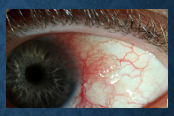
OCULAR SURFACE TUMORS

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COURSE OUTLINE

- Recognition and Differentiation
  - Do I Monitor
  - Do I Refer
- Conjunctival Lesions
  - Benign lesions
  - Pre-Malignant lesions
  - Malignant lesions





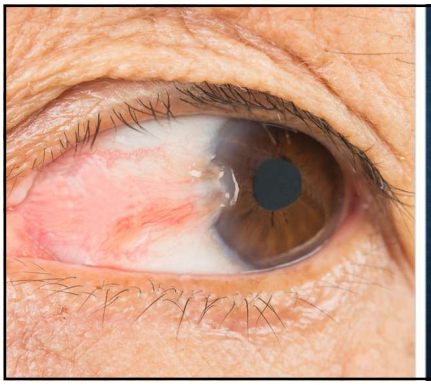
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LARGE STUDY OF 5002 PATIENTS FROM AN ONCOLOGY CENTER

- BENIGN- 52%
- PRE-MALIGNANT – 18%
- MALIGNANT – 30%
- THERE IS ROUGHLY A 50/50 CHANCE THE LESION WILL BE PRE-MALIGNANT OR MALIGNANT

Shields CL, Chien JL, Surakiatchanukul T, et al. Conjunctival tumors: review of clinical features, risks, biomarkers, and outcomes. The 2017 J. Donald M. Gass Lecture. Asia Pac J Ophthalmol. 2017;6:109-20.

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BENIGN LESIONS PTERYGIUM

Wing-shaped degenerative lesion that grows onto the cornea

Exposure to UV, dust, wind

Removal if lesion grows more than 3mm onto the cornes.

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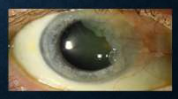
COMMON CONJUNCTIVAL TUMORS

- Ocular surface neoplasia (OSSN-14%)
- Lymphoid tumor (9%)
- Primary Acquired Melanosis (PAM (12%)
- Nevi (23%)
- Melanoma (12%)

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OCULAR SURFACE SQUAMOUS NEOPLASIA: UMBRELLA TERM

- Wide spectrum of dysplastic changes of the epithelium of the cornea, limbus, and conjunctiva
- Pre-invasive: CCIN (corneal epithelial dysplasia and conjunctival intraepithelial neoplasia)
- Carcinoma in situ
- Invasive: Squamous Cell Carcinoma (SCC) & mucoepidermoid carcinoma (more aggressive & recurrent)



Hanan R, Blut P, Foster C S. Conjunctival/corneal intraepithelial neoplasia. International Ophthalmology Clinics. 2009;49(1):63-70.

- CREDIT: HARRIETTE CANELLOS, OD

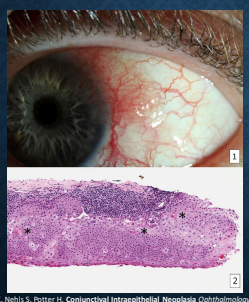
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OCULAR SURFACE SQUAMOUS NEOPLASIA (OSSN)

- Unilateral (usually)
- Vascularized
- Gelatinous mass located in the sun-exposed nasal and temporal limbus
- Range
  - mild epithelial dysplastic changes, e.g. conjunctival intraepithelial neoplasia
  - Can progress to severe invasive lesions-e.g. squamous cell carcinoma (SCC)
- Usually occurs in older Caucasian males with a history of chronic sun exposure
  - In the US, SCC is 5X more common in males
  - In Africa, conjunctival SCC is equally common in men and women and occurs at a younger age

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IT BEGINS- CONJUNCTIVAL INTRAEPITHELIAL NEOPLASIA



Surapaneni K, Nehls S, Potter H. **Conjunctival Intraepithelial Neoplasia** *Ophthalmology*, 1221039

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A: Leukoplakia and corneal involvement
B: Prominent vascularity and feeder vessels
C: OSSN in an HIV patient
D: Deep corneal invasion requiring resection and plaque radiotherapy

Credit: Shields CL, Lally SE, Shields J. A Guide to Conjunctival Tumors. Rev Optom May 2019

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SQUAMOUS CELL CARCINOMA



- Carcinoma in situ: entire epithelium is involved, but the basement membrane is intact & tumor cells have not invaded the stroma
- Squamous cell carcinoma (SCC) invades the basement membrane into the stroma
- SCC can be locally invasive and involve the sclera, uvea, eyelids, & orbit
- Rarely metastasize to distant sites (<1%). Regional lymph nodes- first site.

Nowell A, Romero-Kusabara IL, Frazão MAM. Update in ocular surface squamous neoplasia. Rev Assoc Med Bras. 2024 Jun 7;70 CREDIT: HARRIETTE CANELLOS, OD

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OSSN CHARACTERISTIC AS-OCT FINDINGS

- A **hyperreflective** & thickened epithelium
- Localized primarily **within the epithelium**
- Abrupt transition zone: distinct boundary separates the hyperreflective area from normal epithelium
- Epithelial thickness measuring above a cutoff (typically around **120** µm) suggests OSSN





- **Normal cornea-conj epithelium 50 to 70** µm
- Avg pterygium 80 µm to 101 µm

Huang JJ, Locatelli EVT, Huang JJ, De Arriguraga S, Rao P, Dubovy S, Karp CL, Galor A. It Is All About the Angle: A Clinical and O Surface Squamous Neoplasia and Corneal Pannus. Cornea. 2024 Oct 1;43(10):1249-1256.

- CREDIT: HARRIETTE CANELLOS, OD

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OSSN VS PTERYGIUM ON AS-OCT

OSSN

Hyperreflective & thickened **epithelium**

- Abrupt transition zone





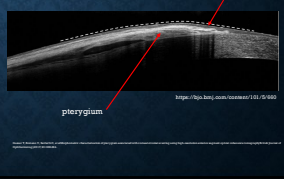
Venkateswaran N, Mercado C, Wali SC, Galor A, Wang J, Karp CL. High-resolution anterior segment optical coherence tomography of ocular surface lesions: A review and handbook. Expert Rev Ophthalmol. 2021;16(5):61-69.

- CREDIT: HARRIETTE CANELLOS, OD

Pterygium

Sub-epithelial lesion

- Epithelium is hyporeflective & remains at normal thickness



https://bjo.bmj.com/content/101/5/660

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PREDISPOSING FACTORS FOR OSSN

- Chronic sun exposure
- Cigarette smoke exposure
- Fair skin complexion
- HIV and Papillomavirus
  - HIV patients can have bilateral, invasive lesions
- Other immune diseases, e.g. autoimmune and immunosuppression from organ transplantation

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TREATMENT FOR OSSN: MONOTHERAPY OR ADJUVANT THERAPY AFTER SURGERY

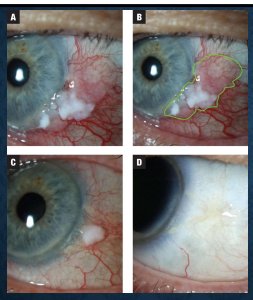
- Immunomodulatory (Interferon Alpha-2b or IFN-2b)
  - Enhances host immune detection
  - Topical drops or sub-conjunctival injection
  - Excellent side effect profile
    - Minimal follicular conjunctivitis
  - High resolution rates
    - 80-95% effective
  - Cons: Expensive, manufacturing shortages

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TREATMENT FOR OSSN

- Topical chemotherapy
  - 5 –Fluorouracil (5 FU)
    - 1% Topical therapy that disrupts DNA and RNA synthesis
    - Pulsed therapy: One week on, Three weeks off to allow epithelial recovery
    - Pain, punctate keratitis
    - Highly effective
- Mitomycin C (MMC) –Second line therapy
  - .02% to .04% topical therapy1 week cycle alternating with 1-3 week "vacation"
  - Severe pain, persistent epithelial defects
  - Risk of limbal cell deficiency (LSCD)

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Treatment was initiated at MMC 0.02% QID. Estimated extent of lesion highlighted. After the first three-week course, the lesion shows dramatic reduction in size. The patient was placed on a washout period of two weeks and instructed to anticipate a second course of MMC. Lesion showed complete resolution following washout.

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SURGICAL MANAGEMENT

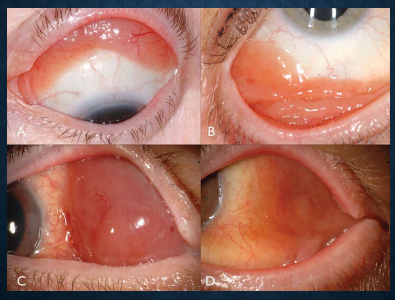
- Reserved for large, rapidly growing and visually threatening lesions
  - "No-touch excision"
    - Surgical resection with 3-4 mm clear conjunctivalmargins
  - Corneal epitheliectomy-alcohol is applied to affected corneal epithelium which is then scaped off
  - Cryotherapy (Freeze-Thaw)
    - Applied to remaining conjunctival margins to destroy remaining cells
  - Reconstruction of Defect Margins
    - Primary closure of margins
    - Amniotic Membrane Transplant (AMT) secured with fibrin glue

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CONJUNCTIVAL LYMPHOID TUMORS

- Arise from proliferation of lymphocytes
- Usually presents in older patients between 60-70 years of age
- Systemic involvement in about 30% of cases (bilateral)
- Predisposing factors include immune dysfunction and autoimmune conditions
- Clinical features
  - Pink
  - Salmon colored
  - Smooth surface
  - **Can resemble follicular or papillary conjunctivits

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Conjunctival lymphoma can be salmon-pink (A) or multilobulated forniceal (B). Medial forniceal conjunctival lymphoma before (C) and after (D) ritiximab.

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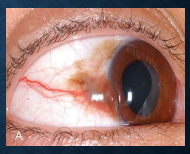
MANAGEMENT

- Complete surgical resection if there is no systemic involvement
- Radiation therapy or rituximab if the tumor is not resectable

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CONJUNCTIVAL MELANOCYTIC TUMORS

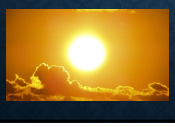
- Are COMMON -more than 50% of conjunctival tumors
- Includes
  - **Conjunctival nevus (45%)**
  - **Primary acquired melanosis (PAM) (25%)**
  - Secondary acquired melanosis
  - Melanoma
  - Metastases to pre-auricular, submandibular and lymph nodes



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INCIDENCE

- In the US:
  - Doubled between 1973 and 1999 from 0.27 per million to 0.54 per million cases
  - Increased 295% in white men, especially in men over 60 years of age
  - Researchers speculate this may be due to increases in **UV exposure**

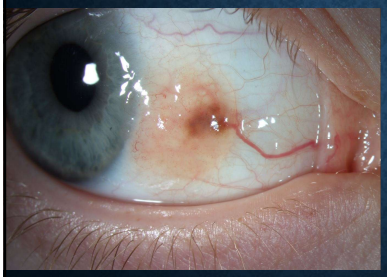


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CLINICAL CHARACTERISTICS

- Pigmented or Non-pigmented
- Can arise from Primary Acquired Melanosis (PAM), Conjunctival nevi or *De Novo*
- Can be found on the limbal, bulbar, fornix or palpebral conjunctiva
- Often accompanied by LARGE Feeder vessels surrounded by flat PAM
- Watch thickness! Anything over 2mm in thickness and invasion into the orbit are at risk for metastasis to lymph nodes (25%)

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BENIGN LESIONS CONJUNCTIVAL NEVUS

Pigmented lesion on the conjunctiva

Feeder vessel may be present

Monitor for growth

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Patient I followed for several years

2018



25

2025



26

2018



2025

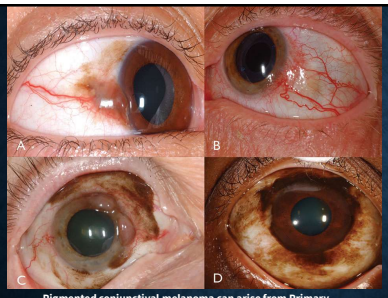


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ANTERION OCT



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Pigmented conjunctival melanoma can arise from Primary Acquired Melanosis (PAM)(A). Non-pigmented conjunctival melanoma may have intense vascularity (B). PAM could also cause mixed pigmented/non-pigmented conjunctival melanoma (C). PAM caused limbal melanoma in this African-American patient (D).

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IS IT CONJUNCTIVAL NEVUS, PAM OR A CONJUNCTIVAL MELANOMA?

- In children, what features differentiate conjunctival nevus from melanoma?
- **CATCH** Melanoma
  - ***C***hildren ***A***ge Older
  - ***T***hickness/base greater
  - ***C***yst lacking
  - ***H***emorrhage
- Differentating PAM from Melanoma
  - PAM is flat Melanoma has thickness





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PREDISPOSING FACTORS

- Long-standing conjunctival nevus or PAM (Primary Acquired Melanosis)
  - 74% of conjunctival melanoma start out as PAM
  - It is estimated 1 in 300 nevi develop into melanoma
  - The larger the area of PAM the greater the risk of transformation inton melanoma
- THEREFORE, PAM must be identified and treated to prevent development into melanoma
  - Surgical excision
  - Cryotherapy
  - Superficial keratectomy if there is corneal involvement

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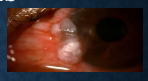
ASSESSMENT OF CONJUNCTIVAL MELANOMA FOR TREATMENT

- Identifying tissue biomarkers for systemic treatment or prevention of metastasis
  - BRAF mutations
  - TERT Promoter mutations
  - PTEN mutations
- Targeted therapies
  - Vemurafenib for BRAF-mutated malignancies

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SUMMARY: HOW TO EVALUATE THESE LESIONS

- Measurement & photo-documentation



- Non-invasive Anterior Segment Imaging
  - Ant Seg OCT: detailed, assessing depth, margins, and characteristics of lesion
- Biopsy: gold standard



nature.com

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SUMMARY

- Conjunctival Tumors
  - Benign (52%)
  - Pre-Malignant (18%)
  - Malignant (30%)
    - Melanoma(12%)
    - Squamous Cell Carcinoma (SCC-9%)
    - Lymphoma (7%)
- Most Common Tumors
  - Ocular surface neoplasia (OSSN-14%)
  - Lymphoid tumor (9%)
  - Primary Acquired Melanosis (PAM (12%)
  - Nevi (23%)
  - Melanoma (12%)

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THANK YOU

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