoria  
• Strabismus • Eye cancer

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