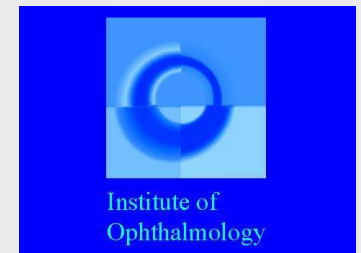


# ***Conjunctival Melanocytic Lesions: pathological aspects***

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University College London**



# ***Declaration of Interests***

- » Senior visiting scientist, IARC, Lyon
- » Former Head of the WHO Classification of Tumours Programme and the Section of Evidence Synthesis and Classification at the International Agency for Research on Cancer, part of the World Health Organisation, Lyon, France.
- » Director, CanTech Ltd, Northamptonshire, UK
- » All opinions expressed are personal, and not those of any of the organisations above.

# ***Introduction***

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- Pigmented lesions of the conjunctiva may not be melanocytic.
- Most adult melanocytic lesions of the conjunctiva cause concern and are often removed for pathological examination.
- They should be placed on card, fixed in formalin, and sent with a full clinical history.
- The classification has been revised in the new 5th edition of the WHO Classification of Tumours of the Eye and Orbit, currently online only.

# ***Classification: Tumours of the conjunctiva and caruncle***

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## **Melanocytic conjunctival tumours**

### Benign melanocytic conjunctival tumours

- Benign epithelial melanosis of the conjunctiva

- Junctional, compound and subepithelial conjunctival naevi

- Inflamed juvenile conjunctival naevus

- Blue naevus of the conjunctiva

- WNT-activated deep penetrating/plexiform melanocytoma (naevus)

- Combined naevus

### Premalignant and malignant melanocytic conjunctival tumours

- Conjunctival melanocytic intraepithelial lesions

- Conjunctival melanoma

From: <https://tumourclassification.iarc.who.int/chapters/65>

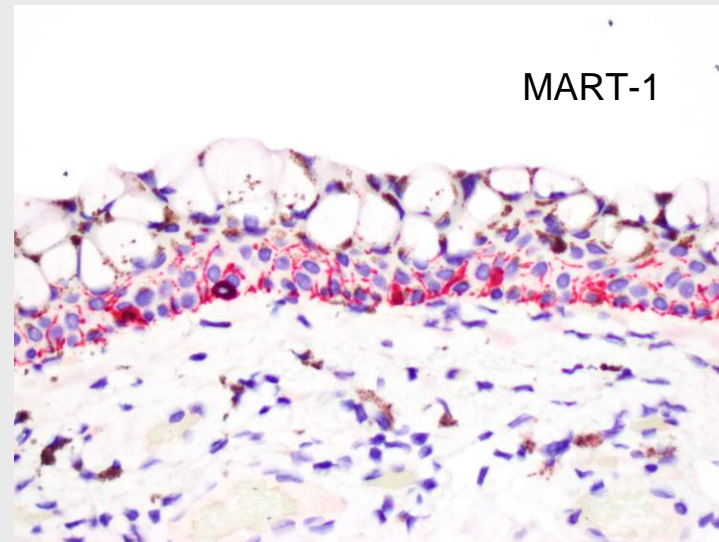
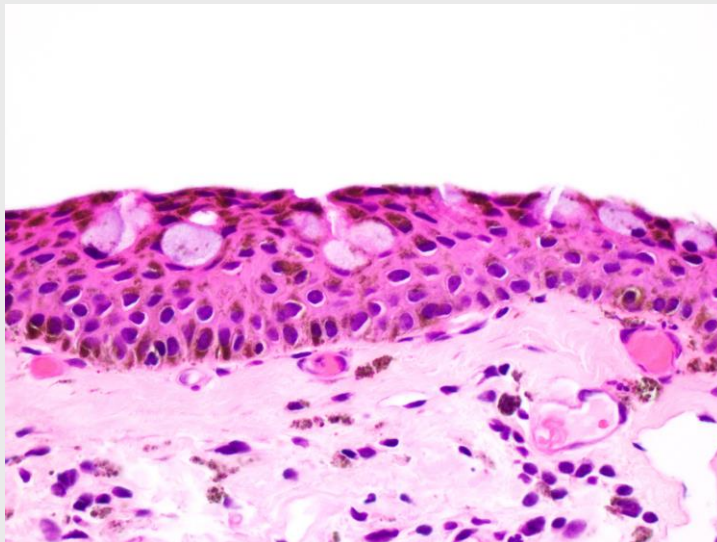
# ***Benign epithelial melanosis of the conjunctiva***

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...characterized by increased production of melanin without significant proliferation of conjunctival melanocytes, which remain normal in size and location, and transfer melanin into adjacent keratinocytes.

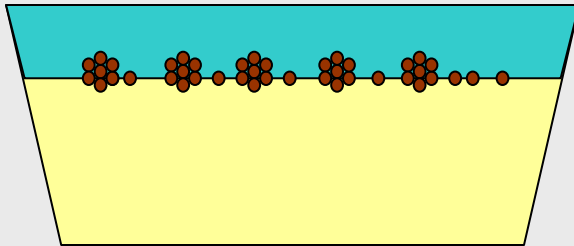
## *Related terminology:*

- Acceptable: constitutional melanosis; complexion-related melanosis
- Not recommended: non-proliferative melanocytic pigmentary patch; ephelis; freckle

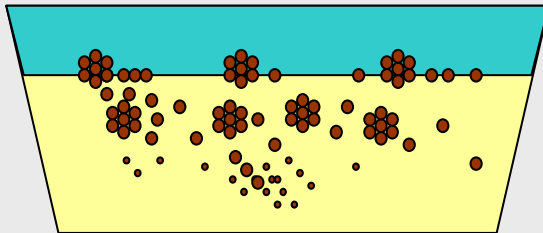


# *Conjunctival Melanonaevi*

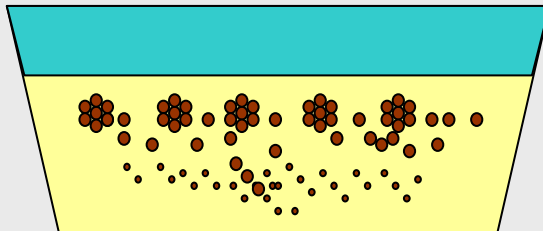
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Junctional



Compound

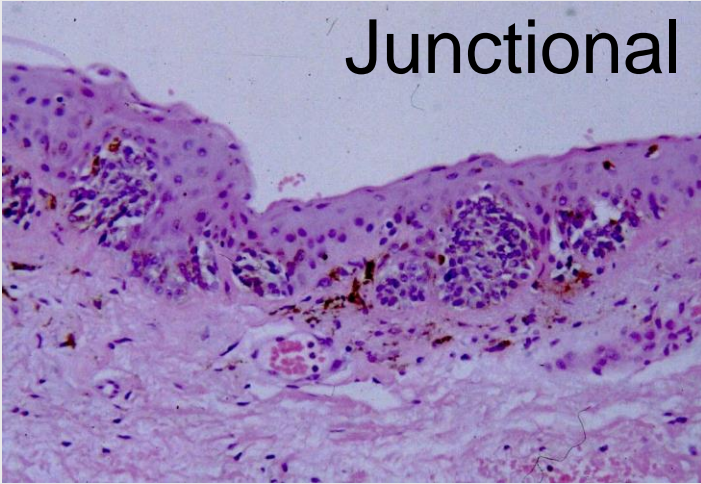


Sub-epithelial  
(stromal)

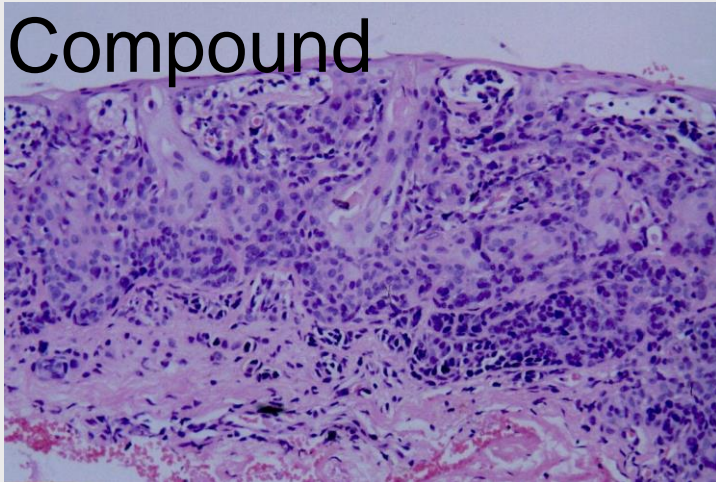
# ***Conjunctival Melanonaevi***

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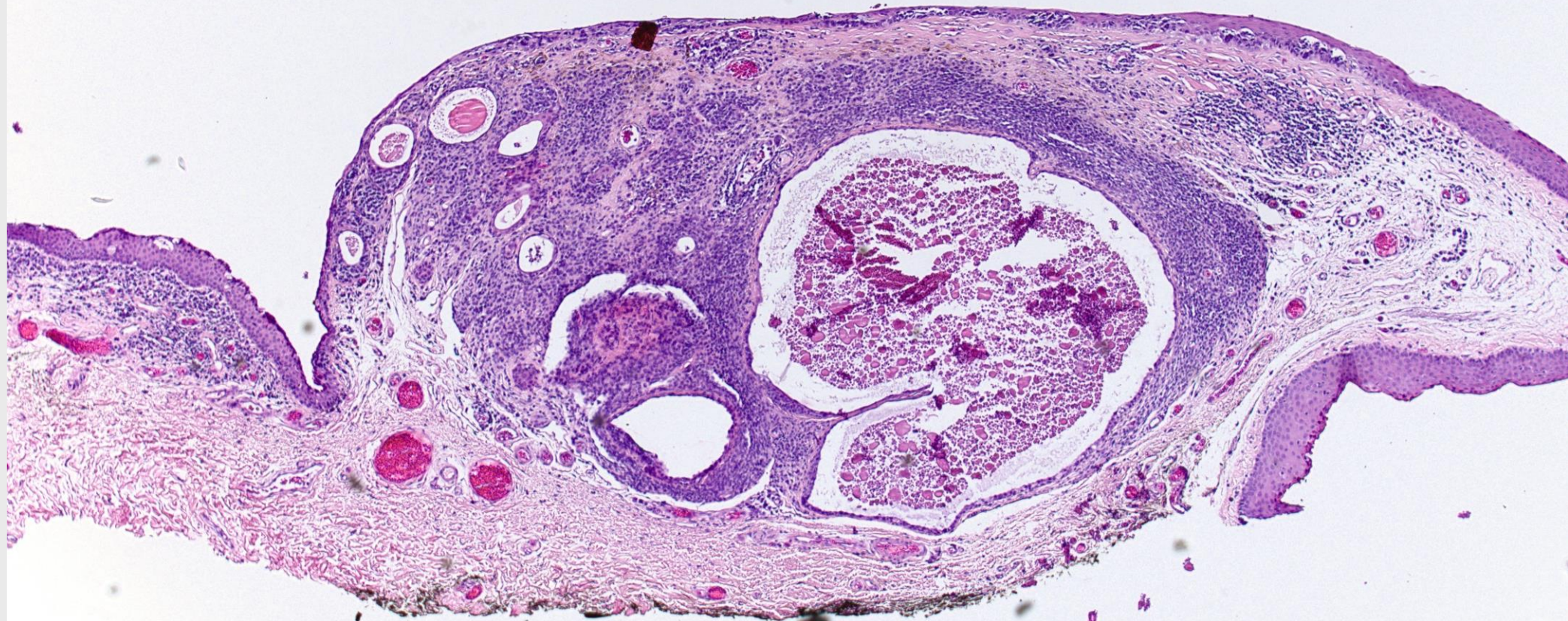
Junctional



Compound



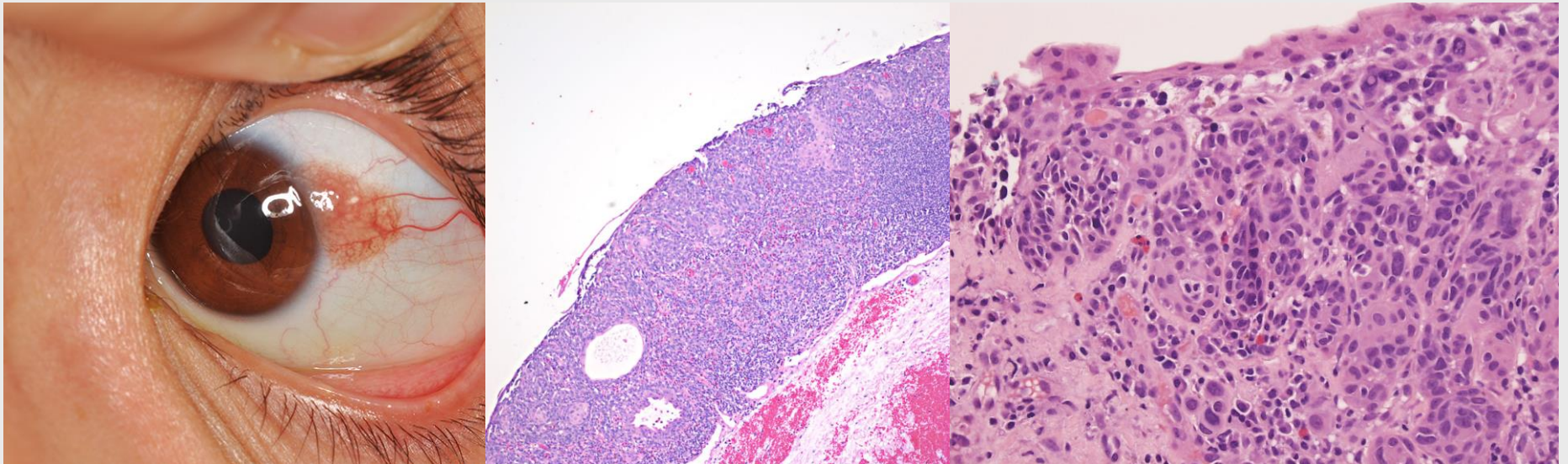
Sub-epithelial  
(stromal)



# ***Inflamed juvenile conjunctival naevus***

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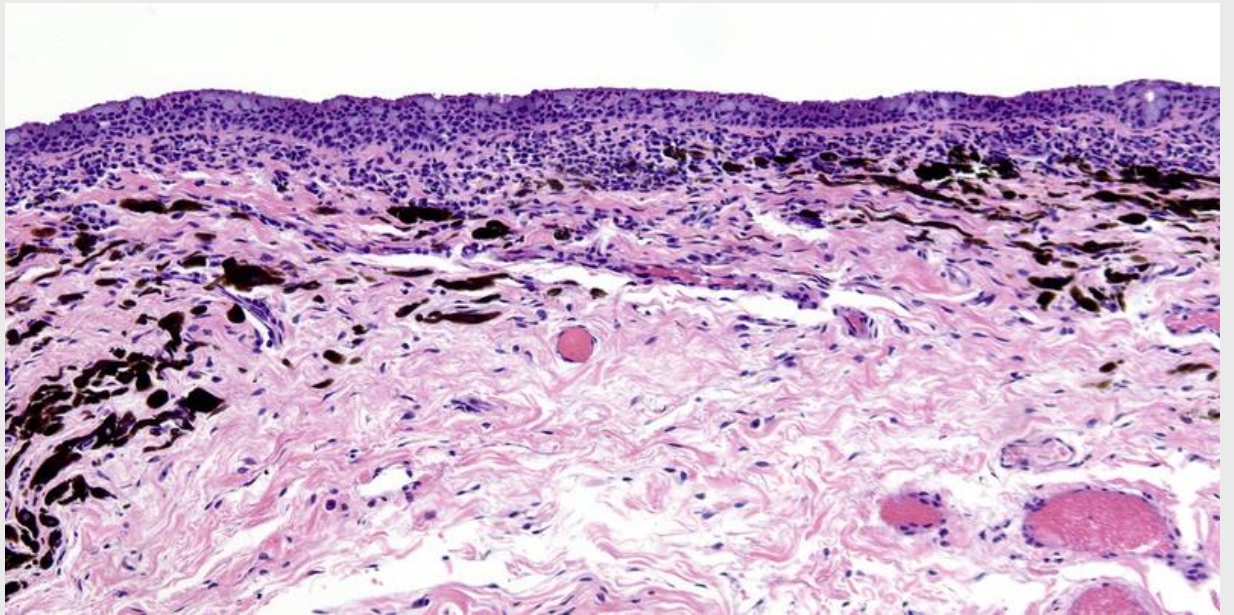
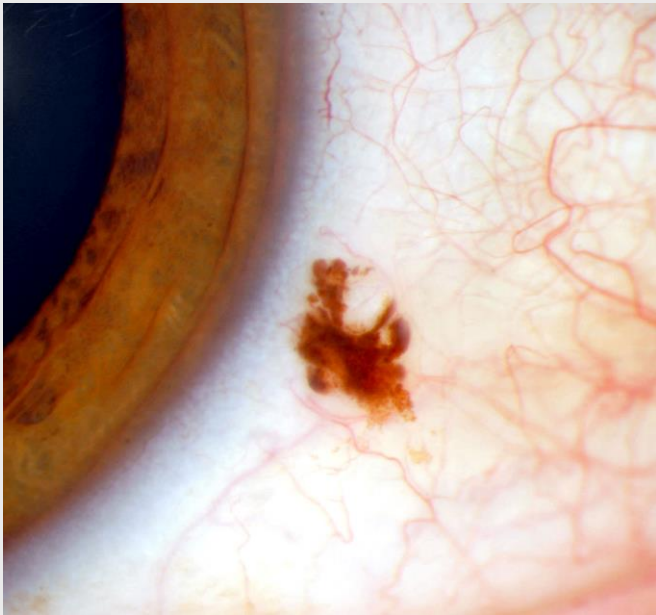
- A compound naevus of childhood and adolescence, with shows inflammation.
- Debatable whether this is a true tumour type, or a subtype.



# ***Blue naevus of the conjunctiva***

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Blue naevus is a stromal melanocytic tumour composed of dendritic, spindle, and / or ovoid cells associated with melanin pigment and stromal sclerosis; it has a blue tinctorial appearance clinically.

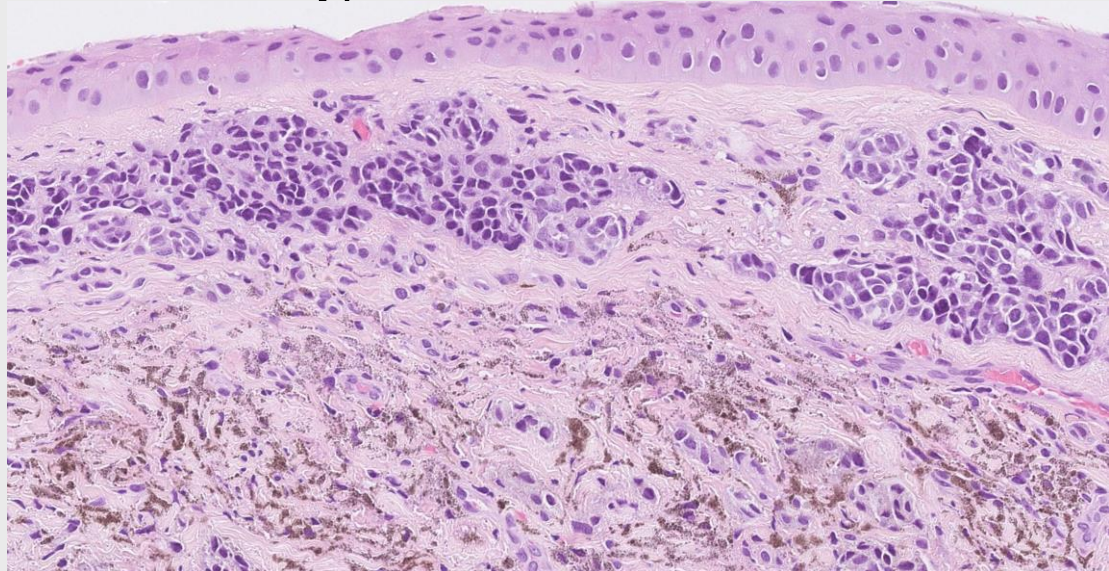




# ***WNT-activated deep penetrating/plexiform melanocytoma (naevus)***

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- A melanocytic tumour composed of relatively large, finely pigmented ovoid or epithelioid melanocytes and genetically characterised by activation of the MAP kinase (*BRAF*) and WNT/beta catenin (usually *CTNNB1*) pathways.
- On the conjunctiva, almost all such lesions present as combined naevi, but not all combined naevi are this tumour type.



# Conjunctival melanocytic intraepithelial lesions

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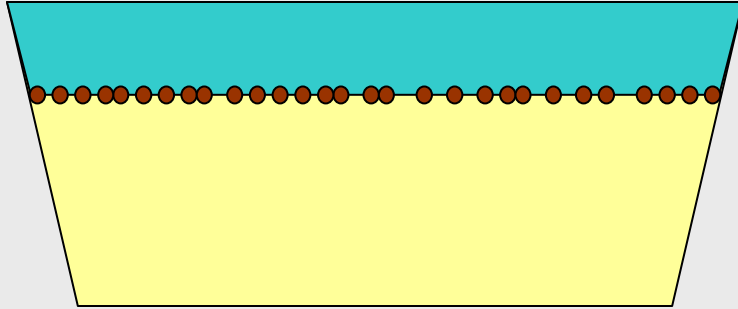
- C-MIL represent a spectrum of morphological changes ranging from melanocytic hyperplasia through degrees of melanocytic atypia to melanoma *in situ*.
- ***Related terminology***
- Acceptable: Conjunctival melanocytic intraepithelial neoplasia (C-MIN); Primary acquired melanosis (PAM); Melanoma in situ
- Not recommended: Precancerous melanosis; premalignant melanosis; intraepithelial melanocytic proliferation with atypia

# ***Conjunctival melanocytic intraepithelial lesions***

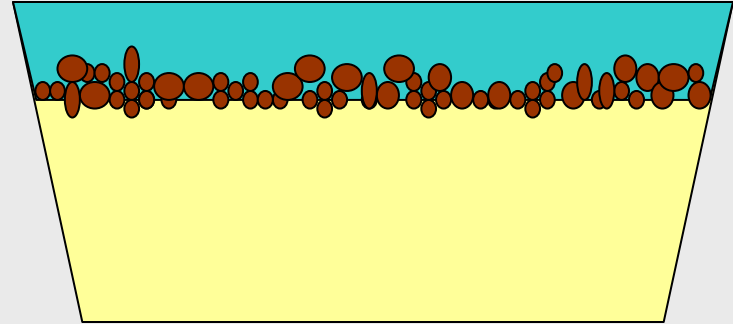
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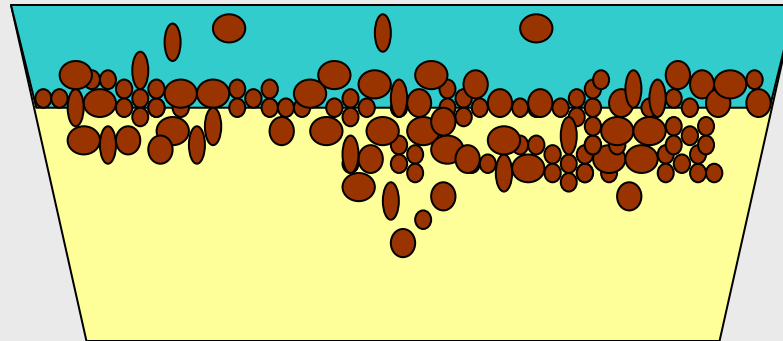
## *Conjunctival melanocytic intraepithelial lesions*



Without Atypia

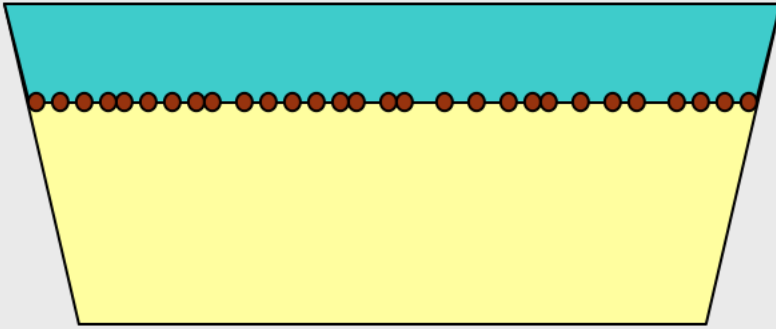


With Atypia

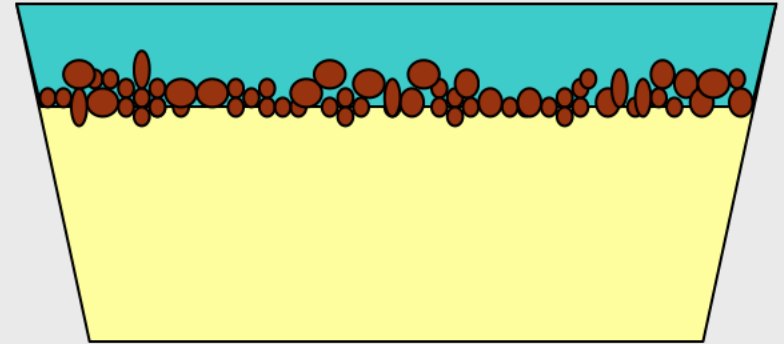


Melanoma

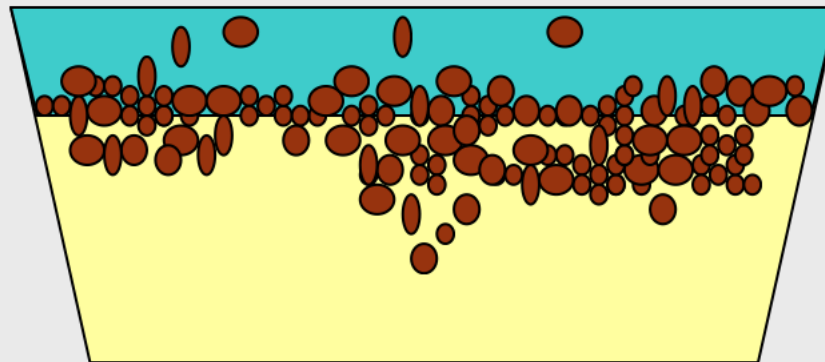
# *Conjunctival melanocytic intraepithelial lesions*



Without Atypia



With Atypia

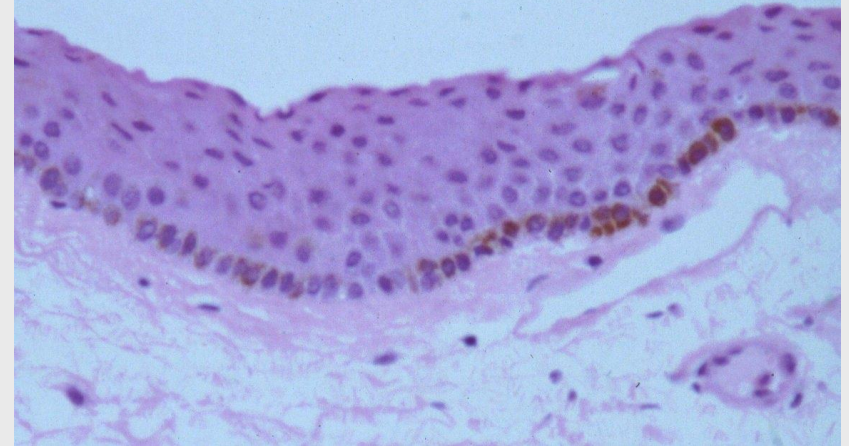


Melanoma

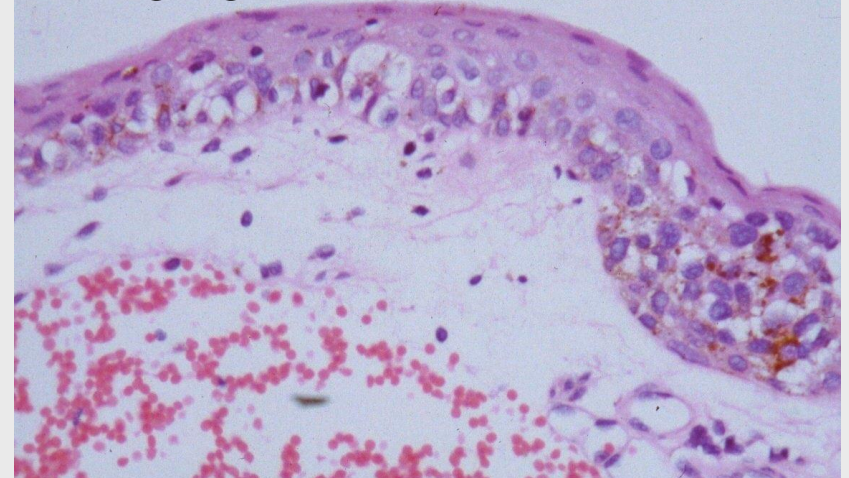
# Conjunctival melanocytic intraepithelial lesions

WHO	Acceptable alternative terminology	Increased cellularity
Not applicable	Benign melanosis c-MIN (grades 0-1) PAM without atypia	No/Minimal
Low-grade C-MIL	PAM with mild atypia c-MIN (grades 2-4)	Yes
High-grade C-MIL	PAM with moderate to severe atypia c-MIN (grade 5-10)	Yes
	Melanoma in situ	Yes

Low grade

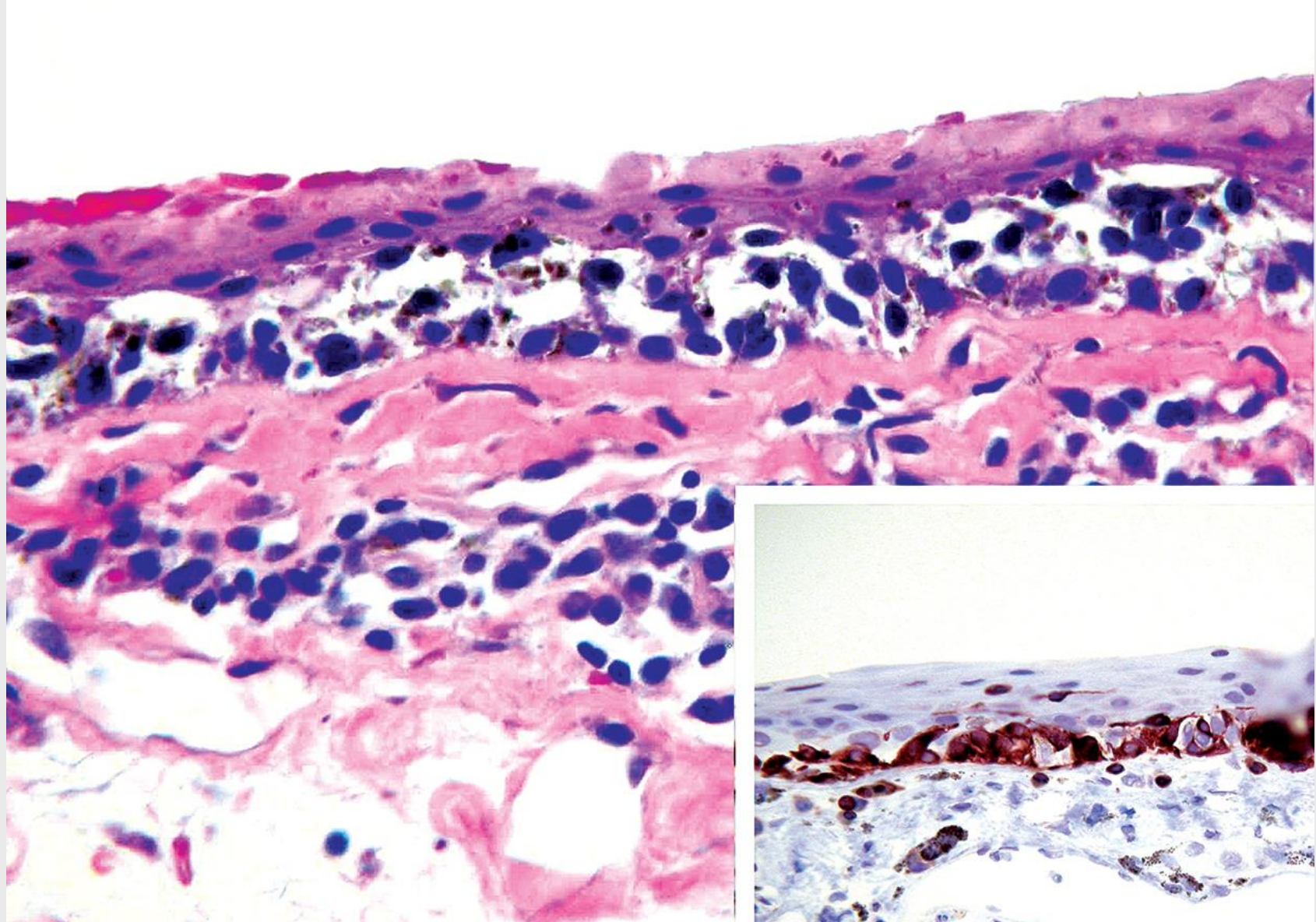


High grade



# ***Conjunctival melanocytic intraepithelial lesions***

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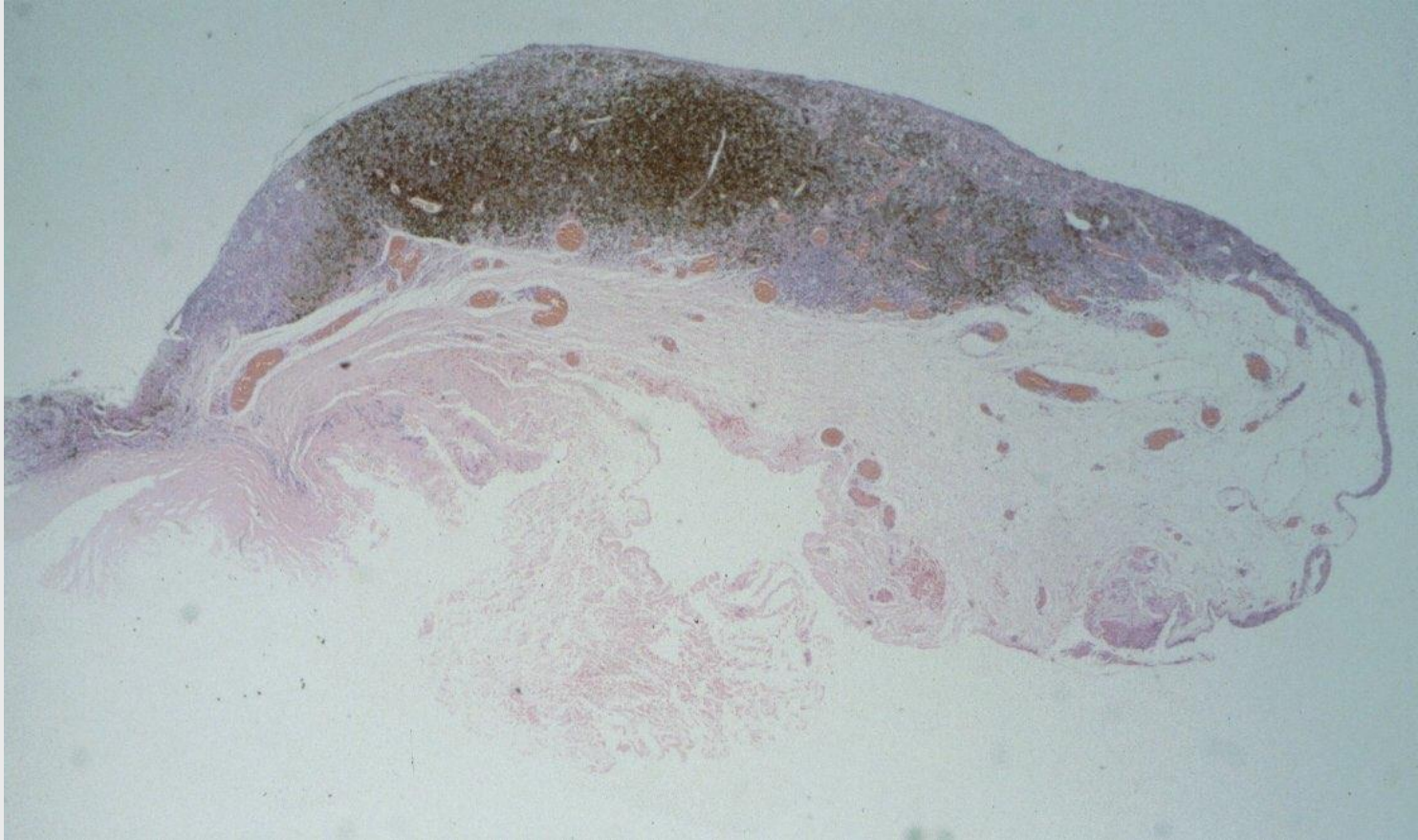
## *When C-MIL turns nasty...*

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- Diffuse infiltration and overcrowding of basal and wing cell layers of epithelium.
- Spindle/epithelioid cells with nuclear pleomorphism and irregular chromatin pattern (cellular atypia).
- Evidence of invasion is not melanosis - it is melanoma.

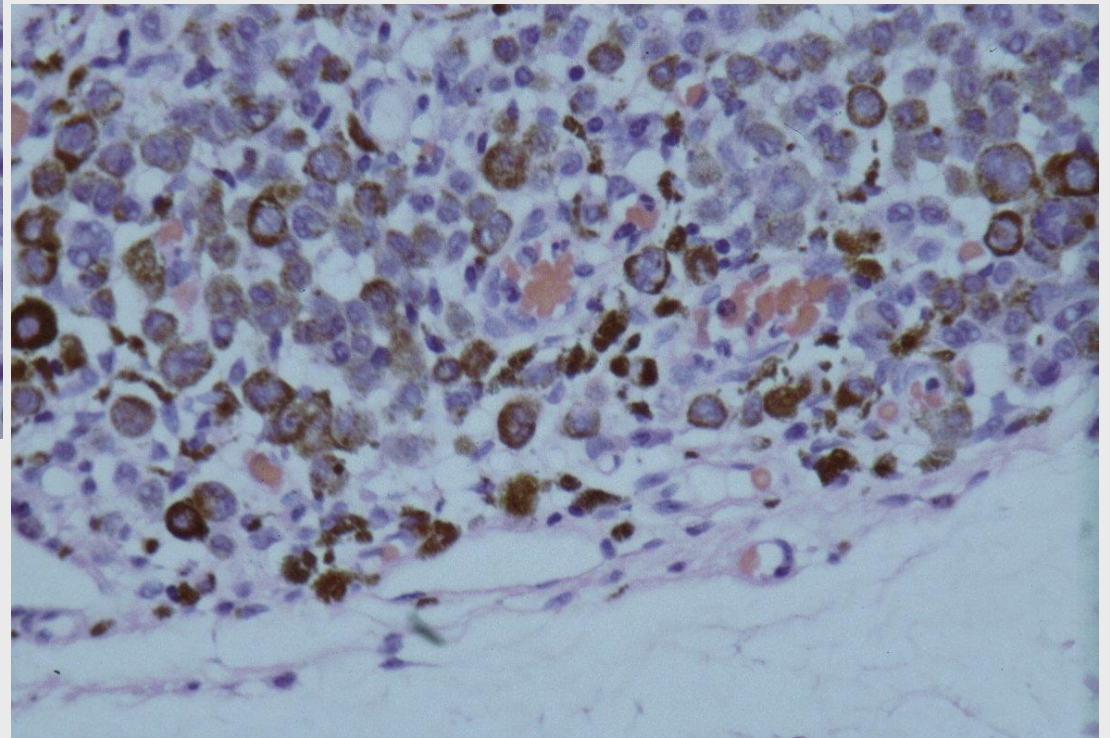
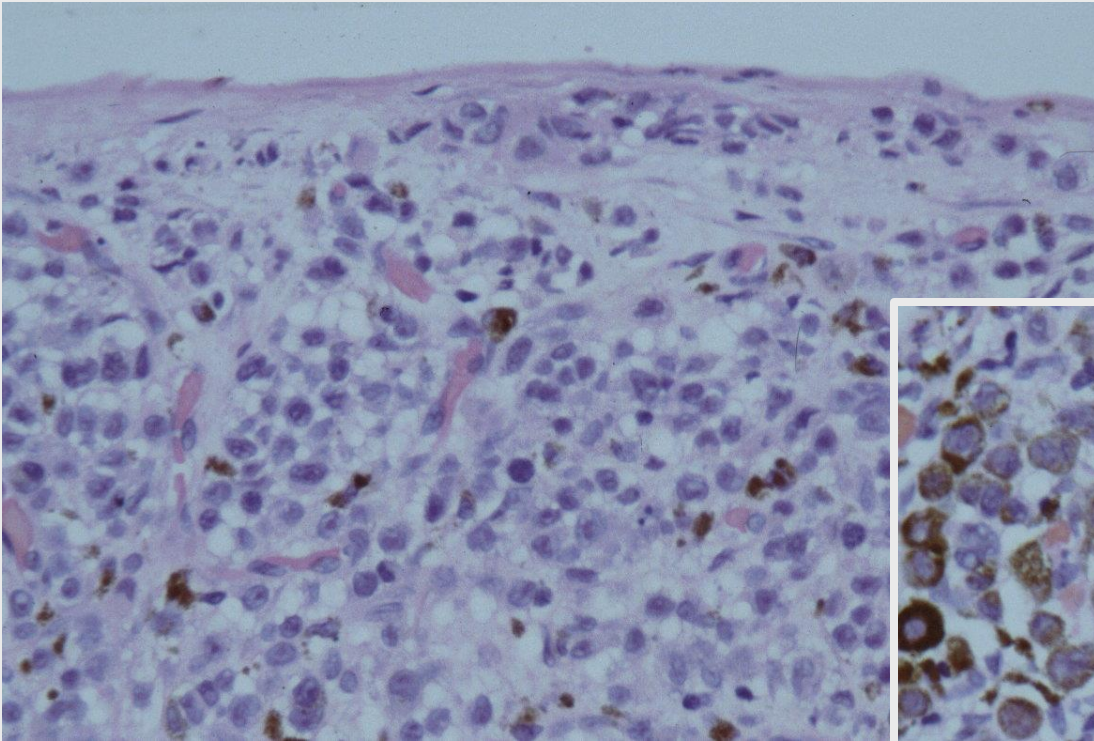
# ***Conjunctival Melanoma***

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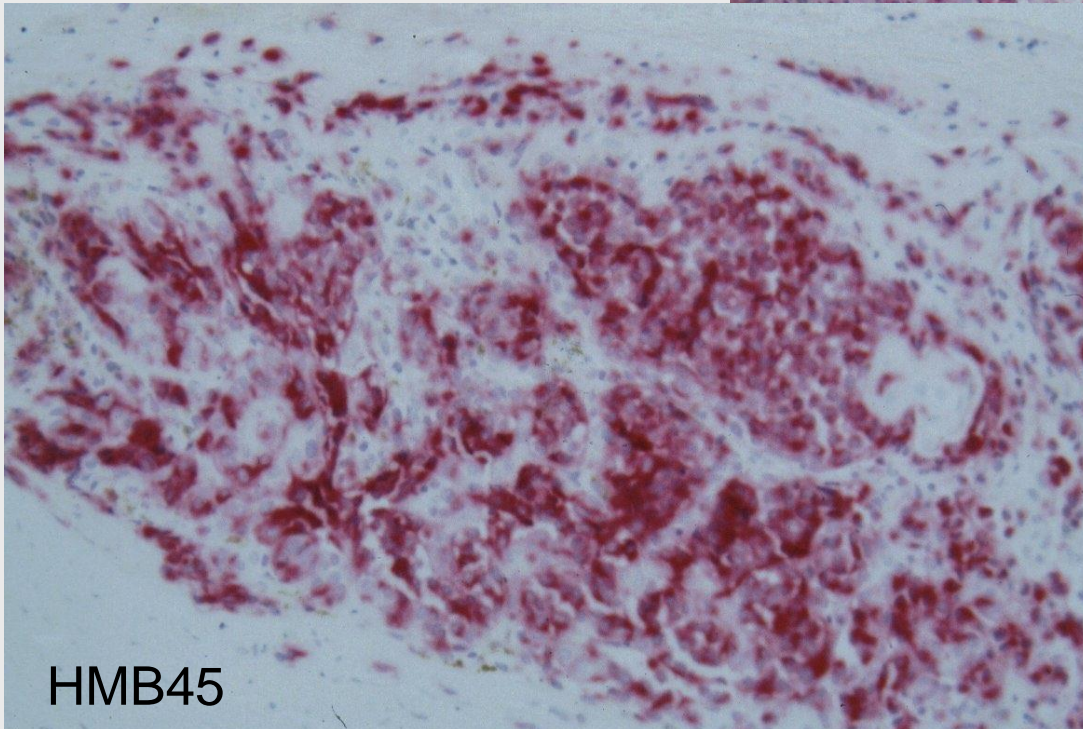
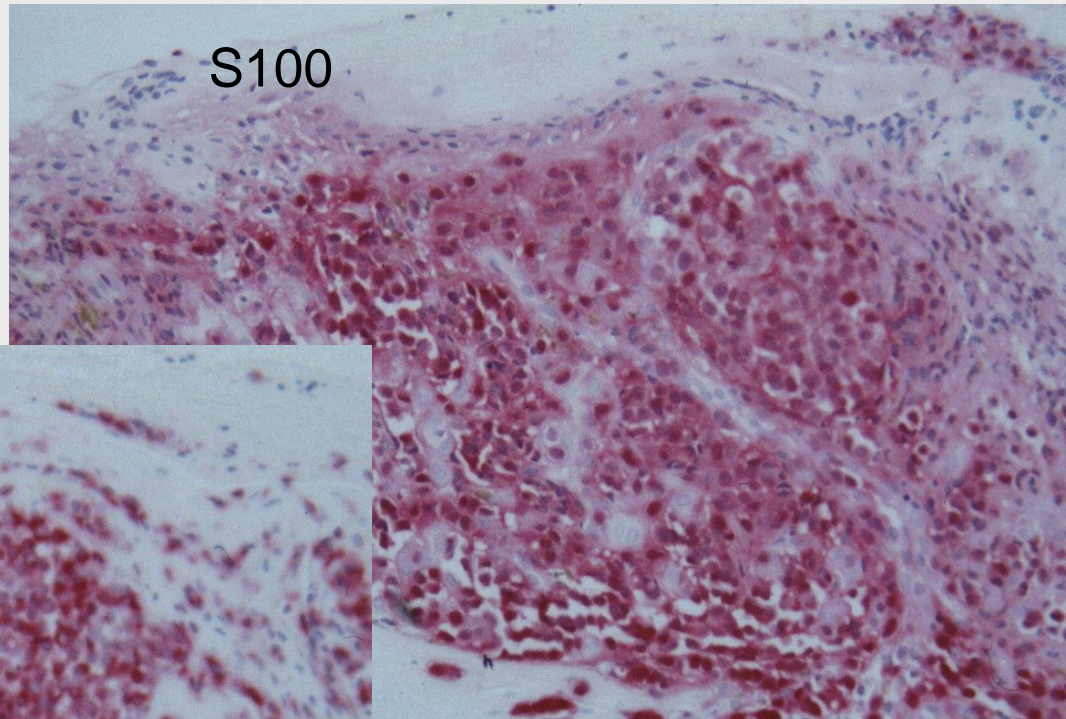
# ***Conjunctival Melanoma***

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# ***Conjunctival Melanoma***

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# Practical Notes

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- If not mounted on card (suture container) conjunctiva will roll up.
- Longitudinal sections ensure cross-cutting and should be avoided - transverse sections are much more likely to be useful.
- Multiple levels may be needed - but keep sections at each level for immunocytochemistry (using Vector Red).
- Use a dataset - e.g. <https://www.rcpath.org/static/d59407d8-310c-46ec-b1c6242f948b74ad/g054datasetconjunctivalmelanomafinaloct07.pdf>

# RCPATH dataset

## APPENDIX C REPORTING PROFORMA FOR CONJUNCTIVAL MELANOMA AND MELANOSIS

Surname	Forenames	Date of Birth
Hospital	Hospital no	NHS no
Date of receipt	Date of reporting	Report no
Pathologist	Surgeon	Sex

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### MACROSCOPIC DESCRIPTION

Specimen type:      Incisional biopsy ☐      Excisional biopsy ☐      Exenteration ☐

Laterality:      Right ☐      Left ☐

Dimension of specimen(s).....

Location of tumour :    Bulbar ☐    Palpebral ☐    Fornix ☐    Caruncle ☐  
                                 Plica semilunaris ☐    Limbus ☐    Cornea ☐    Unspecified ☐

Tumour characteristics:      Unifocal tumour      ☐      Multifocal tumour      ☐

Size of tumour(s).....mm

Non-conjunctival structures involved(specify).....

---

## RCPATH dataset

### MICROSCOPIC DESCRIPTION

Melanosis without atypia: Present ☐ Absent ☐

Melanosis with atypia: Present ☐ Absent ☐

In-situ melanoma	Present <input type="checkbox"/>	Absent <input type="checkbox"/>
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Invasive melanoma: Present ☐ Absent ☐

Maximum invasive melanoma thickness.....mm

Epithelioid cells present in invasive melanoma:                      yes ☐                      no ☐

Lymphatic/blood vessel invasion:                      yes ☐                      no ☐

Growth phase.....

Ulceration	Yes <input type="checkbox"/>	No <input type="checkbox"/>
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Mitotic rate (for invasive melanoma)..... mm<sup>2</sup>Perineural invasion Yes ☐ No ☐

Tumour regression (for invasive melanoma) Yes ☐ No ☐

# RCPATH dataset

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Microsatellites (for invasive melanoma)                      yes ☐                      no ☐

Tumour infiltrating lymphocytes (for invasive melanoma)    yes ☐                      no ☐

Co-existent naevus (for invasive melanoma)                      yes ☐                      no ☐

Anatomical structures involved by invasive melanoma (specify): .....

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## EXCISION MARGINS

Distance to nearest **peripheral** margin by invasive melanoma is .....mm  
(clear / involved)

Distance to nearest **deep** margin by invasive melanoma is.....mm  
(clear / involved).

Distance to nearest **peripheral** margin by in-situ melanoma / atypical melanosis.....mm  
(clear / involved).

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## COMMENTS

Pathological staging (excision specimens only)      pT      pN      pM      (TNM 6<sup>th</sup> Edition)

SNOMED codes T..... / M.....

# *Prognosis of Conj Melanoma*

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- Depth of invasion ( $> 1.5$  mm)
  - Location (Fornix poor, bulbar good)
  - Lymphatic invasion
  - Presence of PAM + Atypia
- 
- Cytology
  - Vascularity

## Conclusions

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- Conjunctival melanocytic lesions show similarities and important differences in comparison with skin lesions.
- Melanoma may be accompanied by preceding melanosis.
- C-MIL may be extensive and non-pigmented - map biopsy may aid management.
- HMB45 and Ki67 staining can be helpful.
- This is not easy pathology and there is potential for diagnostic errors!