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.
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 that 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

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