Retinoblastoma

Epidemiology

- The most common primary intraocular malignancy of childhood
- 3% of all childhood cancers
- The second most common malignant intraocular tumour
- 1 in 18,000 live births
- 25-30% cases are bilateral but asymmetric
- Survival rates are over 95% in specialized centers but are much lower in the developing world.

Genetics & Histopathology

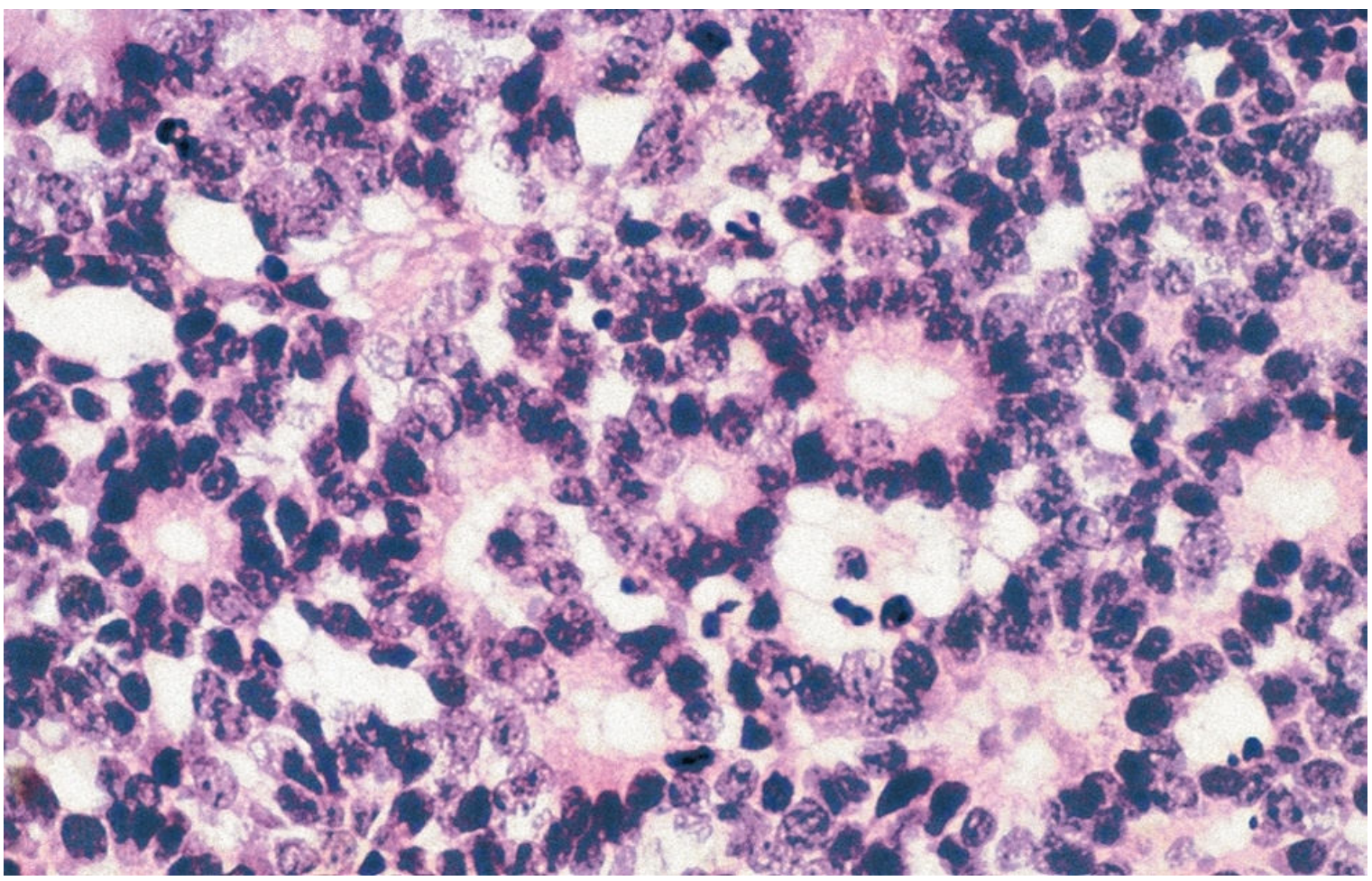
- *RB1 is t*he tumour suppressor gene in which mutations/deletion predisposes to retinoblastoma.
- Tumours are composed of small basophilic cells (retinoblasts) with large hyperchromatic nuclei and scanty cytoplasm.
- Characterized by the formation of structures known as rosettes
- Flexner–Wintersteiner,
- Homer–Wright and fleurettes

- Growth may be endophytic (into the vitreous) with seeding of tumour cells throughout the eye, or
- Exophytic (into the subretinal space) leading to retinal detachment, or mixed, or the retina may be diffusely infiltrated.

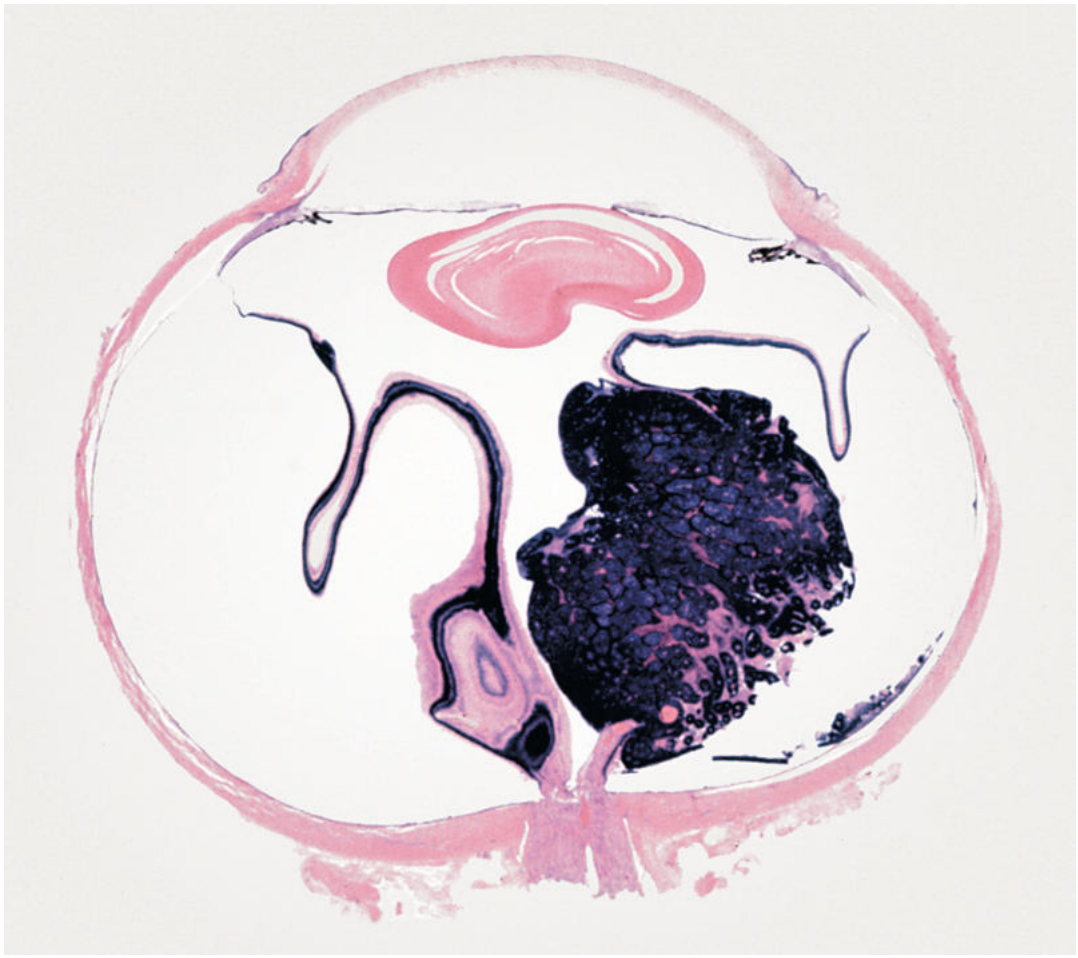
- Optic nerve invasion may occur, with spread of tumour along the subarachnoid space to the brain.

- Metastatic spread is to regional nodes, lung, brain and bone.

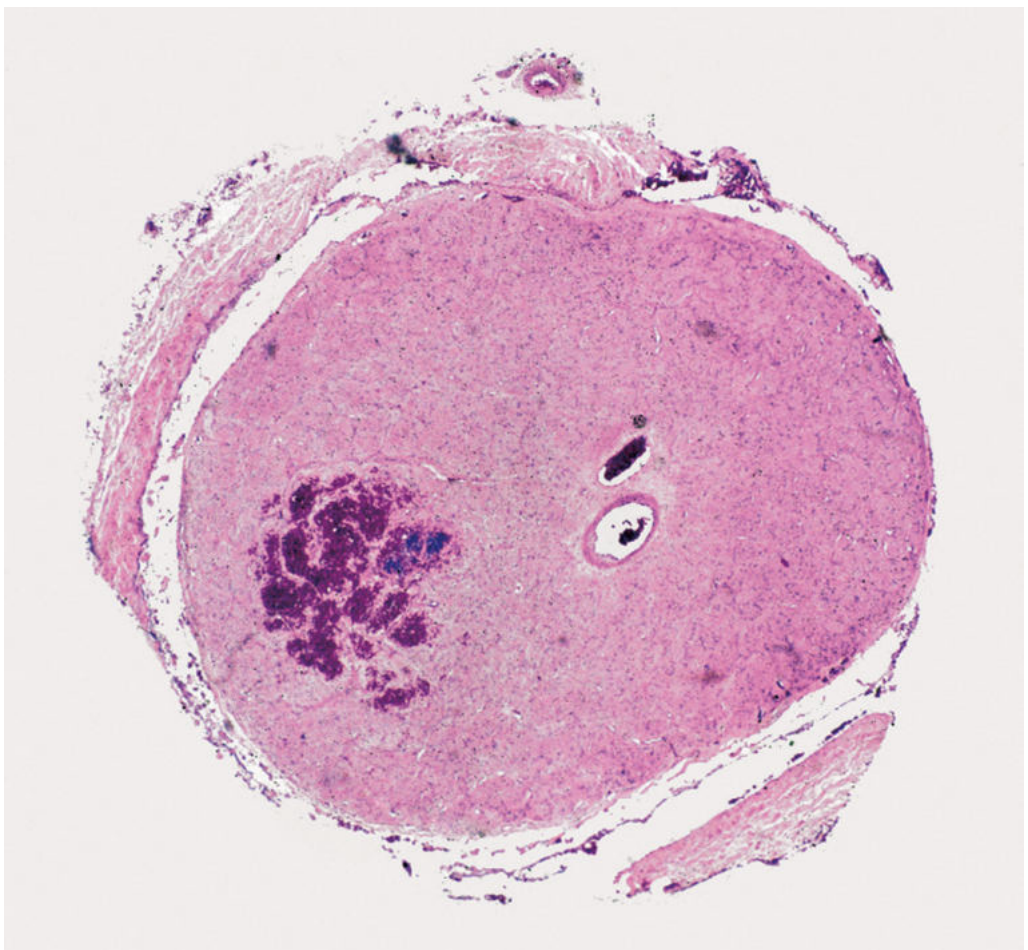
Flexner–Wintersteiner Rosettes



Endophytic growth



Optic nerve infiltration



Types of retinoblastoma

1. Heritable (hereditary, germline) retinoblastoma accounts for 40%.

- One of the pair of alleles of *RB1 is mutated in all the cells in the body*.
- *When a further* mutagenic event ('second hit' according to the 'two-hit' hypothesis proposed by Knudson) affects the second allele, the cell may then undergo malignant transformation.

- Because of the presence of the mutation in all cells, a large majority of these children develop bilateral and multifocal tumours.
- Pinealoblastoma ('trilateral retinoblastoma', which occurs in up to 10%, usually before the age of 5),
- Osteosarcomas,
- Soft tissue sarcomas and melanomas

- The risk of a second malignancy is about 6%
- Increases five-fold if external beam

irradiation has been used to treat the original tumour,

- The second tumour tends to arise within the irradiated field.

2. Non-heritable (non-hereditary, somatic) retinoblastoma.

- 60% Cases
- The tumour is unilateral,
- Non transmissible and
- Does not predispose the patient to second non-ocular cancers.

- If a patient has a solitary retinoblastoma and no positive family history, Its very likely that
- Non-heritable
- The risk in each sibling and the patient's offspring is about 1%.

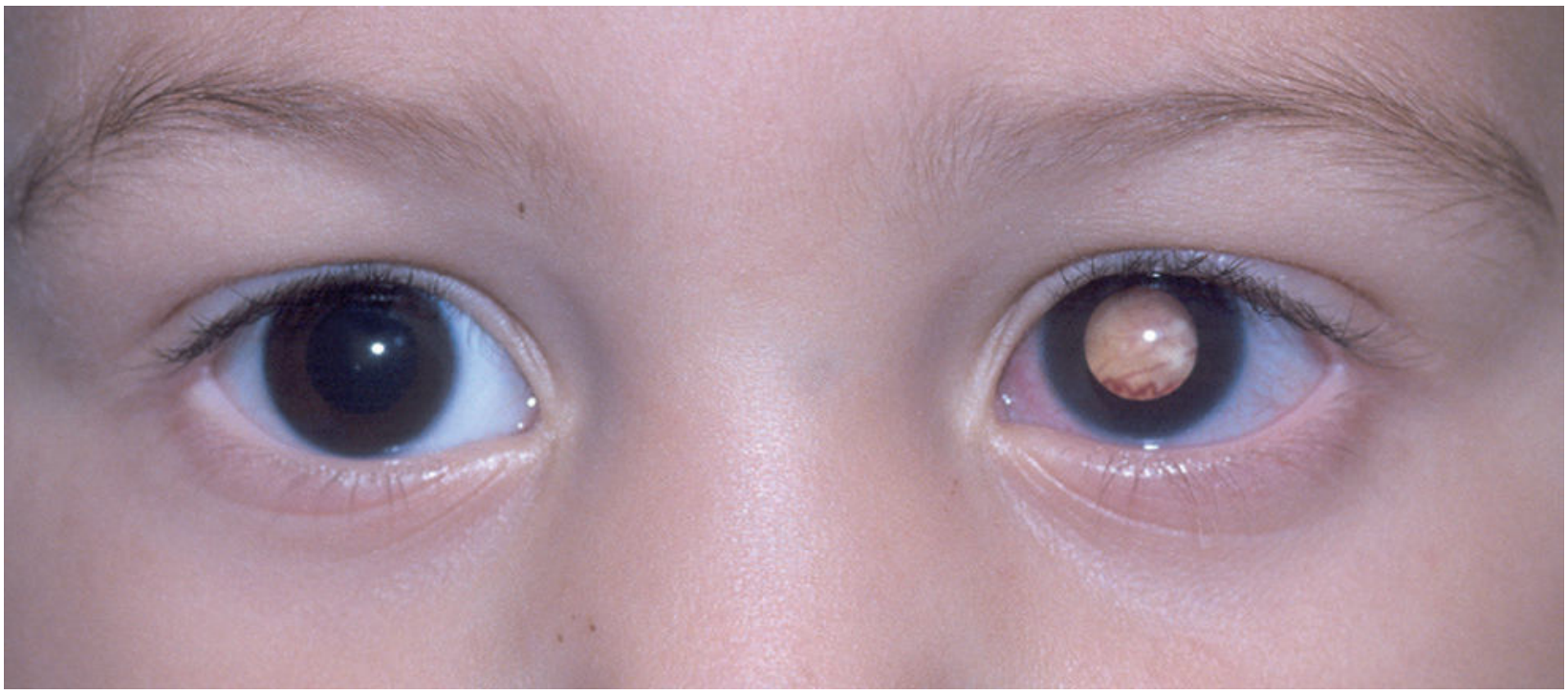
- **Screening of at-risk family members.**
- Siblings at risk of retinoblastoma should be screened by
- Prenatal ultrasonography,
- Ophthalmoscopy soon after birth and
- Then regularly until the age of 4 or 5 years.

- Early diagnosis correlates with a higher chance of preserving vision, salvaging the eye and preserving life.
- If a child has heritable retinoblastoma, the risk to siblings is 2% if the parents are healthy, and 40% if a parent is affected.
- Parents should also be screened

Clinical features

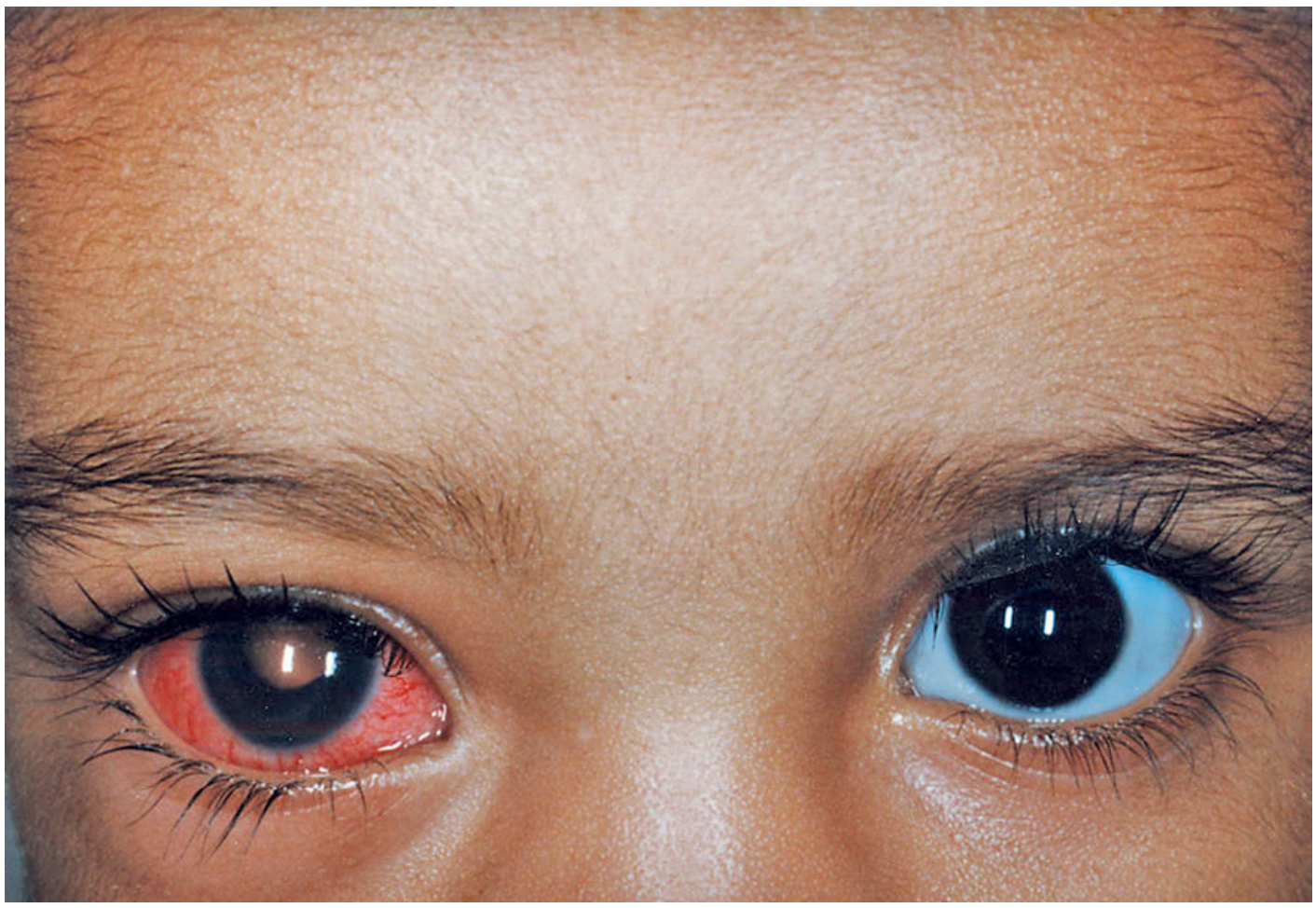
- Bilateral cases present with in 1 yr of age
- Unilateral cases present up to 2 yrs of age
- Leukocoria (white pupillary reflex) is the commonest presentation (60%) and may first be noticed in family photographs.

Leukocoria

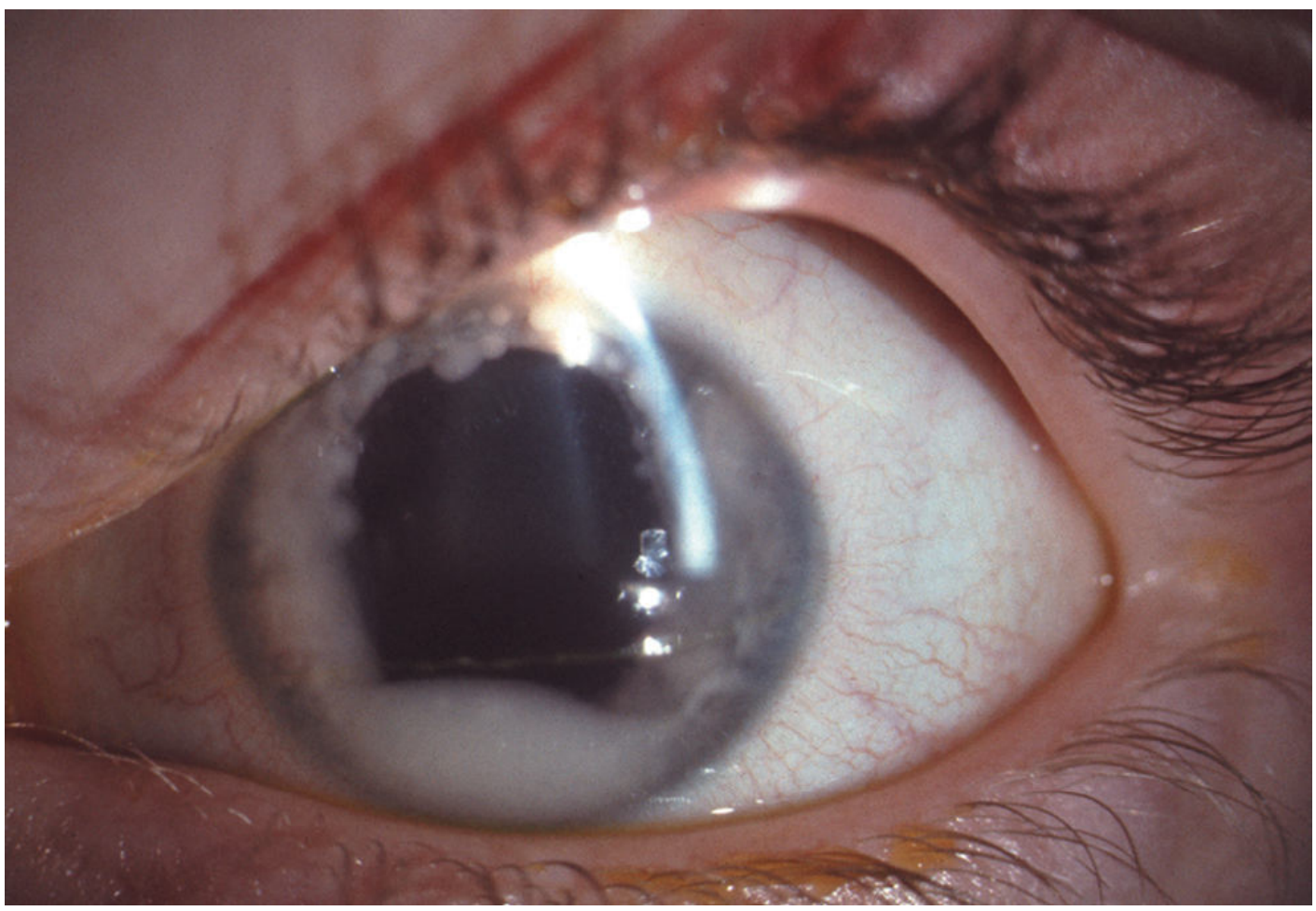


- Strabismus is the second most common (20%); fundus examination is therefore mandatory in all cases of childhood squint.
- Painful red eye with secondary glaucoma
- Painful red eye with uveitis
- Poor vision.
- Inflammation or pseudoinflammation
- Nystagmus

Uveitis



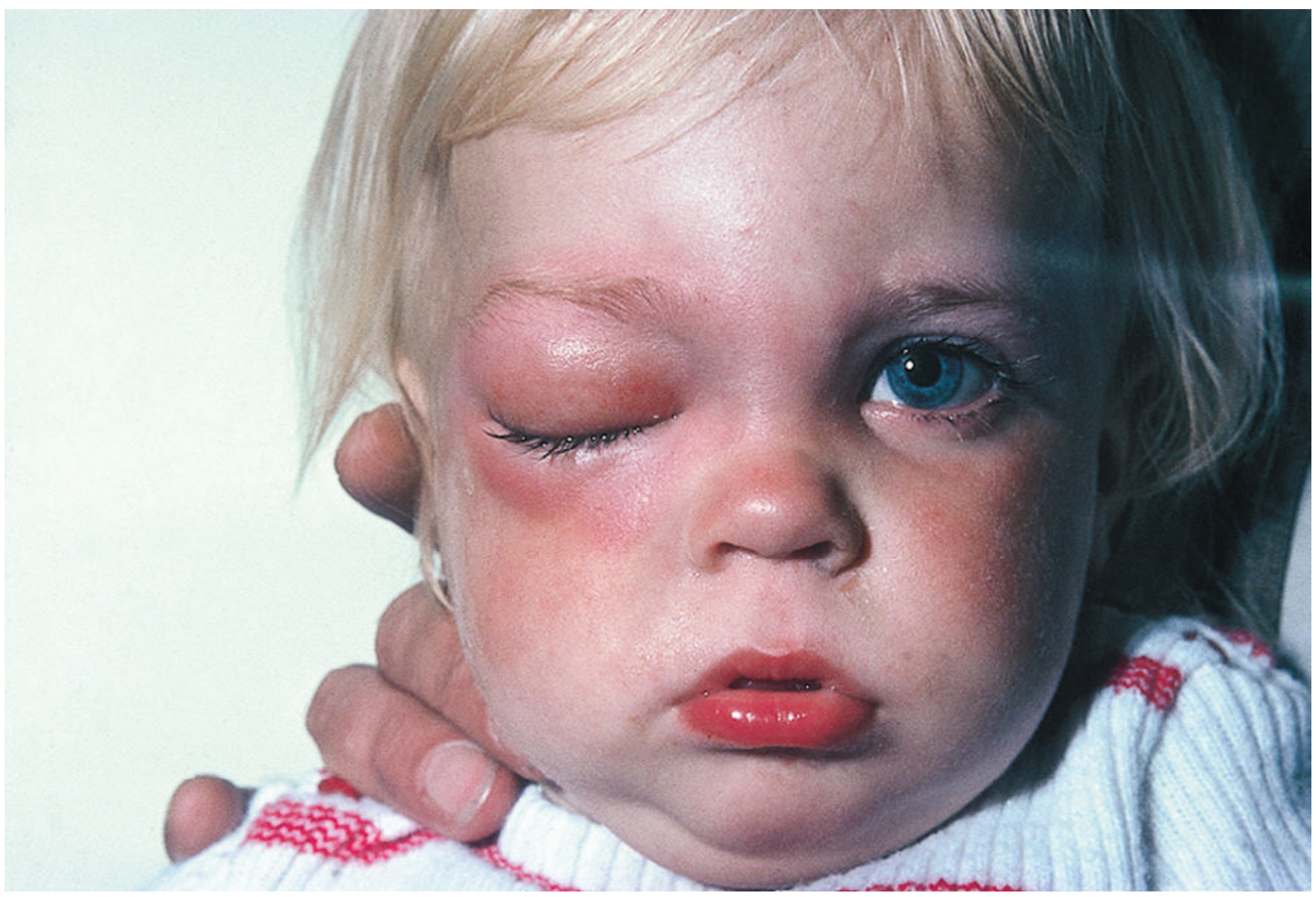
Iris nodules with pseudohypopyon



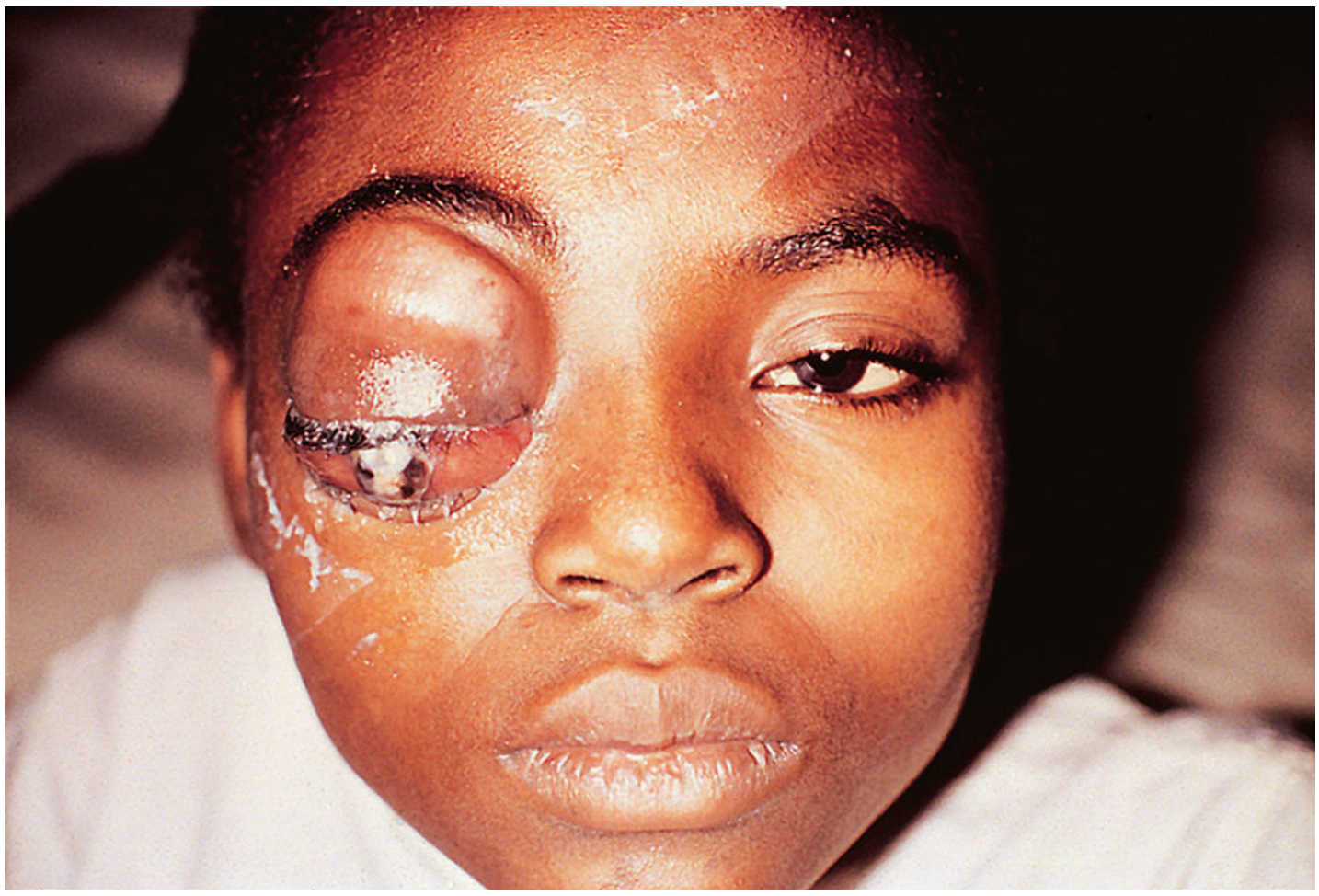
Clinical features

- Routine examination of a patient known to be at risk.
- Orbital inflammation mimicking orbital or preseptal cellulitis may occur with necrotic tumours
- Orbital invasion or visible extraocular growth
- Metastatic disease involving regional lymph nodes and brain before the detection of ocular involvement is rare.

Orbital cellulitis

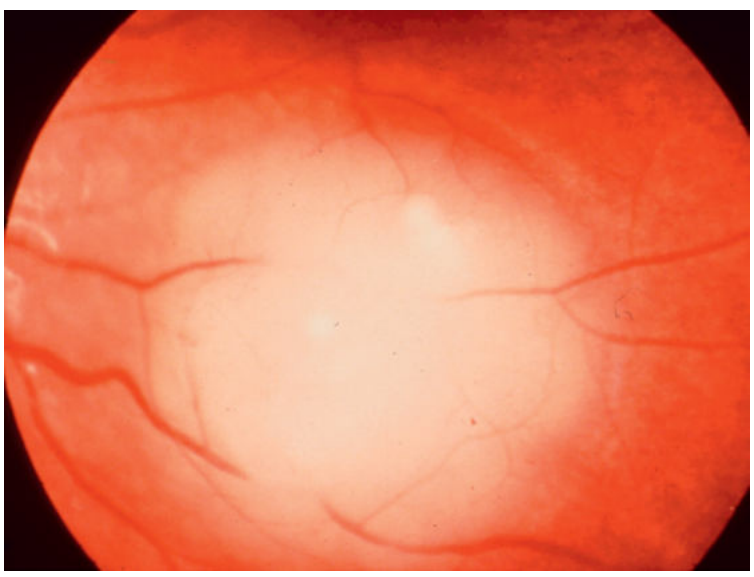


Orbital invasion



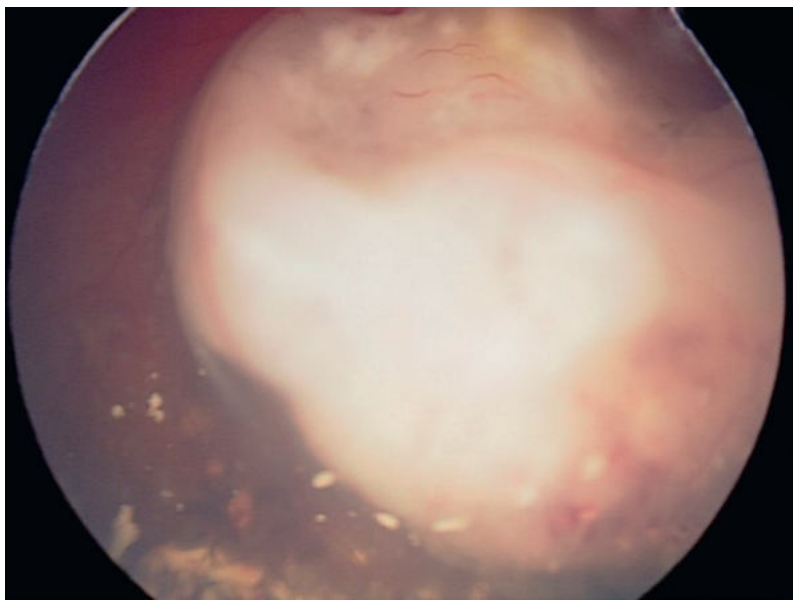
Signs

- An intraretinal tumour is a homogeneous, dome-shaped white lesion that becomes irregular, often with white flecks of calcification.



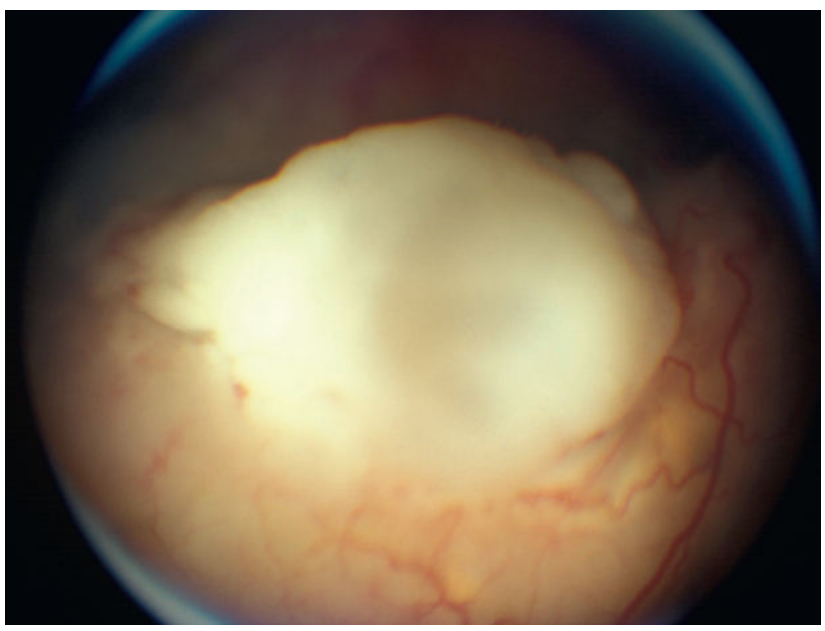
Signs

- An endophytic tumour projects into the vitreous as a white mass that may 'seed' into the gel.



Signs

- An exophytic tumour forms multilobular subretinal white masses and causes overlying retinal detachment



Clinical Stages

- I. *Quiescent stage.*
- II. *Glaucomatous stage.*
- III. *Stage of extraocular extension.*
- IV. *Stage of distant metastasis.*

Clinical Stages

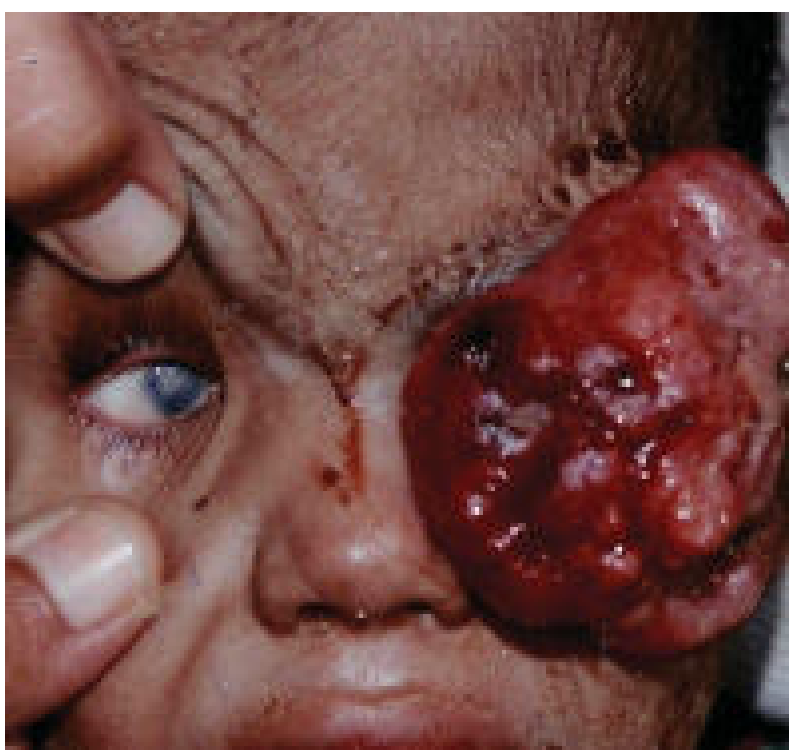
- I. *Quiescent stage.*
- Lasts for about 6 months to1year.
- Leukocoria
- Nystagmus
- Strabismus
- Diminution of vision
- Retinal detachment

Clinical Stages

- **II. *Glaucomatous stage.***
- Pain, redness, watering.
- Eyeball is enlarged leading to proptosis.
- Conjunctival congesion.
- Corneal haze.
- Increased intraocular pressure.
- Rarely acute iridocyclitis.

Clinical Stages

- **III. *Stage of extraocular extension.***
- Fungation and involvement of extraocular tissues resulting in marked proptosis



Clinical Stages

- **IV.** ***Stage of distant metastasis.***
- 1. Lymphatic spread to preauricular and neighbouring lymph nodes.
- 2. Direct extension by continuity to the optic nerve and brain is common.
- 3. Metastasis by blood stream involves cranial and other bones.

Investigations

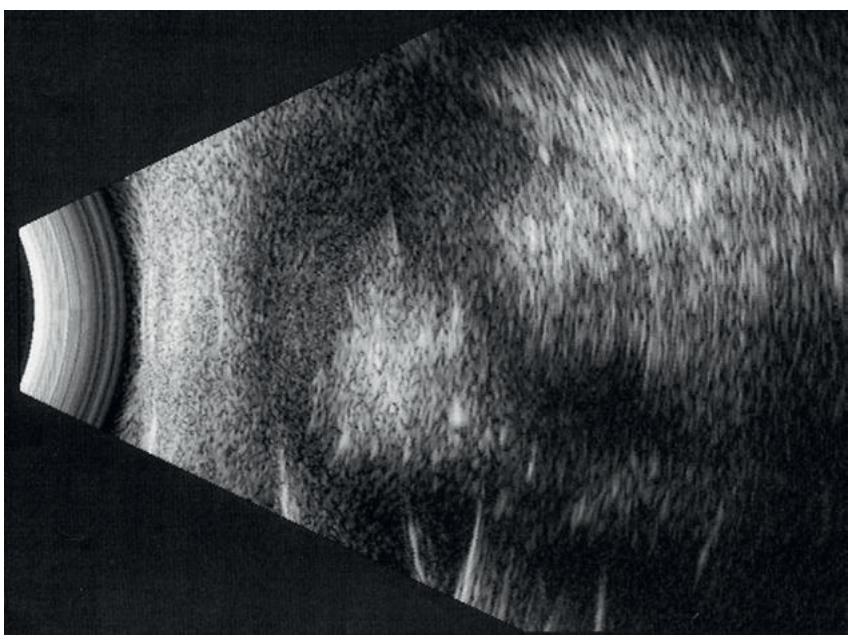
- **Red reflex testing** with a distant direct ophthalmoscope
- **Examination under anaesthesia**
- General examination
- Tonometry.
- Measurement of the corneal diameter
- Anterior chamber examination
- Ophthalmoscopy,
- Cycloplegic refraction.

Investigations

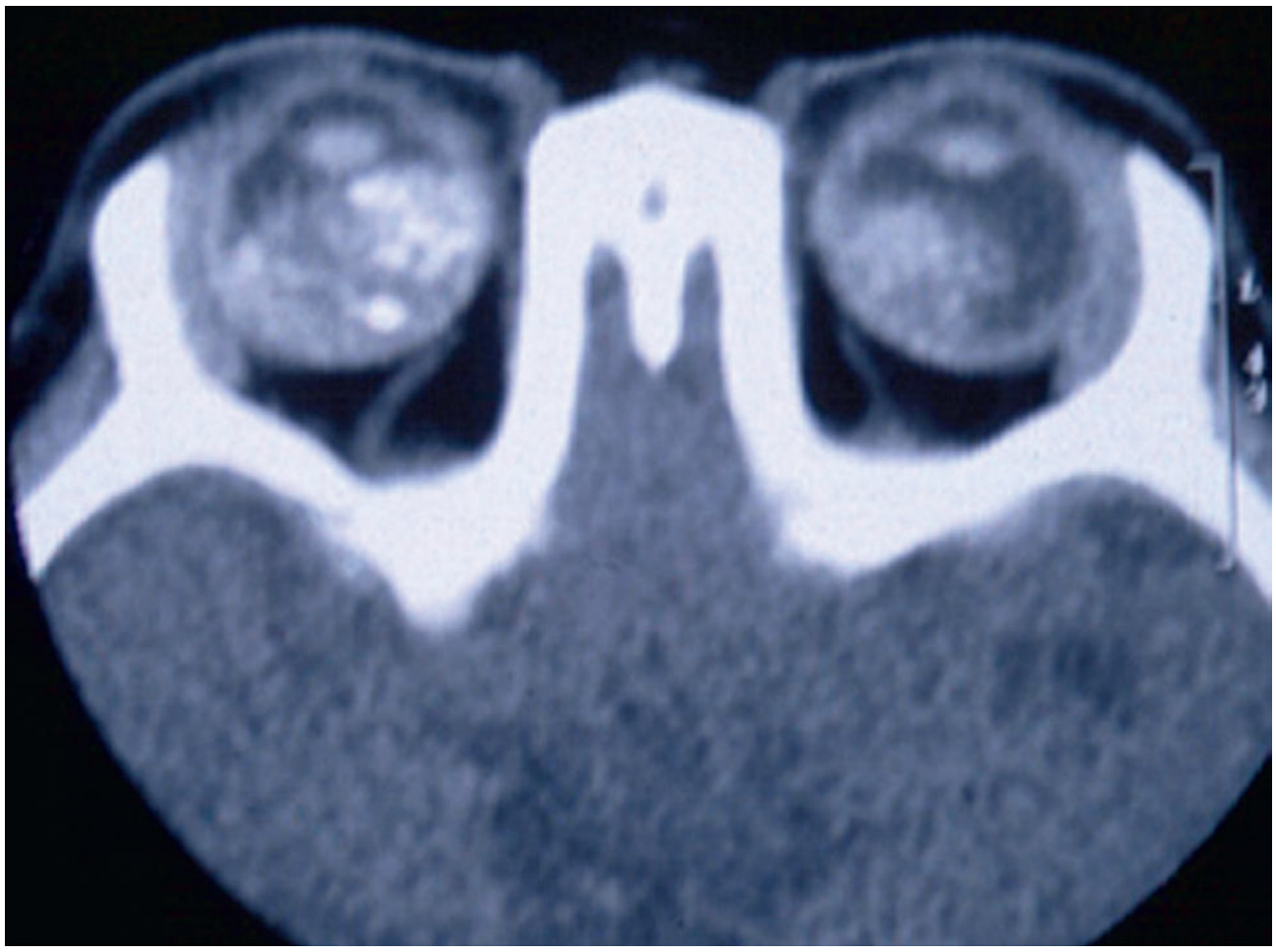
- Ultrasonography
- Aqueous LDH levels
- Wide field photography
- CT scan
- MRI for optic nerve evaluation
- Bone scans and bone marrow aspiration
- Genetic study

USG

- B Scan displays a caulifiower like mass arising from the retina.
- A scan through the mass shows a characteristic V-Y pattern.



CT SCAN



Differential diagnosis

- **Persistent anterior fetal vasculature** (persistent hyperplastic primary vitreous)
- **Coats disease**
- **Retinopathy of prematurity**
- **Toxocariasis**
- **Uveitis**
- **Vitreoretinal dysplasia**
- **Endophthalmitis**

Treatment

- 1. ***Tumour destructive therapy.***
- When tumour is involving less than half of retina and optic nerve is not involved
- Chemoreduction followed by local therapy

(Cryotherapy, thermochemotherapy or brachytherapy) for large tumours (>12mm in diameter)

- Tumour <12 mm in diameter and <8mm in thickness Radiotherapy (external beam radiotherapy or brachytherapy) combined with chemotherapy is recommended for medium size.
- Cryotherapy is indicated for a small tumour (<4.5 mm indiameter and <2.5 mm in thickness) located anterior to equator.

- Laser photocoagulation is used for a small tumour located posterior to equator <3 mm from fovea.

- Thermotherapy with diode laser is used for a small tumour located posterior to equator away from macula

- **2. *Enucleation***
- Tumour involves more than half of the retina.
- Optic nerve is involved.
- Glaucoma is present and anterior chamber is involved.
- Followed by radiotherapy and chemotherapy if optic nerve is involved.
- Intravenous carboplatin, etoposide and vincristine (CEV) are given in three to six cycles according to the grade of retinoblastoma.

- **Careful review** at frequent intervals is generally required following treatment, in order to detect recurrence or the development of a new tumour, particularly in heritable disease.

- Palliative therapy
- Retinoblastoma with orbital extension,
- Retinoblastoma with intracranial extension, and
- Retinoblastoma with distant metastasis.

- Chemotherapy,
- Surgical debulking of the orbit or orbital exentration, and
- External beam radiotherapy

Prognosis

- If untreated the prognosis is almost always bad and the patient invariably dies.
- Rarely, spontaneous regression with resultant cure and shrinkage of the eyeball may occur due to necrosis followed by calcification

- Prognosis is fair (survival rate 70-85%) if the eyeball is enucleated before the occurrence of extraocular extension.

MCQs

1. Gene Rb1 responsible for retinoblastoma is located at:

A. 13q14
B. 14q13
C. 13p14
D. 14p13

MCQs

2. Pathognomic feature of retinoblastoma is:

A. Necrosis
B. Calcification
C. Granulomatous reaction
D. None

MCQs

3. Characteristic histopathological feature of retinoblastoma is:

A. Flexner–Wintersteiner rosettes,
B. Granulomatous reaction
C. Homer–Wright and fleurettes
D. None

4. On A scan characteristic pattern of Retinoblastoma is:

A. Collar stud appearance
B. V-Y Pattern
C. Cauliflower pattern
D. All

5. The most common clinical presentation of retinoblastoma is:

A. Nystagmus
B. Leukocoria
C. Strabismus
D. Secondary glaucoma

6. Which not a clinical presentation of Retinoblastoma

A. Nystagmus
B. Leukocoria
C. Strabismus
D. Growth retardation

7. Which not a differential diagnosis for Retinoblastoma

A. Coat's disease
B. Persistent hyperplastic primary vitreous
C. Endophthalmitis
D. Central retinal vein occlusion

8. Leucocoria is seen in:

A. Cataract
B. Coat's disease
C. Retinopathy of prematurity
D. All

9. If retinoblastoma involves more than half of the retina, the treatment of choice is:

A. Chemotherapy
B. External beam radiotherapy
C. Enuclaetion
D. Cryotherapy

10. The most preferred combination of chemotherapy for retinoblastoma is:

A. Methotrexate, etoposide & vinblastin
B. Methotrexate, etoposide & vincristin
C. Carboplatin, etoposide & vinblastin
D. Carboplatin, etoposide & vincritin

Thank You