

REVIEW OF OPHTHALMIC TUMORS

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This review covers the most important aspects of selected benign and malignant tumors and related lesions of the eyelids, conjunctiva, globe, and orbit. It is designed as a review for the practicing ophthalmologist and as a preparatory course for the candidate for board examinations in ophthalmology. A self-assessment quiz will be given, followed by a didactic lecture and then the quiz will be repeated. Subjects of less importance will be included in the outline but mentioned only briefly in the lecture. Subjects of greater importance will be covered in more detail.

It is not possible to cover all ocular tumors in this outline or in the discussion. For more comprehensive reading, please see the textbooks cited at the end of this outline. They cover all pertinent aspects of intraocular and adnexal tumors and related lesions and are designed to assist the applicant for OKAP and board examinations and also to assist in care of patients with ophthalmic tumors and many other related conditions.

Review of Ophthalmic Tumors

Self-assessment Quiz

1. This eyelid lesion in an 80-year-old patient has shown slowly progressive enlargement for two years. Which statement is true?
 - A. This viral induced lesion will eventually involute.
 - B. Even though it is malignant, it lacks potential to metastasize.
 - C. The affected patient is most likely HIV positive.
 - D. This lipid-containing lesion is often confused with chalazion.
 - E. It originates from mechanoreceptors for touch.

2. Which of the following has been described as a complication of corticosteroid injection of the condition shown in the photograph?
 - A. Central retinal artery obstruction.
 - B. Linear subcutaneous fat atrophy.
 - C. Adrenal gland suppression.
 - D. None of the above.
 - E. All of the above.

3. This conjunctival lesion has shown slow enlargement in a 55-year-old person for 8 years. Which statement is true?
 - A. Fundus exam will probably detect uveal melanoma.
 - B. Local resection is impossible and exenteration is advisable.
 - C. Staging biopsies and cryotherapy would be advisable.
 - D. These findings should prompt an evaluation for lymphoma.
 - E. The patient is likely to have a history of cutaneous melanoma.

4. A 30-year-old attorney from Philadelphia's main line, who worked for years as a lifeguard, develops this conjunctival lesion over a 2-week period. Which statement is true?
 - A. He is probably a descendent of a Halawa Indian.
 - B. The rapid onset strongly suggests a pyogenic granuloma.
 - C. Biopsy would reveal a pure proliferation of lymphoid cells.
 - D. Unlike squamous carcinoma, this tumor is often multifocal.
 - E. The lesion probably resulted from prior sunlight exposure.

5. A 30-year-old woman is found to have the fundus lesion shown in the photograph. Which statement is true?
 - A. An immediate breast biopsy is indicated.
 - B. Calcium and phosphorus levels will probably be abnormal.
 - C. She has an increased chance for familial colon cancer.
 - D. This flat lesion is too small to delineate with CT.
 - E. None of the above.

6. A 55-year-old man is referred for the lesion shown. Which statement is true?
 - A. The prominent blood vessels suggest choroidal hemangioma.

- B. Photocoagulation is the treatment of choice.
 - C. He is very likely to have a primary lung cancer.
 - D. This type of lesion often metastasizes to liver.
 - E. Many patients with this lesion develop renal malignancy.
7. A 3-year-old child is referred for the lesion shown. Which statement is false?
- A. Peripheral fundus would show light bulb vascular changes.
 - B. Cardiac rhabdomyoma is often seen in such patients.
 - C. This is the most common ocular tumor of childhood.
 - D. The child's playful puppy should be promptly killed.
 - E. All of the above.
8. A young child with pigmented cutaneous macules and painless progressive visual loss for 12 months develops ipsilateral axial proptosis as shown. Which statement is true?
- A. Abdominal exam would likely reveal an adrenal mass.
 - B. The visual loss is probably due to a macular astrocytoma.
 - C. This lesion is a common cause of orbital "chocolate cyst".
 - D. Seizures and cerebral calcification are often seen.
 - E. Examination is likely to show bilateral iris nodules.
9. A 30-year-old patient with excellent vision develops painless axial proptosis and CT shows this orbital mass. Which differential diagnosis is most acceptable.
- A. Optic nerve astrocytoma, lymphoma, cavernous hemangioma.
 - B. Fibrous histiocytoma, capillary hemangioma, schwannoma.
 - C. Schwannoma, cavernous hemangioma, fibrous histiocytoma.
 - D. Metastasis, schwannoma, inflammatory pseudotumor.
 - E. Optic nerve meningioma, fibrous histiocytoma, schwannoma.
10. A 12-year-old child presents with the lesion shown. Which group of systemic findings is compatible with this lesion.
- A. Lisch nodules, cafe' au lait spots, congenital glaucoma.
 - B. Nevus flammeus, congenital glaucoma, choroidal hemangioma.
 - C. Brain calcification, depigmented macules, skin angiofibromas.
 - D. Cerebellar hemangioma, pheochromocytoma, hypernephroma.
 - E. None of the above.

I. EYELIDS AND LACRIMAL DRAINAGE SYSTEM

A. Benign tumors of the epidermis of the eyelids

1. Papilloma

a. Clinical

- 1 Rough-surfaced elevated, well-defined lesion
- 2 Can be sessile or pedunculated lesion

b. Pathology

- 1 Finger-like processes of vascularized connective tissue.
- 2 Hyperkeratosis

c. Management

- 1 Observation
- 2 Complete excision

2. Keratoacanthoma

a. General considerations

1. Specific form of pseudoepitheliomatous hyperplasia
2. Resembles basal cell carcinoma clinically
3. Resembles squamous cell carcinoma pathologically
4. Possibly of viral etiology
5. More common in immunosuppressed patients
6. Recently believed to represent squamous cell carcinoma

b. Clinical features

1. Rapidly developing hyperkeratotic lesion
2. Often develops a central crater
3. May spontaneously regress if not excised

c. Pathology

1. Acanthotic and dyskeratotic epithelium
2. Resembling squamous cell carcinoma
3. Usually has inflammatory cells

d. Treatment

1. Observation
2. Complete excision

3. Seborrheic keratosis

a. Clinical

1. Circumscribed, rough-surfaced, elevated brown to gray lesion
2. Likened unto a button on the skin

b. Pathology

1. Outward acanthosis, proliferation of basal cells

2. Typical keratin cysts within the basaloid proliferation
- c. Treatment
 1. Observation
 2. Remove by shaving excision

B. Premalignant and malignant tumors of the surface epithelium of the eyelids

1. Actinic keratosis

- a. General considerations
 1. Most often in older fair-skinned males
 2. History of chronic sunlight exposure
- b. Clinical
 1. Multiple, slightly elevated erythematous lesions
 2. Can occasionally appear as a cutaneous horn
- c. Pathology
 1. Elastotic degeneration in dermis
 2. Hyperkeratosis, elongated rete pegs
- d. Treatment:
 1. Local excision of more suspicious lesions
 2. Topical 5-Fluorouracil (Effudex)

2. Basal Cell Carcinoma

- a. General Considerations
 1. Accounts for over 90% of eyelid malignancies
 2. Classified as malignant because of its local invasiveness
 3. Almost never develops distant metastasis
 4. Lower lid 55%, medial canthus 30%. upper lid 10%, lateral canthus 5%.
- b. Nodular or nodulo-ulcerative type
 1. Clinical features
 - a. Vary from case to case
 - b. Usually an elevated mass
 - c. Thickened, fairly well-defined erythematous margins
 - d. Central crater or ulcer
 - e. Loss of cilia
 2. Histopathology
 - a. Well-defined lesion
 - b. Central ulcer
 - c. Lobules of closely-packed nuclei

- d. Connective tissue septa
 - c. Morpheaform or sclerosing type
 - 1. Clinical features
 - a. Poorly defined border
 - b. May lack ulceration
 - c. Loss of cilia
 - 2. Histopathology
 - a. Poorly defined margins and cords of tumor cells
 - b. Deeper invasion into dermis
 - d. Treatment
 - 1. Small lesion--primary excision; Larger lesion: biopsy prior to definitive surgery
 - 2. Final surgery depends on extent of lesion
 - 3. Frozen sections of chemosurgery usually advisable
 - 4. Closure: primary closure, skin flap or graft
 - 5. Cryotherapy: recurrent lesions, usually in medial canthus
 - 6. Orbital exenteration for deep invasive lesions
 - 7. Irradiation for recurrent cases
 - e. Nevoid basal cell carcinoma syndrome (Gorlin-Goltz Syndrome)
 - Autosomal dominant, 0.7% of basal cell tumors, multiple basal cell tumors, odontogenic keratocysts bifid ribs, plantar and palmar pits,
3. Squamous Cell Carcinoma
- a. General considerations
 - 1. Less than 5% of malignant eyelid tumors
 - 2. Often arises from actinic keratosis
 - b. Clinical
 - 1. Elevated keratinizing mass
 - 2. Similar to basal cell carcinoma
 - 3. Can metastasize to regional lymph nodes
 - c. Pathology
 - 1. Proliferated invasive squamous cells
 - 2. Dyskeratosis and mitotic activity
 - d. Treatment: Similar to basal cell carcinoma; may require orbital exenteration

C. Glandular and Adnexal Tumors of the Eyelids

- 1. Sebaceous Gland Carcinoma
 - a. General Considerations

1. About 5 % of all malignant eyelid tumors; can metastasize
2. Can metastasize to regional lymph nodes and distant organs
3. Origins: Meibomian glands, Zeis glands, or caruncle
4. May be multicentric in origin

b. Clinical features

1. More common in upper eyelid
2. Usually presents as a solitary yellow nodule, resembling a chalazion
3. Loss of cilia
4. Unlike basal cell carcinoma, it does not ulcerate early
5. Diffuse form resembles unilateral blepharoconjunctivitis.
6. Diffuse form is a result of pagetoid growth pattern
7. Can involve both eyelids and conjunctiva
8. Zeis gland tumor--yellowish nodule near eyelid margin

c. Pathology

1. Lobules or sheets of malignant tumor cells
2. More anaplastic than basal cell carcinoma
3. Contain lipid that can be seen with lipid stains

d. Clinical course and prognosis

1. Orbital invasion 17%
2. Lymph node metastasis 28%
3. Tumor deaths 14% (AFIP series)
4. Tumor deaths 40% (Chinese series)
5. More recent series suggest improving prognosis

e. Management

1. Same as for basal cell carcinoma
2. Map biopsies of eyelids and conjunctiva
3. Wide local excision and close follow up

f. Muir-Torre Syndrome

1. Hereditary: usually autosomal dominant
2. Sebaceous gland tumors (hyperplasia, adenoma or carcinoma)
3. Keratoacanthomas
4. Internal malignancy (colon cancer and others)

2. Sweat Gland Tumors

- a. Syringoma
- b. Eccrine acrospiroma
- c. Carcinoma

3. Hair Follicle Tumors

- a. Trichoepithelioma

- b. Trichofolliculoma
- c. Trichilemmoma
- d. Pilomatrixoma (Calcifying epithelioma of Malherbe)

D. Melanocytic Tumors of the Eyelids

1. Nevus

- a. Clinical
 1. Smooth elevated lesion near the eyelid margin
 2. Pigmented or nonpigmented
 3. Cilia usually intact
- b. Pathology
 1. Typical nesting of slightly atypical melanocytes
 2. May be junctional or compound
- c. Management
 1. Observation or local resection
 2. Wide excision if malignant transformation suspected

2. Oculodermal melanocytosis (Nevus of Ota)

a. Clinical

1. Congenital periocular flat cutaneous pigmentation
2. Associated epibulbar and uveal pigmentation
3. Increased incidence of uveal melanoma (about 0.4 %)
4. Slightly higher incidence of orbital and brain melanoma
5. Eyelid and conjunctival melanoma extremely rare

b. Pathology

1. Scattered dendritic dermal melanocytes
2. Resembles a blue nevus

c. Management

1. Periodic examinations
2. Look for ipsilateral uveal melanoma

3. Lentigo maligna (Melanotic freckle of Hutchinson)

a. Clinical

1. Acquired cutaneous pigmentation
2. Often in the periocular region
3. Middle aged or older patients
4. Associated conjunctival pigmentation (PAM)
5. Can give rise to eyelid melanoma (about 30%)
6. Better prognosis than superficial spreading or nodular melanoma
6. Can also give rise to conjunctival melanoma

b. Management

1. Close observation
2. Surgical excision for suspicious or growing lesions

4. Malignant Melanoma

a. General considerations

1. Relatively rare in the eyelids
2. Clinically and pathologically similar to other cutaneous melanomas

b. Clinical features

1. Variably pigmented eyelid nodule
2. Progressive growth
3. Can metastasis to regional nodes and systemically

c. Pathology

1. Nodule of neoplastic melanocytes

2. Invades dermis
- d. Management
 1. Similar to other cutaneous melanomas
 2. Wide surgical excision
 3. Systemic follow up

E. Neurogenic Tumors of the Eyelids

1. Neurofibroma

- a. Clinical
 1. Solitary eyelid nodule without neurofibromatosis
 2. Diffuse plexiform variant typical of neurofibromatosis
 - Early S-shaped curve to upper eyelid
 - Proptosis due to orbital component
- b. Pathology
 1. Proliferation of axons, Schwann cells and fibroblasts
 2. Mucinous degeneration
- c. Treatment
 1. Observation or resection
 2. Plexiform type may be very difficult to completely excise

2. Neurilemoma (Schwannoma)

- a. General considerations
 1. Benign tumor
 2. Arises from Schwann cells
 3. Usually not associated with neurofibromatosis
- b. Clinical
 1. Solitary eyelid nodule
 2. Subcutaneous; may resemble a chalazion
- c. Pathology
 1. Pure proliferation of Schwann cells
 2. (See section on orbit for more detailed description)
- d. Treatment
 1. Observation
 2. Local excision usually preferable

3. Merkel Cell Tumor (neuroendocrine carcinoma of skin)

- a. General considerations
 - 1. Recently recognized to affect eyelids
 - 2. Malignant tumor
 - 3. Arises from Merkel cells (mechanoreceptors for touch)
- b. Clinical
 - 1. Occurs in older patients
 - 2. Reddish-blue sausage-shaped lesion
 - 3. Usually in upper eyelid
 - 4. Metastasis and death in 25%
- c. Pathology
 - 1. Nodules of large basophilic cells
 - 2. May resemble sebaceous gland carcinoma
- d. Management
 - 1. Excision and eyelid reconstruction
 - 2. Similar to basal cell carcinoma

F. Vascular Tumors of the Eyelids

1. Capillary Hemangioma

- a. Clinical
 - 1. Appears in infants as a strawberry birthmark.
 - 2. Grows during the first few months of life; then regresses
 - 3. Main complications are amblyopia and strabismus
- b. Pathology
 - 1. Proliferating benign endothelial cells
 - 2. Numerous small vascular channels
- c. Management
 - 1. Controversial
 - 2. Refraction; treat any amblyopia
 - 3. Corticosteroids
 - a. Local injection
 - b. Systemic
 - c. Be aware of complications of steroids
 - 4. Surgical excision in selected cases
 - 5. Sclerosing agents and irradiation rarely used today

2. Nevus Flammeus

- a. Clinical
 - 1. Congenital port wine stain

2. Distribution along branches of fifth cranial nerve
 3. Grows with patient; does not regress
 4. Relationship to Sturge-Weber syndrome discussed later
- b. Pathology-Not a true cavernous hemangioma. May be mixed
 - c. Treatment
 1. Observation
 2. Cosmetics
 3. Laser ablation
3. Kaposi's sarcoma
- a. Clinical
 1. Blue-red subcutaneous mass; resembles hemorrhage
 2. Solitary or multiple
 3. More common in patients with AIDS
 - b. Pathology
 1. Malignant proliferation of vascular tissue
 2. Typical slit-like vascular channels
 - c. Management
 1. Chemotherapy
 2. Low dose irradiation

G. Lymphoid Tumors of the Eyelids

1. Clinical
 - a. B-cell lymphoma--firm subcutaneous mass
 - b. T-cell lymphoma--more superficial (mycosis fungoides)
 - c. Frequently associated with systemic lymphoma
2. Pathology--spectrum ranging from benign to malignant
3. Management
 - a. Systemic evaluation for lymphoma
 - b. If systemic disease present, consider chemotherapy
 - c. If no systemic disease--consider ocular irradiation

H. Xanthomatous Tumors of the Eyelids

1. Xanthelasma
 - a. Clinical
 1. Bilateral placoid yellow eyelid lesions

- 2. Isolated or associated with systemic xanthomatoses
 - 3. Familial hyperlipidemia, Erdheim-Chester disease, etc
 - b. Pathology
 - 1. Lipid laden cells in dermis
 - 2. Often concentrated around blood vessels
 - c. Treatment: Observe or excise for cosmetic reasons
2. Others (Rare; see orbit section)

I. Metastatic Tumors to the Eyelids

- 1. General considerations
 - a. Most often from breast or lung; kidney, melanoma, etc
 - b. Eyelid mass can be first sign of malignancy
- 2. Clinical
 - a. Rapidly growing eyelid nodule
 - b. May initially resemble a chalazion
- 3. Pathology
 - a. Varies with the primary lesion
 - b. If poorly differentiated, primary may be hard to identify

J. Tumors of the Lacrimal Drainage System

- 1. General considerations
 - a. Primary lacrimal sac tumors are uncommon
 - b. Secondary tumors from eyelids and conjunctiva
 - c. Squamous papilloma is the most common
 - can evolve into squamous cell carcinoma
 - d. Squamous cell carcinoma, melanoma, and others
- 2. Clinical
 - a. Firm mass near medial canthus
 - 2. Must be differentiated clinically from dacryocystitis
- 3. Management
 - 1. Dacryocystectomy
 - 2. Irradiation or chemotherapy
 - 3. May later require reconstruction of drainage system

II. CONJUNCTIVAL TUMORS

A. Congenital tumors (usually choristomas)

1. Dermoid

a. Clinical features

1. Solid yellow-white tumor (choristoma)
2. Usually at limbus or on the cornea at birth
3. May be associated with Goldenhar syndrome
 - a. Sporadic; non hereditary
 - b. Limbal dermoids
 - c. Dermolipomas
 - d. Auricular appendages
 - e. Vertebral anomalies
 - e. Facial, GI, GU anomalies

b. Pathology

1. Mass of dense fibrous tissue
2. Contains hair, sebaceous glands and other appendages

c. Treatment

1. Observation
2. Local excision

2. Epibulbar Osseous Choristoma

a. Clinical

1. Rock hard mass
2. Usually on bulbar conjunctiva superotemporally

b. Pathology

1. Simple choristoma
2. Composed of mature bone

c. Treatment: Observation or local excision

3. Complex choristoma

a. Clinical

1. Variable clinical features
2. Diffuse or localized conjunctival-corneal mass
3. Can be associated with sebaceous nevus of Jadassohn (Organoid nevus syndrome)

b. Pathology

1. Complex choristoma
2. Cartilage

3. Ectopic lacrimal gland tissue
4. Other choristomatous elements

B. Benign Tumors of Surface Epithelium of Conjunctiva

1. Papilloma

a. General considerations

1. Two distinct forms
2. Childhood and adulthood forms

b. Childhood form

1. Children or young adults
2. Usually in forniceal or bulbar conjunctiva
3. Occasionally in palpebral conjunctiva
4. May be multiple and bilateral
5. Usually small and self-limited
6. Infectious etiology--human papillomavirus
7. Benign

c. Adulthood form

1. Older adults
2. Usually arises near limbus
3. Spreads over conjunctiva and cornea
4. Unilateral and solitary
5. Continued growth
6. May obtain massive proportions
7. Benign

d. Pathology

1. Cores of fibrovascular tissue lined by
2. Acanthotic conjunctival epithelium

e. Treatment

1. Cryotherapy
2. Local excision
3. Steroids occasionally effective
4. Oral cimetidine (Tagamet) has initial promise in childhood form

2. Hereditary Benign Intraepithelial Dyskeratosis

a. Clinical

1. Bilateral fleshy, placoid lesions
2. Bulbar conjunctiva near limbus
3. Similar dyskeratotic plaques on buccal mucosa
4. Originally seen in tri-racial families in North Carolina

b. Pathology

1. Acanthosis, dyskeratosis, prominent rete pegs

2. Benign; has not been known to become malignant

c. Treatment : Observation or local excision

C. Premalignant and Malignant Tumors of Surface Epithelium of Conjunctiva

1. General considerations

- a. Conjunctival intraepithelial neoplasia (CIN)
- b. Invasive squamous cell carcinoma
- c. The above 2 may be indistinguishable clinically
- d. Therefore, they are discussed together under squamous cell carcinoma

2. Conjunctival squamous cell carcinoma

a. Clinical

1. Fleshy, placoid limbal mass
2. Usually in interpalpebral fissure
3. Occasionally in fornices
4. May show leukoplakia (hyperkeratosis)
5. May have a papillomatous configuration
6. Can invade the orbit and globe
7. Distant metastasis very rare

b. Pathology

1. Neoplastic cells arising in epithelium
2. Conjunctival intraepithelial neoplasia (CIN)
 - (a) Mild : ("Dysplasia")
Partial thickness replacement of epithelium by neoplastic cells
 - (b) Severe : ("Carcinoma in situ")
Full thickness replacement of epithelium by neoplastic cells
3. Invasive squamous cell carcinoma
 - a. Breaches the basement membrane
 - b. Invades the conjunctival stroma
 - c. Can invade the globe and orbit
 - d. Mucoepidermoid and spindle cell variants more invasive

c. Treatment--surgical

1. Varies with the clinical findings
2. Good preoperative clinical evaluation
3. Local retrobulbar anesthesia
4. Superficial alcohol partial epitheliectomy
5. Excision by partial lamellar sclerokeratoconjunctivectomy
6. "no touch" approach
7. Double freeze-thaw cryotherapy to conjunctival margins
8. Closure of conjunctiva with absorbable sutures

d. Supplemental treatment

1. Topical chemotherapy--mitomycin C or 5-fluorouracil (5FU)

2. Irradiation (plaque or external beam) D. Melanocytic Tumors of the
Conjunctiva

1. Nevus

a. Clinical

1. Children and young adults
2. Discrete
3. Elevated
4. Cysts
5. Variably pigmented
6. Stationary

b. Pathology: May be junctional, compound, or deep, as in eyelid nevi

c. Management: Observation; excision if growth occurs

2. Primary Acquired Melanosis

a. Clinical

1. Middle age
2. Diffuse, patchy
3. Flat
4. No cysts
5. Always pigmented
6. Wax and wane

b. Pathology

1. Abnormal melanocytes in basal layer of the epithelium.
2. May show atypia

c. Chances of evolution into melanoma (AFIP series)

- | | |
|-------------------|------|
| 1. Overall | 32% |
| 2. Without atypia | 0% |
| 3. With atypia | 46 % |
| 4. Severe atypia | 75% |

d. Most recent Wills Eye Institute series (Shields JA et al Zimmerman Lecture 2006)

- | | |
|-------------------|-----|
| 1. Overall | 4% |
| 2. Without atypia | 0% |
| 3. With atypia | 3% |
| 4. Severe atypia | 13% |

d. Surgical management

1. Varies with the clinical findings
2. Good preoperative clinical evaluation
3. Local retrobulbar anesthesia
4. Superficial alcohol keratectomy

5. Local excision of highly suspicious nodules
6. Quadrantic map biopsies
7. Limbal peritomy 360
8. Cryotherapy from underside of conjunctival
9. Closure of conjunctiva with absorbable sutures

e. Supplemental management: chemotherapy-mitomycin-C or 5 FU

3. Malignant Melanoma

a. Origin

1. PAM
2. Pre-existing nevus
3. De novo

b. Clinical

1. Variably pigmented mass
2. Prominent conjunctival vessels
3. Can involve cornea
4. Can involve fornices
5. Can invade the orbit and globe

c. Pathology--Malignant melanocytes; spindle or epithelioid cells

d. Treatment--Same as for squamous cell carcinoma--surgical

1. Varies with the clinical findings
2. Good preoperative clinical evaluation
3. Local retrobulbar anesthesia
4. Superficial alcohol partial epitheliectomy
5. Excision by partial lamellar sclerokeratoconjunctivectomy
6. A "no touch" approach should be employed
7. Double freeze-thaw cryotherapy to conjunctival margins
8. Closure of conjunctiva with absorbable sutures
9. Supplemental treatment
 - a. Topical chemotherapy--mitomycin C
 - b. Amnion or mucous membrane grafting
 - c. Irradiation (plaque or external beam)

E. Stromal Tumors of the Conjunctiva

1. Vascular

a. Pyogenic granuloma

1. Misnomer : Neither pyogenic nor a granuloma
2. Clinical

- a. Fleshy reddish-pink mass
 - b. Occurs at site of prior surgery or trauma
- 3. Pathology
 - a. Proliferation of granulation tissue
 - b. Small vascular channels
 - c. Inflammatory cells
- b. Cavernous hemangioma
 - 1. Rare
 - 2. Blue to red lobular mass
- c. Lymphangioma
 - 1. Prominent mass of lymphatic channels
 - 2. Often continuous with orbital lesion
 - 3. Frequent hemorrhage--chocolate cysts
 - 4. Management--Difficult; surgical debulking
- d. Kaposi's sarcoma
 - 1. Clinical features
 - a. Recently seen more frequently in AIDS patients
 - b. One or more red lesions, simulating conjunctival hemorrhage
 - 2. Management
 - a. Excision
 - b. Irradiation
 - c. Chemotherapy
- 2. Lymphoid Tumors
 - a. Fleshy "salmon patch" lesion on the conjunctiva
 - b. Sometimes associated with systemic lymphoma
 - c. Discussed in more detail in the orbit section
- 3. Metastatic Tumors
 - a. Conjunctival metastasis relatively rare
 - b. Usually from breast or lung
 - c. Fleshy yellow pink mass; metastatic melanoma is usually pigmented
 - d. Management: Excision, irradiation, chemotherapy
- F. Caruncular Tumors and Cysts
 - 1. Tumors may have origin from dermal or conjunctival elements
 - 2. Review of surgically-excised lesions (Shields C et al, WEH)

3. Specific lesions

Papilloma	32 %	
Nevus	24 %	
Pyogenic granuloma		9 %
Inclusion cyst	7 %	
Chronic inflammation	7 %	
Oncocytoma	4 %	
Miscellaneous	12 %	
Malignant lesions	5 %	
Melanoma		
Squamous cell carcinoma		
Sebaceous gland carcinoma		

G. Other Conjunctival Tumors (Less common)

III. INTRAOCULAR TUMORS

A. Tumors of the Uveal Stroma

1. Melanocytic tumors of the Iris

a. Nevus

1. Clinical

- a. Localized or diffuse lesion of iris stroma
- b. Variably pigmented; relatively flat
- c. Ectropion iridis, angle involvement, sector cataract

2. Pathology

- a. Usually low-grade spindle cells
- b. Occasional deeply pigmented round cells (melanocytoma)

3. Management

1. Observation
2. Less than 5% show growth in 5 years

b. Malignant melanoma

1. Circumscribed type

a. Clinical

1. Nodular mass arising from iris stroma
2. Secondary ectropion, angle involvement, cataract
3. Spontaneous hyphema can occur
4. Growth is the most reliable sign of malignancy

b. Pathology

1. Usually low-grade spindle B cells
2. Occasional epithelioid cells

c. Management

1. Varies with clinical circumstances
2. Usually removal by sector iridectomy
3. Iridocyclectomy if trabecular meshwork involved
4. Plaque radiotherapy or enucleation if not resectable

2. Diffuse type

a. Clinical features

1. Acquired hyperchromic heterochromia
2. Ipsilateral secondary glaucoma
3. Gonioscopy shows angle involvement

- b. Pathology
 - 1. Often spindle cells
 - 2. Loosely cohesive epithelioid cells are frequent
- c. Management
 - 1. varies with clinical circumstances
 - 2. Often require enucleation
 - 3. Fine need aspiration prior to enucleation
 - 4. Plaque radiotherapy in selected cases
- d. Prognosis
 - 1. Metastatic patterns similar to posterior uveal melanoma
 - 2. Metastasis most often involves liver
 - 3. Mortality rates vary from 5 to 14%

2 Melanocytic Tumors of the Posterior Uvea

a. Choroidal Nevus

- 1. Clinical
 - a. Flat or minimally elevated choroidal lesion
 - b. Overlying drusen
 - c. Usually slate gray; can be amelanotic
- 2. Suspicious signs for growth and malignant transformation
 - a. Thickness > 2 mm
 - b. Fluid Subretinal
 - c. Symptoms
 - d. Orange pigment
 - e. Margin < 3mm from disc to optic disc

TFSOM = To find small ocular melanoma
 If more than 3 factor—50 % chance of growth

- 3. Regarding above risk factors for growth in 5 years
 - a. If no risk factors <5%
 - b. If all 5 risk factors 95%
- 4. Pathology
 - a. Usually low grade benign spindle cells
 - b. Occasional round deeply-pigmented cells (melanocytoma)
- 5. Management Consider risk factors
 - a. Baseline fundus photographs
 - b. Baseline ultrasonography for elevated lesions

- c. Periodic observation
 - d. If growth documented, consider treatment as small melanoma
- b. Posterior uveal melanoma
1. Clinical Features--ciliary body melanoma
 - a. Usually pigmented ciliary body mass
 - b. Occult location posterior to iris
 - c. May attain a large size before clinical diagnosis
 - d. External signs
 1. Dilated episcleral blood vessels (sentinel vessels)
 2. Nodule of extraocular extension
 - e. May encroach on lens
 1. Lenticular astigmatism
 2. Subluxation
 3. Cataract
 - f. Occasional vitreous hemorrhage
 2. Clinical features--choroidal melanoma
 - a. Considerable variation in shape and color; usually pigmented
 - b. Usually dome shaped pigmented choroidal mass
 - c. May be amelanotic and diffuse
 - d. Surface orange pigment
 - e. Secondary retinal detachment
 - f. Break through Bruch's membrane--mushroom shape
 - g. Prominent vessels in dome of mushroom
 - h. Occasional vitreous hemorrhage
 3. Diagnosis of posterior uveal melanoma (ciliary body and choroid)
 - a. Indirect ophthalmoscopy: Usually diagnosed by this method
 - b. Fluorescein angiography
 1. Beginning fluorescence in early venous phase
 2. Late mottled staining
 3. Visible prominent tumor vessels ("double circulation?")
 - c. Ultrasonography
 1. A scan: Low to medium reflectivity
 2. B scan: Acoustic hollowness; choroidal excavation
 3. Particularly valuable in eyes with opaque media
 - d. Transillumination

1. Can often be performed in office
 2. Most melanomas cast a shadow
- e. Computed tomography
1. Can demonstrate posterior uveal melanoma
 2. Usually adds little to ocular diagnosis
 3. Not used routinely
- f. Magnetic Resonance Imaging
1. Can demonstrate posterior uveal melanoma
 2. Usually adds little to ocular diagnosis
 3. Not used routinely
- g. Radioactive phosphorus uptake test
1. Very accurate method
 2. Usually requires conjunctival incision
 3. Used less often because of clinical experience and FNAB
- h. Fine needle aspiration biopsy (FNAB)
1. Very reliable diagnostic method
 2. Reserved for difficult cases
 3. Technique difficult; requires experienced
 3. Requires experienced cytopathologist
4. Pathology of Posterior Uveal Melanoma
Spindle, mixed or epithelioid cell type
5. Management of Posterior Uveal Melanoma
- a. Concepts continue to change
 - b. Irradiation and enucleation appear to have similar prognosis
 - c. Observation
 1. Small tumors that lack risk factors for growth and metastasis
 2. Risk factors for growth and metastasis have been identified
 3. Presence of risk factors may prompt earlier treatment
 4. Risk factors for growth of small melanocytic choroidal lesions
 - a. Thickness greater than 2 mm
 - b. Surface orange pigment
 - c. Subretinal fluid
 - d. Proximity to optic disc
 - e. Symptoms
 5. Risk factors for metastasis of small melanocytic choroidal lesions
 - a. Thickness greater than 2 mm
 - b. Symptoms

- c. Proximity to optic disc
 - d. Documented growth
6. In none of risk factors present--metastasis < 1%.
7. If all 4 risk factors present--metastasis about 20%
- d. Laser photocoagulation
 - 1. Method of treating selected small melanomas
 - 2. Used less often today
 - 3. Has been replaced by transpupillary thermotherapy
 - e. Transpupillary Thermotherapy (TTT)
 - 1. Infrared radiation for hyperthermia
 - 2. Used for selected small and medium choroidal melanoma
 - 3. Probably fewer complications than radiotherapy
 - 4. Preliminary studies show encouraging result
 - f. Episcleral plaque brachytherapy
 - 1. Most common method of treatment used today
 - 2. Results encouraging
 - h. Charged particle irradiation
 - 1. Alternative method of radiotherapy
 - 2. Similar results as plaque brachytherapy
 - i. Local resection
 - 1. Used for selected ciliary body and choroidal melanoma
 - 2. Most common method is partial lamellar sclerouvectomy (PLSU)
 - 3. Avoids enucleation and complications of radiation therapy
 - 4. Difficult and time-consuming technique
 - 5. Results are encouraging
 - 6. Internal resection techniques under investigation
 - j. Enucleation
 - 1. Used for advanced tumors; little hope for useful vision
 - 2. Usually greater than 15 mm in diameter
 - 3. Usually greater than 10 mm in thickness
 - 4. Gentle minimal manipulation technique advised
 - 5. Several orbital implants : hydroxyapatite, medpor, etc.
 - k. Orbital exenteration
 - 1. Used for tumors with massive orbital extension
 - 2. Eyelid-sparing technique usually advisable
 - l. Chemotherapy and immunotherapy
 - 1. Historically, results were discouraging
 - 2. May have promise in future

6. Prognosis for posterior uveal melanoma

- a. Can metastasize to liver and other organs (30- 50%)
- b. Factors that affect prognosis
 - 1. Cell type--mixed epithelioid have worst prognosis
 - 2. Tumor size and growth pattern
 - 3. Presence of extraocular extension,
 - 4. Mitotic activity
 - 5. Others
- c. Cytogenetics : new developments
 - 1. Several abnormalities, Chromosomes 3,6,8,9.
 - 2. Chromosome 3 disomy – 95% five year survival
 - 3. Chromosome 3 monosomy – 50% five year survival
 - 4. Enucleation. Tumor cells obtained by harvesting tissue
 - 5. Plaque radiotherapy. Tumor cells by needle biopsy

7. Collaborative Ocular Melanoma Study (COMS)

- a. Medium sized melanoma.
 - (1) Enucleation vs plaque radiotherapy
 - (2) No difference in prognosis (about 30% 5 year mortality)
- b. Large melanoma
 - (1) Pre-enucleation radiation vs enucleation alone
 - (2) No difference in prognosis
- c. Issues not addressed in COMS
 - (1) juxtapapillary, ciliary body, iris melanoma
 - (2) extraocular extension
 - (3) Early subclinical metastases

c. Metastatic tumors to the uvea and retina

1. General Considerations

- a. Most are carcinomas; melanoma and sarcoma less common
- b. Breast and lung cancer most common primary tumors
- c. Other primaries: Carcinoid, renal cell, GI tract, melanoma, etc
- d. May be multifocal and bilateral
- e. Predilection for posterior choroid
- f. Unknown primary in 10%
- g. No prior history of cancer 25%

2. Clinical features

- a. Iris metastasis
 - 1. Usually a loosely-cohesive yellow or pink mass
 - 2. May produce a tumor-induced pseudohypopyon
 - 3. May simulate endophthalmitis
 - 4. Metastatic melanoma to iris usually pigmented

- b. Ciliary body metastasis
 - 1. May be difficult to visualize clinically
 - 2. Can simulate iridocyclitis
 - c. Choroidal metastasis
 - 1. Creamy-yellow mass
 - 2. Usually in posterior choroid
 - 3. May be multifocal and bilateral
 - 4. May cause extensive retinal detachment
 - e. Optic disc metastasis
 - 1. Usually extension from choroidal metastasis
 - 2. Can be confined to optic disc without choroidal component
 - 3. Appears as a swollen, infiltrated disc
 - f. Retinal metastasis
 - 1. Very rare
 - 2. Tumor foci in retina, around blood vessels
3. Diagnostic modalities
- a. Fluorescein angiography
 - 1. Relatively hypofluorescent early
 - 2. Late staining similar to melanoma
 - b. Ultrasonography
 - 1. Similar to choroidal hemangioma
 - 2. A-scan--medium to high reflectivity
 - 3. B-scan--acoustic solidity
 - c. Computed tomography and MRI
 - 1. Can demonstrate larger choroidal metastasis
 - 2. Not usually necessary for ocular diagnosis
 - d. Fine needle aspiration biopsy
 - 1. Reserved for difficult cases
 - 2. Used frequently in ocular oncology
 - 3. Very reliable diagnostic methods
 - 4. Requires experienced cytopathologist
4. Pathology
- a. Gross
 - 1. Usually diffuse; occasionally dome-shaped
 - 2. Almost always amelanotic
 - 3. Metastatic melanoma usually pigmented
 - b. Microscopic

1. Varies with primary neoplasm
 2. Some are poorly differentiated
5. Management

- a. Chemotherapy for systemic disease
- b. Observation if vision not threatened
- c. Radiotherapy if vision is threatened

d. Vascular Tumors of the Uvea

1. Circumscribed choroidal hemangioma

a. Clinical

1. Red-orange choroidal mass
2. Usually in the posterior choroid; near macular area.
3. Symptoms similar to central serous chorioretinopathy

b. Diagnosis

1. Fluorescein angiography
 - a. Fluorescence in arterial phase
 - b. Late staining similar to melanoma
 - c. "Multilake" staining of overlying retinal cysts
2. Indocyanine green angiography may be helpful
 - a. Early hyperfluorescence
 - b. Typical late "wash-out" phenomenon
2. Ultrasonography
 - a. A scan--high internal reflectivity
 - b. B scan--acoustic solidity
 - c. No choroidal excavation

c. Pathology

1. Choroid thickened by tumor
1. Cavernous vascular spaces lined by thin endothelial cells
2. Overlying cystic retinopathy

d. Management

1. Observation if asymptomatic
2. Surface laser photocoagulation if retinal detachment
3. Transpupillary thermotherapy being investigated
4. Radiotherapy if extensive detachment present
 - a. Plaque brachytherapy
 - b. External radiotherapy

2. Diffuse choroidal hemangioma

- a. Seen with variations of the Sturge-Weber syndrome
 - b. Bright red fundus reflex ("Tomato catsup fundus") on affected side
 - c. Mentioned in phakomatosis section
- e. Osseous, Myogenic, and Neurogenic Tumors of the Uvea
- 1. Choroidal osteoma
 - a. Clinical
 - 1. Yellow-orange placoid choroidal lesion
 - 2. Most often in juxtapapillary or circumpapillary location
 - 3. Unilateral or bilateral
 - 4. More common in young adult women
 - 5. Can spawn a choroidal neovascular membrane
 - 6. Can become decalcified with time
 - b. Diagnosis
 - 1. Typical clinical appearance
 - 2. Fluorescein angiography-gradual hyperfluorescence
 - 3. Ultrasonography and CT--dense plaque in choroid
 - c. Pathology
 - 1. Plaque of mature bone
 - 2. Involves full thickness choroid
 - 3. Relative sparing of RPE and sensory retina
 - d. Management
 - 1. No effective treatment
 - 2. Laser for choroidal neovascularization
 - 2. Myogenic tumors
 - a. Leiomyoma
 - 1. Amelanotic mass, usually in ciliary body
 - 2. May resemble amelanotic melanoma
 - 3. More common in young adult women
 - 4. Transmits light readily
 - 5. Although benign, can grow and cause complications
 - 6. Pathology
 - a. Spindle cells; smooth muscle origin
 - b. Immunohistochemistry important in diagnosis
 - 7. Management: local resection or enucleation
 - b. Rhabdomyosarcoma
 - 1. Can occur in iris or ciliary body of children
 - 2. Amelanotic, fleshy iris mass

3. Proliferation of rhabdomyoblasts
3. Neurogenic tumors
 - a. Neurilemoma (Schwannoma) (rare)
 1. Amelanotic mass that resembles melanoma
 2. Ciliary body or choroidal location
 3. Usually solitary
 4. Occasionally associated with neurofibromatosis
 5. Benign proliferation of Schwann cells
 - Antoni A and B patterns

- b. Neurofibroma

1. Amelanotic uveal mass
2. Solitary, multiple, or diffuse
3. Usually associated with neurofibromatosis

B. Tumors of the Nonpigmented Ciliary Epithelium (NPCE)

1. Congenital tumors of NPCE--Medulloepithelioma

- a. General considerations

1. Only important congenital tumor of NPCE
2. Embryonic tumor that arises from the medullary epithelium
3. Usually diagnosed during the first decade of life.
4. Usually involves ciliary body; occasionally optic nerve

- b. Clinical

1. Fleshy yellow to pink ciliary body mass
2. Can cause congenital lens "coloboma"
3. Neoplastic, vascularized cyclitic membrane
4. Subluxed lens, cataract, retinal detachment, secondary glaucoma

- c. Pathology

1. Nonteratoid or teratoid types
2. Nonteratoid type-pure proliferation of embryonic NPCE
3. Teratoid type-also has heterotopic elements(cartilage, rhabdomyoblasts)
4. Cytologically benign (20%) or malignant (80%)
5. Can be locally invasive but rarely metastasizes

- d. Management

1. Observation generally not advisable: lesion is usually progressive
2. Small, circumscribed tumor: can be resected locally

3. Many require enucleation
2. Acquired tumors of NPCE
 - a. Reactive hyperplasia
 1. Not a true neoplasm
 2. Reaction to inflammation or trauma
 - b. Involutional hyperplasia (Fuchs' adenoma)
 1. Rarely seen clinically
 2. Usually detected in enucleated or autopsy eyes
 3. More common with increasing patient age
 4. Small white mass in pars plicata
 5. Pathologically--proliferation of NPCE with abundant basement membrane
 - c. Adenoma and adenocarcinoma
 1. General considerations
 - a. Arises from mature adult NPCE
 - b. Diagnosed in adulthood
 - c. Involves primarily the ciliary body
 2. Clinical
 - a. Amelanotic ciliary body mass
 - b. Usually irregular surface
 - c. Transmits light readily
 3. Pathology
 - a. Circumscribed amelanotic ciliary body mass
 - b. Several histopathologic variations
 - c. Proliferation on adult NPCE cells
 4. Management
 - a. Observation for small asymptomatic lesions
 - b. Local resection for growing or symptomatic lesions
 - c. Enucleation for more advanced cases.
- C. Tumors and cysts of the pigmented epithelium
 1. Tumors of the iris pigmented epithelium
 - a. Classified as adenoma (benign) or adenocarcinoma (malignant)
 - b. The vast majority are adenomas
 - c. Clinical:

1. Deeply pigmented; black or dark brown
 2. Circumscribed; sometimes multinodular
 3. Displaces iris stroma
 4. Does not directly involve iris stroma
 - b. Pathology
 1. Low grade proliferation of pigment epithelial cells
 2. Pseudocysts containing pigment-laden macrophages
 - c.. Management
 - a. Usually observation
 - b. Resection if growth or secondary glaucoma
2. Cysts of the iris pigmented epithelium
- a. General
 1. Not true tumors
 2. Important in differential diagnosis or pigmented tumors
 3. Classified in several types
 4. Each type has different clinical features and clinical course
 - b. Classification
 1. Peripheral (iridociliary)
 2. Midzonal (retroiridic)
 3. Central (pupillary)
 4. Dislodged
 - a. Free-floating
 - b. fixed
3. Solitary congenital hypertrophy of the RPE (CHRPE)
- a. Clinical Features
 1. Well circumscribed flat black lesion at level of RPE
 2. May have depigmented halo and lacunae
 3. May sometimes demonstrated slight basal growth
 4. Can occasionally give rise to nodular outgrowth
 - b. Diagnosis
 1. Typical clinical appearance
 2. Fluorescein angiography
 - a. Hypofluorescence of pigmented areas
 - b. Hyperfluorescence of lacunae (transmission defect)
 - c. Pathology
 1. RPE cells taller and more pigmented
 2. Large compact spherical melanosomes
 - d. Management: observation

4. Multifocal CHRPE (congenital grouped pigmentation; "bear tracks")
 - a. Clinical Features
 1. Multiple flat gray to black lesions at level of RPE
 2. Usually assume a sector distribution
 3. Larger lesions anteriorly
 - b. Diagnosis: typical ophthalmoscopic appearance
 - c. Pathology: probably identical to solitary CHRPE
 - d. Management: observation
5. RPE lesions of familial adenomatous polyposis (FAP) and Gardner's syndrome
 - a. Multiple atypical RPE lesions associated with bowel cancer syndromes
 - b. Unlike typical CHRPE, the lesions are multifocal, irregular, and bilateral
 - c. This condition has a high association with FAP and Gardner's syndrome
 - d. Gardner's syndrome--FAP plus extracolonic manifestations (osteoma, etc)
 - e. The fundus lesions have been called CHRPE in literature
 - f. This led to concern that all CHRPE is associated with bowel cancer
 - g. Typical solitary and multifocal CHRPE are not usually associated with FAP
6. Combined hamartoma of the RPE and sensory retina
 - a. Clinical Features
 1. Sessile gray lesion of the sensory retina and RPE
 2. Usually near optic disc; can be located peripherally
 3. Tortuous or corkscrew retinal vessels within lesion
 4. Surface glial tissue causes traction on sensory retina
 - b. Diagnosis
 1. Characteristic clinical features
 2. Fluorescein angiography shows the abnormal vascular pattern
 - c. Pathology
 1. Cords or proliferated pigment epithelium in sensory retina
 2. Abnormal retinal vessels in lesion
 3. Surface glial tissue causing wrinkling of internal limiting membrane
 - d. Management
 1. Observation
 2. Vitrectomy and membrane for severe traction
7. Adenoma and adenocarcinoma of the CPE and RPE
 - a. General considerations
 1. Adenoma and adenocarcinoma may be clinical indistinguishable

2. Can be locally aggressive but does not metastasize
- b. Clinical features
 1. Usually a deeply pigmented lesion
 2. Can cause subluxed lens, cataract, vitreous hemorrhage
 3. Prominent retinal vessels and exudative retinal detachment
 4. Should be differentiated from melanoma
- c. Pathology
 1. CPE--Pigmented cells with numerous vacuoles
 2. RPE--Cords and tubules of RPE cells
- d. Management
 1. Observation if small and asymptomatic
 2. Local resection (iridocyclectomy) for tumors of CPE
 3. Radiation or enucleation for aggressive tumors of posterior RPE

D. Tumors of the Sensory Retina and Optic Disc

1. Retinoblastoma

a. General considerations

1. Most common primary intraocular malignancy of childhood
2. 1: 15,000 live births

b. Genetics : Hereditary and non-hereditary forms.

1. The hereditary form appears to have an autosomal dominant inheritance
2. However, it is a recessive suppresser gene
3. Deletion on long arm of chromosome 13 (13q-14)
4. Second tumors
 - a. Develop in 25% to 30% of children with germ line retinoblastoma
 - b. Many types, but osteosarcoma of the femur is the most common
 - c. Trilateral retinoblastoma
 1. An important second tumor
 2. Bilateral retinoblastoma plus pinealoblastoma or parasellar tumor
5. Genetic counseling is an important aspect of management

c. Clinical features (Sequence)

1. Initially, small, transparent, and difficult to visualize
2. Gradually becomes more opaque
3. Elevated dome-shaped white retinal mass
4. Then develops prominent retinal feeder and drainer blood vessels
5. Secondary retinal detachment and vitreous seeding
6. Leukocoria
7. Growth patterns
 - a. Initially intraretinal
 - b. Endophytic growth pattern--simulates endophthalmitis
 - c. Exophytic growth pattern-- simulates Coats' disease
 - d. Diffuse infiltrating pattern
8. Diffuse infiltrating retinoblastoma
 - a. Usually unilateral and nonfamilial
 - b. Somewhat older children
 - c. Simulates inflammatory disease
 - d. High incidence of misdiagnosis and misdirected therapy
 - e. Management--usually enucleation
9. Far advanced cases
 - a. Neovascular glaucoma
 - b. Optic nerve and orbital extension
 - c. Massive extraocular extension
 - d. Intracranial extension

- e. Distant metastasis
- 10. Spontaneous regression or arrest
 - a. Occurs in 5% of cases
 - b. Typical clinical features
 - c. Usually no treatment indicated
- d. Pathology
 - 1. Gross
 - a. White intraocular tumor
 - b. Arises from sensory retina
 - c. Endophytic or exophytic growth
 - 2. Microscopic
 - a. Viable tumor appears blue with hematoxylin-eosin
 - b. Necrotic tumor appears pink
 - c. Calcification appears blue
 - d. Poorly differentiated--Anaplastic retinoblasts
 - e. Well differentiated--Flexner-Wintersteiner rosettes and fleurettes
- e. Differential diagnosis
 - 1. PHPV, Coats disease, ocular toxocariasis, and several others
 - 2. Discussed elsewhere and beyond the scope of this discussion
- f. Diagnostic approaches
 - 1. Clinical history
 - 2. Slit lamp biomicroscopy
 - 3. Ophthalmoscopy
 - 4. Ultrasonography
 - 5. Fluorescein angiography
 - 6. Computed tomography; magnetic resonance imaging
 - 8. Fine needle aspiration biopsy--rarely indicated
- g. Management
 - 1. General considerations
 - a. Enucleation being used less often
 - b. External beam irradiation being used less often
 - c. More conservative methods being employed
 - 2. Enucleation
 - a. Advisable for advanced cases
 - b. Important to obtain a long section of optic nerve.
 - c. Integrated implant (hydroxyapatite) can be used
 - 3. External beam irradiation
 - a. Moderately advanced tumors
 - b. Multiple tumors

- c. Vitreous or subretinal seeds
 - d. Increased incidence of second tumors in hereditary cases
4. Episcleral plaque brachytherapy
 - a. Used more frequently today for circumscribed tumors
 - b. Less irradiation to orbital bone and soft tissue
 - c. Apparently no increased incidence of second cancers
 - d. Used most often after failure of other treatments
 5. Cryotherapy
 - a. Small pre-equatorial tumors without vitreous seeding
 - b. Triple freeze-thaw technique is effective
 6. Laser photocoagulation
 - a. Small post-equatorial tumors without vitreous seeding
 - b. Used less often since introduction of thermotherapy
 - a. Recently introduced technique
 7. Chemothermotherapy
 - a. Chemotherapy to sensitize tumor to laser light.
 - b. Carboplatin administered
 - c. Followed by transpupillary or transcleral heat treatment
 8. Systemic (intravenous) chemoreduction
 - a. Recently popularized technique
 - b. Chemotherapy given to reduce size of tumor(s)
 - c. Subsequent treatment with conservative methods
 - d. Goal is to avoid enucleation and external irradiation
 9. Intra-arterial chemotherapy (melphalan)
 - a. Intra-arterial chemotherapy
 - b. Done in Japan for > 20 yrs (Kaneko et al)
 - c. Recently used in USA (Sloan-Kettering)
 - d. Used at Wills Eye Institute for 3 years
 Caution:
 1. Enucleation alone is still appropriate for very advanced intraocular cases.
 2. 98 % survival with enucleation alone without any chemotherapy agents.
 3. Very controversial at this time
 4. Needed: better studies; more follow up
- h. Prognosis
1. Improving considerably
 2. Affected eyes being salvaged more often
 3. About 95 % survival in USA today for retinoblastoma

4. Second tumors often prove fatal
 - i. International Classification of Retinoblastoma
 1. Designed to address eye salvage after chemoreduction
 2. Stages correlate well with prognosis for eye salvage

2. Vascular tumors of the retina and optic disc

a. General considerations

1. Always important to specify the type of retinal hemangioma
2. Each has different features, complications, and systemic associations
3. Capillary, cavernous, racemose, and acquired vasoproliferative types

b. Retinal hemangioblastoma (Capillary hemangioma)

1. General

- a. Benign congenital vascular tumor
- b. Frequent association with von Hippel-Lindau (VHL) syndrome
- c. Von Hippel-Lindau syndrome discussed in phakomatosis section

2. Clinical

- a. Reddish retinal mass
- b. Peripheral tumor has dilated feeder and drainer retinal vessels.
- c. Exudative form: Retinal exudation and exudative detachment
- d. Yellow intraretinal exudation has predilection for foveal area
- e. Vitreoretinal form: vitreal and retinal traction
- f. Tumor can occur at optic disc--feeder vessels may be absent
- g. More aggressive when seen with VHL syndrome

3. Diagnosis

- a. Typical clinical appearance
- b. Characteristic angiographic features
 1. Rapid filling of tumor through feeder artery
 2. Intense hyperfluorescence of tumor

4. Pathology

- a. Intraretinal mass
- b. Proliferation of endothelial and glial cells
- c. Numerous small blood vessels

5. Management

- a. Observation for some small and asymptomatic lesions
- b. Laser photocoagulation for small posterior lesions
- c. Cryotherapy for larger peripheral lesions
- d. Radiotherapy (external or plaque) for selected cases
- e. There are specific techniques for above treatments

c. Cavernous hemangioma

1. General

- a. Benign congenital vascular tumor
- b. Sometimes associated with CNS and cutaneous hemangiomas
- c. No eponym for this syndrome

2. Clinical
 - a. Blue-red retinal mass--peripheral or at optic disc
 - b. Resembles a bunch of grapes
 - c. No feeder vessels--located along course of retinal vein
 - d. Usually no retinal detachment
 - e. Vitreous hemorrhage is most frequent complication
 - f. Can occur at optic disc
3. Diagnosis
 - a. Typical clinical appearance
 - b. Classic (perhaps pathognomonic) angiographic features
 1. Slow filling in late venous phase
 2. Late staining with blood-fluorescein interface
4. Pathology
 - a. Intraretinal vascular mass
 - b. Composed of large dilated congested retinal veins
5. Management
 - a. Observation--the majority require no treatment
 - b. Vitrectomy for recurrent vitreous hemorrhage
 - c. Membrane peeling if severe traction and visual loss
- d. Racemose hemangioma
 - 1 General
 - a. Benign congenital vascular lesion
 - b. Actually an arteriovenous communication
 - c. Can be mild or severe
 - d. Association with midbrain lesions--Wyburn-Mason syndrome
 2. Clinical Features
 - a. Retinal arteriovenous communication
 - b. No intervening capillary bed
 - c. Can range from mild to severe
 - d. Usually no exudation or detachment
 - e. Complications: vitreous hemorrhage, BRVO (rare)
 3. Diagnosis
 - a. Typical clinical appearance
 - b. Fluorescein angiography-arteriovenous communication without leakage
 4. Pathology: Large endothelial-lined channels
 5. Management: Observation--the majority require no treatment
- e. Acquired vasoproliferative tumor of fundus

1. Recently recognized vascular fundus lesion
 2. Previously called presumed acquired nonfamilial retinal hemangioma
 3. Now divided into primary and secondary types
 - a. Primary type
 1. Usually idiopathic
 2. Older individuals, often with hypertension
 3. Yellow red mass usually near inferior equator
 4. Relatively stable, but often exudative detachment
 - c. Secondary type--associated with pre-existing ocular diseases
 1. Inflammation--Intermediate uveitis, toxocariasis
 2. Retinitis pigmentosa
 3. Coats' disease
 4. Trauma
 5. Long-standing retinal detachment
 6. Others
 4. Pathology
 - a. Little histopathology available
 - b. Probably composed of blood vessels, RPE, and glial cells
 5. Management
 - a. Observation--Many require no treatment
 - b. Cryotherapy
 - c. Laser photocoagulation
 - d. Irradiation
3. Glial tumors of the retina and optic disc
- a. Reactive gliosis
 1. Reactive proliferation of astrocytes and Muller cells
 2. Can sometimes assume tumorous proportions (“massive gliosis”)
 3. Can be nodular or diffuse, sometimes entirely filling the eye
 4. Usually secondary trauma, inflammation, or vascular disease
 - b. Astrocytic hamartoma
 1. General
 - a. Benign congenital vascular lesion
 - b. Associated with tuberous sclerosis (Bourneville syndrome)
 - c. Usually diagnosed in childhood
 2. Clinical Features
 - a. Noncalcified type
 1. Gray-yellow sessile lesion in nerve fiber layer

- 2. No enlarged feeder vessels
 - b. Calcified type
 - Glistening yellow calcified bodies
 - c. Exudation and detachment: very rare
 - d. Usually relative stable. Occasional slow growth and detachment
 - e. Occasional aggressive behavior, detachment, glaucoma
3. Diagnosis
- a. Typical clinical appearance
 - b. Fluorescein angiography: slow uptake, late staining
 - c. No large feeder vessels as seen with retinoblastoma
4. Pathology
- a. Benign tumor of astrocytes
 - b. Calcified deposits, like psammoma bodies
5. Management
- a. Observation
 - b. Most require no treatment
 - c. Laser treatment for small progressive tumors
 - d. Enucleation occasionally necessary
- c. Acquired retinal astrocytoma
1. General
- a. Benign acquired glial tumor
 - b. Usually no apparent association with tuberous sclerosis
 - c. Similar to acquired intracranial astrocytoma
2. Clinical Features
- a. Elevated gray-yellow retinal mass
 - b. Usually a noncalcified lesion
 - c. Generally diagnosed in adulthood
 - d. Progressive enlarge is common
 - e. Exudative retinal detachment frequent
3. Diagnosis
- a. Rather typical clinical appearance
 - b. Clinical diagnosis not often made because lesion is rare
 - c. Fluorescein angiography-slow uptake, late staining

4. Pathology

- a. Benign tumor of astrocytes
- b. No significant calcium

5. Management

- a. Observation if asymptomatic
- b. Progressive or symptomatic lesions--treat
- c. Role of laser, cryotherapy and radiation not established

E. Melanocytoma of the optic nerve

1. General

- a. Benign pigmented lesion in optic disc
- b. Probably congenital
- c. Previously misdiagnosed as melanoma
- d. Actually represents a various of melanocytic nevus
- e. Malignant transformation rare

2. Clinical Features

- a. Deeply pigmented tumor located over the optic disc
- b. May have choroidal and nerve fiber layer involvement
- c. Usually stable; subtle growth noted in 15%

3. Diagnosis

- a. Typical clinical appearance
- b. Fluorescein angiography: generally hypofluorescent
- c. Visual field defects: enlarged blind spot; arcuate scotoma

4. Pathology

- a. Deeply pigmented mass: bleaching necessary
- b. Round to ovoid cells
- c. Uniform nuclei; usually no prominent nucleoli
- d. Choroidal and nerve fiber layer components

5. Management

- a. Observation: the majority require no treatment
- b. If malignant transformation suspected--consider enucleation

F. Intraocular Lymphoid Tumors

1. General considerations

- a. May be benign or malignant
- b. Benign and malignant forms may be indistinguishable in uvea

2. Benign lymphoma (Uveal lymphoid infiltration; BRLH)

- a. Clinical

1. Diffuse or multiple yellow uveal infiltrations
 2. May occur in iris, ciliary body, or choroid
 3. Secondary retinal detachment common
 4. Salmon pink lesions in conjunctiva and orbit can suggest the diagnosis
 5. May be associated with myeloma and Waldenstrom's macroglobulinemia
 6. May eventually evolve into malignant lymphoma
- b. Diagnosis
1. Clinical suspicion
 2. Fluorescein angiography--similar to uveal metastasis
 3. Ultrasonography, CT, MRI--Uveal thickening and orbit involvement
 4. Conjunctival, orbital, or choroidal biopsy
- c. Pathology
1. Polymorphic--benign lymphocytes and plasma cells
 2. Germinal centers and Dutcher bodies (intranuclear inclusion bodies)
- d. Management
1. Steroids not usually highly effective
 2. Responds well to low doses of radiotherapy (1500-2000 cGy)
3. Malignant Lymphoma
- a. General considerations
1. Classification of lymphoma (REAL classification)
 - a. Non-Hodgkin's lymphoma (NHL)
 - b. Hodgkin's lymphoma
 2. Intraocular lymphoma
 - a. A form of extranodal lymphoma
 - b. Usually non-Hodgkin's B-cell lymphoma
 - c. Two forms recognized-- uveal and retinovitreal
 - d. In advanced cases, the 2 types can overlap
 - e. Markedly increased incidence in immunosuppressed patients
- b. Uveal form
1. General considerations
 - a. Usually associated with visceral, extranodal NHL
 - b. Probably reaches uvea via ciliary circulation
 - c. Usually middle aged or elderly patients
 2. Clinical features
 - a. Amelanotic, yellow uveal stromal mass
 - b. May affect iris, ciliary body or choroid
 - c. Unilateral or bilateral

- 4. May be solitary, multifocal, or confluent
- d. May be indistinguishable from benign uveal infiltration
- e. May resemble metastasis , birdshot choroiditis, or sarcoidosis

3. Diagnosis

- a. Typical clinical features
- b. Examine conjunctiva--look for salmon patch lesion
- c. Fluorescein angiography
- d. Ultrasonography--choroidal mass, high internal reflectivity
- e. Ultrasonography, CT, MRI
 - 1. Uveal mass
 - 2. May show adjacent orbital involvement
- f. Uveal biopsy (iris, ciliary body, choroid) in selected cases

4. Management

- 1. Appropriate chemotherapy if systemic involvement present
- 2. Ocular radiotherapy if no systemic involvement

c Retinovitreal form (primary CNS lymphoma)

1. General considerations

- a. Prior names now considered inaccurate
 - 1. Microgliomatosis
 - 2. Reticulum cell sarcoma
 - 3. Histiocytic lymphoma

b. Usually associated with CNS lymphoma

c. Usually middle aged or elderly patients

2. Clinical features

- a. Signs of uveitis and vitritis
- b. Most cases are bilateral--frequently asymmetric
- c. Sub RPE typical yellow infiltrates

3. Diagnosis

- a. Typical clinical features
- b. Evaluation for CNS lymphoma--lumbar puncture, MRI.
- c. Vitreous biopsy

4. Management

- a. Vitrectomy at time of vitreous biopsy
- b. Ocular irradiation
- c. CNS irradiation if brain involvement detected
- d. Intrathecal chemotherapy
- e. Intraocular chemotherapy being investigated

G. Intraocular leukemia

1. Intraocular involvement usually hemorrhage only
2. Intraocular involvement by leukemic cells less common
3. Can affect iris, posterior uvea, retina, optic nerve or vitreous
4. Clinical features
 - a. Iris thickening: tumor induced pseudohypopyon
 - b. Choroidal and retinal infiltration; often hemorrhagic
 - c. Swollen optic disc
 - d. Vitreal cells
5. Management: systemic chemotherapy and/or ocular radiotherapy

IV. ORBITAL TUMORS

A. General considerations

1. Knowledge of clinical features of orbital lesions is important
2. Office evaluation is different from routine ocular examination
3. Familiarity with incidence of various orbital lesions is important
4. Imaging studies (CT, MRI) have greatly improved diagnosis and management
5. Clinical judgment regarding management options is extremely important
 - a. Observation
 - b. Incisional biopsy
 - c. Excisional biopsy
 - d. Needle biopsy
 - e. Medical management (corticosteroids, etc)
 - f. Irradiation
 - g. Chemotherapy
6. Convenient to divide orbital lesions into 2 groups
 - a. Orbital tumors that occur primarily in childhood
 - b. Orbital tumors that occur primarily in adulthood
 - c. Not always a clear distinction between the two.

B. Orbital Tumors That Occur Primarily in childhood

1. Dermoid Cyst

a. General

1. Congenital cystic mass
2. Sometimes not recognized until months or years after birth
3. Entrapment of epithelium in deeper location
4. Can occur and bony sutures or soft tissue sites
5. Usually no systemic associations

b. Clinical Features

1. Subcutaneous mass deep to the epidermis
2. Most often at superolateral orbital rim (zygomaticofrontal suture)
3. Less often nasally
4. About 5% occur in orbital soft tissue, usually nasally
5. May occasionally occur in deep orbit
6. May have dumbbell shape--inside and outside orbit
7. Draining cutaneous fistula sometimes occurs
8. Can rupture, leading to localized inflammation

c. Diagnosis

1. Typical clinical features

- 2. Imaging studies--Non-enhancing mass
- d. Pathology
 - 1. Epithelial-lined cyst
 - 2. Typical dermoid cyst--lined by epidermis (keratinizing)
 - 3. Conjunctival dermoid cyst--lined by conjunctival epithelium (nonkeratinizing)
 - 4. Dermal appendages in wall and hair in lumen of cyst
 - 5. Ruptured cyst can lead to granulomatous inflammation
- e. Management : Observation or excision, depending on clinical findings

2. Teratoma

- a. General
 - 1. Rare cause of congenital proptosis
 - 2. Usually very evident at birth
- b. Clinical Features
 - 1. Can produce marked proptosis and displacement of globe
 - 2. Globe itself is often normal
- c. Pathology
 - 1. Complex mass with variable findings from case to case
 - 2. True teratoma has elements of all three germ layers
 - 3. Dermal, respiratory, intestinal, glandular components
 - 4. Rare case of poorly formed fetus in orbit
- d. Management
 - 1. Orbital exenteration often performed in past
 - 2. Exenteration can be avoided in less advanced cases
 - 3. Obtain good imaging studies
 - 4. Remove teratoma and salvage globe when possible

3. Capillary Hemangioma

- a. General considerations
 - 1. Most common orbital vascular tumor of childhood
 - 2. Similar clinical course to eyelid capillary hemangioma
- b. Clinical Features
 - 1. Proptosis in first two weeks of life
 - 2. Sometimes associated periocular cutaneous hemangioma
 - 3. Enlarges for several months, then slowly regresses without treatment

c. Diagnosis

- 1. Proptosis in an infant, exacerbated by crying or straining
- 2. CT, MRI
 - a. Usually diffuse or irregular orbital mass

- b. Occasionally well-circumscribed
- c. Marked enhancement
- d. Pathology
 1. Proliferation of plump endothelial cell
 2. Numerous small capillaries
- e. Management
 1. Refraction
 2. Correct refractive error
 3. Patching for amblyopia of potential amblyopia
 4. Systemic or local corticosteroids (See eyelid section)
 5. Local surgical resection for small anterior tumors

4. Lymphangioma

- a. Clinical
 1. Proptosis may be present at birth
 2. Sometimes detected later in life following trauma and hemorrhage
 3. Eyelid often blue due to subcutaneous involvement
 4. Conjunctiva may show clear or hemorrhagic lymph channels
 5. Proptosis may be exacerbated after trauma or upper respiratory infection
 6. Hemorrhage into lymph channels called "chocolate cysts"
 7. Slowly progressive, does not tend to regress
- b. Diagnosis
 1. Characteristic clinical features
 2. CT, MRI: Irregular multicystic mass with blood in cysts
- c. Pathology
 1. Irregular mass composed of bloodless, ectatic lymph channels
 2. Spaces lined by flattened endothelial cells
 3. Hemorrhages into spaces produce the "chocolate cysts"
 4. Lymphoid tissue often seen in septae
 5. May microscopically resemble varix or cavernous hemangioma
- d. Management
 1. May be very challenging; parents often eager for a "cure"
 2. Best to temporize if signs and symptoms are minor
 3. Large blood cysts can be managed by aspiration
 4. Surgical excision or debulking sometimes necessary

5. Juvenile Pilocytic Astrocytoma (Optic Nerve Glioma)

- a. General considerations
 1. Most common primary optic nerve tumor
 2. Usually becomes apparent during the first few years of life
 3. About 70% associated with neurofibromatosis

4. About 15% of patients with NF-1 have optic nerve glioma
 5. Often bilateral
 6. Can be limited to orbit or extend into CNS
- b. Clinical features
 1. Painless visual loss
 2. Axial proptosis
 - c. Diagnosis
 1. Typical clinical features
 2. Look for signs of neurofibromatosis
 3. CT, MRI
 - a. Very typical ovoid or fusiform mass of optic nerve
 - b. May show a characteristic kink in the mass
 - c. Coronal sections important to show optic nerve origin
 - d. MRI with enhancement helps identify CNS involvement
 - d. Pathology
 1. Well-circumscribed benign tumor of optic nerve
 2. Composed of compact well-differentiated fibrillary astrocytes
 3. Surrounded by dura mater
 4. Reasons for apparent growth seen clinically
 - a. Arachnoidal proliferation (simulates meningioma)
 - b. Intratumoral mucin deposition
 - c. Intratumoral hemorrhage
 - e. Management
 1. Controversial; depends on overall clinical situation
 2. Observation, resection, or radiotherapy, chemotherapy
6. Rhabdomyosarcoma
 - a. General
 1. Most common primary malignant orbital of childhood
 2. Most occur in first decade; Mean age eight years
 3. Occasionally congenital or onset in adulthood
 4. Can metastasize
 5. Cure rate now over 90%
 - b. Clinical features
 1. Rather rapid onset
 2. Proptosis and displacement of globe
 3. Eyelid edema, conjunctival chemosis
 4. May resemble idiopathic orbital inflammation
 - c. Diagnosis
 1. Must have high index of suspicion
 2. CT, MRI

- a. Round, ovoid or irregular mass
 - b. Initially well circumscribed; later diffuse
 - c. Enhancement with contrast
 - d. Usually in orbital soft tissue
 - e. Can invade orbit from nasopharynx through bone
- d. Pathology
1. Tumor composed of poorly differentiated rhabdomyoblasts
 2. Characteristic strap cells with cross striations
 3. Large round ganglioform cells
 4. Embryonal form most common; Alveolar form most malignant
 5. Immunohistochemistry helpful in difficult cases
- e. Management
1. Biopsy to establish diagnosis
 2. Remove as much as possible without damaging vital structures
 3. Remove entire tumor if it is small and well-circumscribed
 4. Systemic evaluation; chest x-ray
 5. Combined irradiation and chemotherapy by appropriate specialists
 6. Close ocular and systemic follow up
7. Granulocytic Sarcoma ("Chloroma")
- a. General
1. Soft tissue infiltration by myelogenous leukemia
 2. Usually occurs in young children
 3. Orbital lesion can occur prior to diagnosis of leukemia
- b. Clinical features
1. Rather rapid onset
 2. Proptosis and displacement of globe
 3. May see swelling of temporal fossa
 4. Often a palpable anterior orbital mass
- c. Diagnosis
1. CT and MRI
 2. Circumscribed enhancing orbital mass
 3. Usually in anterior aspect of orbit
- d. Pathology
1. Solid mass of leukemia cells
 2. May resemble lymphoma
 3. Leder stain may assist in confirming granulocytic origin of tumor cells
- e. Management
1. Biopsy: excisional if possible
 2. Treatment of systemic leukemia
 3. Sensitive to chemotherapy and irradiation

8. Burkitt's Lymphoma

a. General

1. Originally described as endemic in some parts of Africa
2. Non-Burkitt's and AIDS-related variants being recognized more often
3. Association with Epstein -Barr virus

b. Clinical features

1. Rapid proptosis or globe displacement in a child
2. African variant mainly affects maxilla and viscera--orbital involvement secondary
2. Non-African variants often initially confined to orbit

c. Diagnosis

1. CT and MRI
2. Usually a circumscribed orbital mass
3. May be ovoid or oblong
4. Can be located anywhere in orbit

d. Pathology

1. Closely-packed malignant B-lymphocytes
2. Foci of histiocytes impart a "starry sky" appearance on low magnification

e. Management

1. Chemotherapy for systemic disease
2. Orbital irradiation

9. Histiocytic Tumors

a. General

1. Previously called "histiocytosis X" group of diseases
 - a. Eosinophilic granuloma
 - b. Hand-Schuller-Christian disease
 - c. Letterer-Siwe disease
2. Birbeck granules (feature of Langerhan's cells) seen in cytoplasm with EM
3. Therefore, Langerhan's cell histiocytosis has become a preferable term
4. Eosinophilic granuloma is the most common form in the orbit

b. Clinical features

1. Solitary bony mass, usually in anterior superotemporal aspect of orbit
2. May resemble an inflamed dermoid cyst
3. Mass arises within bone--does not compress bone

c. Diagnosis

1. CT, MRI
2. Bone destructive orbital mass
3. May extend into intracranial cavity
4. May resemble metastatic neuroblastoma or ruptured dermoid cyst

d. Pathology

1. Proliferation of Langerhan's cells
2. Multinucleated giant cells
3. EM: cytoplasmic evidence of Birbeck granules

e. Management

1. Biopsy and curettage
2. Corticosteroids if necessary
3. Observation: many are self-healing

10. Metastatic tumors

a. General considerations

1. Less common than in adults
2. Reach orbit by hematogenous routes
3. Three main tumors recognized
 - a. Neuroblastoma
 - b. Wilm's tumor (nephroblastoma)
 - c. Ewing's tumor
 - d. Others

11. Metastatic tumors--neuroblastoma

a. General

1. Most important metastatic tumor to the orbit in children.
2. Primary tumor usually in adrenal gland
3. Primary neoplasm usually diagnosed prior to orbital involvement
4. Orbital mass diagnosed before adrenal primary in only 3-5%

b. Clinical features

1. Rapid proptosis and globe displacement
2. Unilateral or bilateral
3. Eyelid ecchymosis is a characteristic feature

c. Diagnosis

1. Abdominal evaluation for adrenal neuroblastoma
2. Orbital CT, MRI
3. Bone-destructive orbital mass--usually superotemporally
4. May be similar to Langerhan's' cell histiocytosis and ruptured dermoid cyst

d. Pathology

1. Poorly differentiated neuroblastic cells
2. May resemble retinoblastoma

e. Management

1. Chemotherapy for systemic disease
2. Orbital irradiation

B. Orbital Tumors That Occur Primarily in Adulthood

1. Idiopathic Orbital Inflammation (“Inflammatory pseudotumor”)

a. General

1. Inflammatory mass that resembles a neoplasm
2. Frequently seen in childhood as well as adulthood
3. Etiology usually uncertain

b. Clinical features

1. Usually in adults; often in children
2. Acute or subacute onset of pain and eyelid and conjunctival edema
3. Proptosis or displacement of globe

c. Diagnosis

1. CT, MRI findings vary from case to case
2. Usually a well-defined or irregular orbital mass
3. Can involve one or more orbital soft tissues

4. CT, MRI variations

- a. Localized or diffuse mass; usually confined to soft tissues
- b. Involvement of one or more rectus muscles (orbital myositis)
- c. Involvement of optic nerve sheaths
- d. Involvement of sclera and choroid (scleritis, choroiditis)
- e. Diffuse involvement of all orbital tissues

d. Pathology

1. Infiltration of affected tissues by chronic inflammatory cells (mostly lymphocytes)
2. Usually nongranulomatous-- no epithelioid cells or giant cells
3. In children, eosinophils are frequent

e. Management

1. Oral corticosteroids or other anti-inflammatory drugs
2. If vision is threatened, then consider I.V. steroids
3. If no response, consider biopsy to rule out neoplasm or granuloma
4. Irradiation in cases that fail to respond to medical treatment

2. Mucocele

a. General

1. Usually in adults; seen in children with cystic fibrosis
2. Cystic lesion extending into orbit, usually from frontal or ethmoid sinus
2. History of chronic sinusitis
3. Can become secondarily infected (pyocele)

b. Clinical features

1. Gradual displacement of globe--inferiorly and temporally
2. Superonasal or nasal fluctuant subcutaneous mass

- c. Diagnosis
 1. CT, MRI
 2. Cystic, non-enhancing, bone destructive mass
 3. Usually continuous with frontal or ethmoid sinus
 4. Opaque sinuses due to chronic sinusitis
 - d. Pathology
 1. Cystic lesion lined by sinus epithelium
 2. Chronic or acute inflammatory cells
 - e. Management
 1. Systemic antibiotics
 2. Surgical excision, removing mass and sinus mucosa
3. Cavernous Hemangioma
- a. General
 1. Most common orbital vascular tumor of adulthood
 2. Usually solitary and not associated with systemic diseases
 - b. Clinical features
 1. Slowly progressive proptosis (usually axial) in an adult
 2. No significant inflammatory signs
 3. Visual acuity and ocular motility usually good
 - c. Diagnosis
 1. CT, MRI
 2. Circumscribed round to ovoid orbital mass
 3. Moderate enhancement
 4. Most often in intraconal location
 - d. Pathology
 1. Encapsulated mass
 2. Large, congested vascular channels with flattened endothelial cells
 3. Smooth muscle in wall of vessels
 - e. Management
 1. Serial observation for small asymptomatic lesions
 2. Surgical excision of larger symptomatic lesions
 - a. Cutaneous approach
 - b. Conjunctival approach
 - c. Osteotomy (Kronlein approach) usually not necessary
4. Neurilemoma (Schwannoma)
- a. General
 1. Most important peripheral nerve tumor of the orbit
 2. Arises from Schwann cells of ciliary nerves

3. Does not arise from optic nerve which has no Schwann cells
 - b. Clinical features
 1. Generally occurs in young to middle aged adults
 2. Usually painless proptosis
 3. Usually downward displacement of globe due to superior location
 4. Unlike neurofibroma, it is not usually associated with neurofibromatosis
 - c. Diagnosis
 1. CT, MRI-- Usually enhancing ovoid mass
 2. Anywhere in orbit, but usually superior (supraorbital nerve)
 - d. Pathology
 1. Encapsulated mass composed bland spindle cells
 2. Neural features; Antoni A and Antoni B patterns
 3. Electron microscopy --wide spacing collagen (Luse bodies)
 - e. Management
 1. Complete excision for circumscribed lesions
 2. Lateral orbitotomy necessary in most cases
5. Fibrous histiocytoma
- a. General
 1. Probably more common than previously realized.
 2. May be benign, locally aggressive or malignant
 3. About 10% are malignant
 4. Can occur at any age--usually middle aged or older adults
 - b. Clinical features
 1. Painless proptosis
 2. Displacement of globe
 3. Advanced or malignant tumors may cause chemosis and visual loss
 - c. Diagnosis
 1. CT, MRI--Well-circumscribed round or irregular mass
 2. Moderate enhancement with contrast
 - d. Pathology
 1. Relatively benign fibroblasts and histiocytes
 2. Sometimes arranged in a storiform pattern
 3. Pleuripotential cells- can differentiate toward fibroblasts and histiocytes
 - e. Management: Usually surgical excision, like other circumscribed tumors
6. Meningioma
- a. General: Two types are likely to produce orbital signs and symptoms

1. Primary optic nerve sheath meningioma (from arachnoid of orbital optic nerve)
 2. Sphenoid ridge meningioma (from arachnoid around sphenoid bone)
 3. Both types have a predilection for adult females
- b. Primary optic nerve sheath meningioma
1. Clinical features
 - a. Initial visual loss and optic atrophy
 - b. Later proptosis
 - c. Retinochoroidal (opticociliary) shunt vessels at disc margin
 - d. May be bilateral
 2. Diagnosis
 - a. CT, MRI
 - b. Usually a diffuse thickening of optic nerve image
 - c. Silhouette of optic nerve within the mass (“railroad sign”)
 3. Pathology
 - a. Benign tumor of arachnoidal meningothelial cells
 - b. May see calcified spherules (psammoma bodies)
 4. Management
 - a. Controversial and difficult
 - b. Observation advisable in most cases
 - c. Surgical excision for massive tumor with severe visual loss
 - d. Radiotherapy for non-resectable lesions
- c. Sphenoid ridge meningioma
1. Clinical features
 - a. Initial proptosis and mass in temporal fossa
 - b. Later visual loss as lesion encroaches on optic canal
 - c. Retinochoroidal shunt vessels less common
 2. Diagnosis
 - a. CT, MRI
 - b. Diffuse thickening of sphenoid bone
 - c. Hyperostosis is characteristic feature
 3. Pathology
 - a. Similar to optic nerve sheath meningioma
 - b. Benign tumor of arachnoidal meningothelial cells
 - c. May see calcified spherules (psammoma bodies)
 4. Management
 - a. Controversial and difficult
 - b. Observation generally advisable in early asymptomatic cases
 - c. Surgical excision for progressive tumors with threat to vision
 - d. Radiotherapy for non-resectable lesions

7. Epithelial tumors of the lacrimal gland (LG)

a. General

1. Non-epithelial masses: about 70%
 - a. Idiopathic inflammation (pseudotumor)
 - b. Granuloma: sarcoidosis, tuberculosis
 - c. Lymphoid tumors (benign or malignant lymphoma)
2. Epithelial tumors: about 30%
 - a. Benign epithelial tumors
 1. Cyst (dacryops)
 2. Pleomorphic adenoma (benign mixed tumor)
 - b. Malignant epithelial tumors
 1. Adenoid cystic carcinoma
 2. Pleomorphic adenocarcinoma (malignant mixed tumor)
 3. Others

b. Pleomorphic adenoma (benign mixed tumor)

1. Clinical features
 - a. Young to middle aged adults
 - b. Painless proptosis, inferior and medial displacement of globe
 - c. Slowly progressive
2. Diagnosis
 - a. CT, MRI
 - b. Round to ovoid superotemporal orbital mass
 - c. May cause bony fossa, but usually no bone erosion
3. Pathology
 - a. Encapsulated mass
 - b. Smooth surface irregularities
 - c. Combination of epithelial cells and stromal elements
4. Management
 - a. Complete excision of mass (excisional biopsy)
 - b. Incisional biopsy and needle biopsy generally contraindicated
 - c. Incomplete excision can lead to recurrence and malignant transformation
5. Prognosis
 - a. Excellent if tumor completely removed
 - b. Incomplete removal--recurrence or possible malignant transformation

c. Malignant epithelial tumors

(Adenoid cystic carcinoma, pleomorphic adenocarcinoma, etc)

1. Clinical features
 - a. Any age, some adenoid cystic carcinoma occur in children
 - b. More rapid onset and progression of proptosis and displacement
 - c. Pain is more common (due to bone and nerve invasion)
 2. Diagnosis
 - a. CT, MRI
 - b. Initially round or ovoid mass; later irregular
 - c. Bone destruction is often present
 - d. Calcium sometimes present
 3. Pathology
 - a. Varies with type of tumor
 - b. Adenoid cystic carcinoma--Swiss cheese pattern; nerve and bone invasion
 - c. Pleomorphic adenocarcinoma--Epithelial and mesenchymal elements
 - d. Mucoepidermoid carcinoma--abundant mucous
 4. Management
 - a. Complete excision if possible
 - b. If not resectable, do generous incisional biopsy
 - c. Frozen sections to confirm tumor presence if necessary
 - d. Await permanent sections
 - e. Then consider orbital exenteration with bone removal
 - f. Supplemental brachytherapy (plaque) option to exenteration in some cases
 5. Prognosis
 - a. Once considered very poor
 - b. Improving, due to earlier diagnosis and treatment
8. Lymphoid Tumors
- a. General
 1. Can be benign (reactive lymphoid hyperplasia), intermediate, or malignant
 2. Benign and malignant difficult to differentiate--biopsy necessary
 3. Classification difficult and controversial
 4. Most orbital lymphoma is non Hodgkin's B-cell type
 5. T-cell lymphoma rare in orbit
 - b. Clinical features
 1. Unilateral or bilateral orbital mass
 2. Usually in the anterior portion of orbit
 3. May be palpable through lid
 4. Sometimes simultaneous conjunctival and uveal involvement
 - c. Diagnosis
 1. Systemic evaluation for lymphoma
 2. Look for conjunctival "salmon patch" and uveal infiltration

3. Orbital CT, MRI
 4. Smooth solid mass that molds to bone and globe
 5. Variable size and shape
 6. Usually soft tissue; bone involvement rare
- d. Pathology
1. Varies from benign, atypical, and malignant lymphoma
 2. Benign--Well-differentiated B-lymphocytes, plasma cells
 3. Malignant--Poorly differentiated B lymphocytes
- e. Management
1. Evaluation for systemic lymphoma
 2. Biopsy to establish the diagnosis
 - a. If small and localized--do excisional biopsy
 - b. If not easily resectable--do incisional biopsy
 - c. If known systemic lymphoma--consider needle biopsy
 - d. Communicate with pathologist--immunohistochemical studies
 3. If systemic lymphoma present--possible chemotherapy
 4. If systemic lymphoma absent: consider orbital irradiation
 - a. 1500-2000 cGy for benign lesion
 - b. 3000-3500 cGy for atypical or malignant
9. Metastatic Tumors
- a. General
1. Like uveal metastasis, most arrive by hematogenous routes
 2. Most are carcinoma; melanoma and sarcoma less common
 3. Breast, lung and prostate are most common primary sites
 4. Bronchial carcinoid, thyroid, kidney, etc, less common
 5. About 25% have no prior history of cancer
- b. Clinical features
1. Rather rapid onset of proptosis and displacement of globe
 2. Pain, diplopia and blurred vision often occur
 3. Usually unilateral, occasionally bilateral
 4. Fibrotic tumors (breast, stomach, etc) may cause enophthalmos
- c. Diagnosis
1. CT, MRI
 2. Features vary with primary lesion and extent of orbital lesion
 3. Lung, carcinoid, melanoma, thyroid, kidney--often circumscribed
 4. Breast--often diffuse and ill-defined
- d. Pathology
1. Varies with the primary tumor
 2. May be poorly differentiated, sometimes making the diagnosis difficult
- e. Management

1. Excisional or incisional biopsy
2. Chemotherapy for systemic metastasis
3. Orbital radiotherapy (3500-4000 cGy)

f. Prognosis

1. Usually poor
2. Some orbital metastasis (i.e., carcinoid) may offer better prognosis

9. Secondary Tumors

a. General

1. Should be differentiated from metastatic tumors
2. Reach orbit by direct extension from adjacent structures
3. Clinical features vary with the location of the primary neoplasm
4. Most of the specific tumors discussed earlier
 - under eyelids, conjunctival and intraocular sections

b. Eyelids

1. Basal cell carcinoma
2. Sebaceous gland carcinoma
3. Squamous cell carcinoma
4. Melanoma

c. Conjunctiva

1. Squamous cell carcinoma
2. Melanoma

d. Intraocular structures

1. Uveal melanoma
2. Retinoblastoma
3. Medulloepithelioma

e. Paranasal sinuses

1. Maxillary sinus carcinoma
2. Ethmoid sinus carcinoma

f. Nasopharynx

1. Nasopharyngeal carcinoma
2. Angiofibroma

g. Cranial cavity

1. Meningioma
2. Meningoencephalocele

h. Diagnosis

1. History
2. CT, MRI
3. Biopsy

i. Pathology

1. Varies with primary lesion
2. Often poorly differentiated

j. Management

1. Varies with type and extend of the tumor
2. Surgical excision: possible orbital exenteration
3. Radiotherapy and chemotherapy for advanced disease

V. SYSTEMIC HAMARTOMATOSES ("PHAKOMATOSES")

A. General Considerations

1. Historical Aspects
 - a. Van der Hoeve (1932) coined term "phakoma"
 - b. Means "mother spot" or birthmark
2. Terminology
 - c. Chorista
 1. A non-tumorous anomaly
 2. Composed of tissues that are not normally present at the involved site
 - b. Choristoma
 1. A tumor-like malformation
 2. Composed of tissues that are not normally present at the involved site
 3. A limbal dermoid is a good example of a choristoma
 - c. Hamartia
 1. A non tumorous anomaly
 2. Composed of tissues that are normally present at the involved site.
 3. An example is the conjunctival telangiectasia of ataxia telangiectasia (Louis-Barr).
 - d. Hamartoma
 1. A tumorous anomaly
 2. Composed of tissues that are normally present at the involved site
 3. Most of the tumors discussed herein are examples of hamartomas
3. Hereditary Aspects
 - a. Many are inherited in autosomal dominant manner with variable penetrance
 - b. Most are now recognized to be due to recessive tumor suppresser gene
 - c. Some have no hereditary pattern (Sturge-Weber and Wyburn-Mason)
4. Principal Tissues Involved
 - a. Neuroectodermal
 1. Tuberous sclerosis
 2. Neurofibromatosis
 3. Others
 - b. Mesodermal
 1. Retinocerebellar Capillary Hemangiomas (von Hippel-Lindau)
 2. Encephalofacial Cavernous Hemangiomas (Sturge-Weber)
5. Relationship to Benign and Malignant Neoplasms
 - a. Most tumors in these syndromes are benign
 - b. Malignant transformation frequently occurs
6. Formes Frustes
 - a. Partial expression of the complete syndrome
 - b. Very common among the phakomatoses

B. Tuberous Sclerosis (Bourneville's syndrome)

1. Heredity
 - a. Usually autosomal dominant pattern with incomplete penetrance
 - b. Recessive suppresser gene
 - c. Abnormality in long arm of chromosome 9 in about one half of cases
 - d. Abnormality in short arm of chromosome 16 in about one half of cases

2. Cutaneous Features
 - a. Facial angiofibromas ("adenoma sebaceum")
 - b. Subungual and periungual angiofibromas
 - c. Shagreen patches
 - d. Vitiligo -- ash leaf sign
 - e. Pigmented macules (cafe au lait spots; more common in neurofibromatosis)

3. Central Nervous System Features
 - a. Subependymal astrocytic hamartomas
 - b. Cortical astrocytic hamartomas
 - c. These tumors may lead to mental deficiency and seizures

4. Other Systemic Involvement
 - a. Renal angiomyolipoma
 - b. Cardiac rhabdomyoma
 - c. Pleural cysts
 - d. Occasional similar hamartomas of liver, thyroid, pancreas, testes, etc.

5. Ocular Involvement
 - a. Astrocytic hamartoma of retina
 - b. Astrocytic hamartoma of optic disc ("giant drusen")
 - c. Juvenile pilocytic hamartoma of optic nerve (rare)

C. Neurofibromatosis (von Recklinghausen's syndrome)

1. Heredity
 - a. Usually autosomal dominant; incomplete penetrance.
 - b. Two types now recognized
 - a. Type 1 (peripheral neurofibromatosis)--Chromosome 17
 - b. Type 2 (central neurofibromatosis)--Chromosome 22
 - c. Some overlap between the two types

2. Cutaneous Features (Mainly in type 1)
 - a. Benign peripheral nerve sheath tumors
 - b. Pigmented macules ("cafe au lait spots")

(More than 5 cafe au lait spots greater than 1.5 cm. in diameter is diagnostic)
 - c. Axillary freckling.
 - d. Nevi

3. Central Nervous System Features (Mainly in type 2)

- a. Astrocytomas (gliomas)
 - b. Pituitary tumors
 - c. Spinal meningiomas
 - d. Acoustic neuromas
 - e. Syringomyelia
4. Other Systemic Involvement
- a. Malignant degeneration of peripheral nerve sheath tumors
 - b. Breast carcinoma
 - c. Cutaneous melanoma
 - d. Pheochromocytoma
 - e. Gastrointestinal and genitourinary malignancies
5. Ocular Involvement--widespread
- a. Eyelids
 - 1. Plexiform neurofibroma
 - 2. Fibroma molluscum
 - 3. Isolated punctate peripheral nerve sheath tumors
 - 4. Cafe au lait spots
 - 5. Nevi
 - b. Conjunctiva
 - 1. Plexiform neurofibroma
 - 2. Other
 - c. Cornea: Occasional prominent corneal nerves
(More common in multiple endocrine neoplasia syndromes)
 - d. Glaucoma
 - 1. Usually congenital--several mechanisms
 - 2. Can be secondary
 - e. Uveal tract
 - 1. Iris--Glial/melanocytic hamartomas-- (Lisch nodules)
 - 2. Diffuse uveal thickening (excess melanocytes and nerves)
 - 3. Nevi
 - 4. Melanomas
 - f. Retina
 - 1. Astrocytic hamartoma
 - a. Similar to that seen with tuberous sclerosis
 - b. However, less likely to be calcified when seen with neurofibromatosis
 - 2. Myelinated nerve fibers--lightly higher incidence than normal
 - 3. Atypical combined hamartoma of retina (seen in type 2)
 - g. Optic Nerve

1. Astrocytic hamartoma (juvenile pilocytic astrocytoma)
2. Meningioma

h. Orbit

1. Plexiform neurofibroma
2. Other orbital tumors (Schwannoma)
3. Orbital bone defects--pulsating proptosis

D. Retinocerebellar Hemangioblastomatosis (von Hippel-Lindau)

1. Hereditary

- a. Usually autosomal dominant pattern with incomplete penetrance
- b. Recessive suppresser gene
- c. Locus on short arm of chromosome 3

2. Cutaneous Features

- a. Rarely see cutaneous hemangioma of limbs or trunk

3. Central Nervous System Features

- a. Cerebellar hemangioblastoma
- b. Syringomyelia
- c. Others

5. Other Systemic Involvement (Frequently bilateral)

- a. Pheochromocytoma
- b. Renal cysts
- c. Hypernephroma
- d. Pancreatic cysts
- e. Epididymal cysts
- f. Others

6. Ocular Involvement--Retinal capillary hemangioma (discussed previously)

- a. Reddish retinal mass
- b. Peripheral tumor--dilated feeder and drainer retinal vessels
- c. Exudative form: retinal exudation and exudative detachment
- d. Yellow intraretinal exudation has predilection for fovea
- e. Vitreoretinal form: vitreal and retinal traction
- f. When tumor occurs at optic disc feeder vessels may be absent
- g. More aggressive when seen with von Hippel-Lindau syndrome

E. Encephalofacial Cavernous Hemangiomatosis (Sturge-Weber syndrome)

1. Heredity--No apparent hereditary pattern

2. Cutaneous Features

- a. Facial hemangioma
 1. "Nevus flammeus"

2. Often irregular-follows distribution of trigeminal nerve
 - b. Other cutaneous hemangiomas
(May overlap the Klippel-Trenaunay -Weber syndrome)
3. Central Nervous System Features
 - a. Leptomeningeal angiomatosis
 - b. Cerebral calcification
 - c. Mental retardation
 - d. Convulsions
4. Other Systemic Involvement: Rare

5. Ocular Involvement

- a. Eyelids
 1. May be affected by the cutaneous hemangioma
 2. Upper lid involvement--suspect congenital glaucoma
- b. Conjunctiva and episclera --Dilated tortuous vessels
- c. Glaucoma--May be congenital or juvenile
- d. Choroid--Diffuse choroidal hemangioma; “tomato catsup fundus”
- e. Retina--Peripheral arteriovenous communications
- f. Other

F. Retinal Cavernous Hemangiomatosis with Skin and CNS Vascular Malformations

1. Heredity
 - a. May be autosomal dominant with low penetrance
 - b. Probable recessive suppresser gene
2. Cutaneous Features--A variety of cutaneous angiomatous lesions can occur.
3. Central Nervous System Features--Similar vascular malformations in the brain.
4. Other Systemic Involvement--rare
5. Ocular Involvement--Retinal cavernous hemangioma (discussed previously)
 - a. May resemble a cluster of grapes in the retina
 - b. Classic appearance with fluorescein angiography

G. Racemose hemangiomatosis (Wyburn-Mason syndrome)

1. Heredity--No clear cut hereditary pattern
2. Cutaneous Features--rare
3. Central Nervous System Features
 - a. Racemose hemangioma in midbrain
 - b. Can also affect pterygoid fossa, mandible and maxilla
4. Other Systemic Involvement--Rare
5. Ocular Involvement
 - a. Racemose hemangioma of retina
 - b. Racemose hemangioma of orbit

H. Other possible phakomatoses

1. Ataxia Telangiectasia (Louis-Barr syndrome)
2. Oculodermal melanocytosis (Nevus of Ota)
3. Organoid nevus syndrome

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