# Retinoblastoma

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Biochem 118Q

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# What is retinoblastoma?

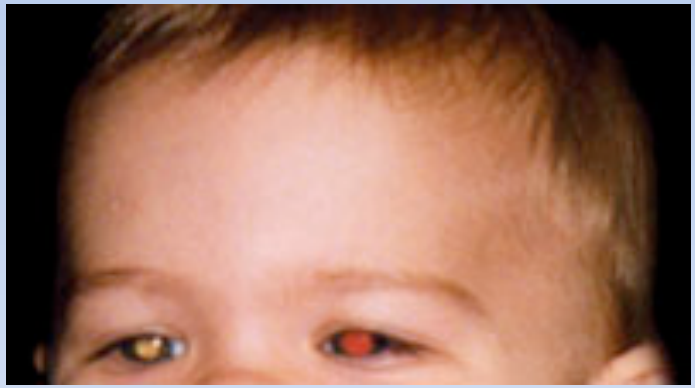
- Cancerous tumor in the retina
- Occurs 1 in 23000 births, affects

~ 300 per year in the U.S.

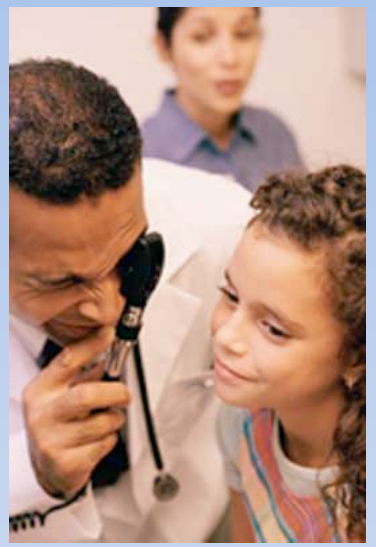
- 90% occurs under 3 years old
- Fatal if untreated; 90% survival

rate if discovered early and treated

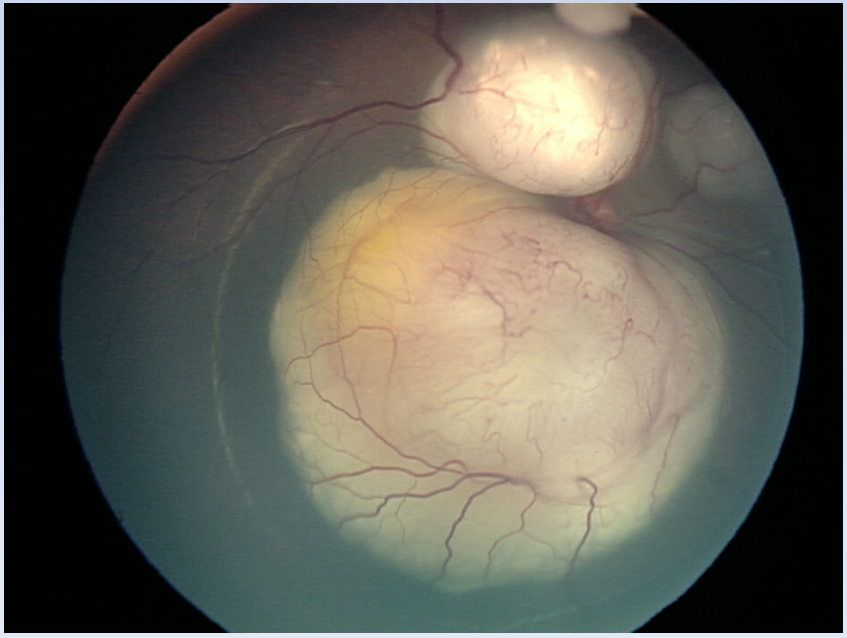
- Could be hereditary or non-hereditary
- 2 forms – unilateral and bilateral



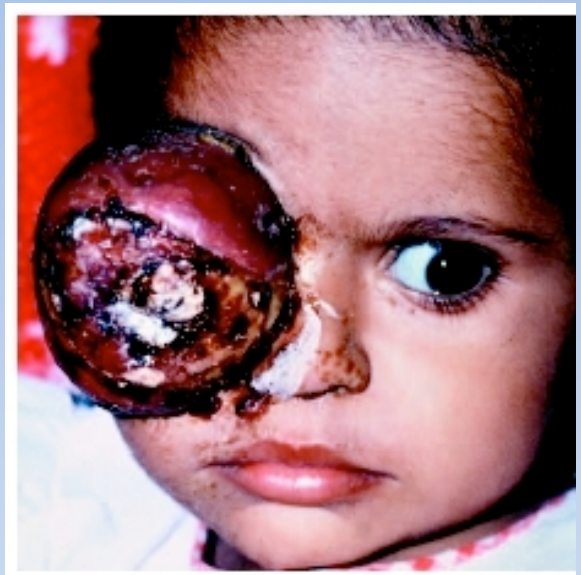
# Classical Diagnosis

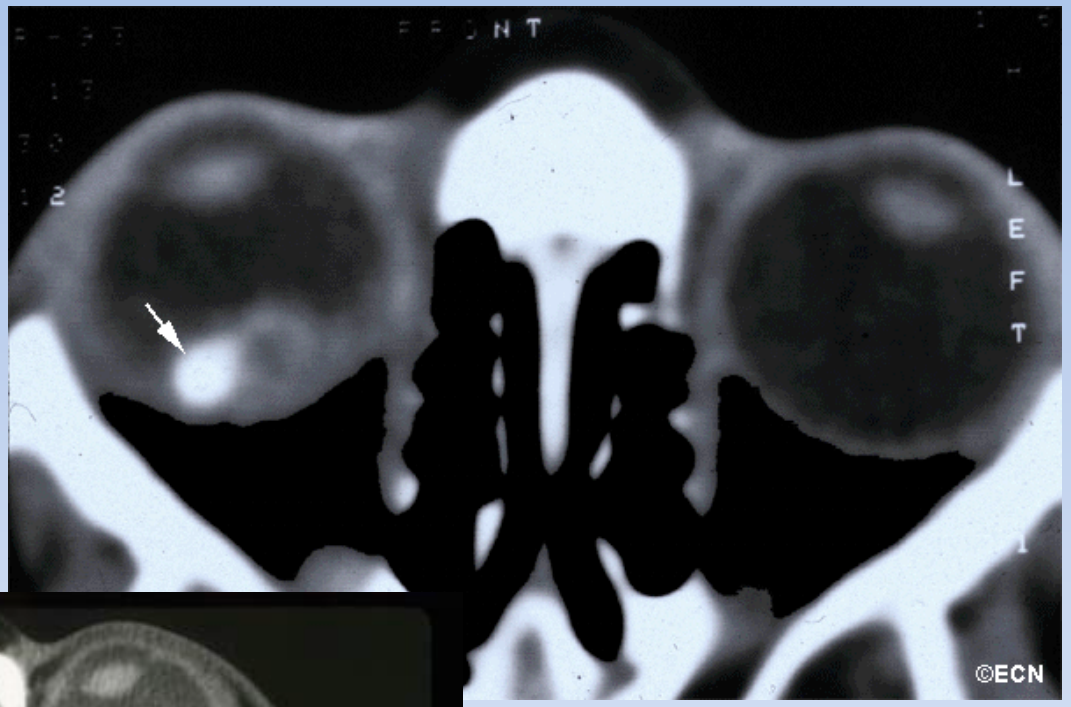


- Symptoms:
  - leukocoria, ‘ white pupil’
  - strabismus, misaligned eyes
  - pain, inflammation, redness
  - glaucoma



- Ophthalmoscopy of the eye with dilation of the pupil
- CT scans, MRI’s, and ultrasound

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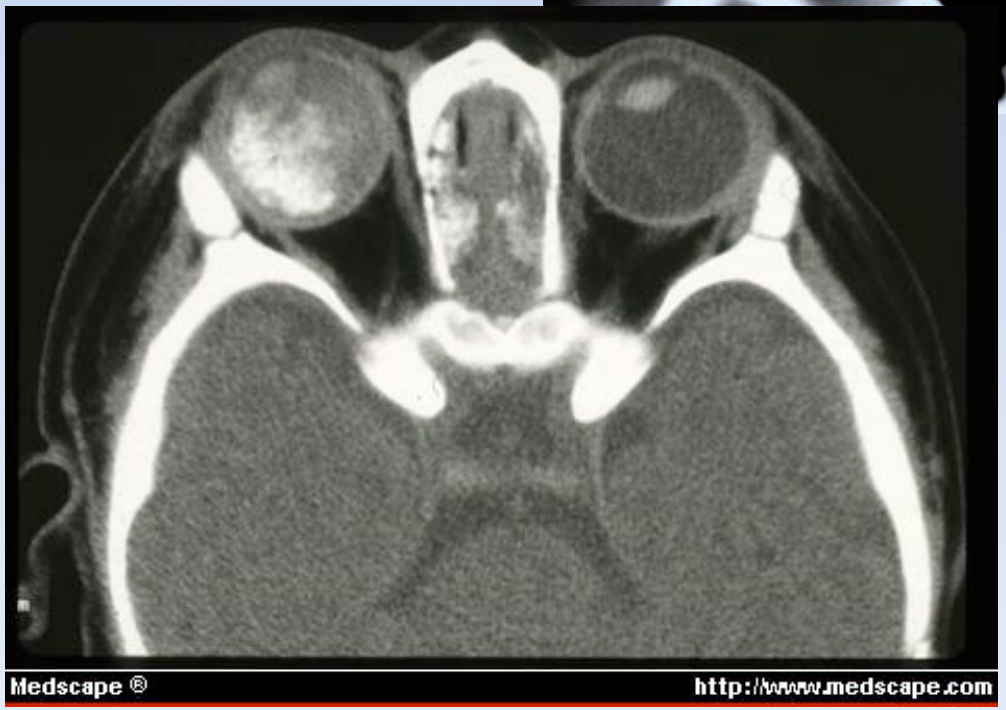
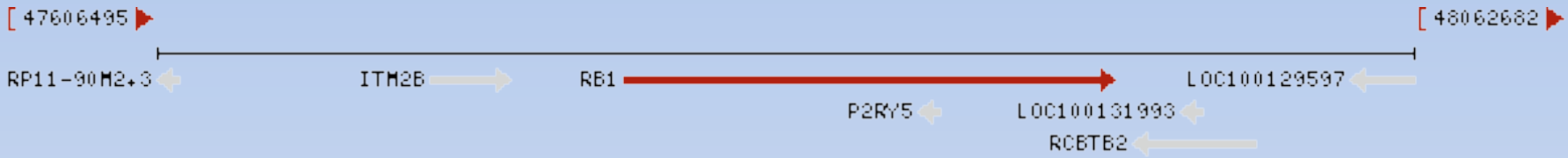

Medscape ®
http://www.medscape.com

# Classical Treatment

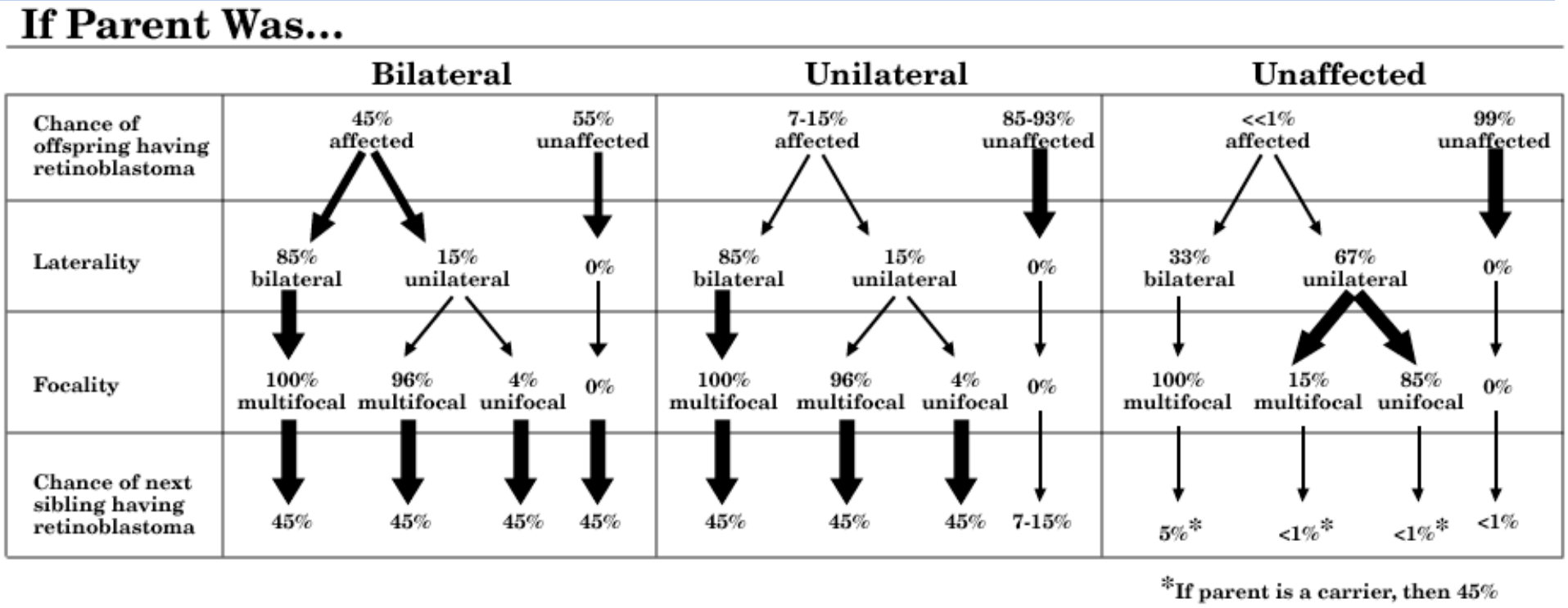
- External beam radiotherapy (X-ray)
- Chemotherapy
- Photocoagulation (laser surgery)
- Local radiotherapy (plaques)
- Cryotherapy
- Enucleation (surgical eyeball removal)

# Genetics of Retinoblastoma




- Single gene mutation of Rb1 on chromosome 13 (locus 13q14.1-q14.2), codes for a cancer suppressor protein
- One of the 1st cancer genes discovered and defined at the molecular level (1970s)
- Mutation is 10% inherited, 20% germinal, and 70% sporadic somatic
- Dominant inheritance
- Incomplete penetrance
- Multiple mutation sites / RFLPs found, no general markers

# Inheritance of Retinoblastoma




*If parent is a carrier, then 45%

# Genetic Diagnosis

| Test Method | | Mutations Detected | Detection Rate of Abnormalities [1] | Test Availability |
|---|---|---|---|---|
| Deletion testing | FISH | Submicroscopic deletions and translocations | >8% | Clinical Testing |
| | Heterozygosity testing | | 8% | |
| | MLPA | Submicroscopic deletions, insertions, and rearrangements | 16% | |
| | Quantitative multiplex PCR | Deletions, insertions | 37% | |
| Mutation scanning | | Single base substitutions, small length mutations | 70%-75% | |
| Sequence analysis | | | | |
| Targeted mutation analysis | | Specific recurrent point mutations | 30% | |
| Methylation analysis | | Hypermethylation of the promoter region | 10%-12% [2] | |
| Analysis of RNA from blood | | (Deep intronic) splice mutations, gross rearrangements | <5% [3] | |

# Genetic Treatment / Future Research

- Currently no cure through genetics
- Genetic counseling
- Prenatal screening possible, but difficult
- Possible novel detection methods though proteomics
- Animal models suggest that retinoblastoma gene may have other functions

# References


- OMIM
- Genetics Review
- Genes and Diseases
- Eye Cancer Network
- National Cancer Institute