

Nail Unit Specimen Processing and the Diagnosis of Common and Important Nail Lesions

Medical Director, CTA Lab

And

Clinical (Affiliate) Professor of Dermatology, Pathology
and Biomedical Engineering

Oregon Health and Sciences University



Objectives

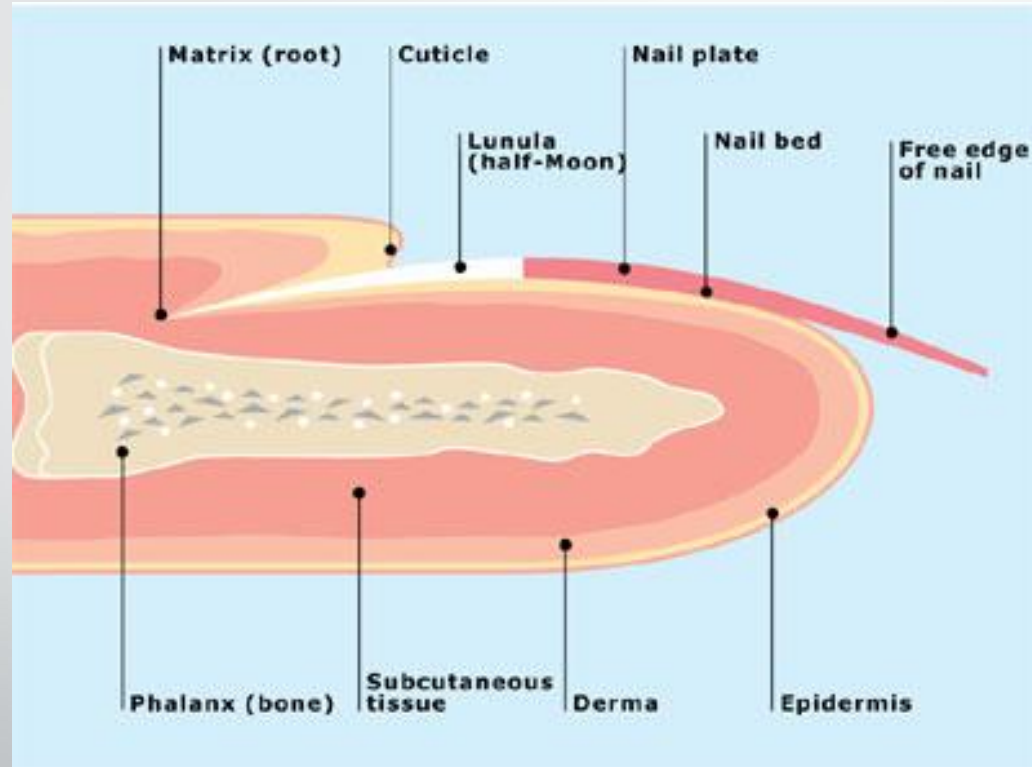
Nail

- Tissue submission/processing

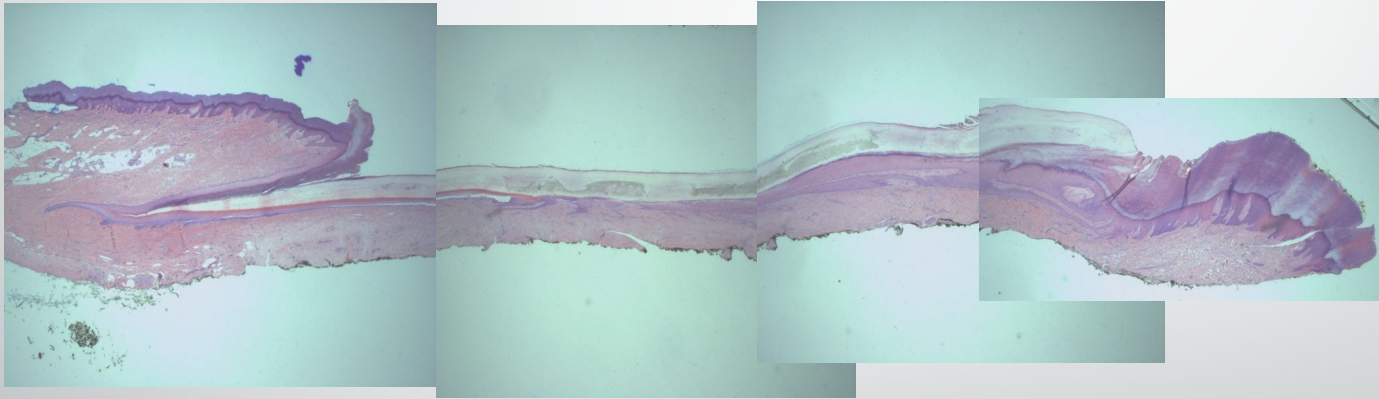
- Fungal identification including mold

- Review of the most common nail lesions

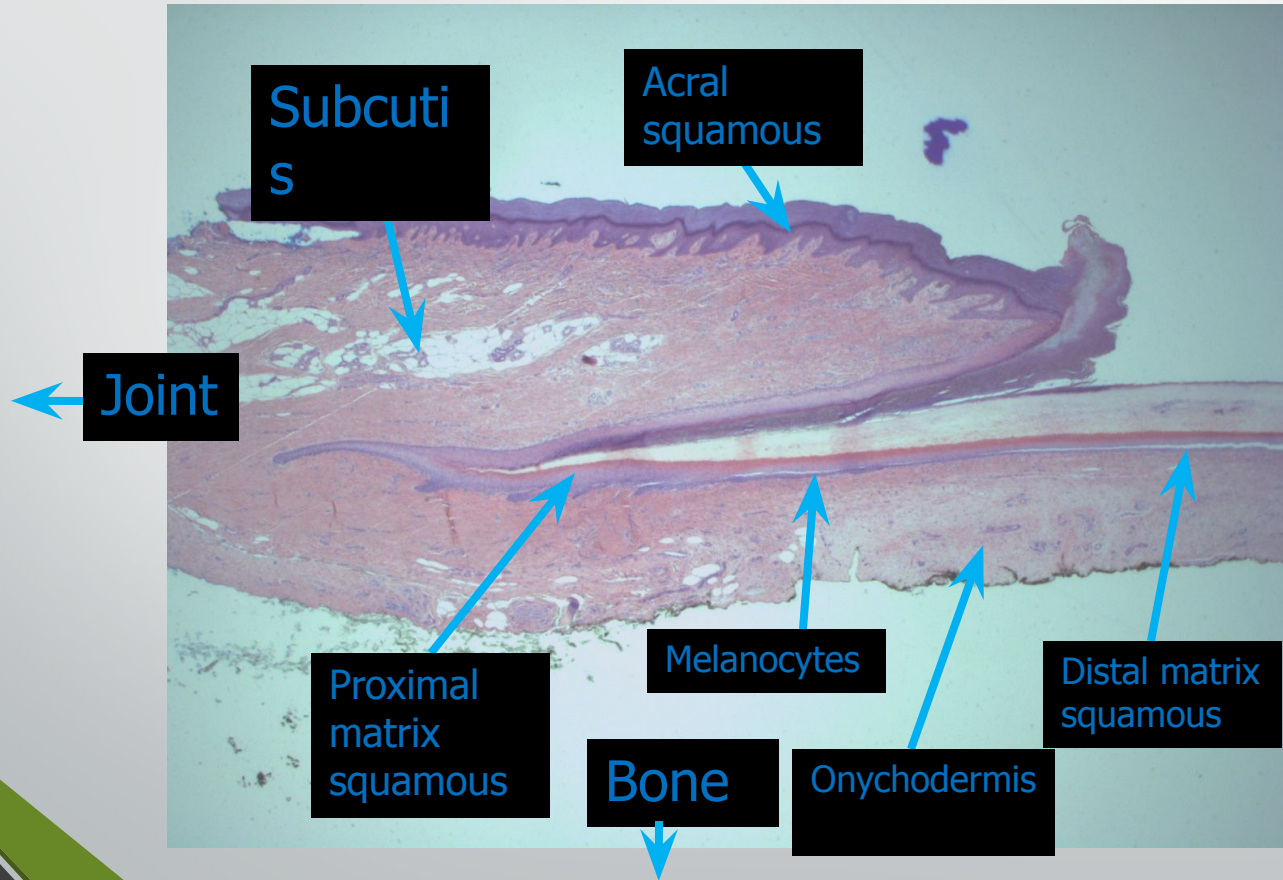
Nail Unit Anatomy and Histology




Nail Unit Anatomy and Histology



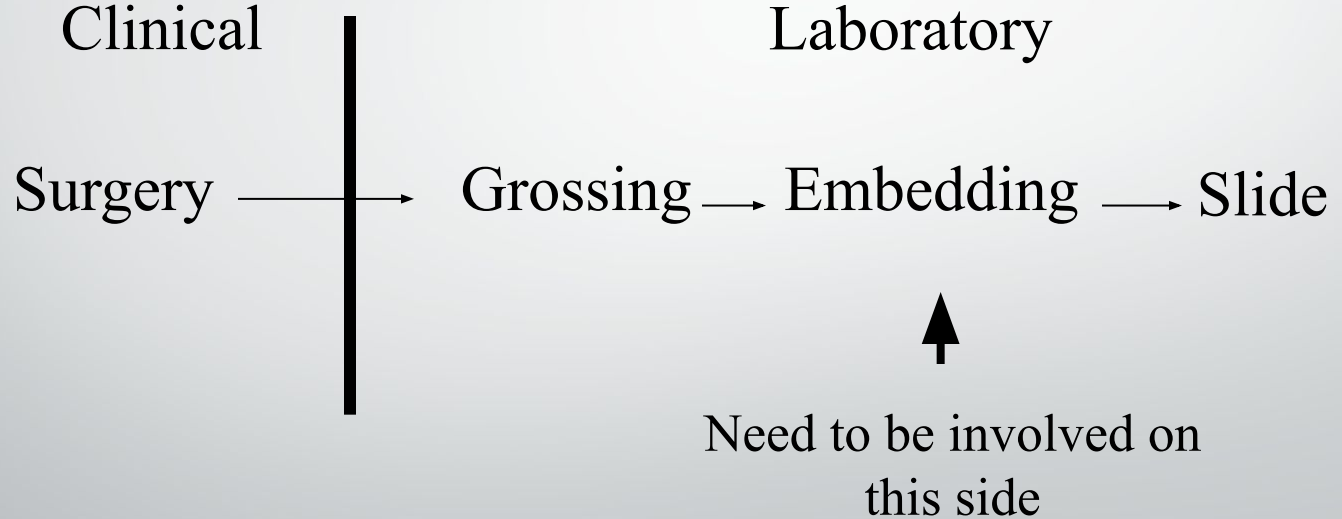
Nail Unit Anatomy and Histology

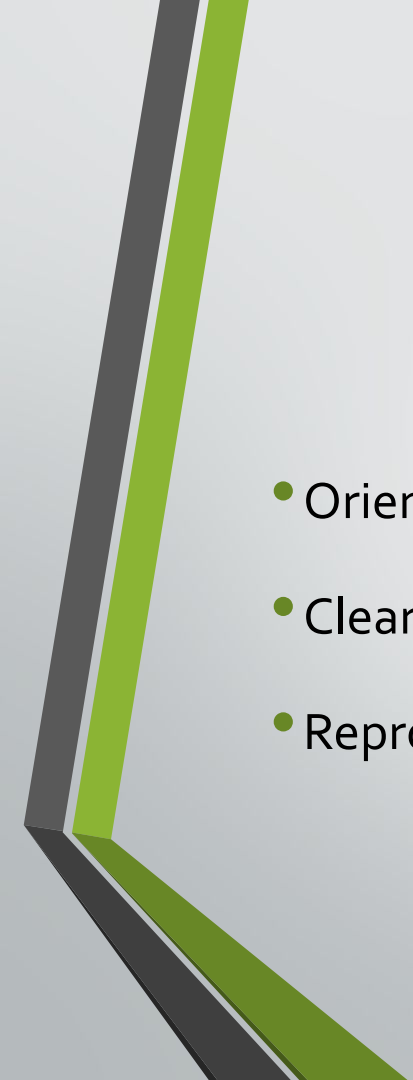




What can the nail surgeon do to submit a
bed/matrix specimen for appropriate
interpretation?

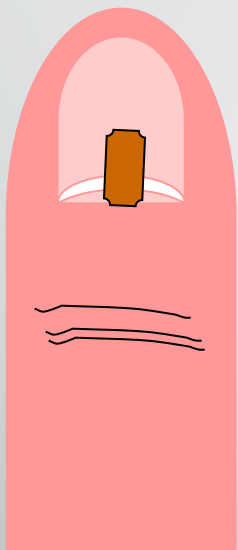
Need to be involved in lab prep



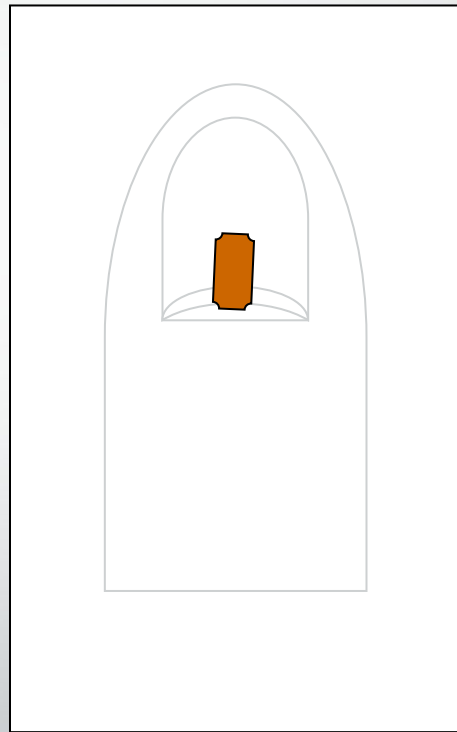
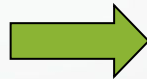
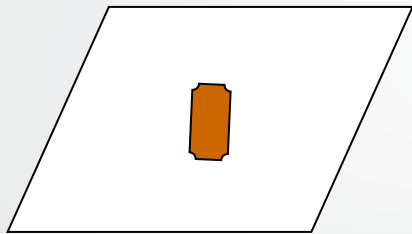


Need concise and clear guidelines for specimen submission

- Orientation of tissue
- Clear information to histotechnicians
- Reproducible among different laboratories



+



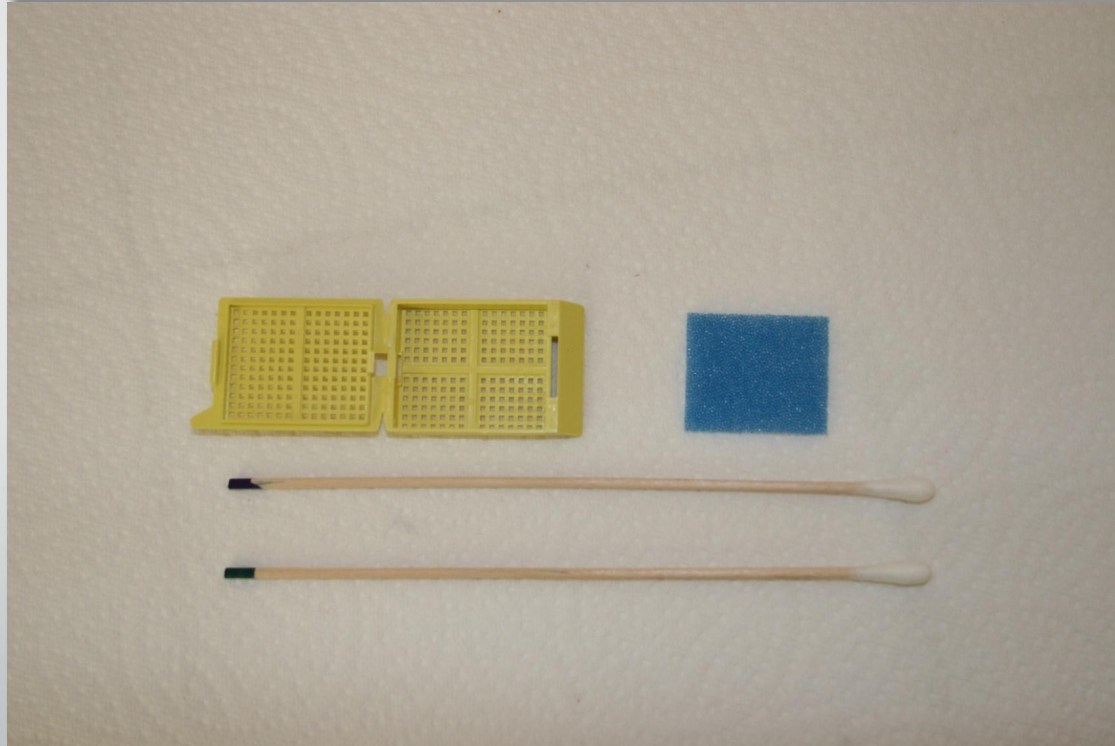


Nail Template



Print template at www.cta-lab.com

Histology Materials



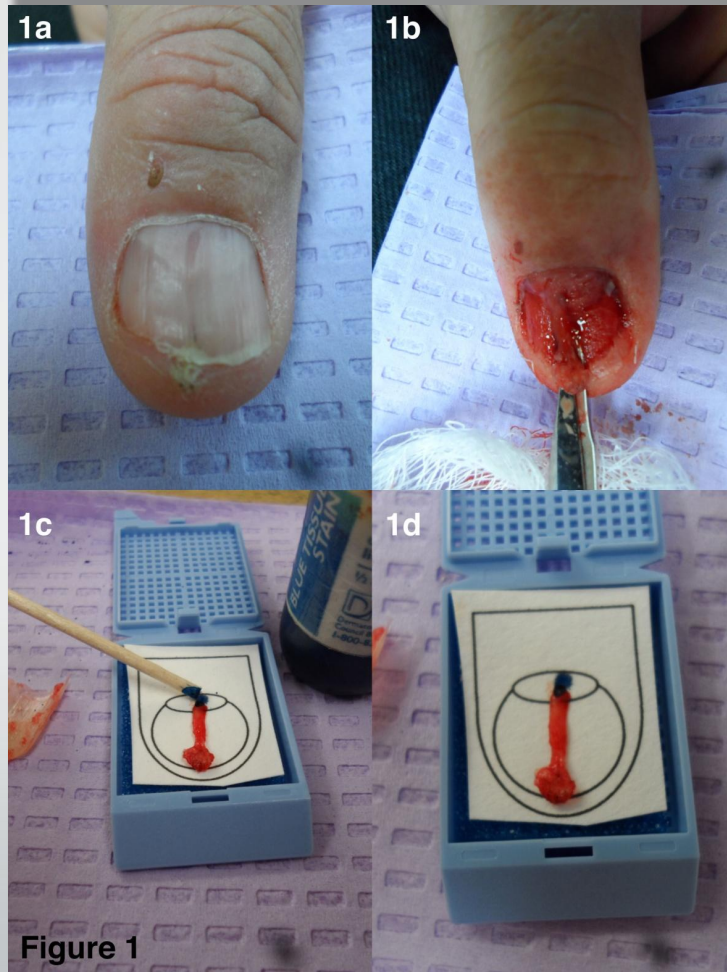
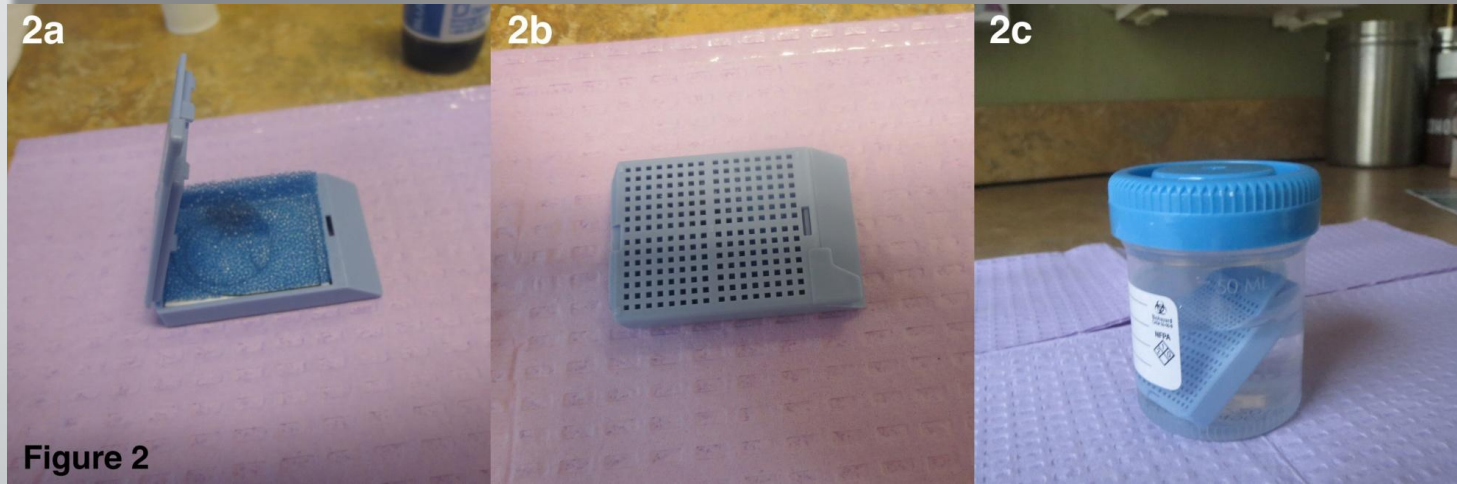
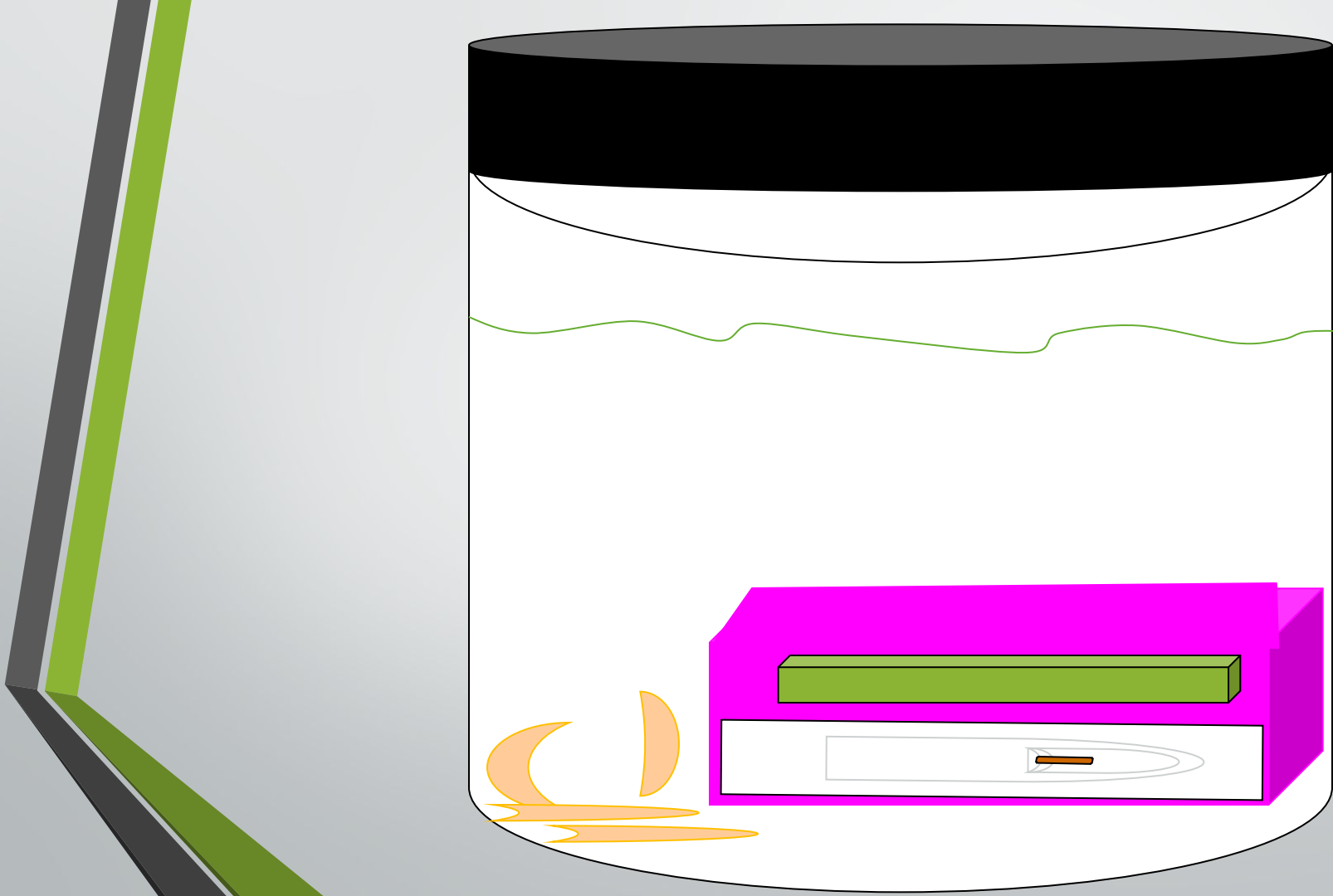


Figure 1





Each specimen is different





Pathologist review before grossing

- Number tissue blocks
- Unstained slides or levels at the start
- Special stains
- Importance of nail
- Reserve nail for culture

Think about the differential diagnosis when grossing

- Onychopapilloma
- Onychomatricoma
- Digital myxoid/mucous cyst
- Squamous cell carcinoma
- Longitudinal melanonychia

Onychopapilloma



Onychopapilloma

- Clinical
 - Longitudinal erythronychia (redness)
 - Distal nail split



Onychopapilloma

- Clinical
 - Longitudinal erythronychia (redness)
 - Distal nail split



Onychopapilloma

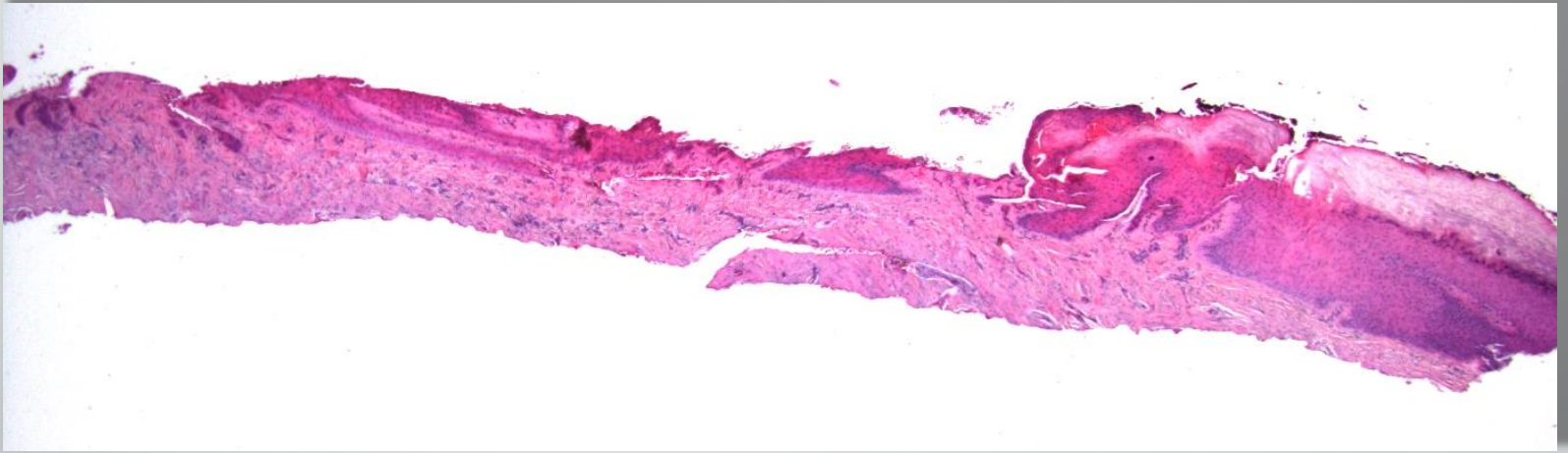
- Clinical
 - Longitudinal erythronychia (redness)
 - Distal nail split



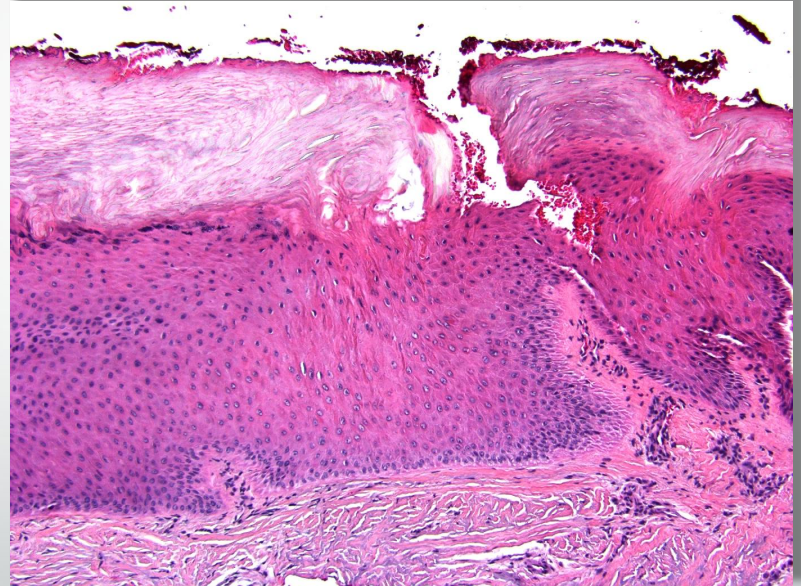
Figure 1

Embed proximal to distal

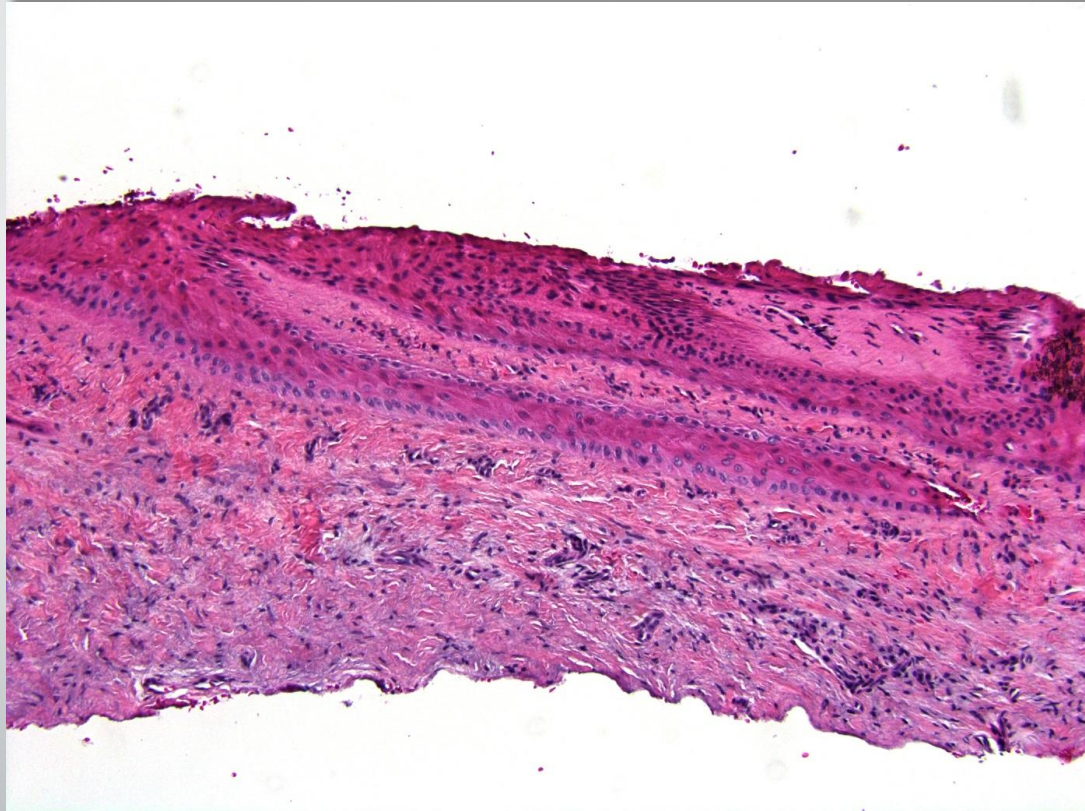
Onychopapilloma—Keratin Producing



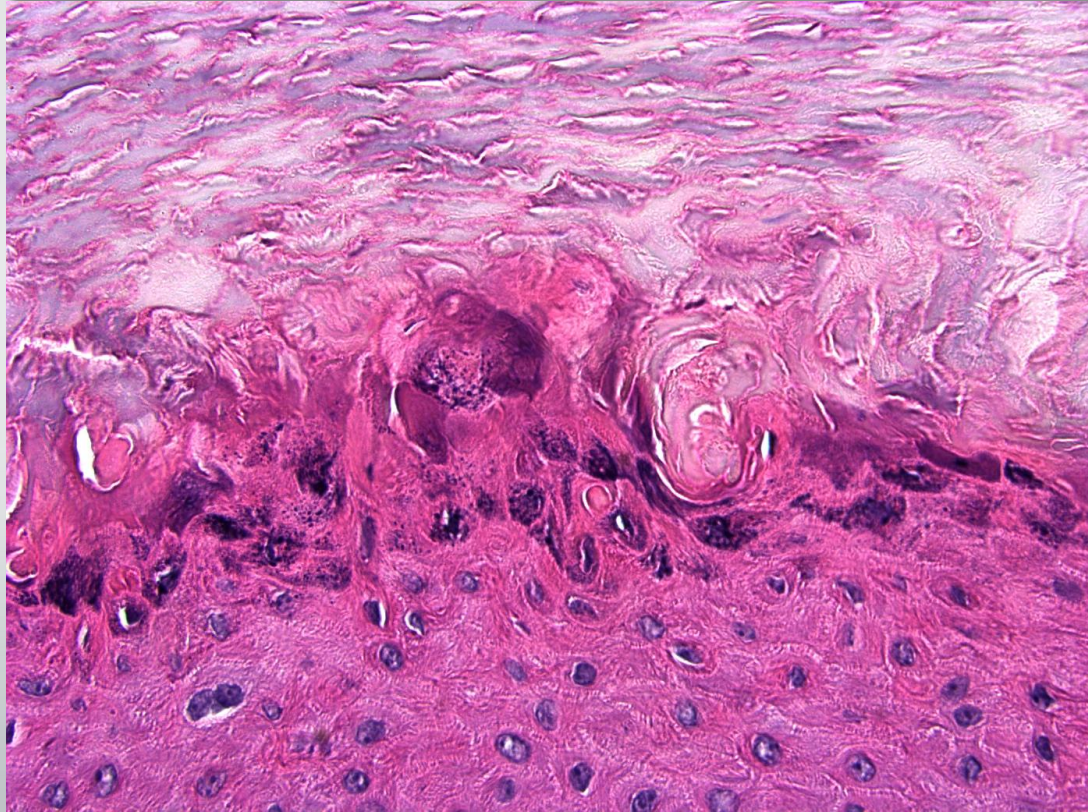
Onychopapilloma—Keratin Producing



Onychopapilloma



Onychopapilloma—Not a wart



Onychomatricoma





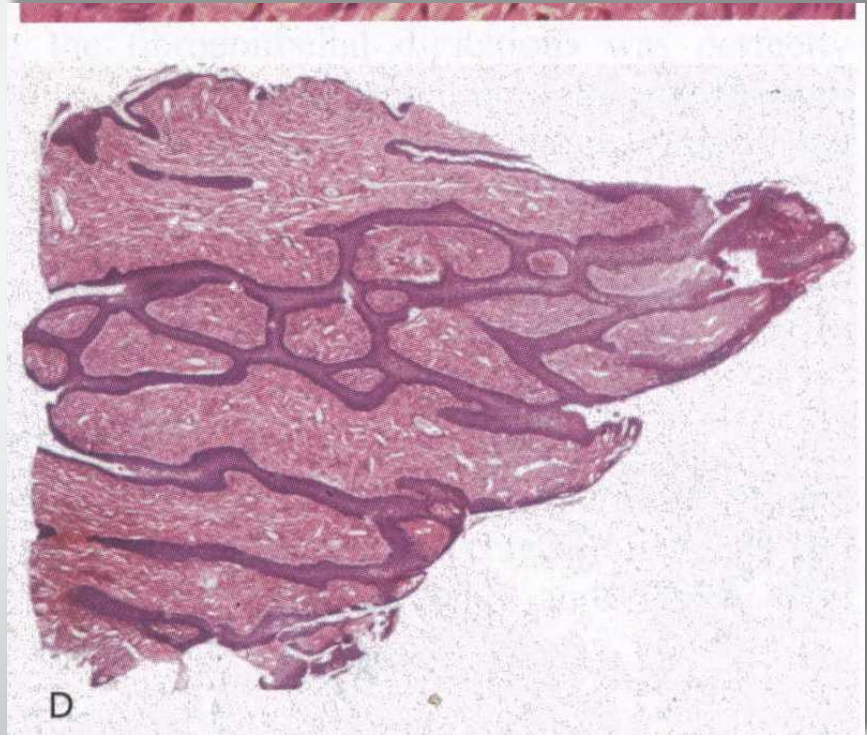
Onychomatricoma

Examine nail for
holes—Transverse
sections of
dystrophic nail

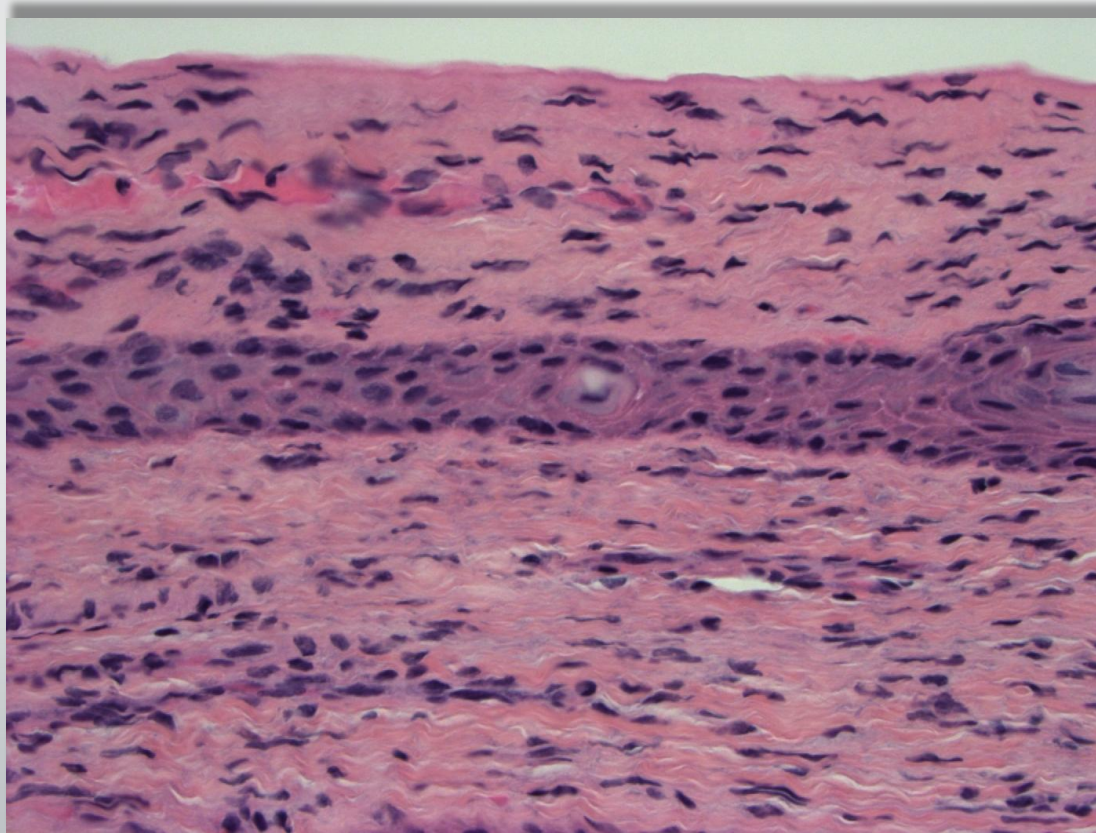


Onychomatricoma

Epithelial and
dermal components

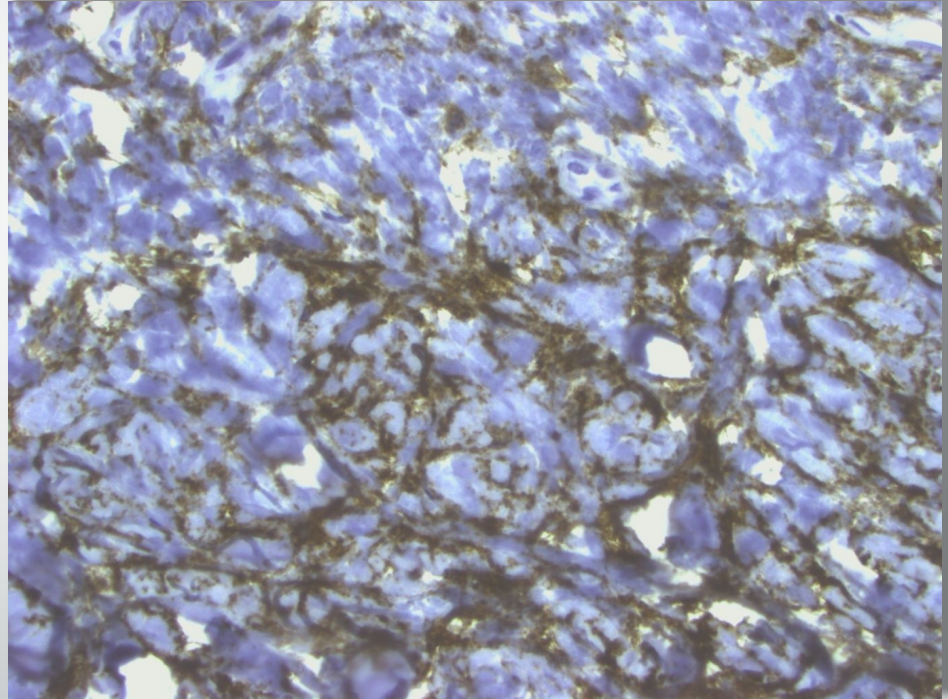


Onychomatricoma



Onychomatricoma

- Onychodermis onychofibroblasts
- CD10+
- CD13+

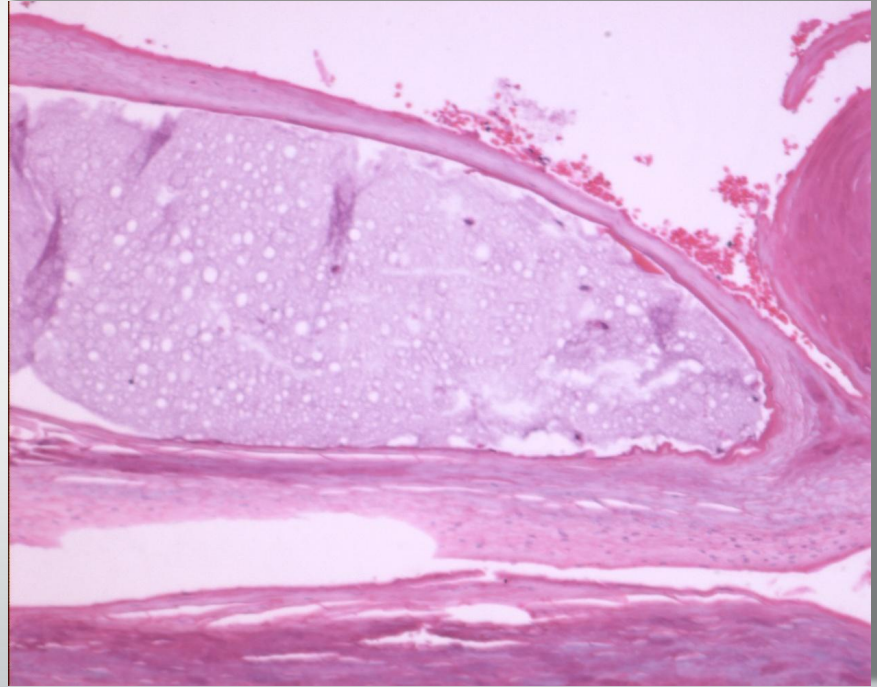


Digital Myxoid/Mucous Cyst

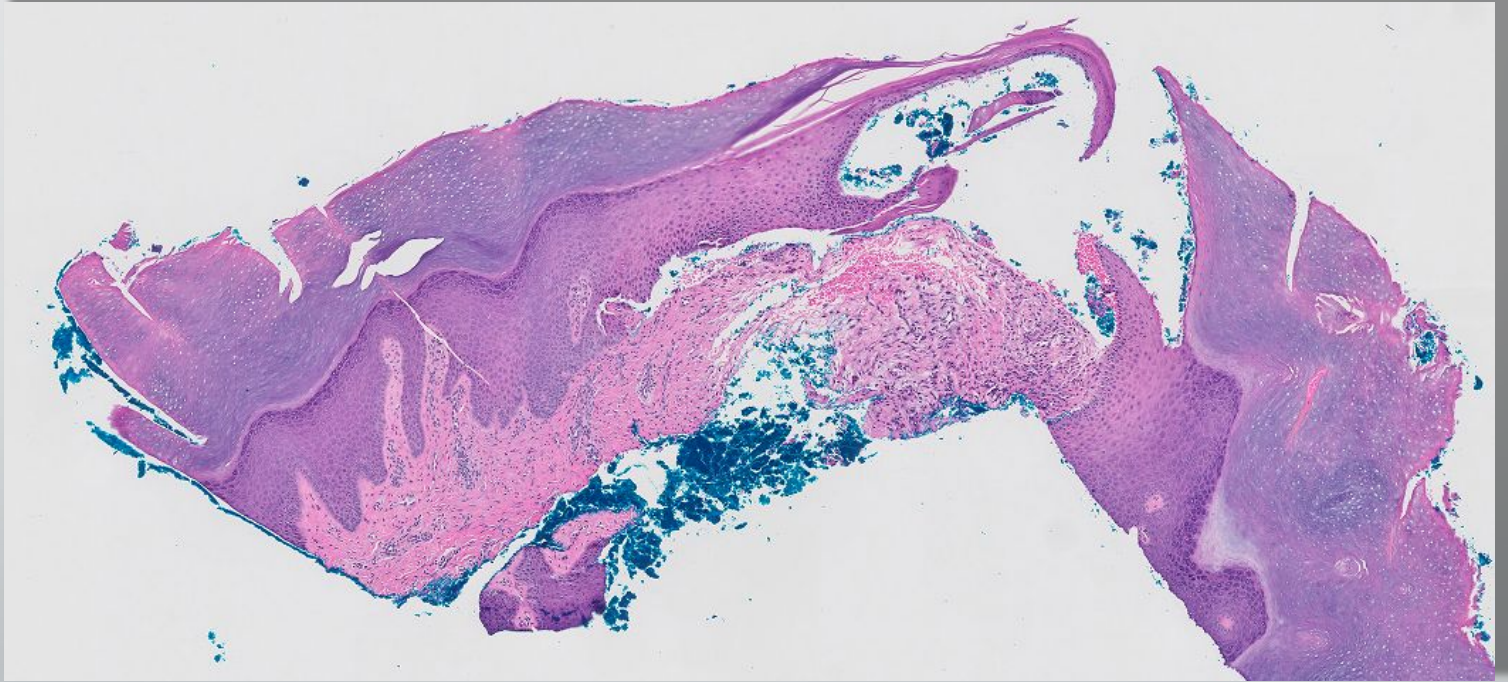


Digital Myxoid/Mucous Cyst

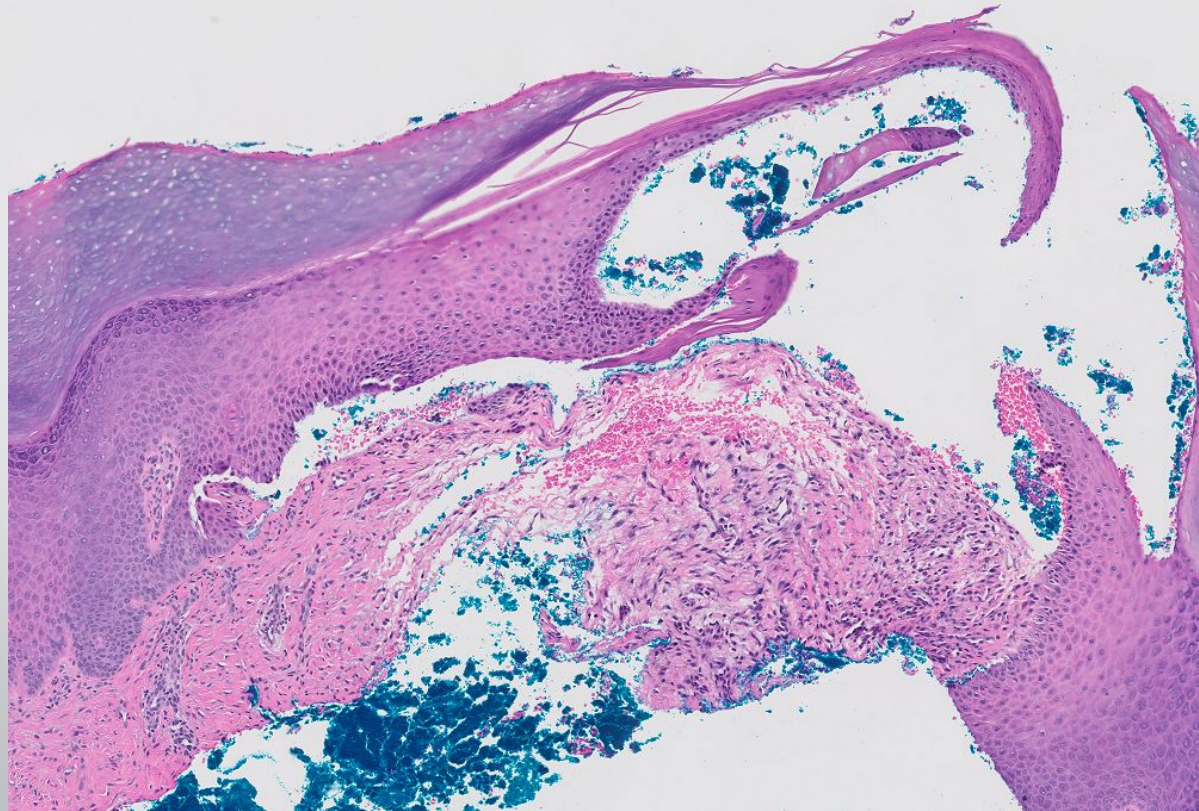
Mucin may
be anywhere



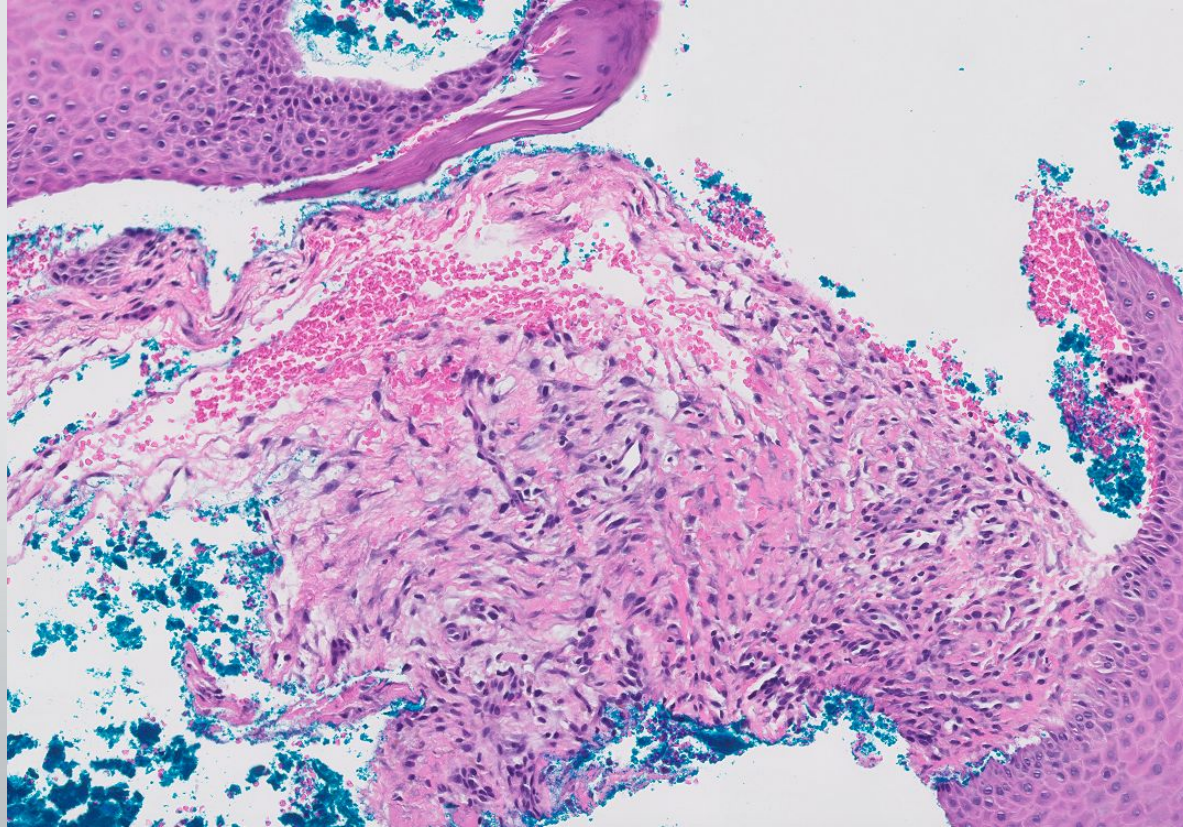
H&E may show only scar and reactive change



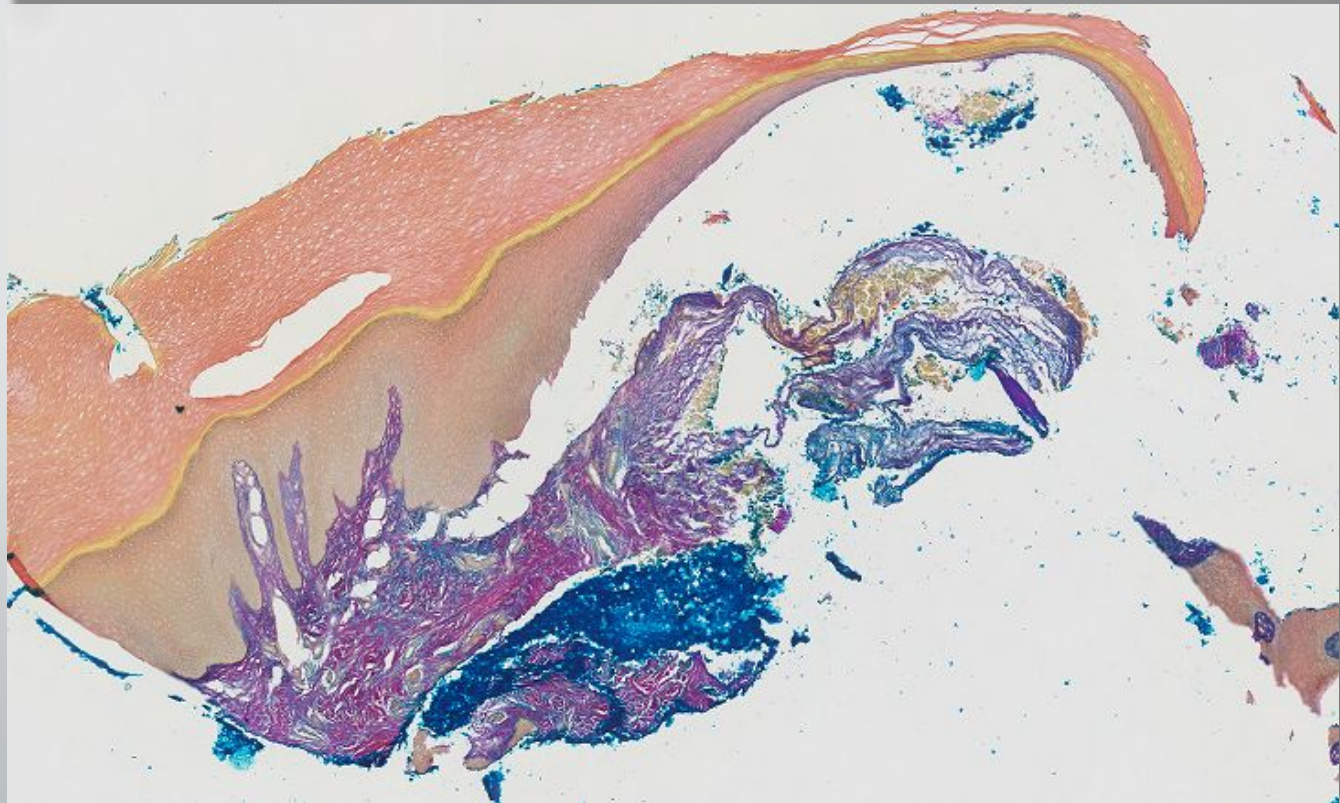
H&E may not show mucin



H&E may not show mucin



Mucin stain often required



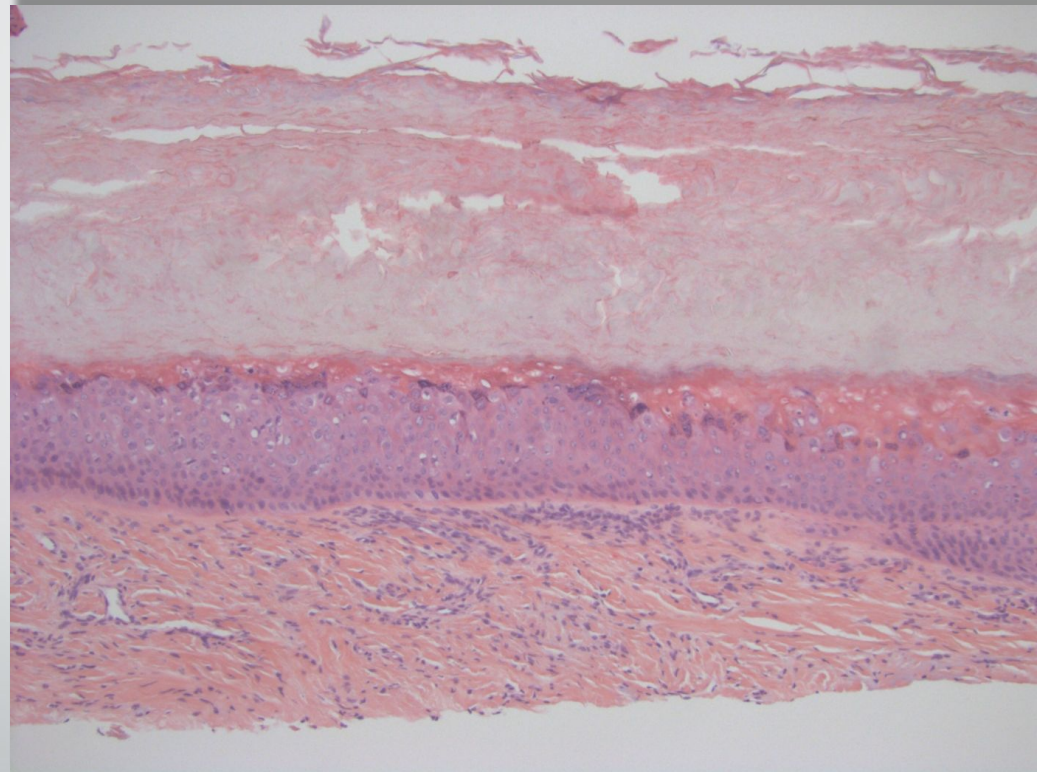
Think about the diagnosis when grossing

- Squamous cell carcinoma
 - Sampling
 - HPV-Verruca etiology

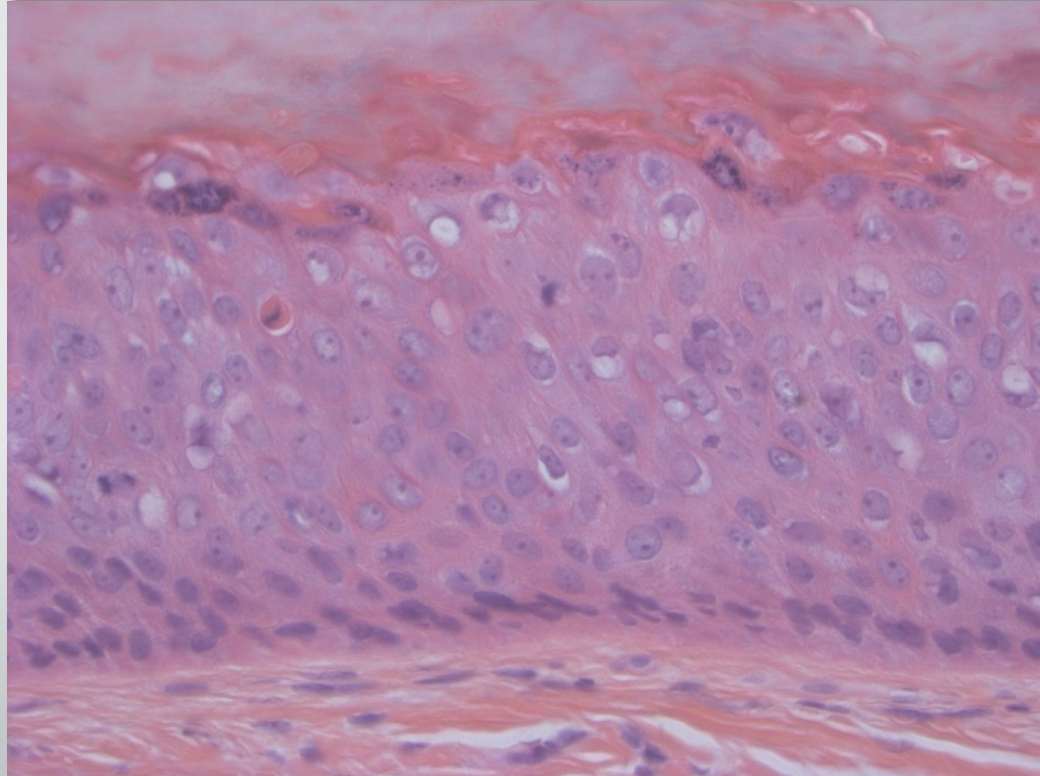
Squamous cell carcinoma



Squamous cell carcinoma

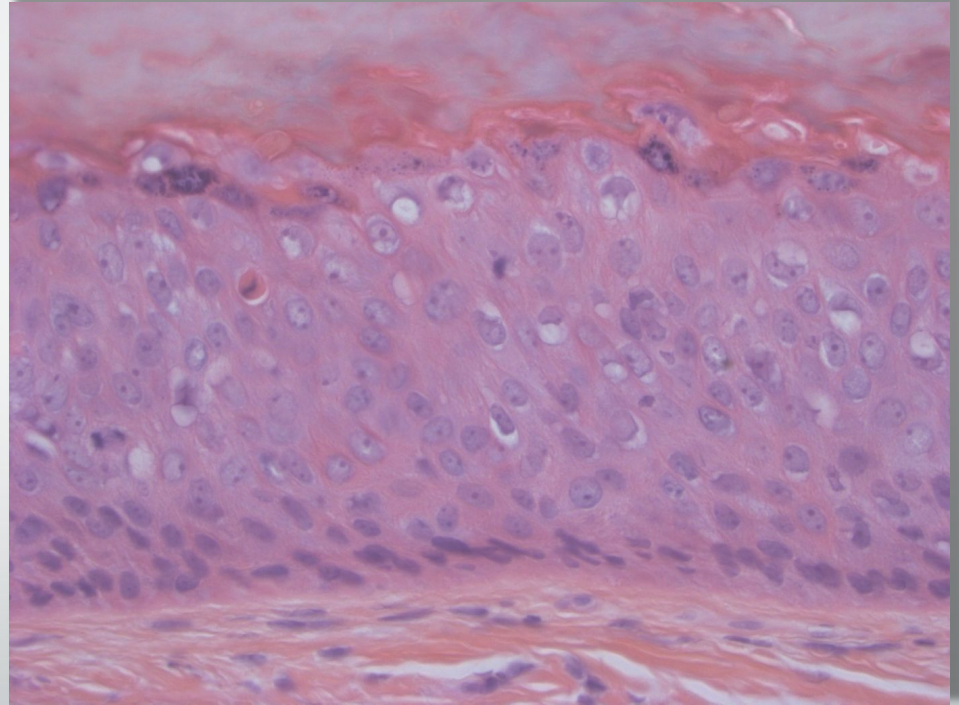


Squamous cell carcinoma in-situ

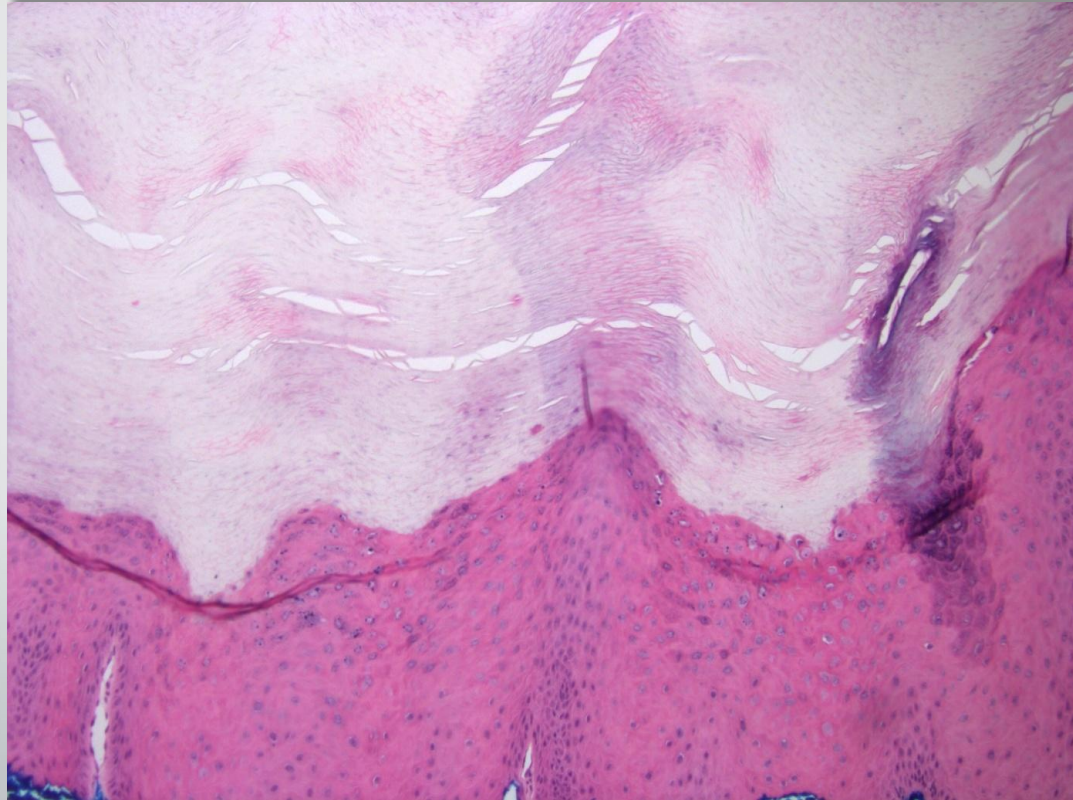


Squamous cell carcinoma in-situ

Human Papillomavirus
(HPV) features



SCC versus Wart/Verruca



SCC versus Wart/Verruca

Clinical correlation often necessary

- Immunosuppression (esp HIV)
- If it is destroying bone, it is not benign!
- Sample more if suspicious



HPV In-situ Hybridization (ISH)

- HPV Subtypes
 - Low risk — Verruca
 - High risk — Squamous cell carcinoma
 - Pan HPV test — Benign and malignant

HPV In-situ Hybridization (ISH)

Comment

Although in an ideal world we would always expect a positive pan-HPV in situ hybridization stain when we see a positive Low-risk HPV stain, we have observed this situation (i.e., a negative pan HPV stain in the face of a positive Low-risk HPV stain) on several occasions in our laboratory. The label "Pan-HPV" is a bit misleading, because although it detects multiple Low-risk and High-risk HPV subtypes, it clearly does not detect every possible type of HPV. Additionally, our Low-risk HPV probe detects HPV type 44, which is an HPV type that is not detected in the Pan-HPV probe that we have available to us. As such, infection with Low-risk HPV type 44 would readily explain the findings in this case.

The HPV in situ hybridization stains were performed using the RNAscope method, which targets HPV-associated RNA in the nucleus and cytoplasm of the target cells. This method has vastly superior sensitivity to the previous methods used at ProPath (which were based on detection of HPV DNA). Unlike DNA-based methods, RNAscope signals can be observed in both the nucleus and cytoplasm. The HPV RNAscope probes used at ProPath are directed at the following HPV types:

Pan-HPV RNAscope probe: Detects HPV types 6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68

Low-risk HPV RNAscope probe: Detects HPV types 6, 11, 42, 43, 44

High / Intermediate risk HPV RNAscope probe: Detects HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68

Thank you for allowing us to study this case.

REFERENCES:

Schache AG, Liloglou T, Jones TM et al: Validation of a novel diagnostic standard in HPV-positive oropharyngeal

HPV In-situ Hybridization (ISH)

- HPV Subtypes
 - Low risk — Verruca
 - High risk — Carcinoma
 - Pan HPV test — Do not use since does not contain all of the subtypes

Think about the diagnosis when grossing

- Longitudinal melanonychia
 - Identify source of clinical pigmentation





Histopathology of benign activation

- Epithelial pigmentation
- Melanophages
- No or only a slight increase in junctional melanocyte density

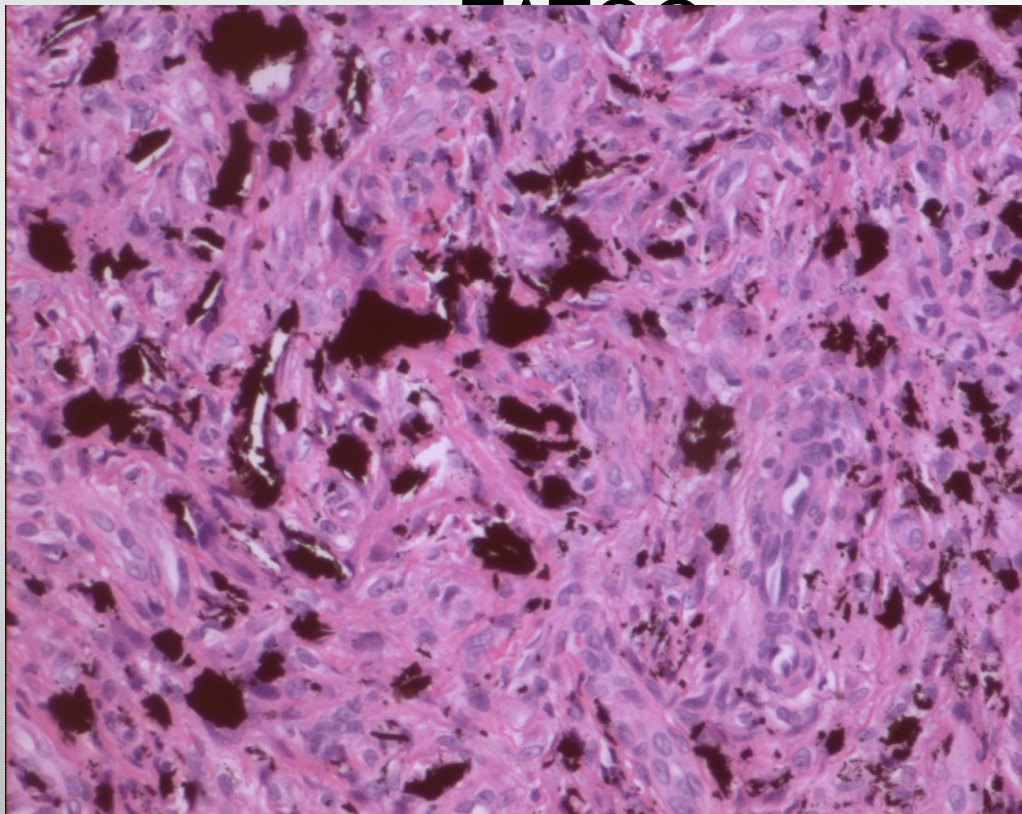
Features of melanotic macule can be subtle

- H&E with initial levels
- MelanA IHC
- Fontana-Masson
- PAS fungus
- Unstained slides

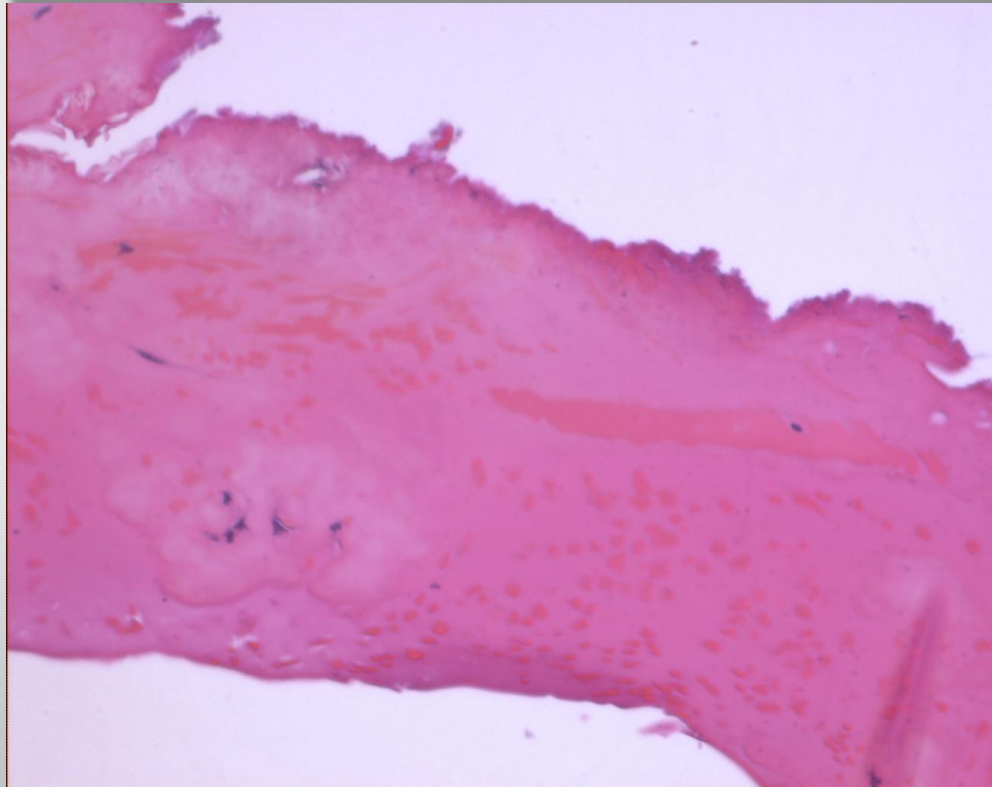
H&E for melanonychia

- H&E level sections
 - Blood
 - Exogenous material
 - Medication deposition

TABLE 2

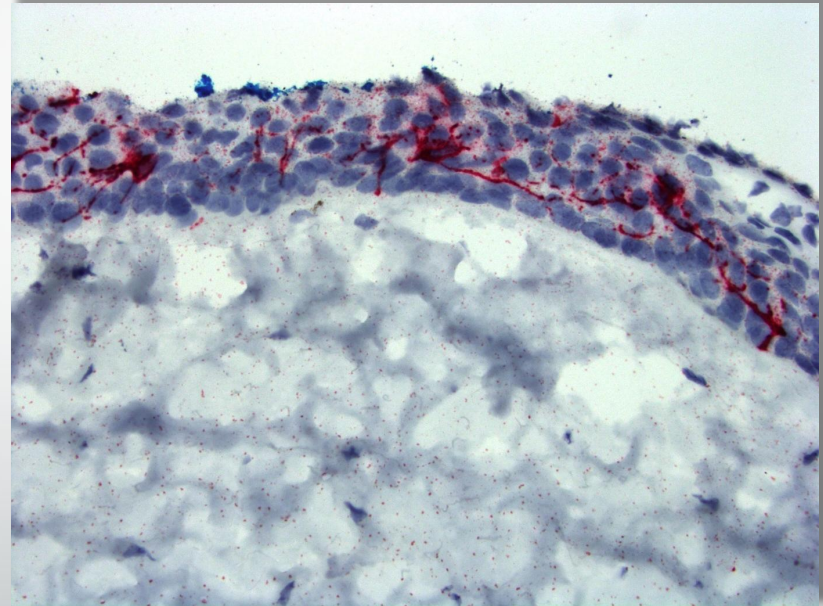


Blood in nail plate

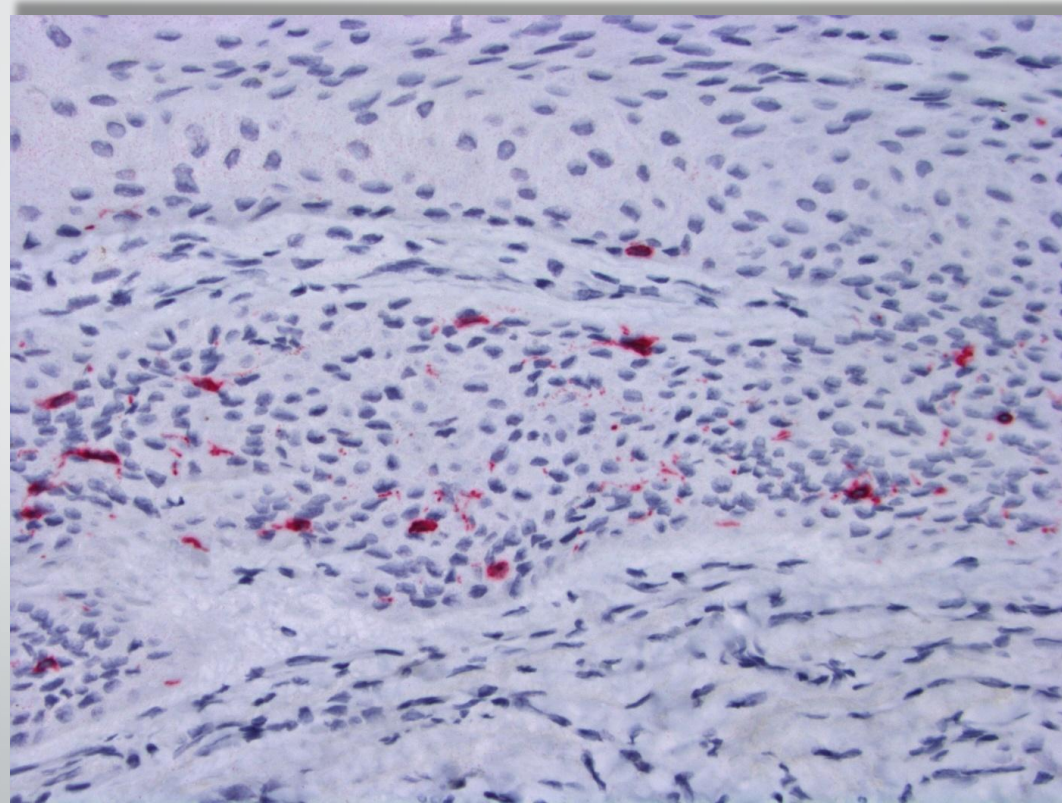


MelanA/Mart1 for melanonychia

- Melanocytes density may vary highly, especially in melanoma in-situ
- Use a red chromogen

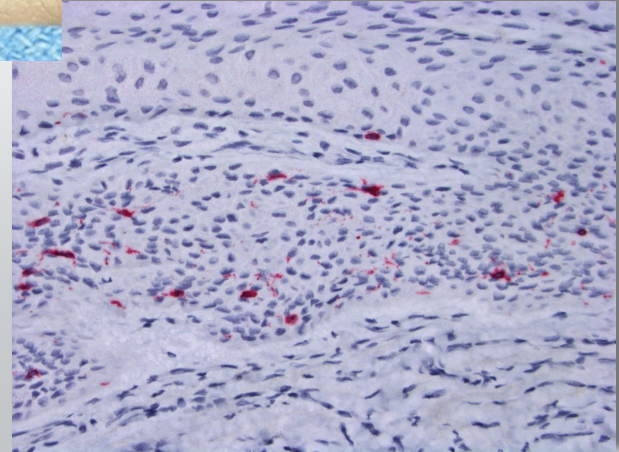


Variable density of melanocytes

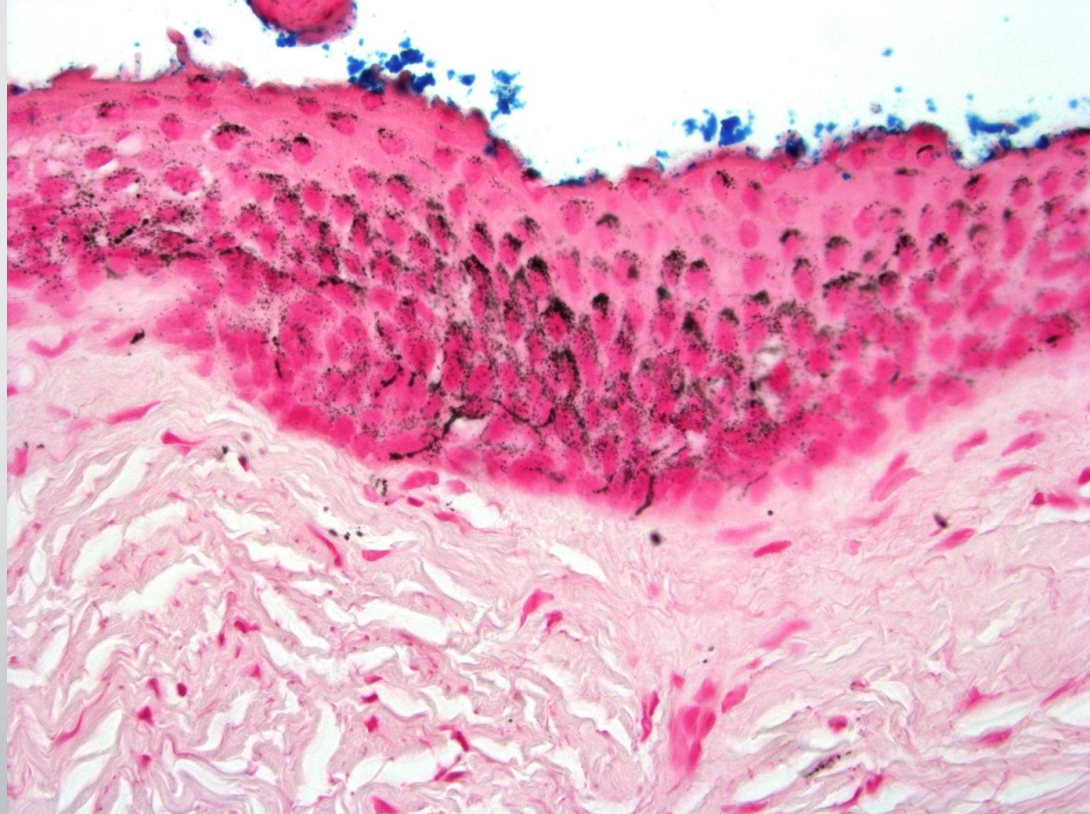


Variable density of melanocytes

Skin type

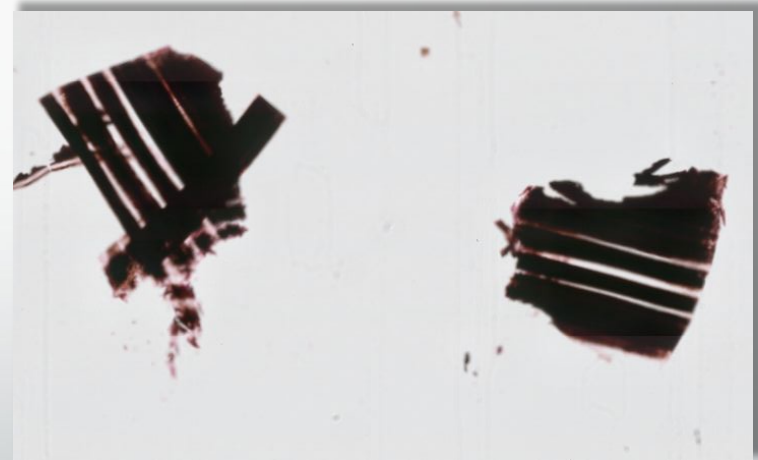


Fontana-Masson for melanonychia



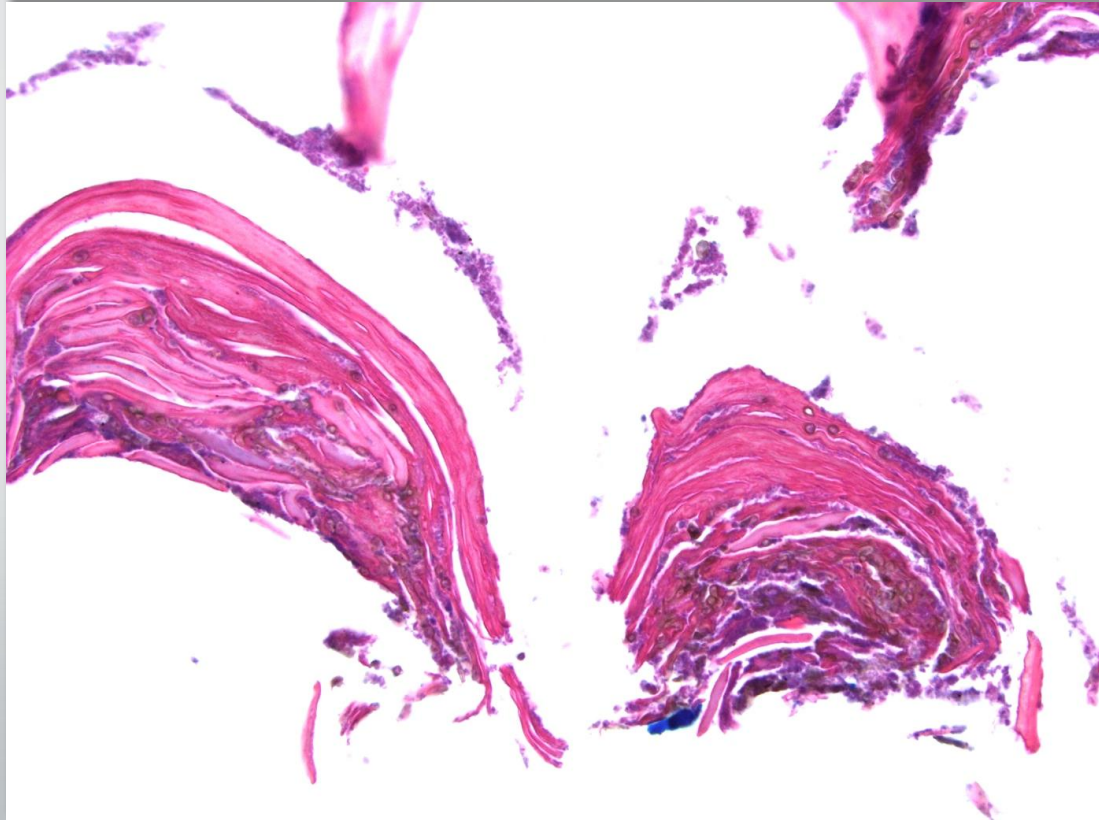
Special stains for pigment do not work in nail plate

- Perl's iron— Fe^{2+} still in heme
- Fontana-Masson—overstains plate—must be diluted

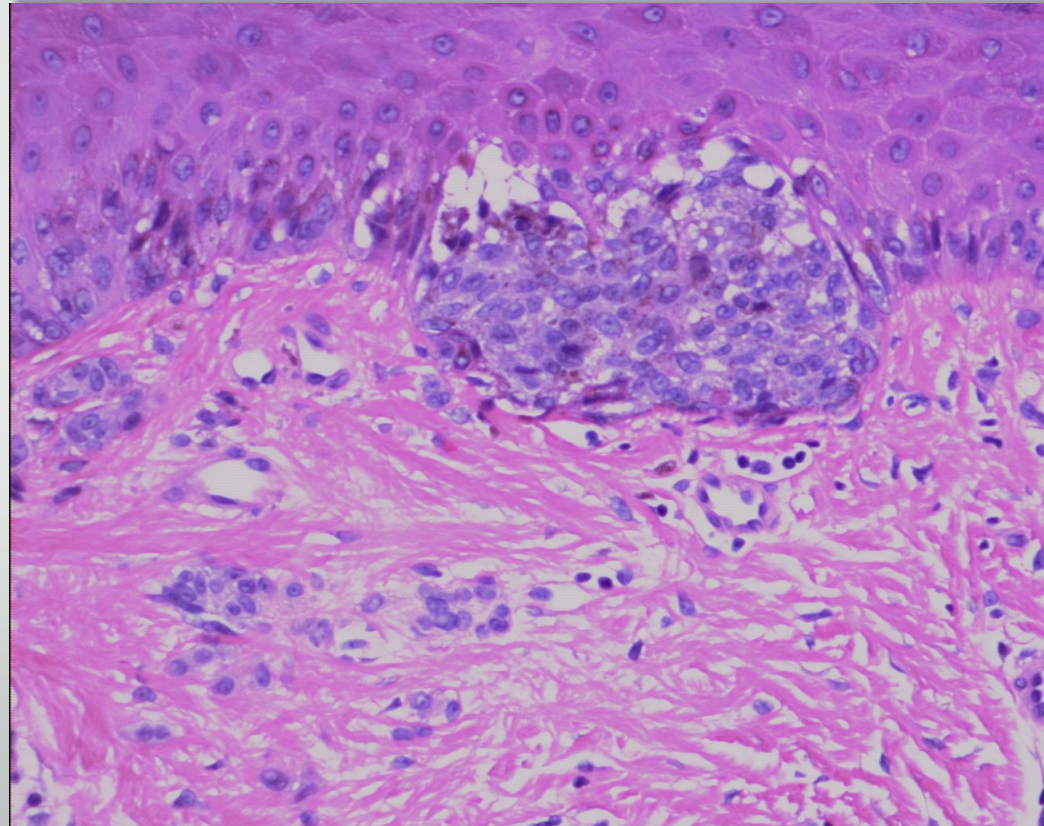




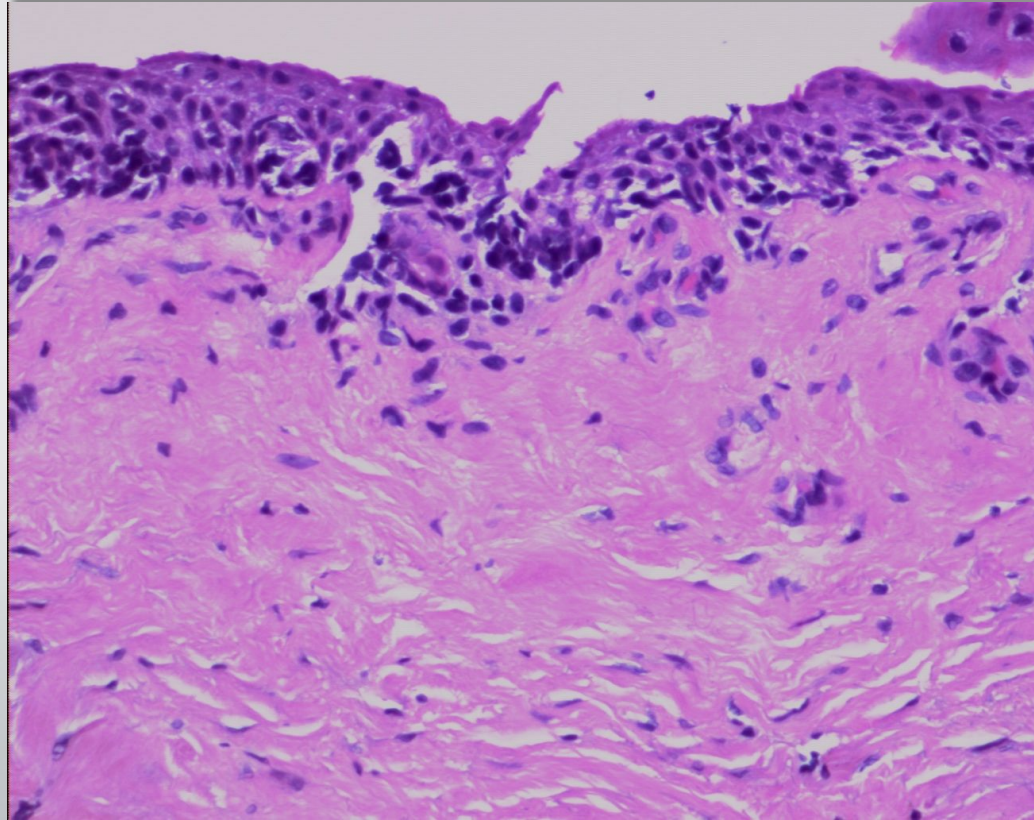
Pigmented fungus



Benign melanocytic nevus

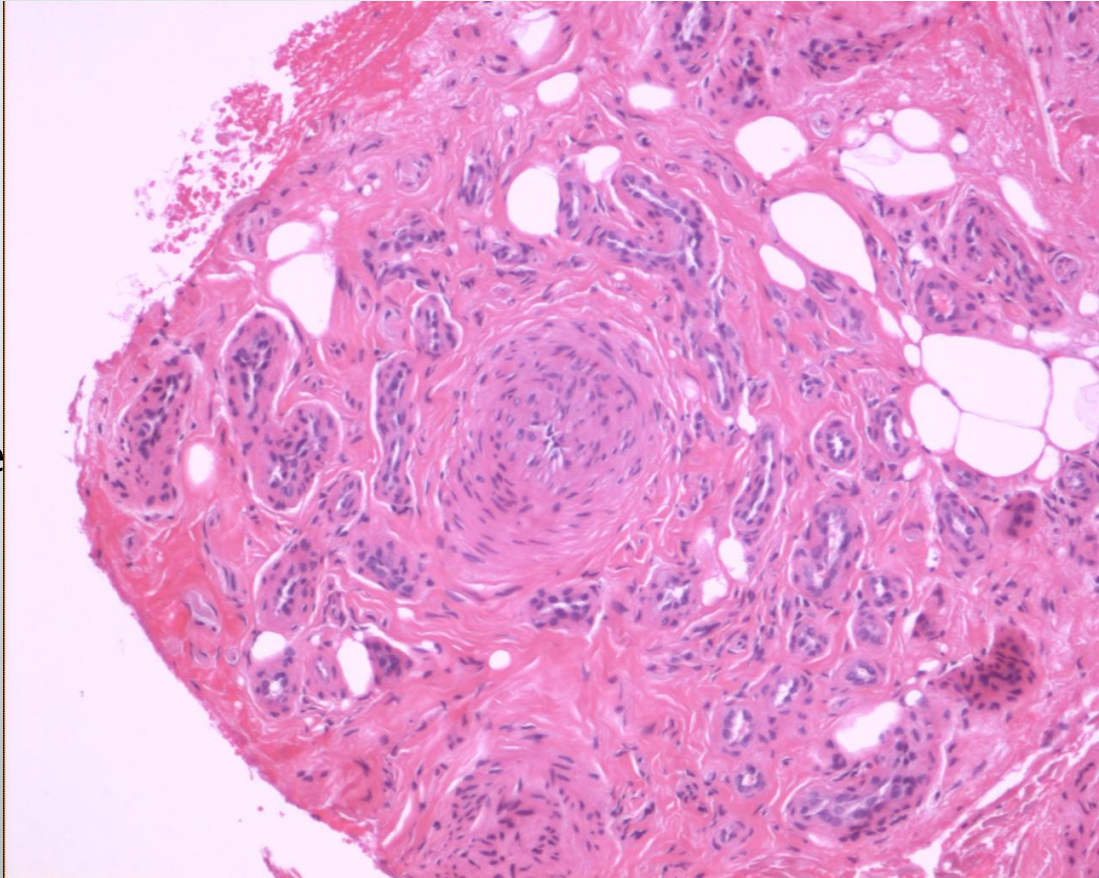


Melanoma in-situ

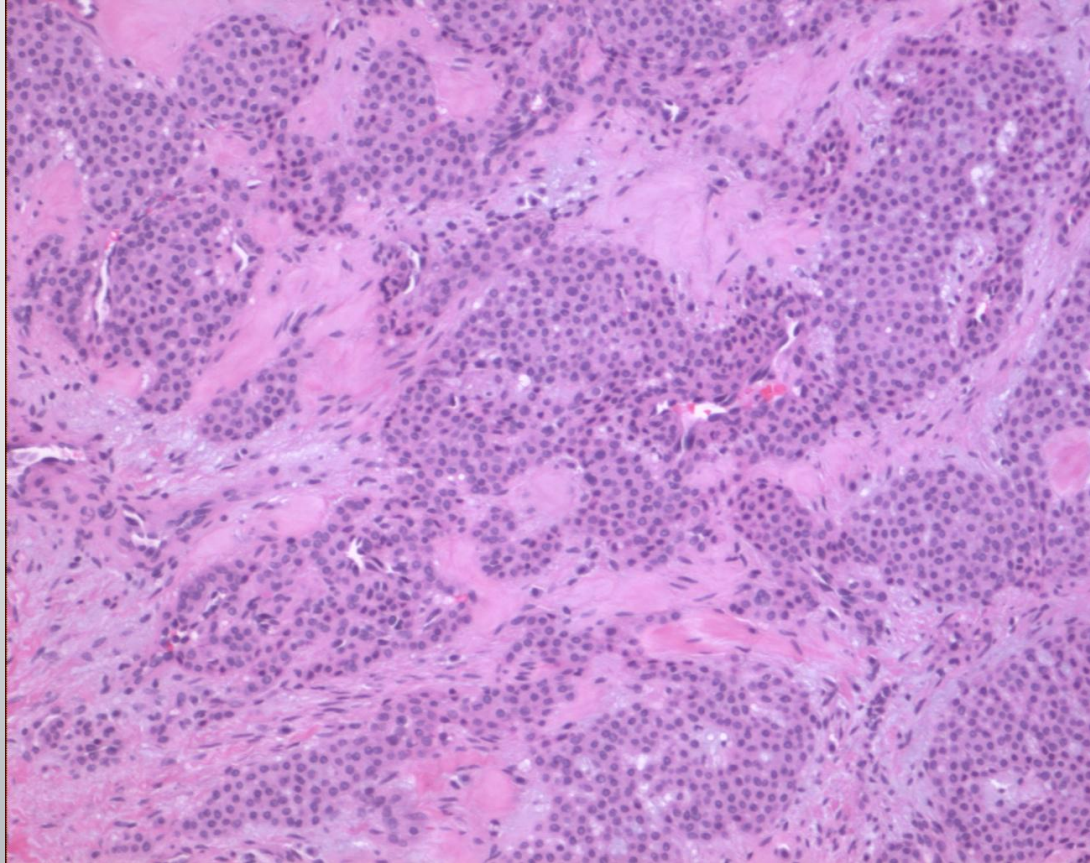


Hemangioma

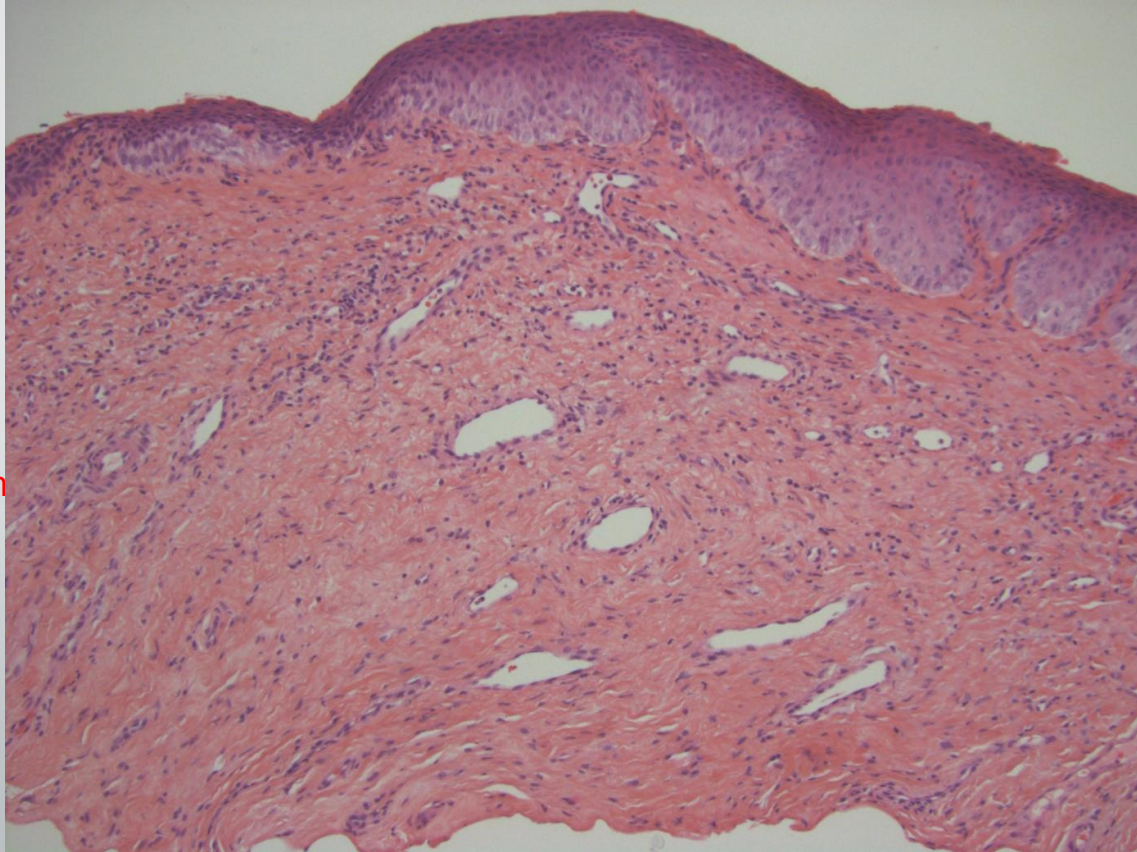
- Often



Glomangioma



Angiofibroma

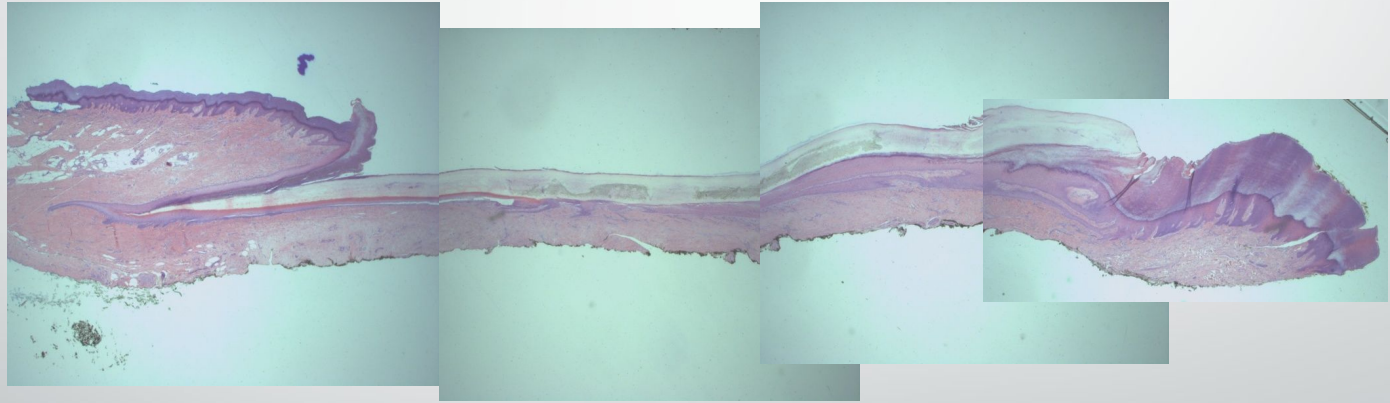


- In

Hutchinson's Sign



Hutchinson's Sign



Dr. Rich's Differential Diagnosis

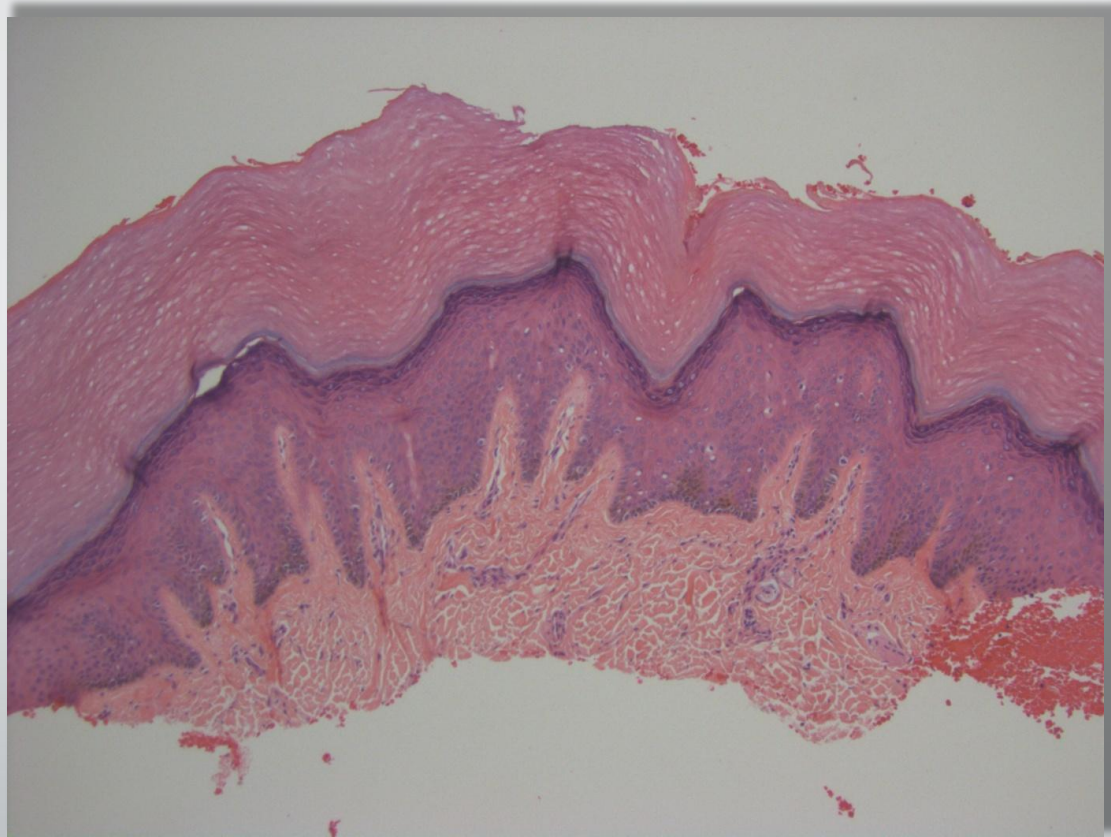
- Trauma pigment
- Nevus
- Lentigo
- R/O Melanoma

Biopsy

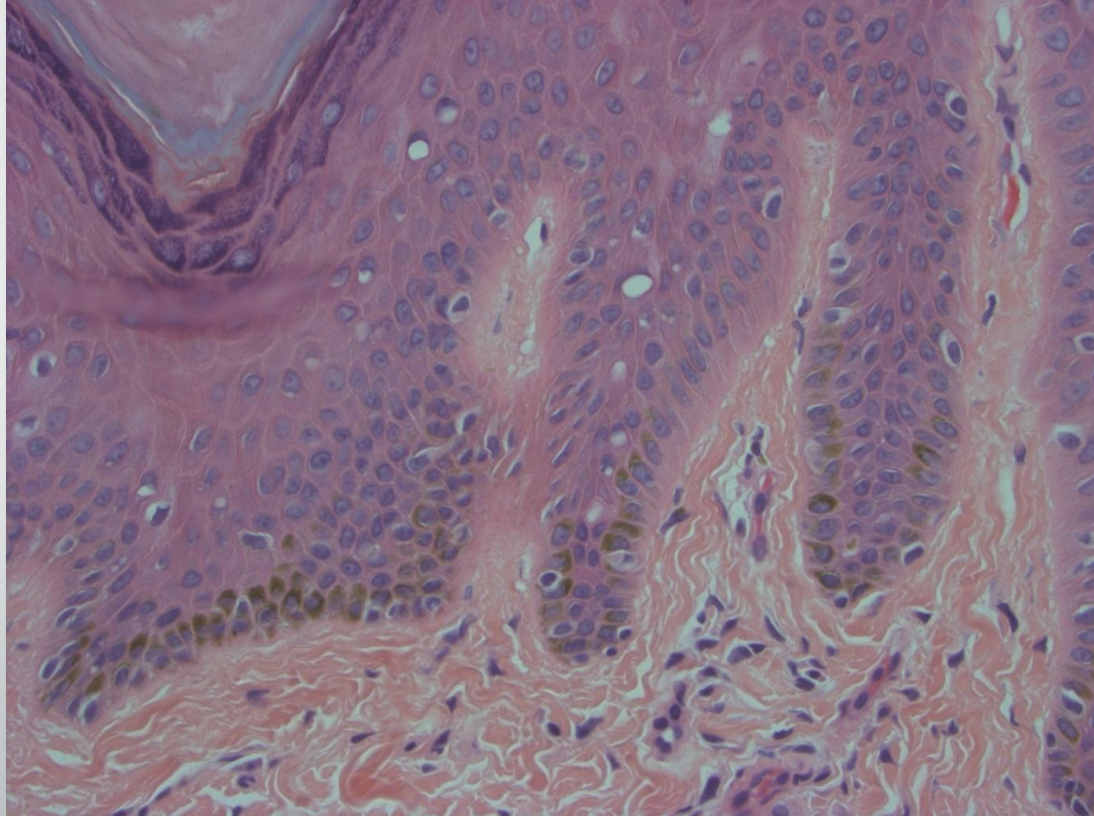
- Nail plate reflected and matrix sampled
- Proximal nail fold sampled



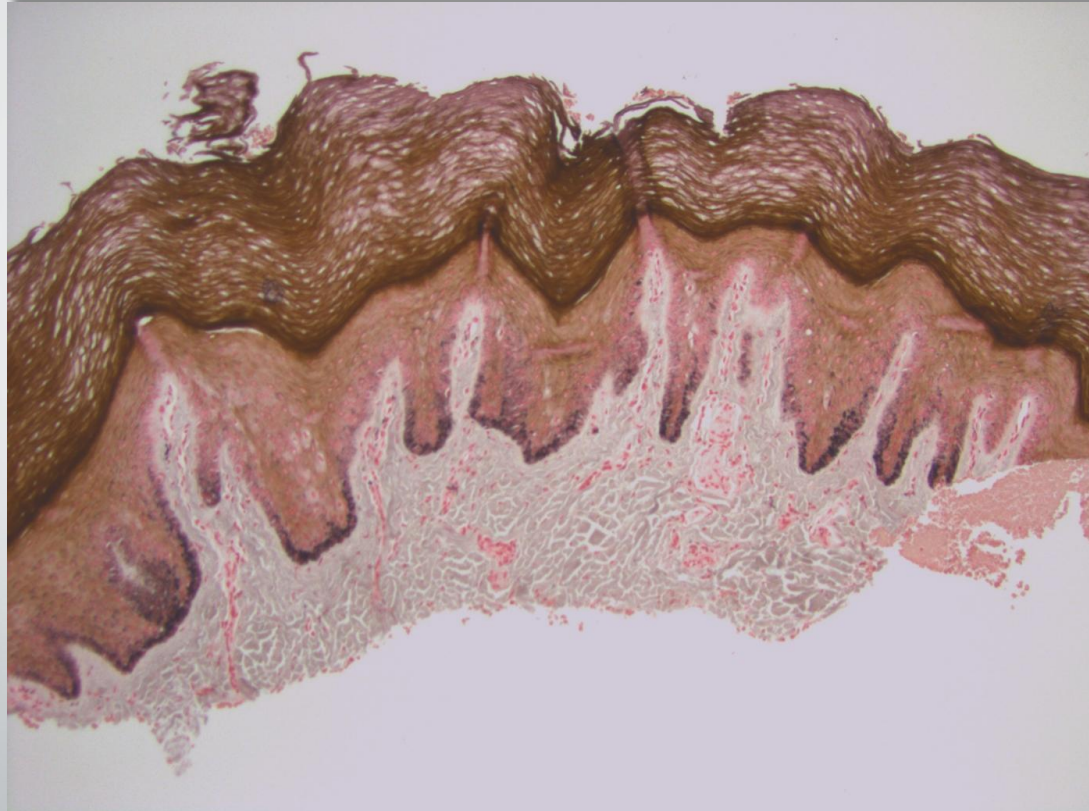
Proximal Nail Fold



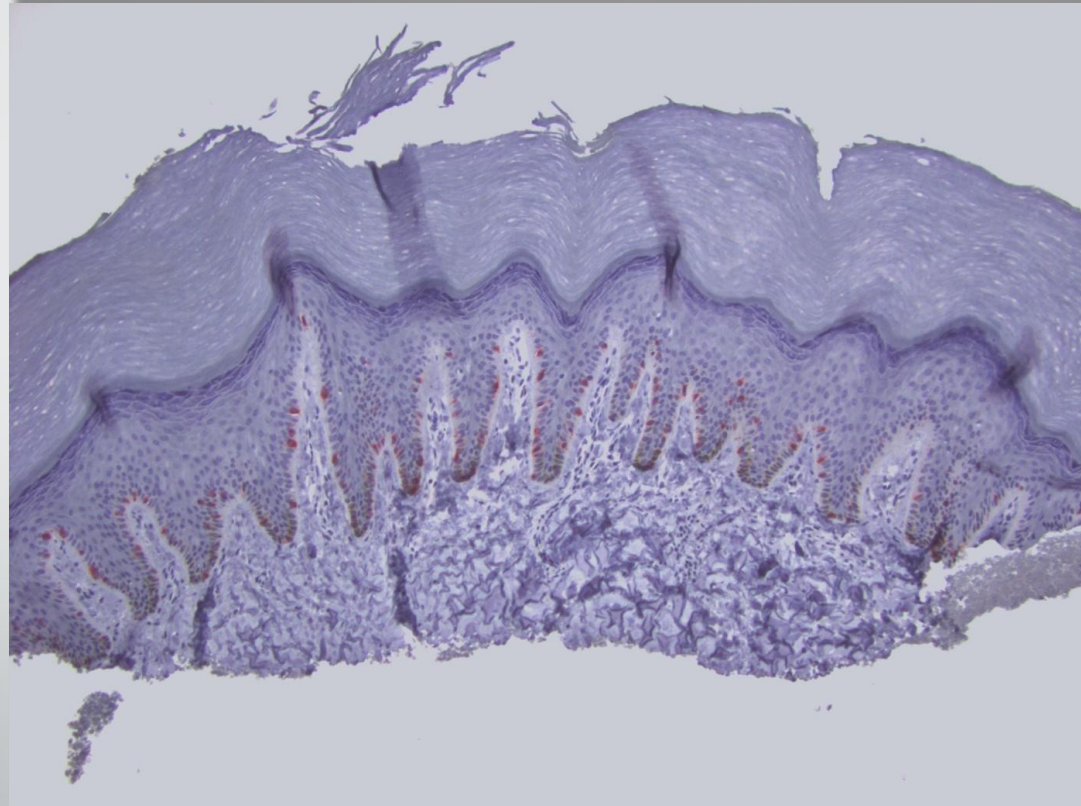
Proximal Nail Fold

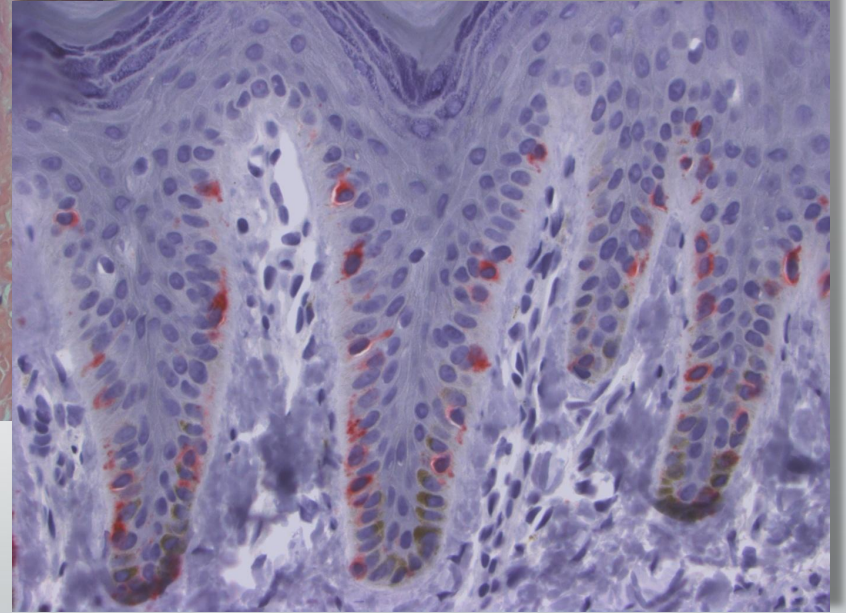
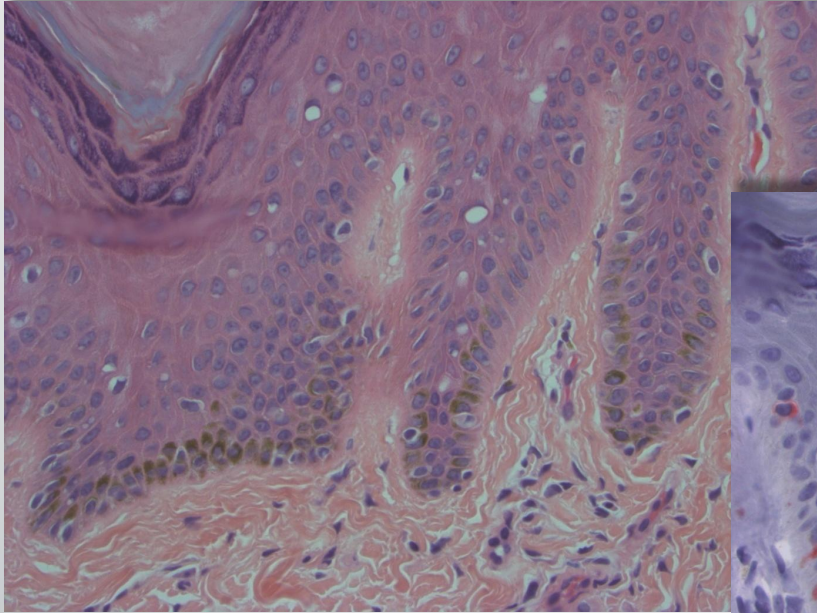


Fontana-Masson Stain

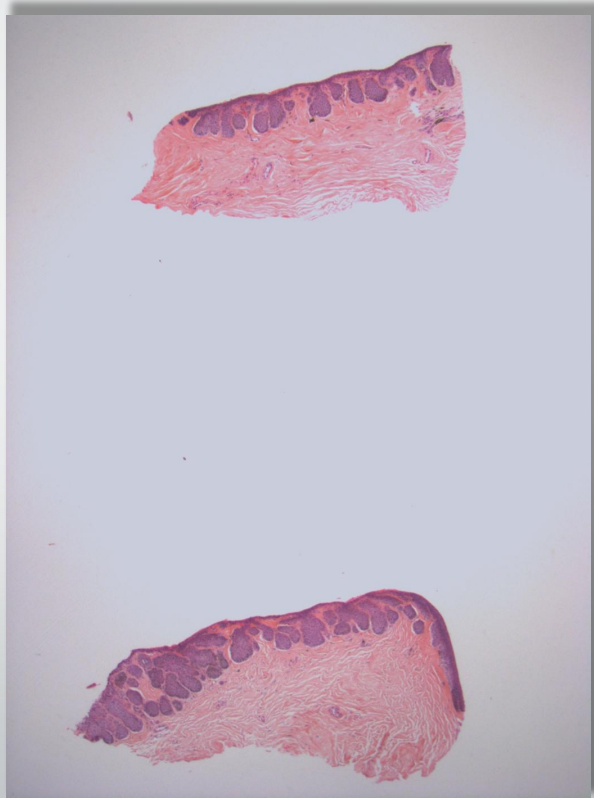


MelanA IHC Study

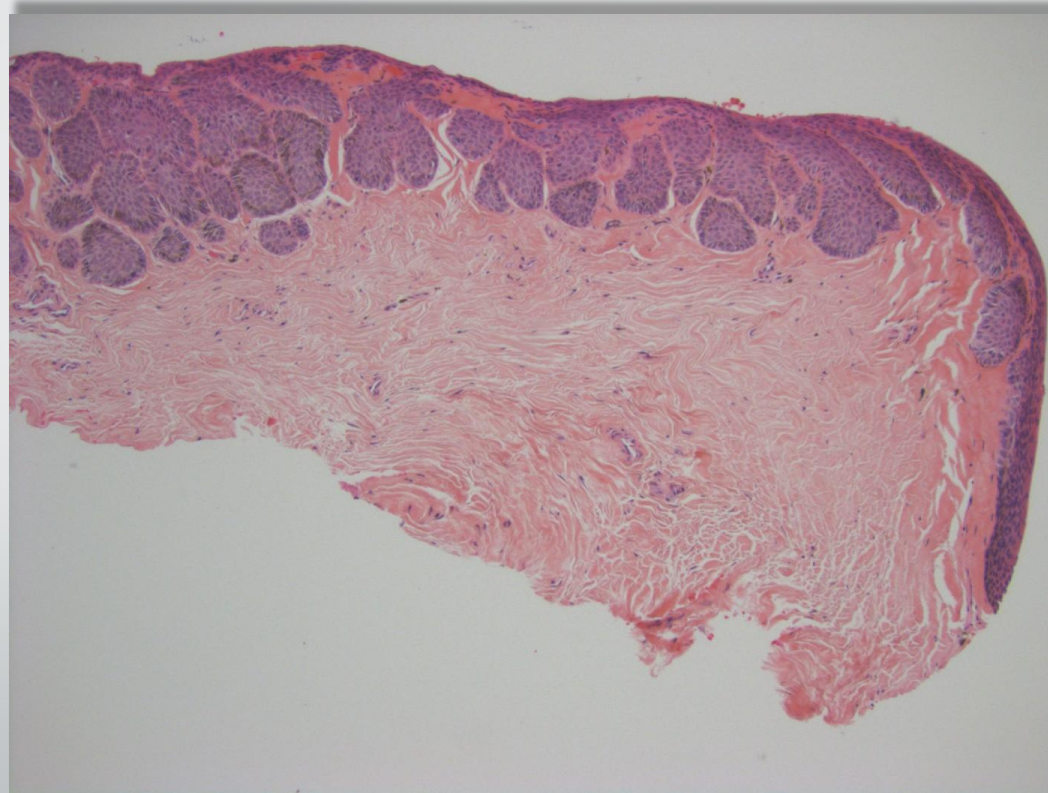




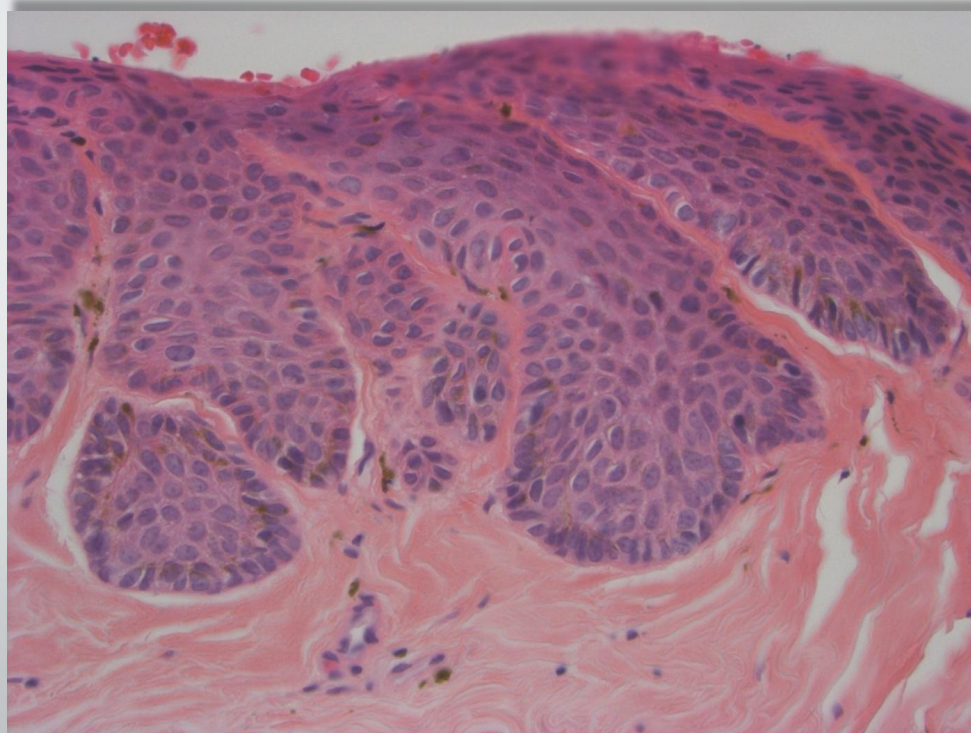
Nail Matrix

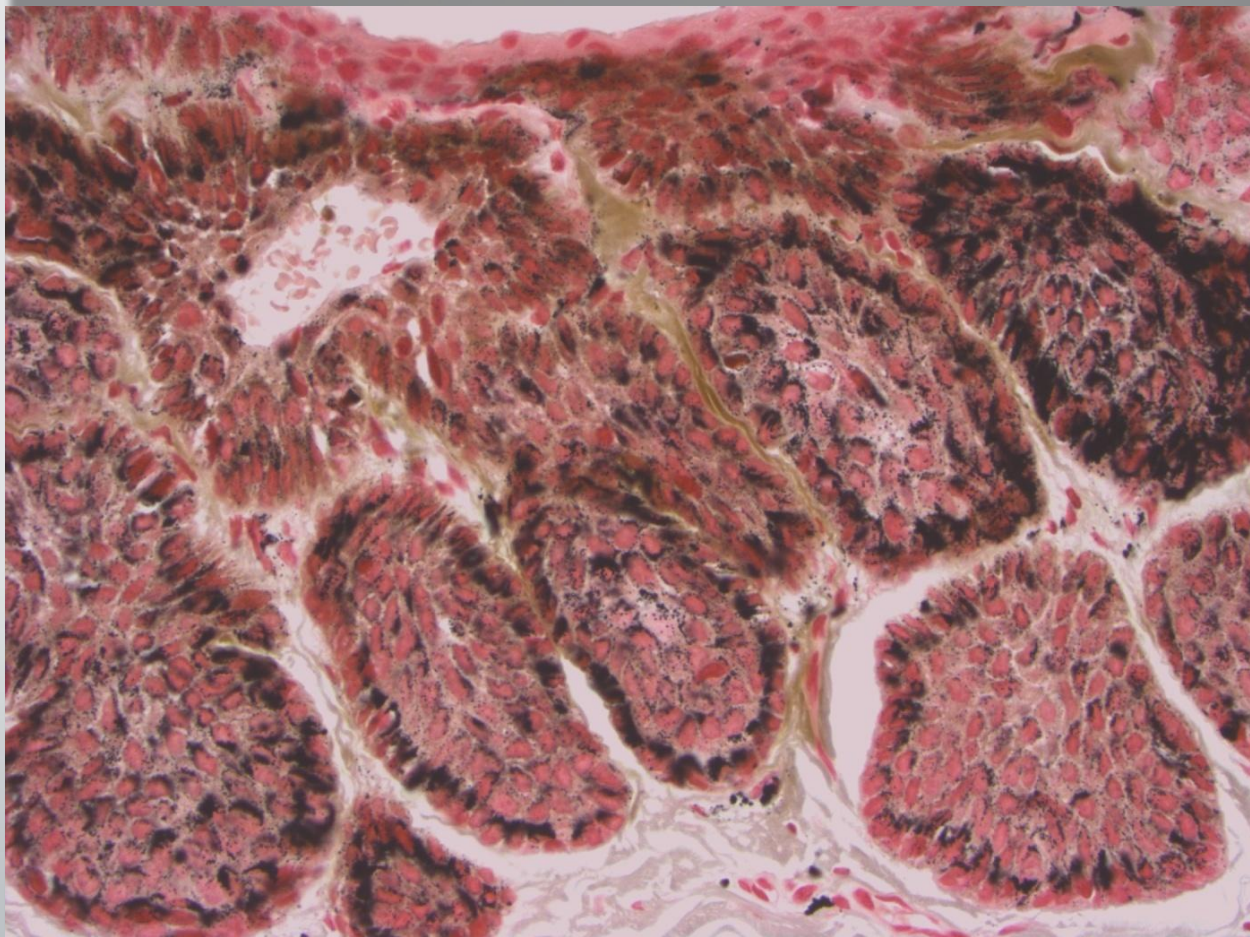


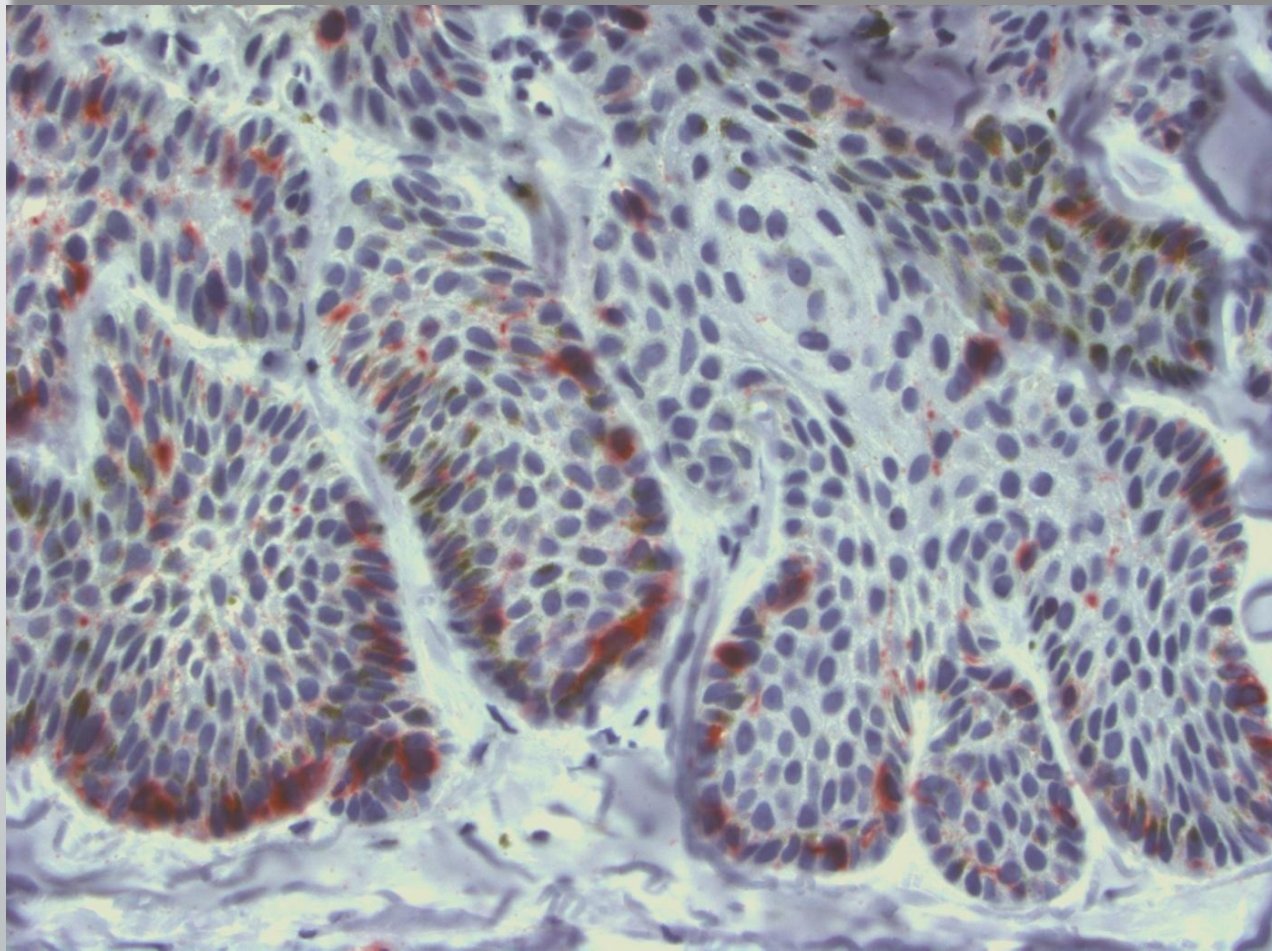
Nail Matrix

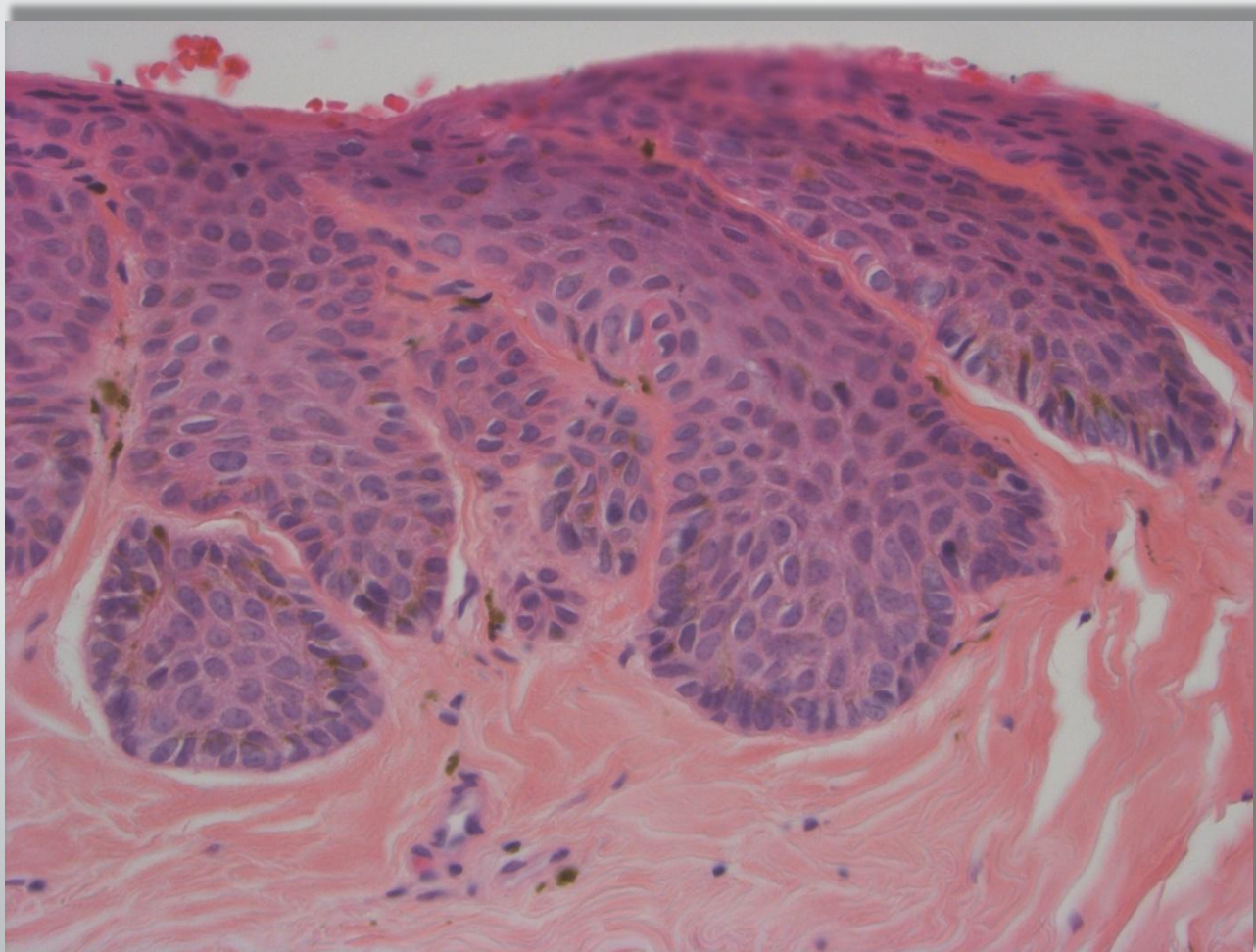


Onychocytic matricoma with a Hutchinson's sign









Onychocytic Matricoma

Am J Dermatopathol. 2012 Feb;34(1):54-9. doi: 10.1097/DAD.0b013e31822c3d8b.

Onychocytic matricoma presenting as pachymelanonychia longitudinal. A new entity (report of five cases).

Perrin C¹, Cannata GE, Bossard C, Grill JM, Ambrossetti D, Michiels JF.

⊕ Author information

Abstract

Among the tumors of the epidermal appendages, only rare tumors have been proved as differentiating in the direction of the nail. Beside onychomatricoma, we report a new matrical tumor of the nail: onychocytic matricoma (acanthoma of the nail matrix producing onychocytes). The main differential diagnosis of onychocytic matricoma is seborrheic keratosis. However, if attention is paid to the nature of the different layers of the tumor and the peculiar microanatomy of the nail matrix, the differentiation is not difficult. Onychocytic matricoma is a localized (monodactylous) longitudinal melanonychia which is slightly raised. The term pachymelanonychia is used to define the 2 clinical features of the tumor. Pachyonychia indicate a localized thickening of the nail plate, and melanonychia indicate its longitudinal pigmented band. Onychocytic matricoma is composed of a basal compartment with a varying admixture of prekeratogenous cells and keratogenous cells. Endokeratinization originating in the deep portion of the tumor and nests of prekeratogenous and keratogenous cells in concentric arrangement are a characteristic feature. Three major patterns can be identified as follows: acanthotic, papillomatous, keratogenous type with retarded maturation. Given the peculiar thickening of the nail plate observed both in pigmented onychomatricoma and onychocytic matricoma, the term pachymelanonychia longitudinal could be proposed to specify clinically these 2 lesions, which the clinician sometimes mistakes for melanoma.

Onychocytic Matricoma

<http://archderm.jamanetwork.com/article.aspx?articleid=1819583>

Observation | March 2014

Onychocytic Matricoma: A New, Important Nail-Unit Tumor Mistaken for a Foreign Body FREE

Karolyn A. Wanat, MD¹; Erika Reid, MD¹; Adam I. Rubin, MD¹

¹Department of Dermatology at the Hospital of the University of Pennsylvania, Philadelphia


JAMA Dermatol. 2014;150(3):335-337. doi:10.1001/jamadermatol.2013.6358.

Onychocytic matricoma (OCM) is a benign acanthoma of the nail unit that presents with localized thickening of the nail plate and melanonychia.¹ This newly described entity has suggestive clinical features and distinctive histopathologic changes.


REPORT OF A CASE

A man in his 40s presented with a history of traumatic injury to the nail unit, after which he noted a dark line under the nail, which he assumed to be a splinter. It persisted for 3 years without any notable change. The patient reported removing portions of it when he would clip the nail back.

Physical examination demonstrated a 2-mm-wide black longitudinal streak extending to the distal lunula with localized nail plate thickening on the right second digit (Figure 1A and B). Dermatoscopic findings were consistent with a foreign body under the nail (Figure 1C and D). Nail clippings of the nail plate were performed to sample the distal portion of the lesion and demonstrated parakeratosis associated with pigmentation.



Onychocytic matricoma versus Seborrheic keratosis of the nail unit



Take home points

Onychocytic matricoma vs Nail unit seborrheic keratosis

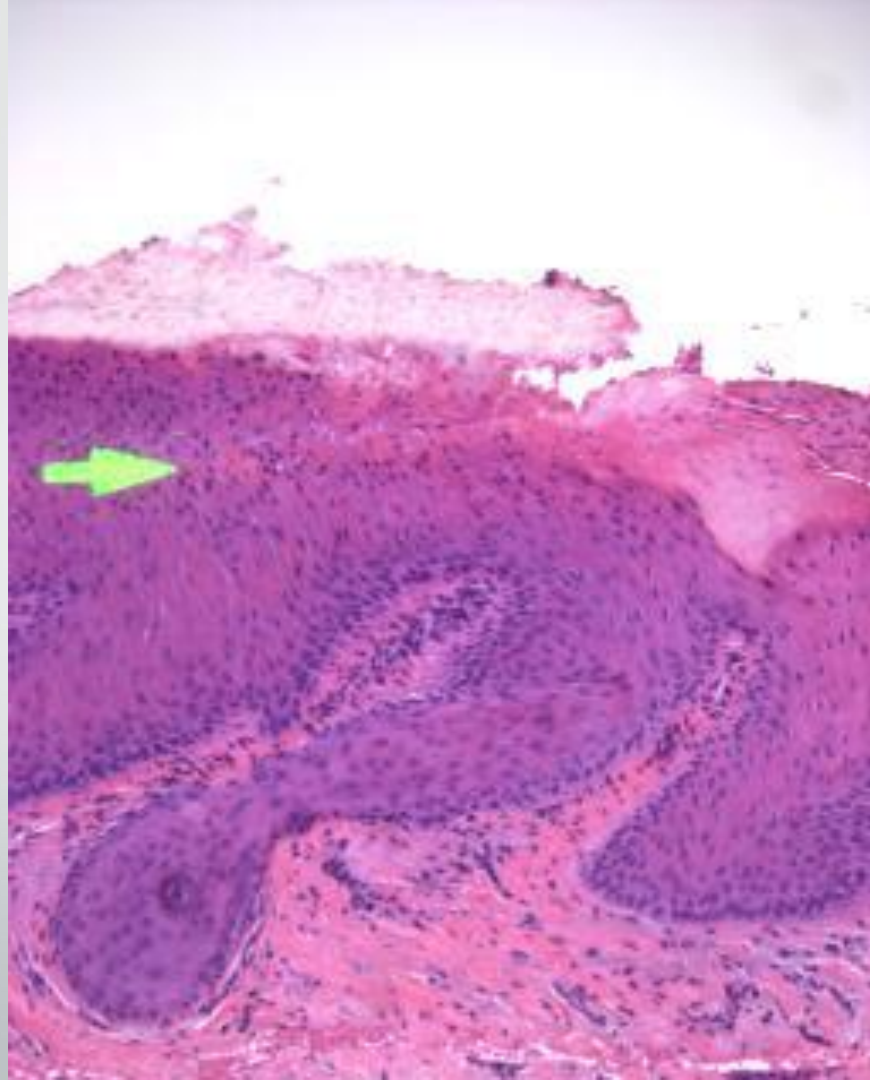
- Semantic difference
- Seborrheic keratosis is very common
- More important is to make sure this is not subtle, pigmented squamous cell carcinoma
- Onychocytic matricoma is a difficult name

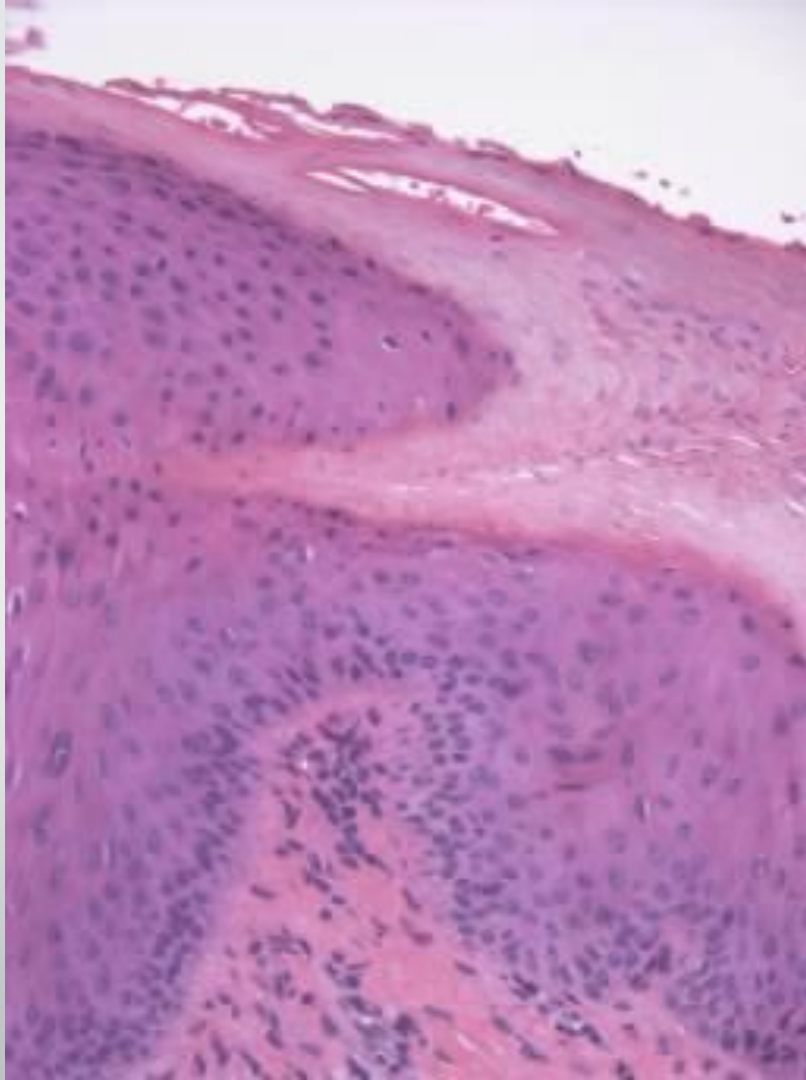
Case

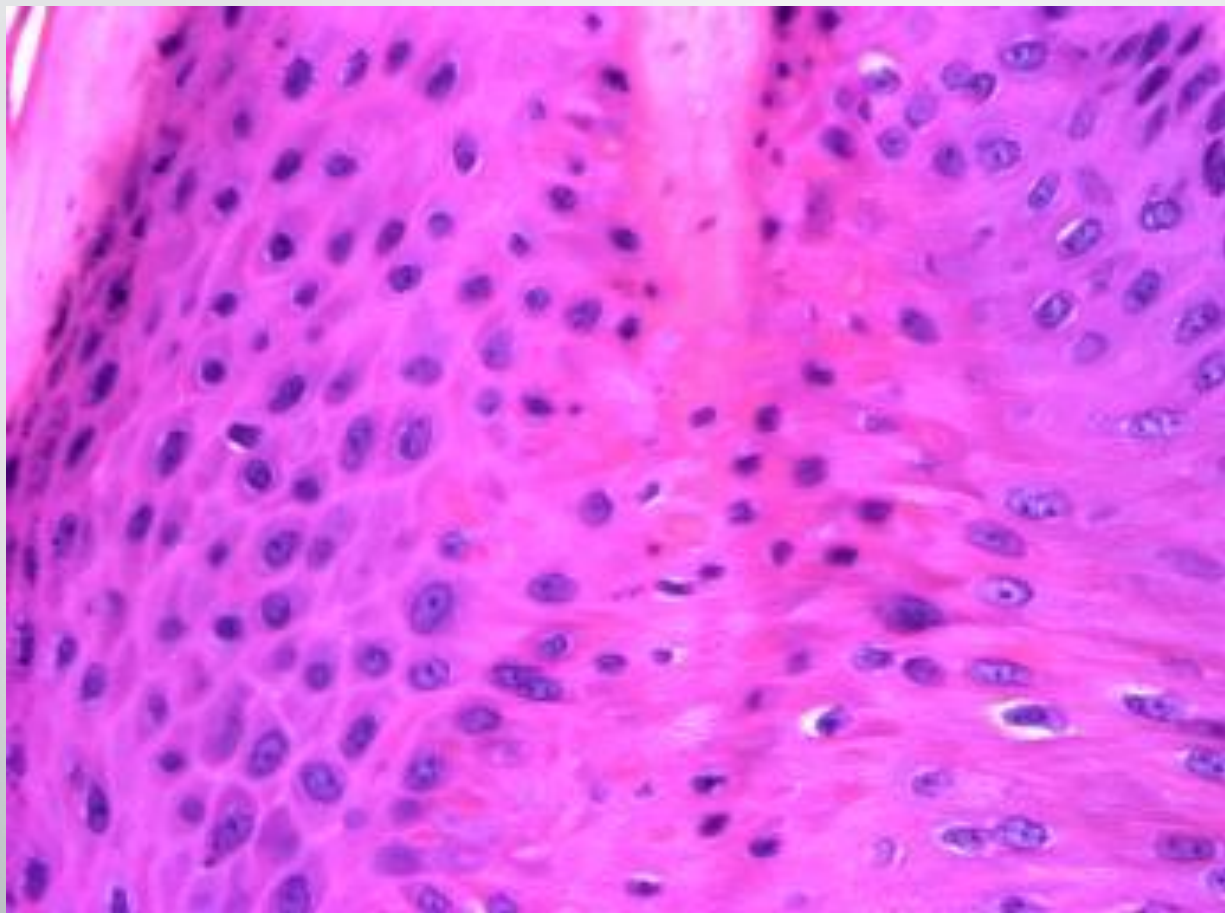
- Vaguely annular formation.



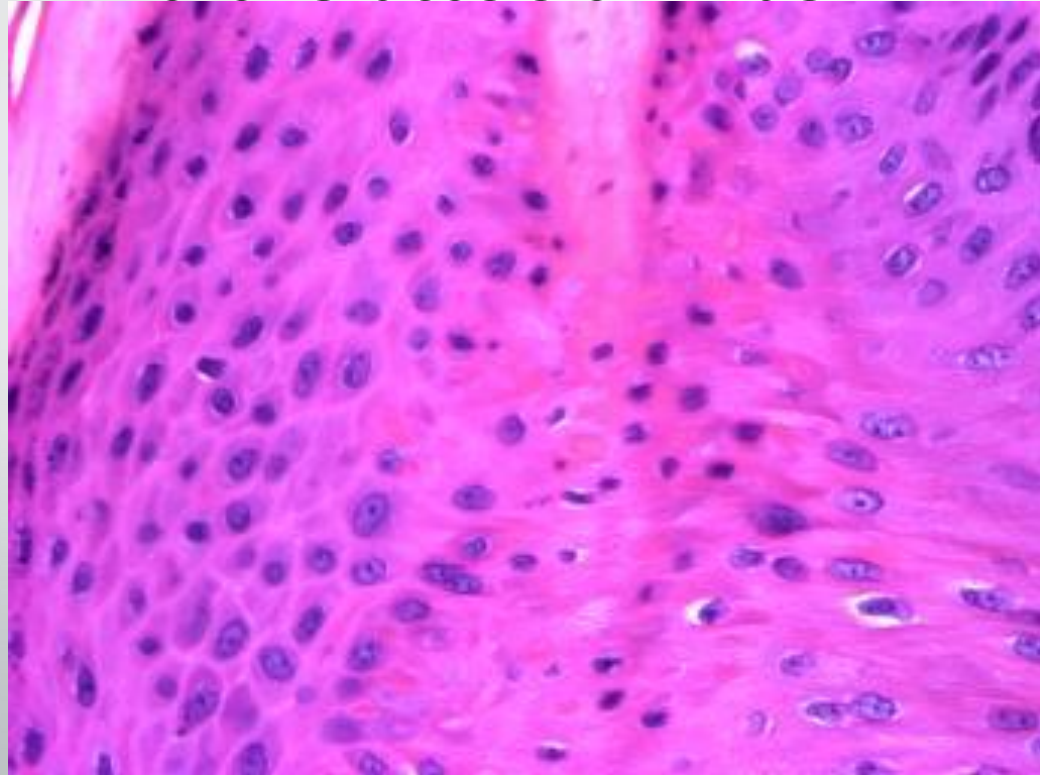
ail with pterygium







Porokeratosis of Mibelli



Nail Fungus Diagnostics

- Sampling is an issue
 - Subungual debris is better than nail plate for sampling

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Subungual debris cytopathology increases sensitivity of fungus detection in onychomycosis

[Christian S. Jordan](#), MD, PhD, [Brandon Stokes](#), CHT, [Curtis T. Thompson](#), MD  

Centrifuge (Cytospin, Fisher HealthCare)



Centrifuge with slide

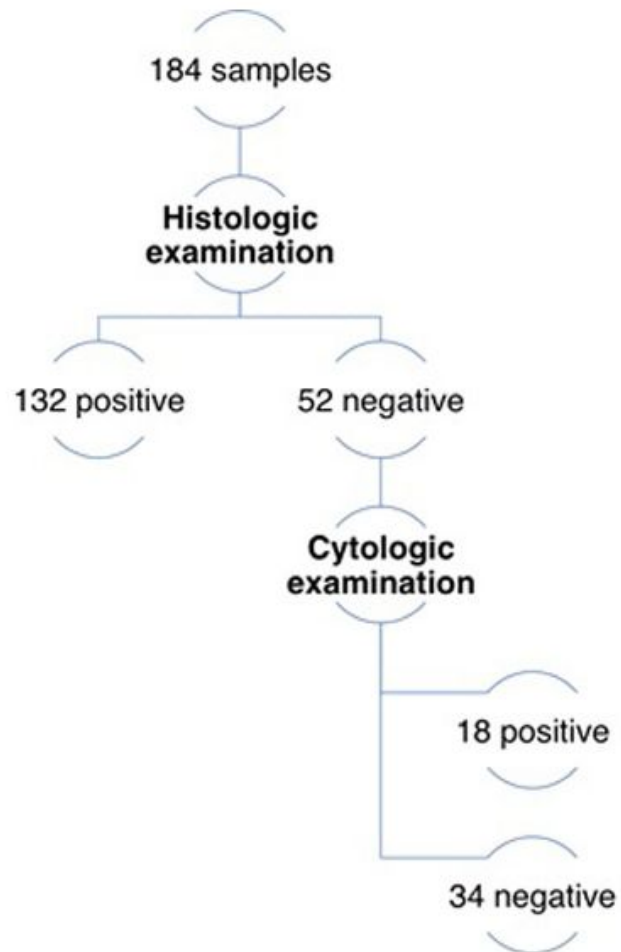


Centrifuge with slide





Fig 1. Onychomycosis. Microscopic examination of PAS-stained subungual debris. (Original magnification: $\times 400$.) Subungual debris was collected by centrifugation of the formalin in which nail clipping specimens were submitted. Microscopic examination of a thin-layer preparation of PAS-stained subungual debris reveals multiple darkly staining fungal forms associated with a single keratin aggregate.



Submit specimen dry in a small envelope

- Test nail plate first
- If plate negative, then centrifuge and PAS

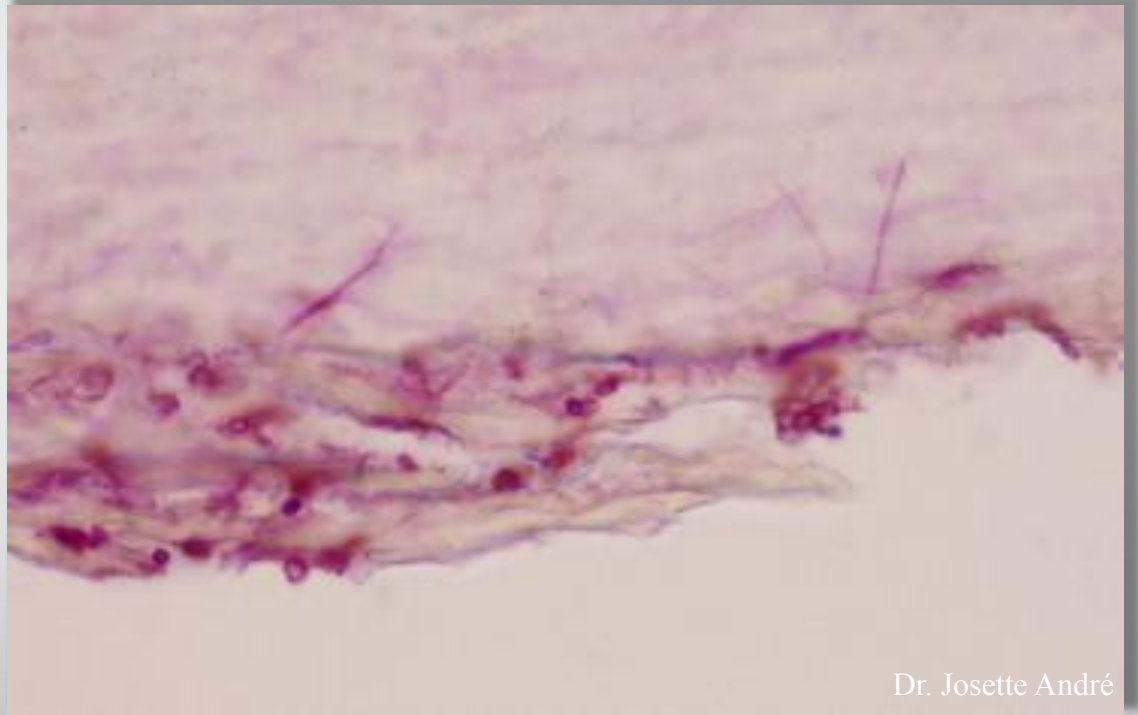


Mold



Mold vs Dermatophyte

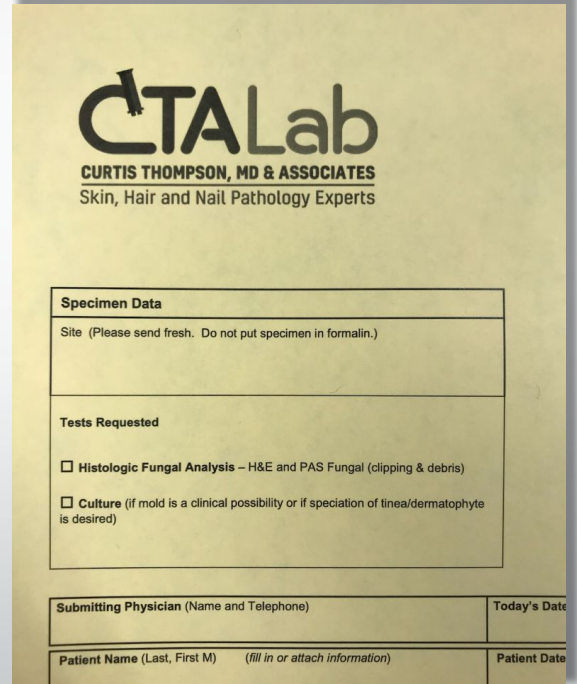
Invades vertical
to nail plate



Dr. Josette André

Mold

- Clinical suspicion
- Culture with cycloheximide-free media
 - Must notify lab of possibility



The image shows a yellow form from CTALab, Curtis Thompson, MD & Associates, Skin, Hair and Nail Pathology Experts. The form contains sections for Specimen Data, Tests Requested, and submission information.

CTALab
CURTIS THOMPSON, MD & ASSOCIATES
Skin, Hair and Nail Pathology Experts

Specimen Data	
Site (Please send fresh. Do not put specimen in formalin.)	
Tests Requested	
<input type="checkbox"/> Histologic Fungal Analysis – H&E and PAS Fungal (clipping & debris)	
<input type="checkbox"/> Culture (if mold is a clinical possibility or if speciation of tinea/dermatophyte is desired)	
Submitting Physician (Name and Telephone)	
Today's Date	
Patient Name (Last, First M) (fill in or attach information)	
Patient Date	

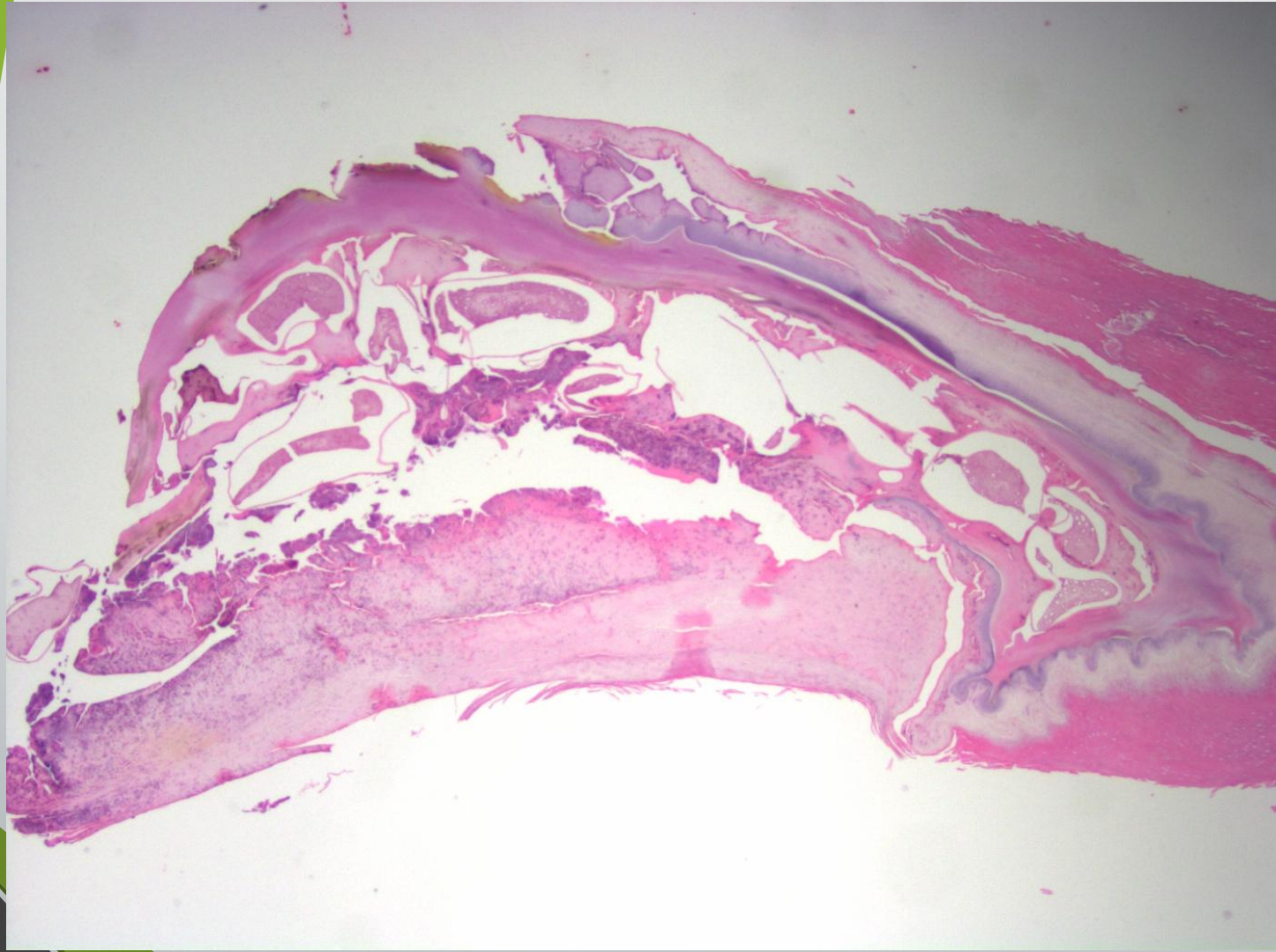
Case

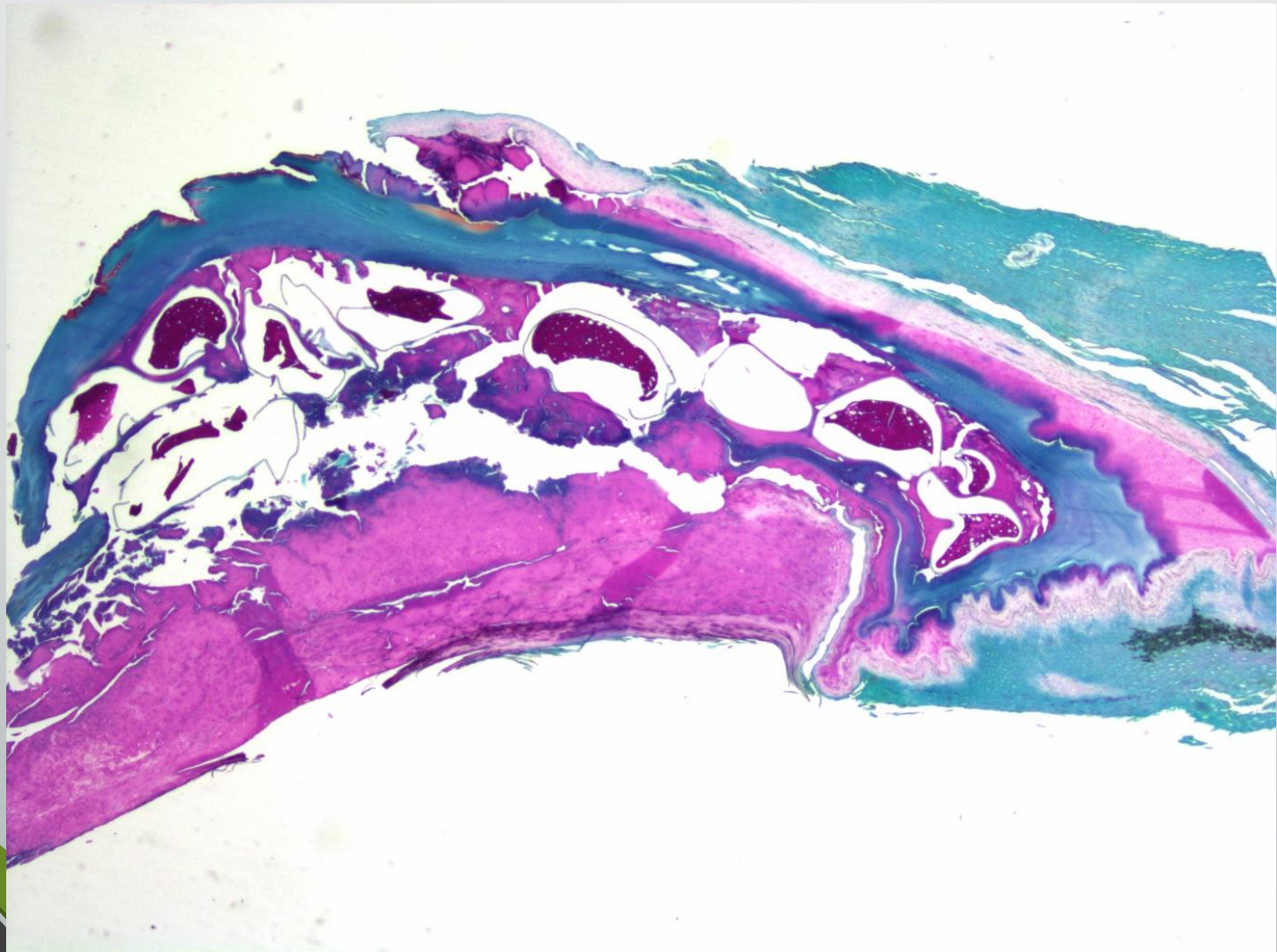
- 63 y/o female
- New lesion of right toenail.
- R/O Squamous cell carcinoma

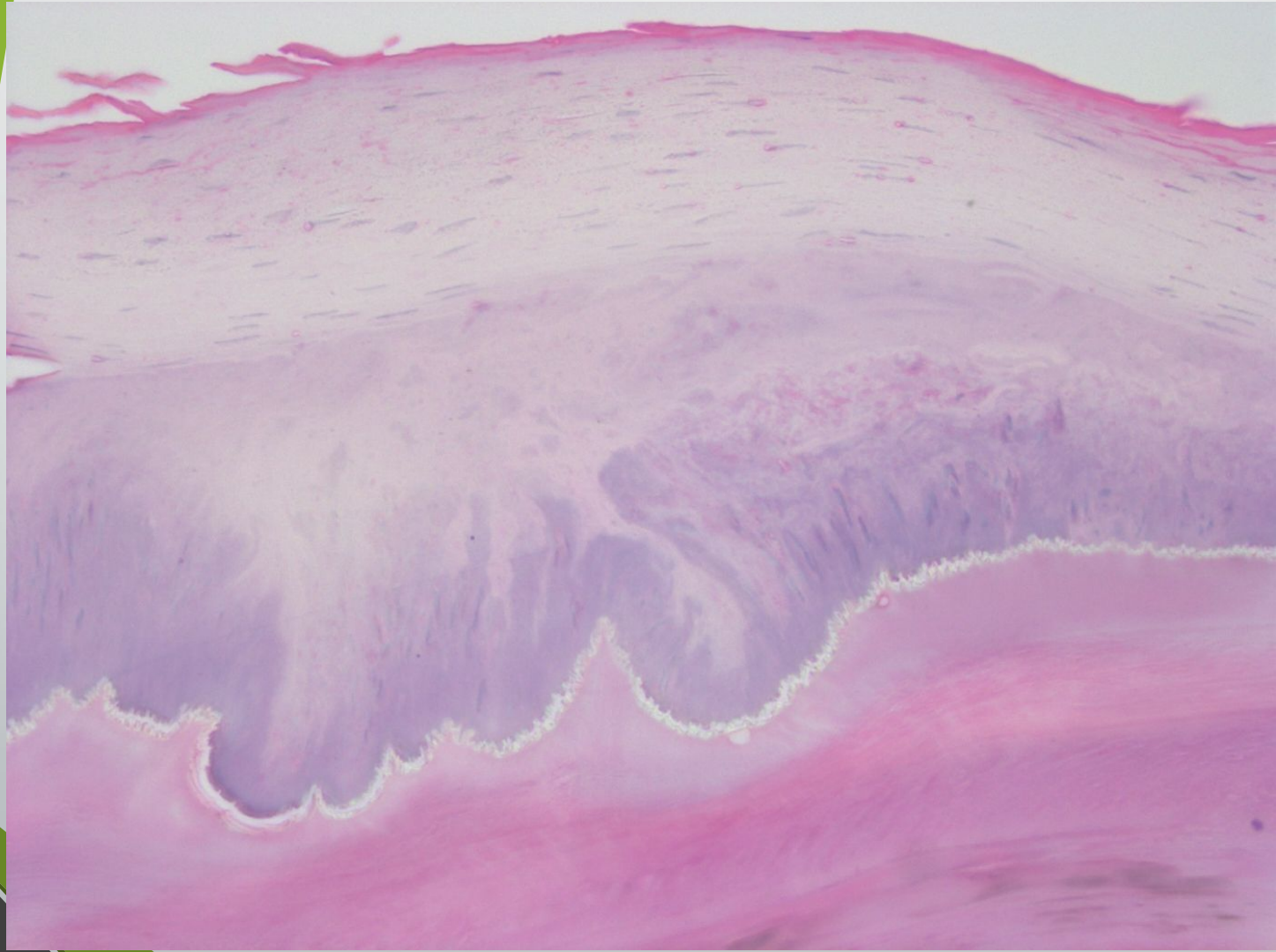
Case

- 63 y/o female
- New lesion of right toenail.
- R/O Squamous cell carcinoma

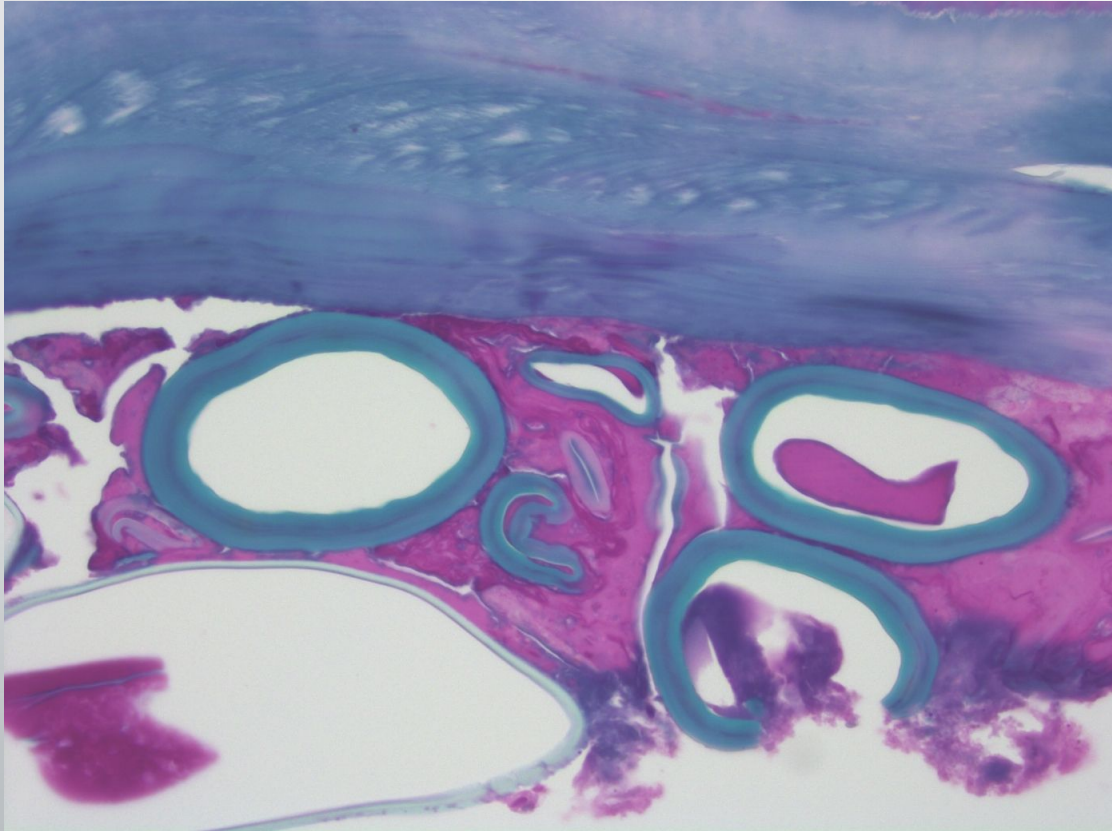
Recent travel to Africa







Tungiasis



Acknowledgements

- Phoebe Rich, Antonella Tosti and Martin Zaiac
- Josette André and Bertrand Richert — Brussels
- Brandon Stokes — Portland

Thank you!

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