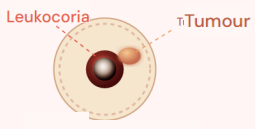
# A Look at *Retinoblastoma*

**1 in 15–20k**
live births
No sex or ethnic predisposition

**<5**
years old
Median diagnosis age — 2 years

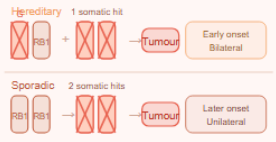
## 01 INTRODUCTION

### WHAT?




- Malignant tumour of developing **retinal cells**
- Primarily affects **infants and young children**
- Caused by loss of **RB1 tumour suppressor gene**[1,2]

### WHY?




- **RB1** controls cell cycle via pRB[1,2]
- Cancer when **both copies inactivated**
- Based on **Knudson's Two-Hit Hypothesis**

### WHO AND WHERE?


- **Unilateral** → somatic mutation[3]
- **Bilateral** → germline mutation
- **Most common** intraocular cancer in children
- Worse outcomes in **low-income countries**[4]

## 02 ETIOLOGY OF RETINOBLASTOMA

### RB1 Gene · tumour suppressor

The RB1 gene encodes **pRB**, an E2F inhibitor blocking the **G1→S phase** transition. Loss of both copies → **uncontrolled proliferation**.[5]

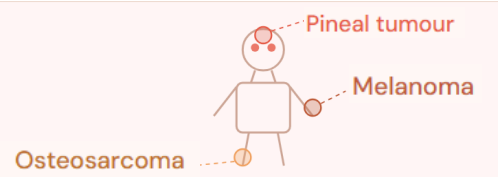
- **13q14 deletion** removes one RB1 allele — only one more hit needed to fully lose RB1[6,7]

### Knudson's Two-Hit Model[7,8]

| Type | Hit 1 | Hit 2 | Onset | Side |
|---|---|---|---|---|
| Hereditary | Germline | Somatic | Early | Bilateral |
| Sporadic | Somatic | Somatic | Later | Unilateral |

### Systemic Cancer Risk · hereditary only

- Germline RB1 = **body-wide susceptibility**, not just the eye[9]
- Risk of **osteosarcoma, melanoma,** pineal tumours
- Sporadic mutations localised to retinal cell of origin




Secondary cancer sites — germline RB1 carriers

## 03 PATHOPHYSIOLOGY

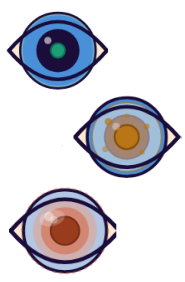
Retinal cone precursor cells have weaker compensatory tumour-suppressor pathways, making them particularly susceptible to malignant transformation when RB1 is lost.[10,11]

### Tumour Growth Patterns

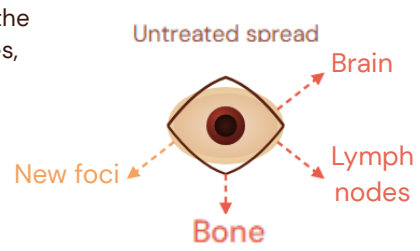
**RT-1 · Focal** Single mass, sharp border. Normal retina preserved.[13]

**RT-2 · Expansive** Large abnormal zones; microtumours in adjacent retina.[13]

**RT-3 · Diffuse** Entire retina involved. Ciliary body and iris affected.[13]



**Progression:** If left untreated, the tumour invades local structures, seeds new foci, and eventually spreads beyond the eye.[12]

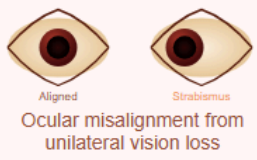



## 04 CLINICAL PRESENTATION

### Common Signs

- Leukocoria (white pupillary reflex) — most classic sign
- Strabismus — misaligned eyes due to vision loss[14,15]
- Persistent red eye, uveitis-like inflammation
- Hyphema, pseudohypopyon, iris heterochromia
- Secondary glaucoma, orbital swelling / proptosis[14]


Normal red reflex vs white pupillary reflex




Ocular misalignment from unilateral vision loss

**Red Flags — refer immediately**

- Leukocoria in photos or clinical exam
- Persistent strabismus or abnormal red reflex
- Unexplained vision loss in child under 5
- Persistent red, painful eye or eye hyphema[15]

[15]

## 05 DIAGNOSIS & SCREENING

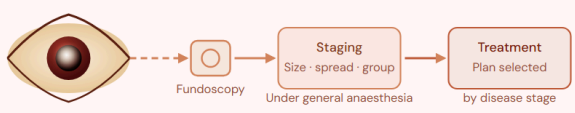
**Primary method:** Ophthalmologic exam under anaesthesia using fundoscopy to directly visualise retinal tumours. Imaging supports staging, spread assessment, and prognosis.[15]

### Supporting Diagnostics

**Imaging**
MRI for optic nerve & brain spread. Ultrasound detects masses. OCT for small tumours & monitoring.[15]
MRI · Ultrasound · OCT

**Genetic (RB1) Testing**
Blood & tumour analysis identifies hereditary vs sporadic. Assesses family risk for genetic counselling.[15]
Germline · Somatic

**Screening**
Children with family history undergo regular dilated eye exams from birth to detect early disease.[16]
High-risk families · From birth




## 06 TREATMENT OPTIONS

### Treatment selection — based on disease stage

| Small / focal | Moderate / bilateral | Advanced intraocular | Metastatic / CNS |
|---|---|---|---|
| focal therapy ± chemo[18] | IVC or IAC + focal[18] | enucleation ± adj. chemo[18] | HD chemo + radiotherapy[18] |

**Focal Therapies**
Locally target the tumour while preserving surrounding tissue. Used for small, localised lesions, often combined with chemotherapy.[18]
Laser photocoagulation · Cryotherapy · Plaque brachytherapy

**Intravenous Chemo (IVC)**
Systemic multi-drug regimen via bloodstream. Shrinks tumours before focal therapy. Also used adjuvantly post-surgery.[19]
Carboplatin · Vincristine · Etoposide

**Intra-Arterial Chemo (IAC)**
Catheter delivers chemo directly to the ophthalmic artery — 10× higher dose to the eye vs IVC. Preferred for unilateral disease. Superior globe-salvage rates.[19]
Unilateral preferred · Globe-salvaging · Melphalan

**Radiation (EBRT)**
High-energy radiation for extraocular spread or orbital involvement. ≥45 Gy orbital / craniospinal. Now less common due to long-term risks in children.[18]
Orbital EBRT · Craniospinal · Long-term risks

**Enucleation · Last Resort**
Surgical removal of the affected eye. Reserved for advanced Group E tumours, failed globe-salvage attempts, or extraocular spread. Major centres have dramatically reduced enucleation rates over the last 30 years in favour of globe-salvaging techniques. Allows histopathologic confirmation and is lifesaving when other options fail.[18]
Group E tumour · Failed IAC/IVC · Extraocular spread · Histopath confirms

*Treatment often involves a multidisciplinary team, including ophthalmologists, radiologists, pathologists, and oncologists.*[18]

**95%**
survival rate
High-income countries with early treatment

**~30%**
without access to care

**~90%**
globe salvage
Eye preserved with modern IAC when treated early

**2–3**
years earlier diagnosis
High-income vs low-income countries

References: