Basics of Nail Pathology

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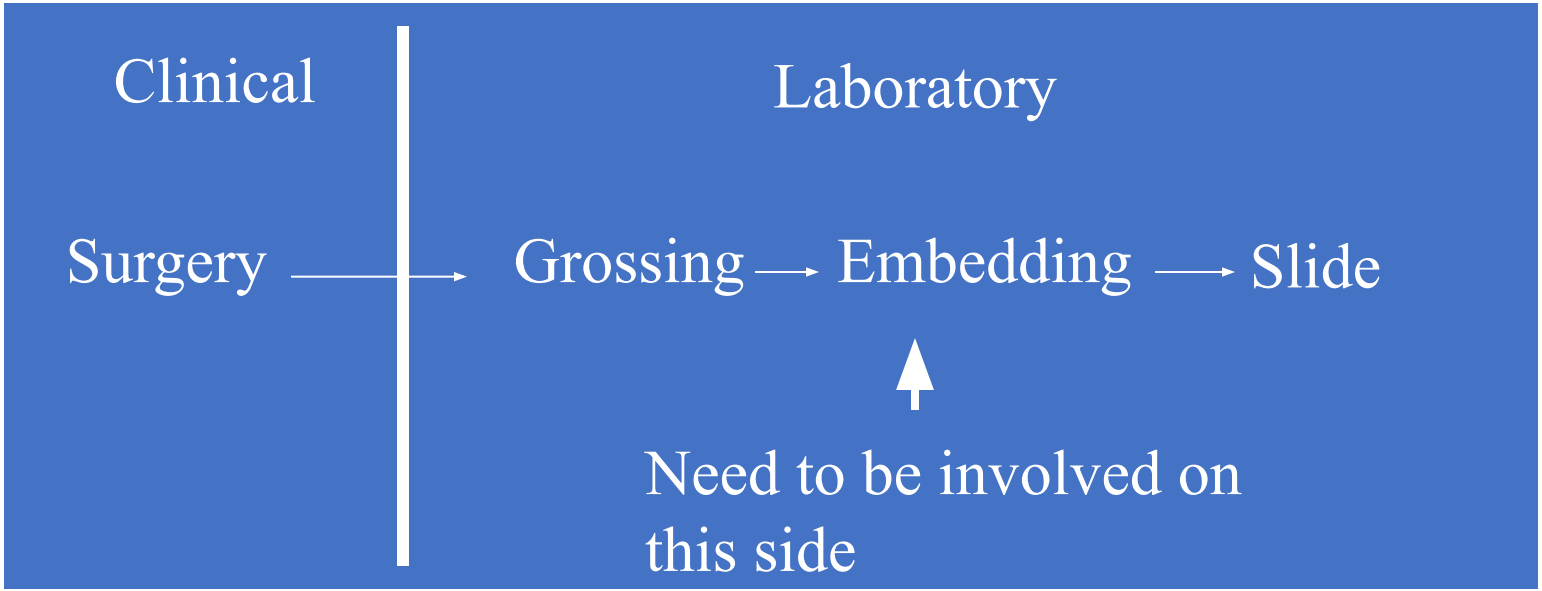
SKIN, HAIR AND NAIL EXPERTS

Objectives

- How/where to biopsy
- How to submit to laboratory
- Laboratory processing
- Special stain utility
- Fungal diagnostics

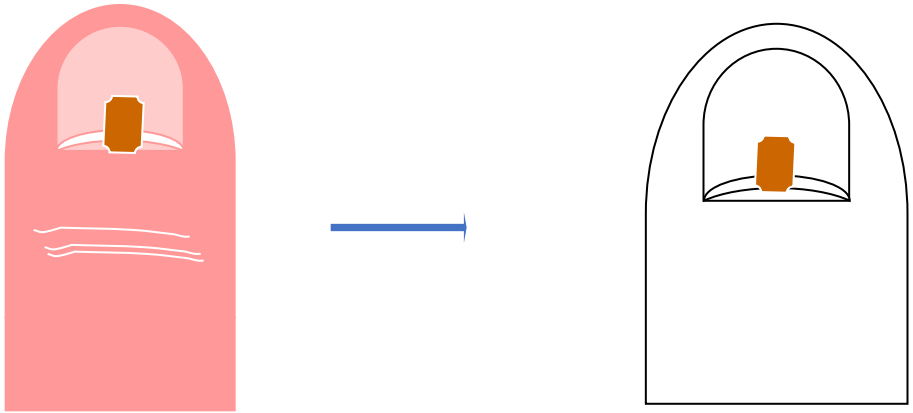
What can the nail surgeon do to submit a bed/matrix specimen for appropriate interpretation?

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

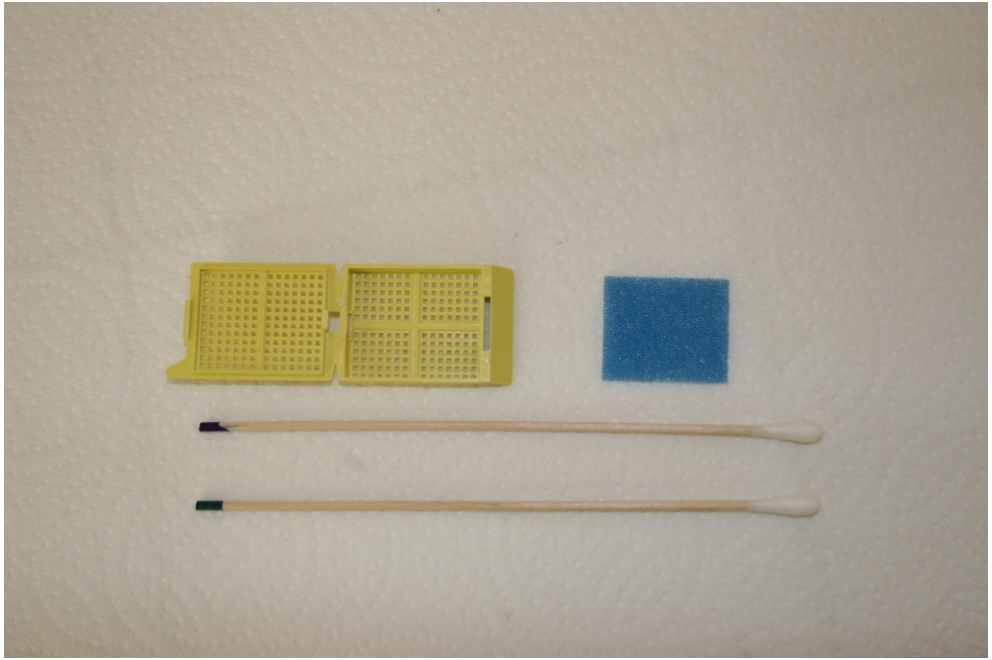


Nail cartoon


Courtesy of Dr. Phoebe Rich

Print template at www.ctapathology.com

Histology Materials



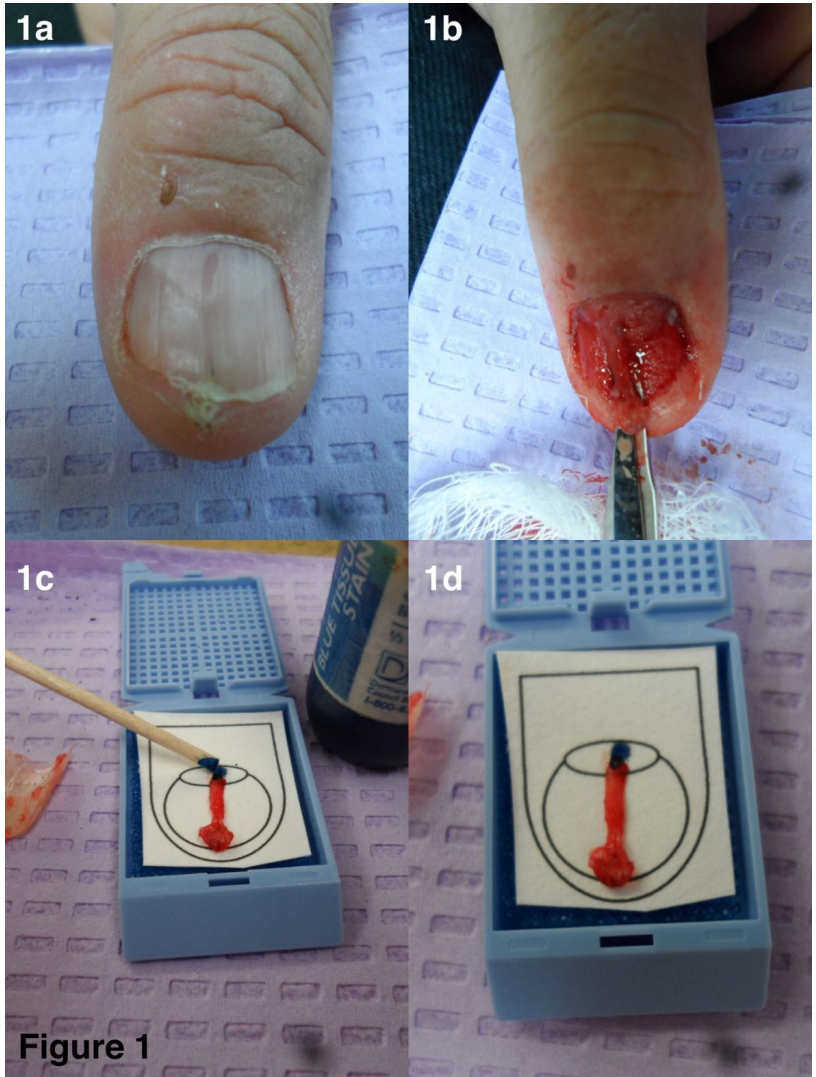


Figure 1

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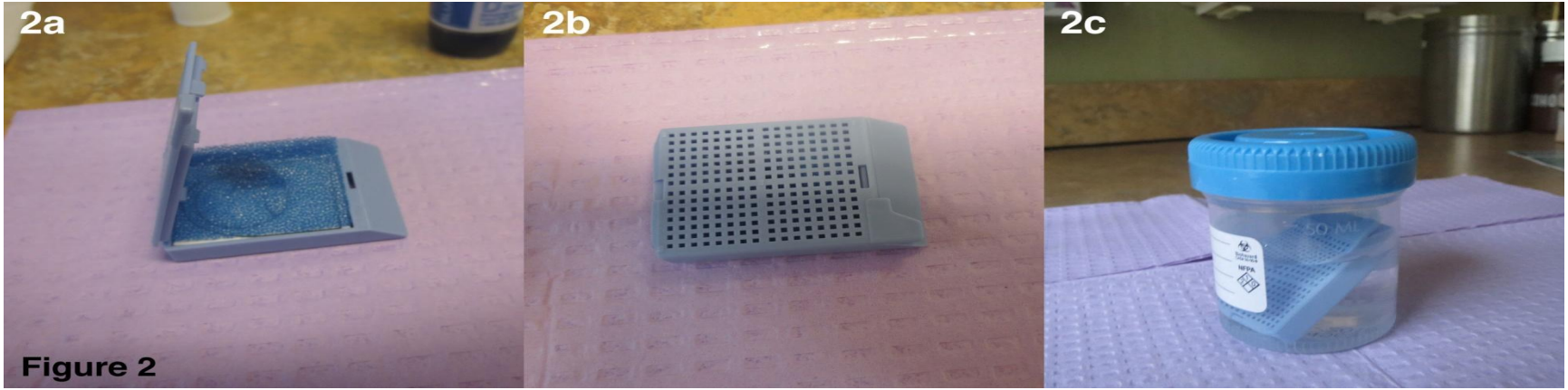
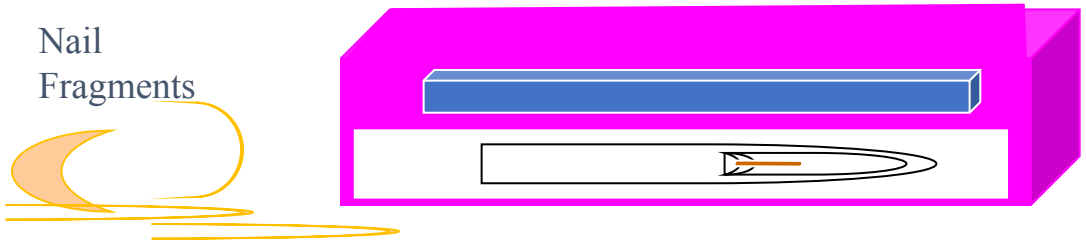

2a
2b
2c
Figure 2

10% formalin

Nail
Fragments



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 fungal testing

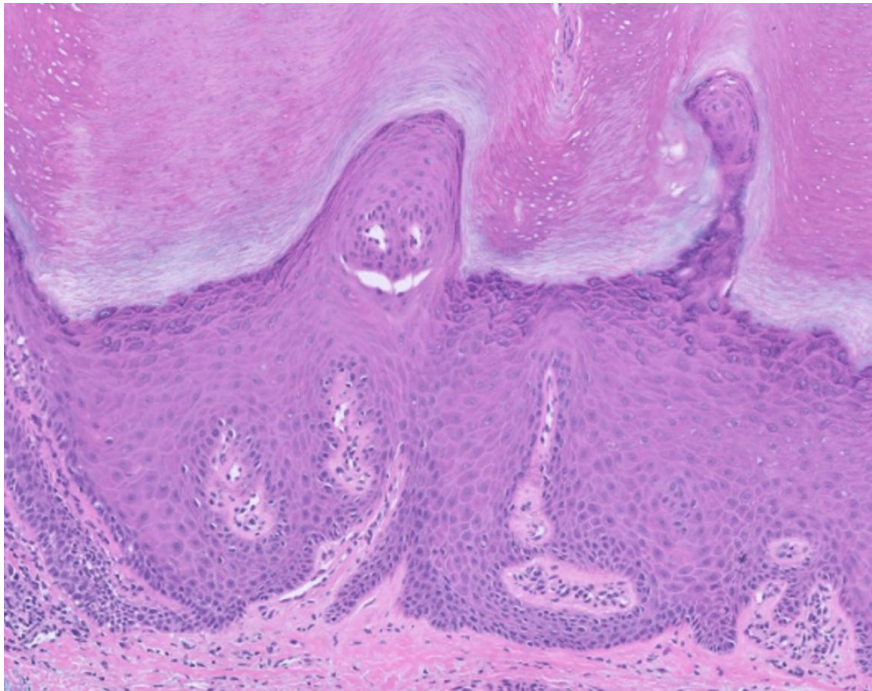
Finding the pigment

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

Neoplasms

- Squamous
  - HPV-related
  - Benign and malignant “Onycho”
- Melanocytic
- Soft tissue
  - Vascular
  - Spindle cells

Squamous neoplasms
HPV benign and malignant



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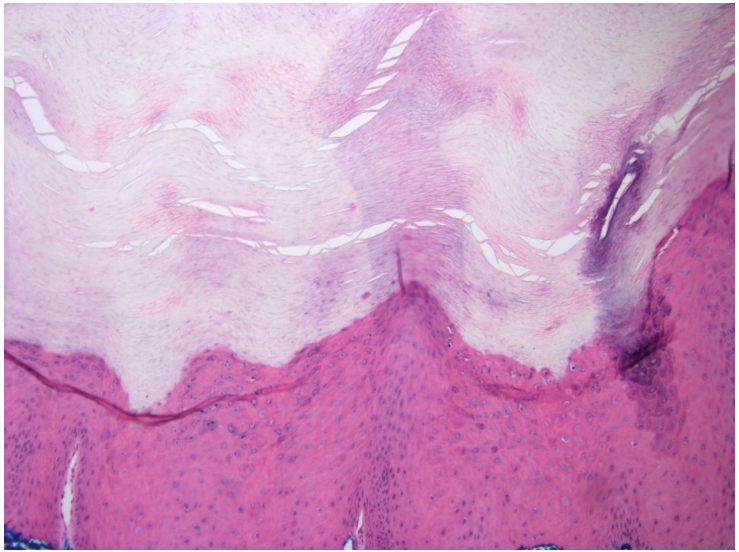
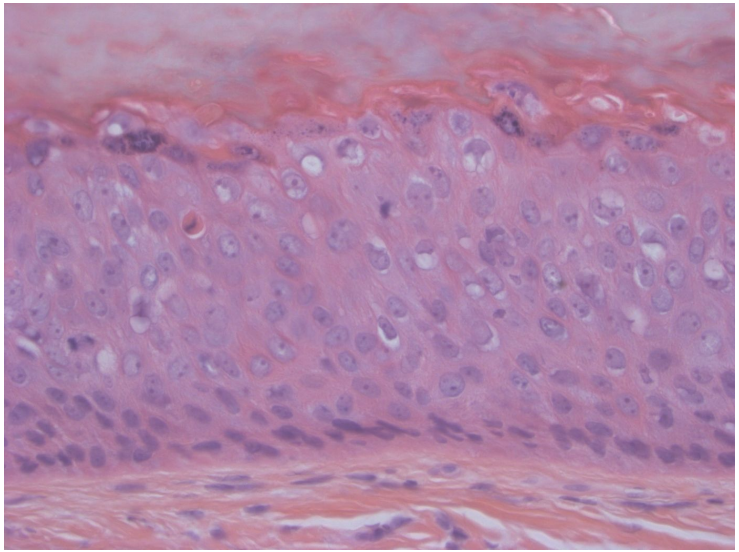
Squamous neoplasms
HPV benign and malignant



Verruca



SCC

Squamous cell carcinoma

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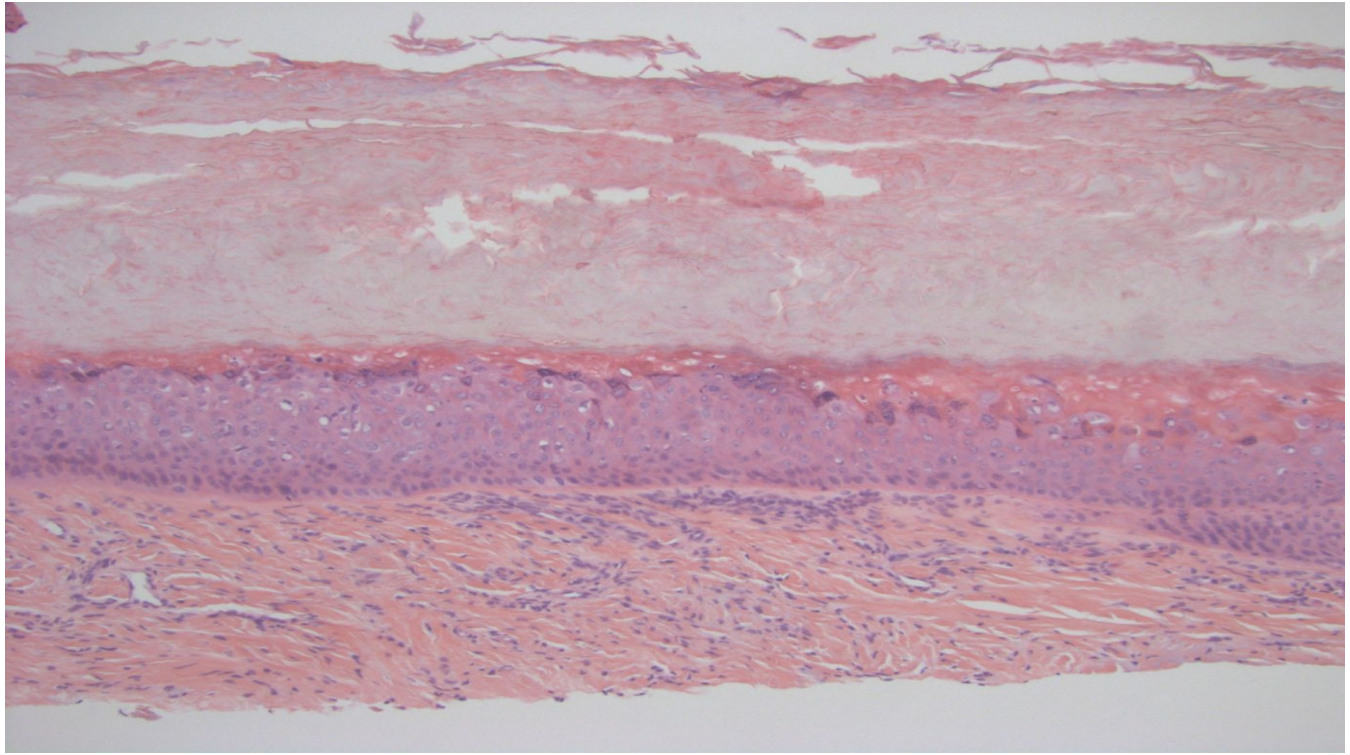
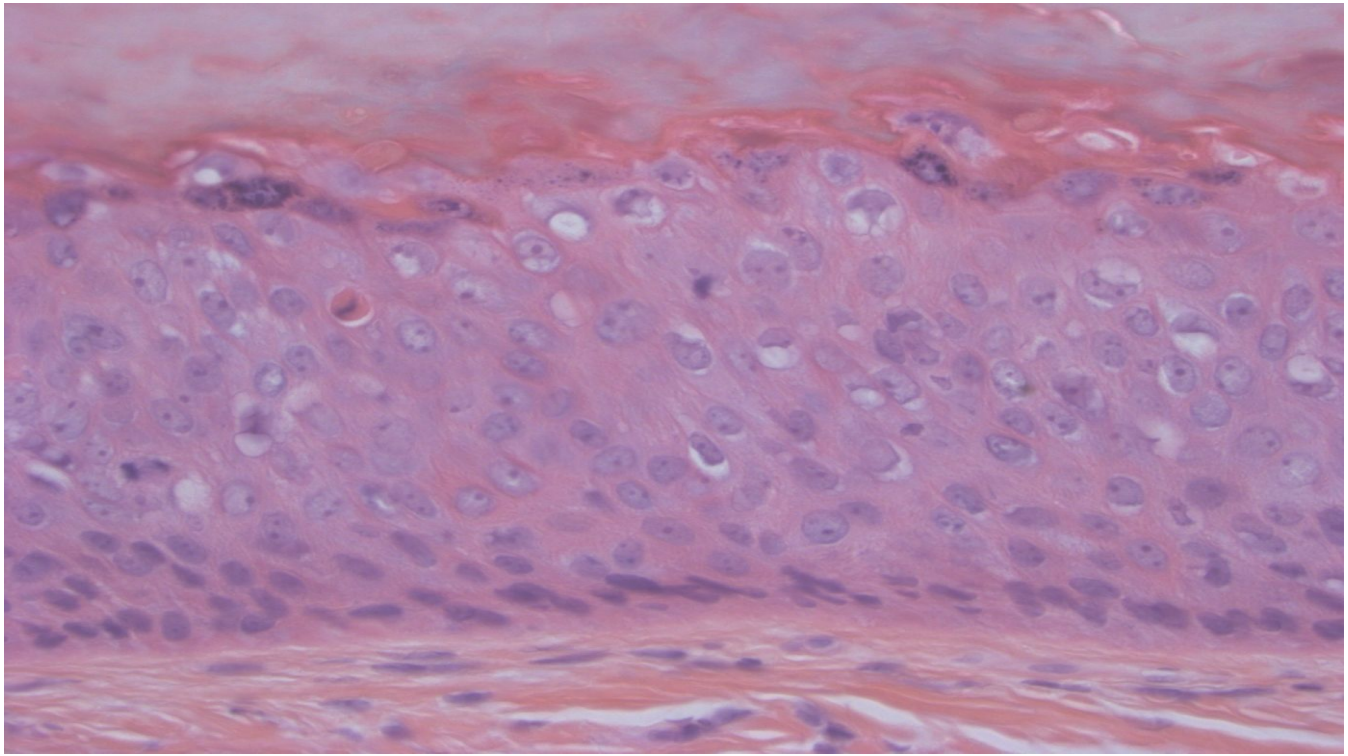
Squamous cell carcinoma

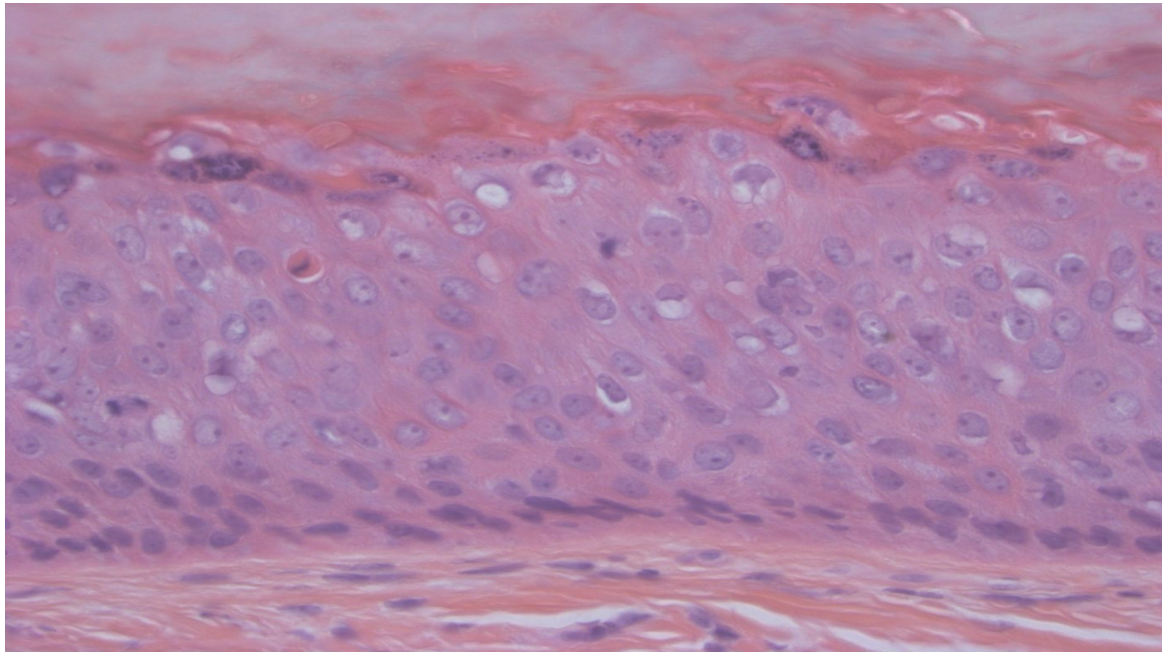


Squamous cell carcinoma in-situ

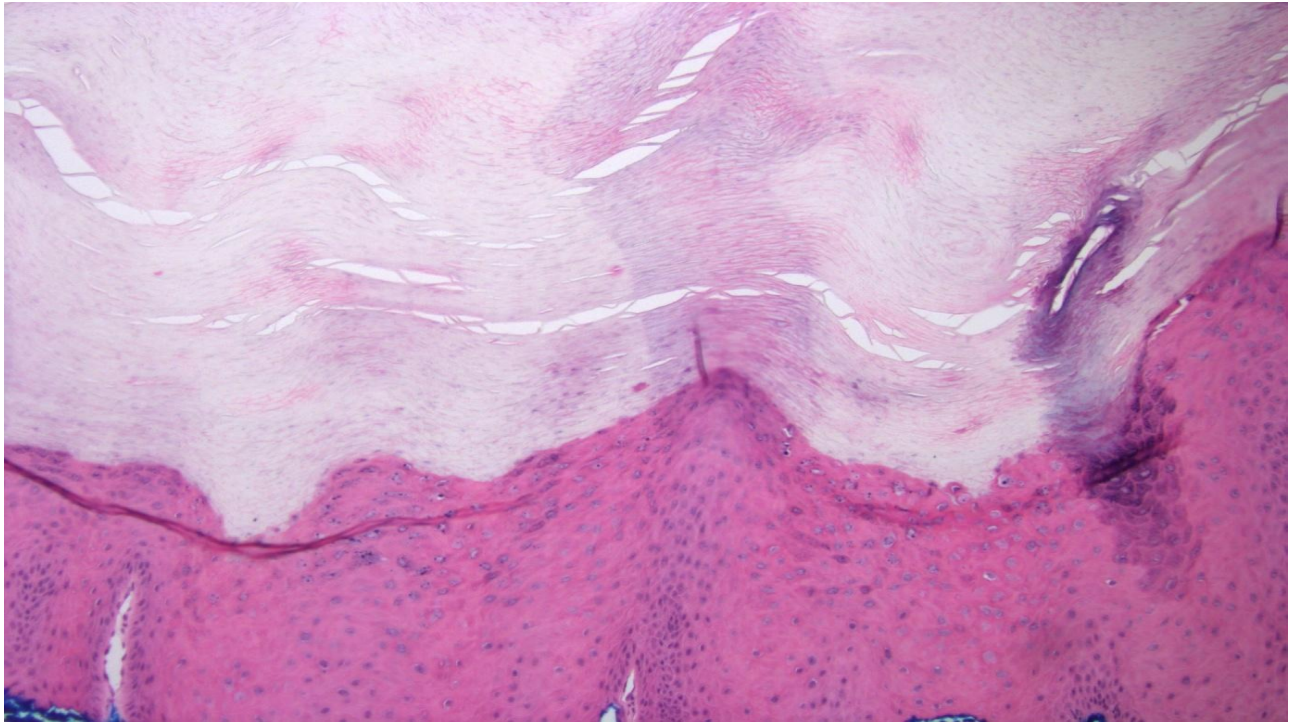


Squamous cell carcinoma in-situ

- Human Papillomavirus (HPV) features



SCC versus Wart/Verruca



SCC versus Wart/Verruca

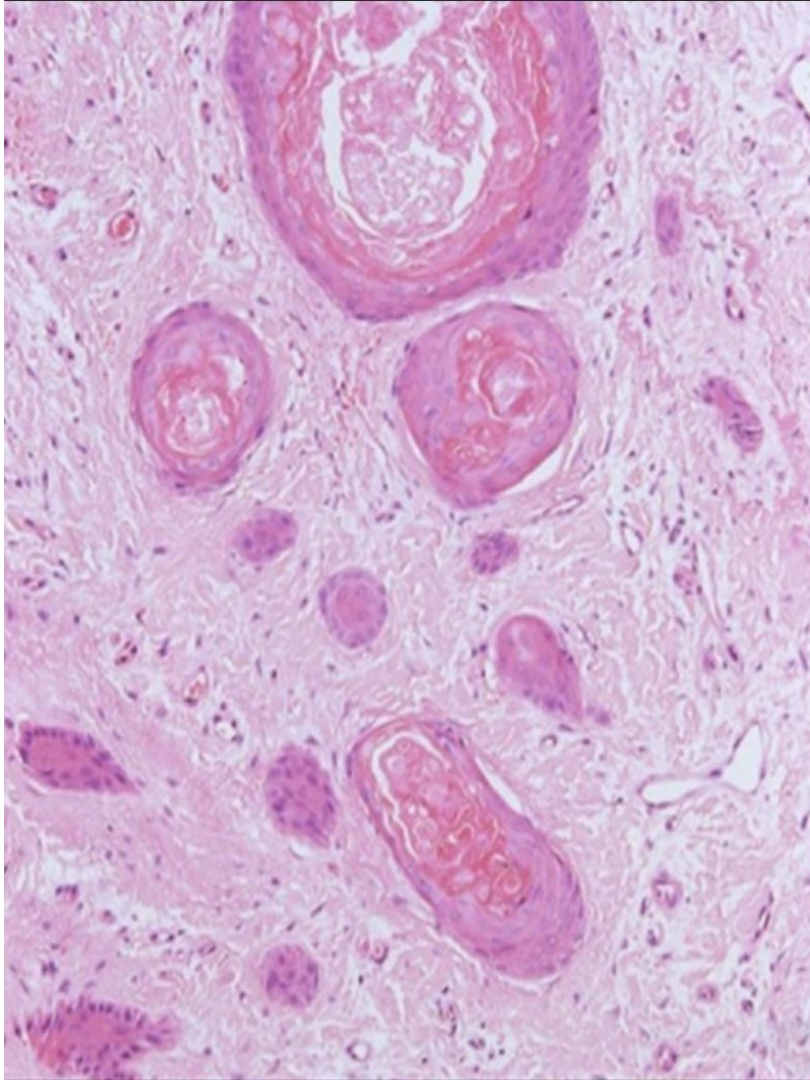
- Clinical correlation often necessary
  - Immunosuppression (esp HIV)
  - If it is destroying bone, it is not benign!
  - Sample more if suspicious

HPV In-situ Hybridization (ISH)

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

Benign squamous inclusions/cyst

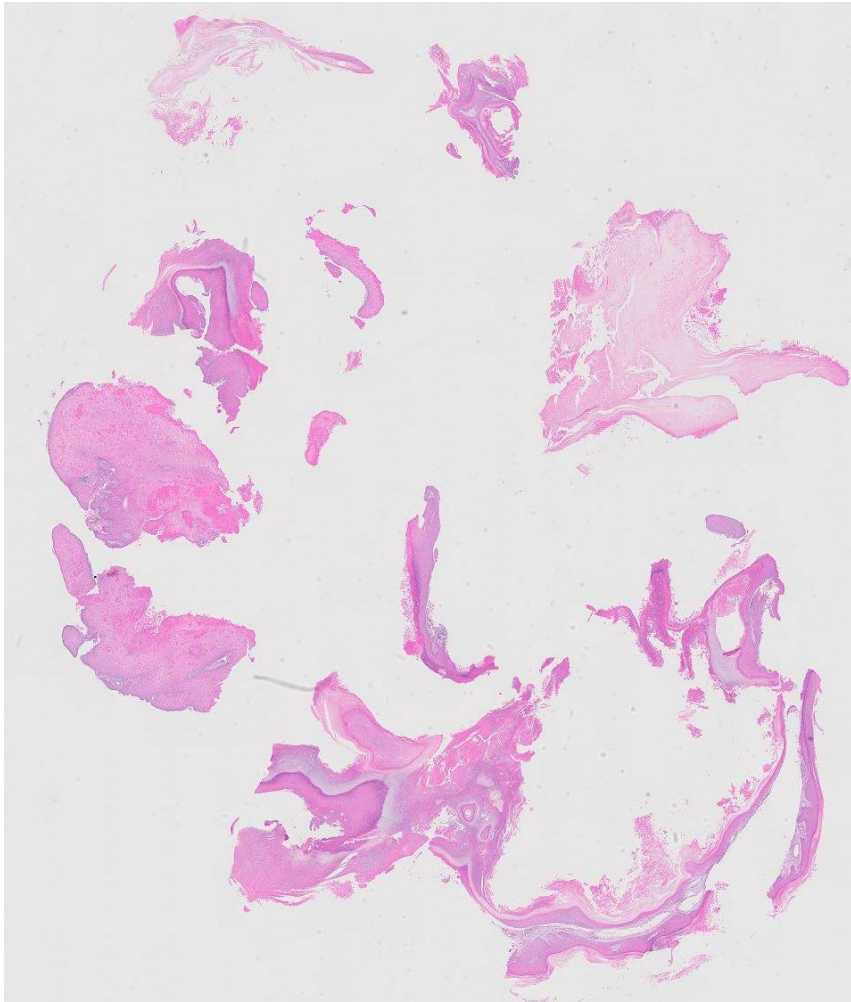
Not squamous cell carcinoma



64 y/o male

- Rapidly enlarging nodule in fingernail for one month
- All other nails normal

64 y/o male



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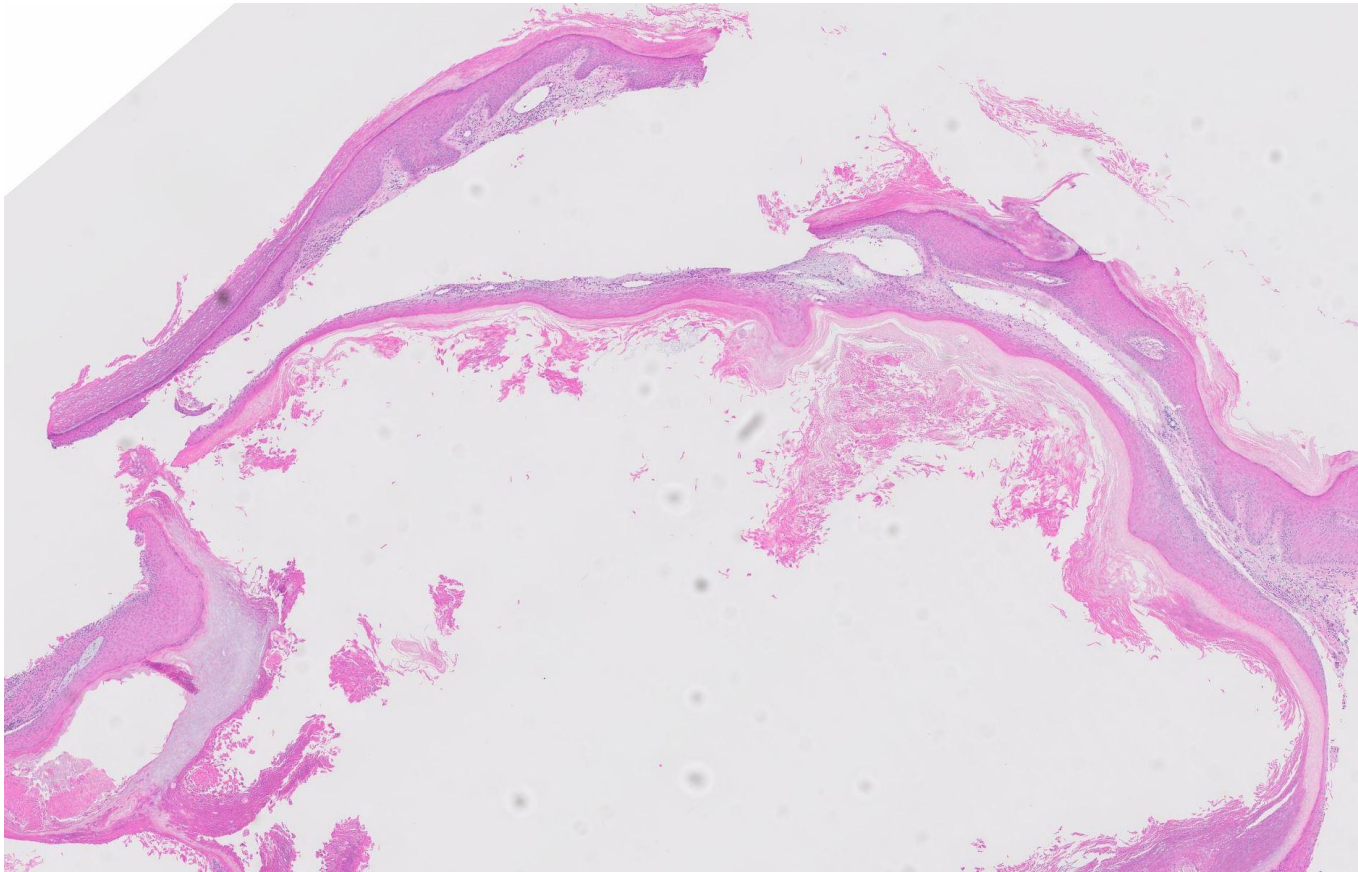
64 y/o male



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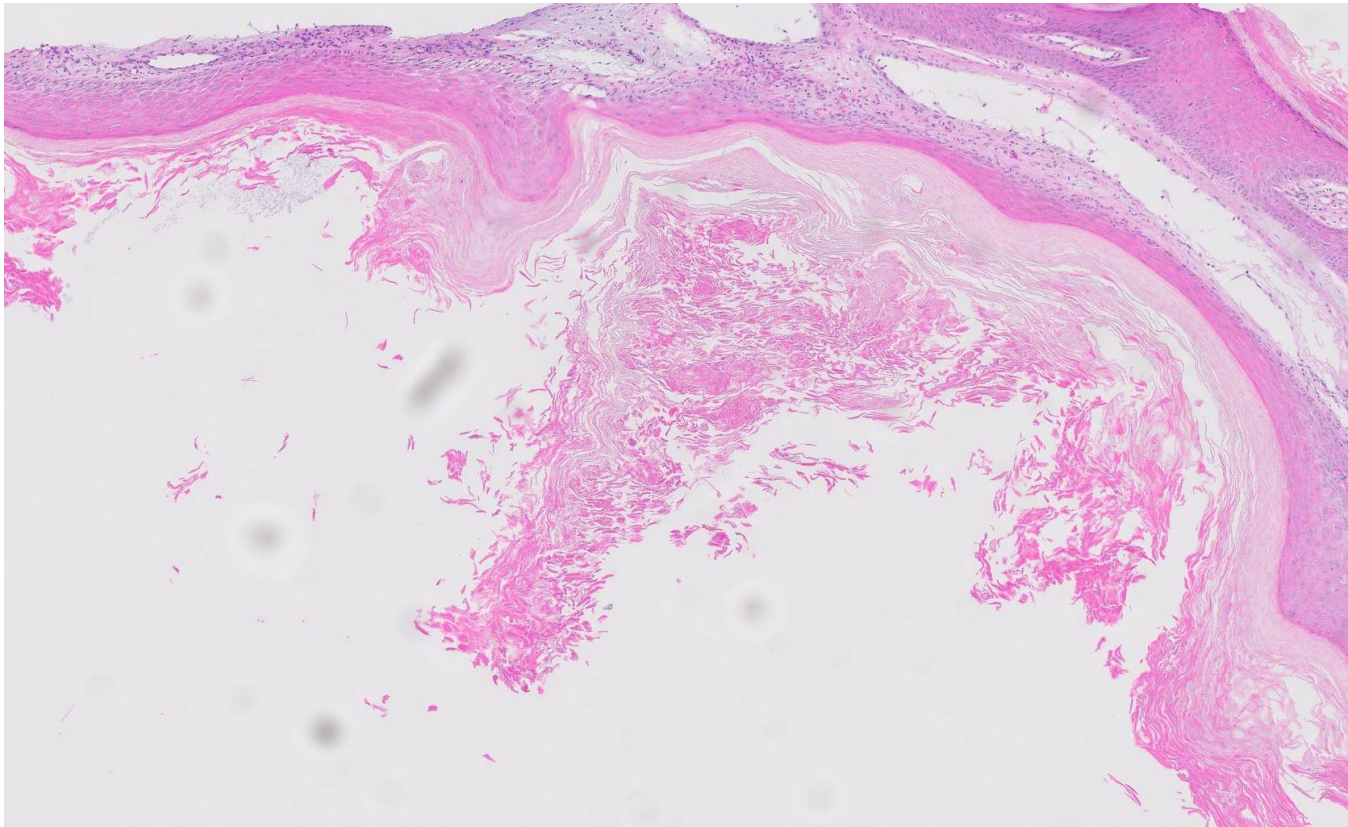

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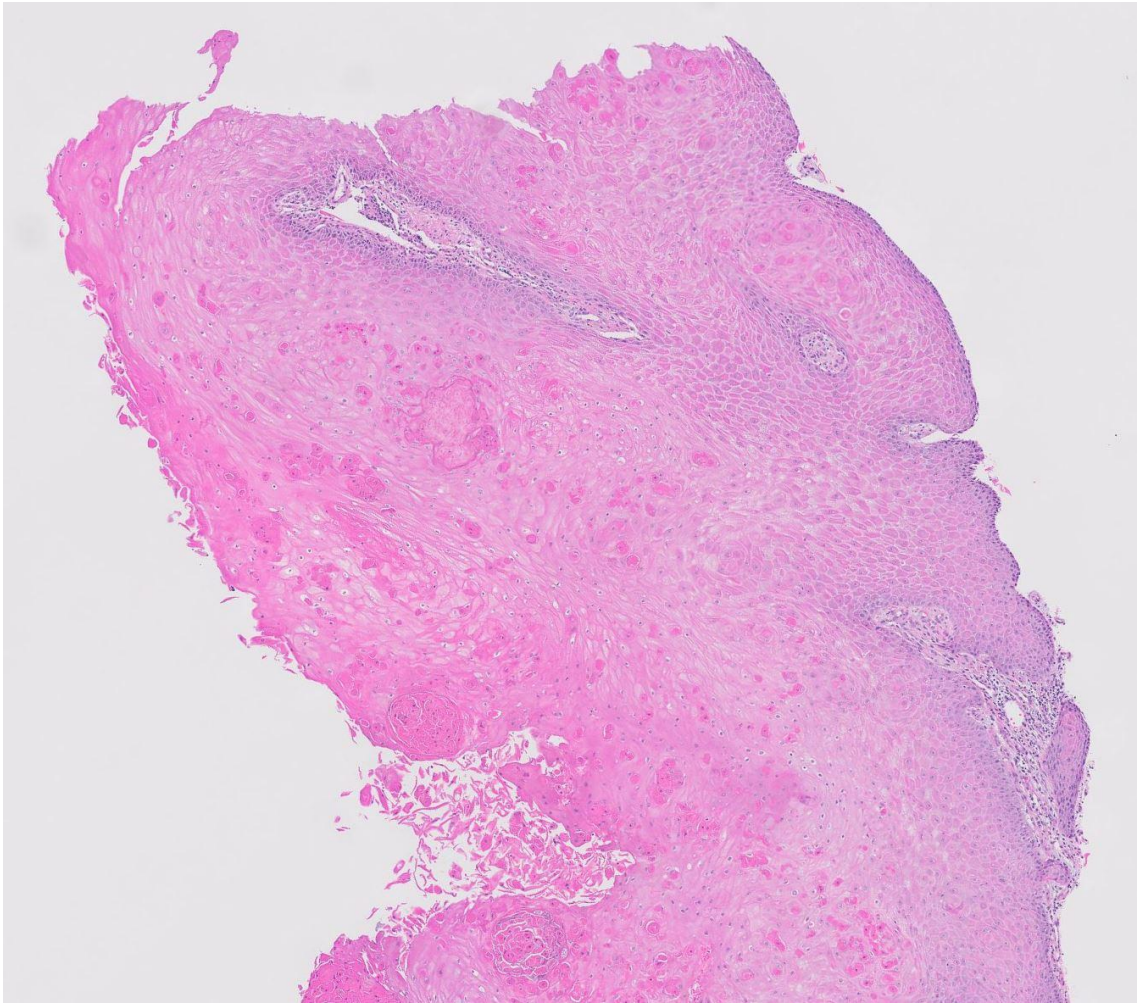

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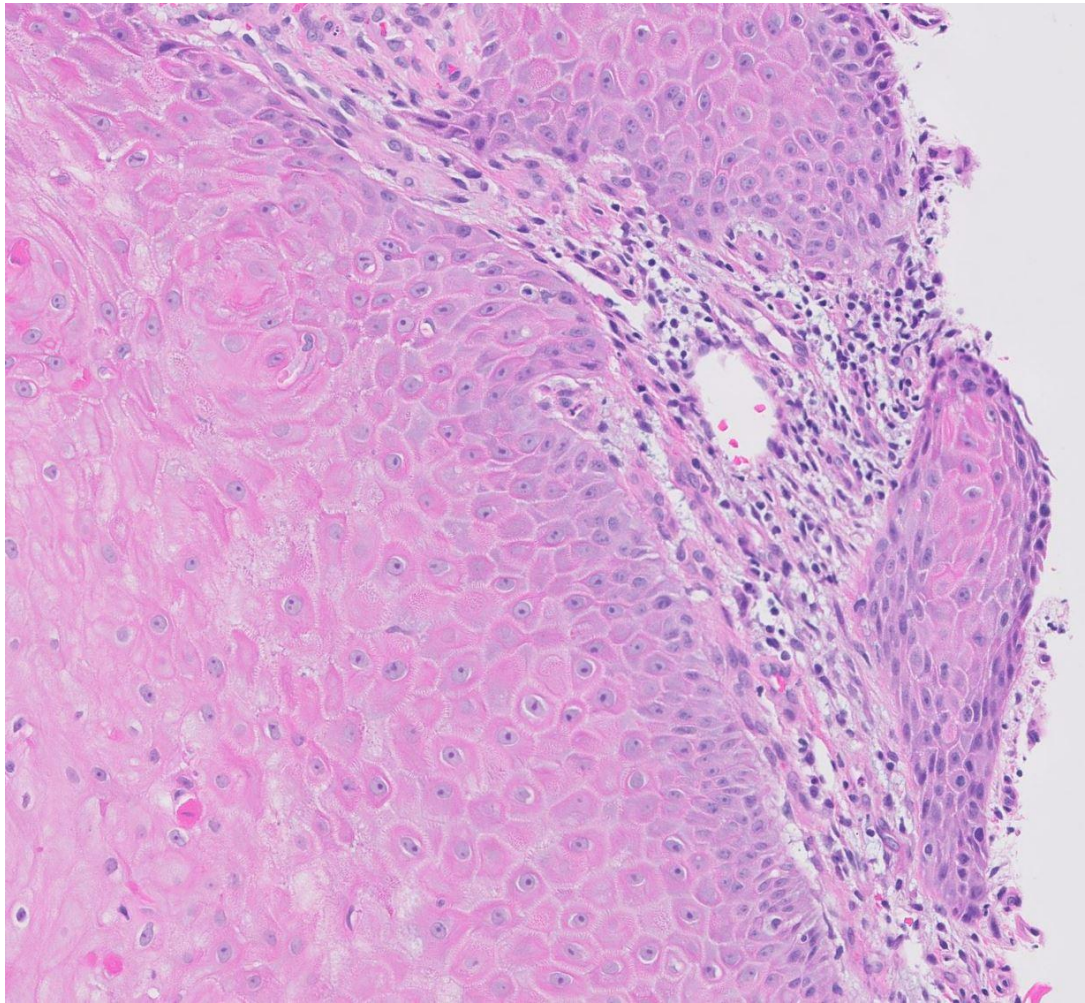

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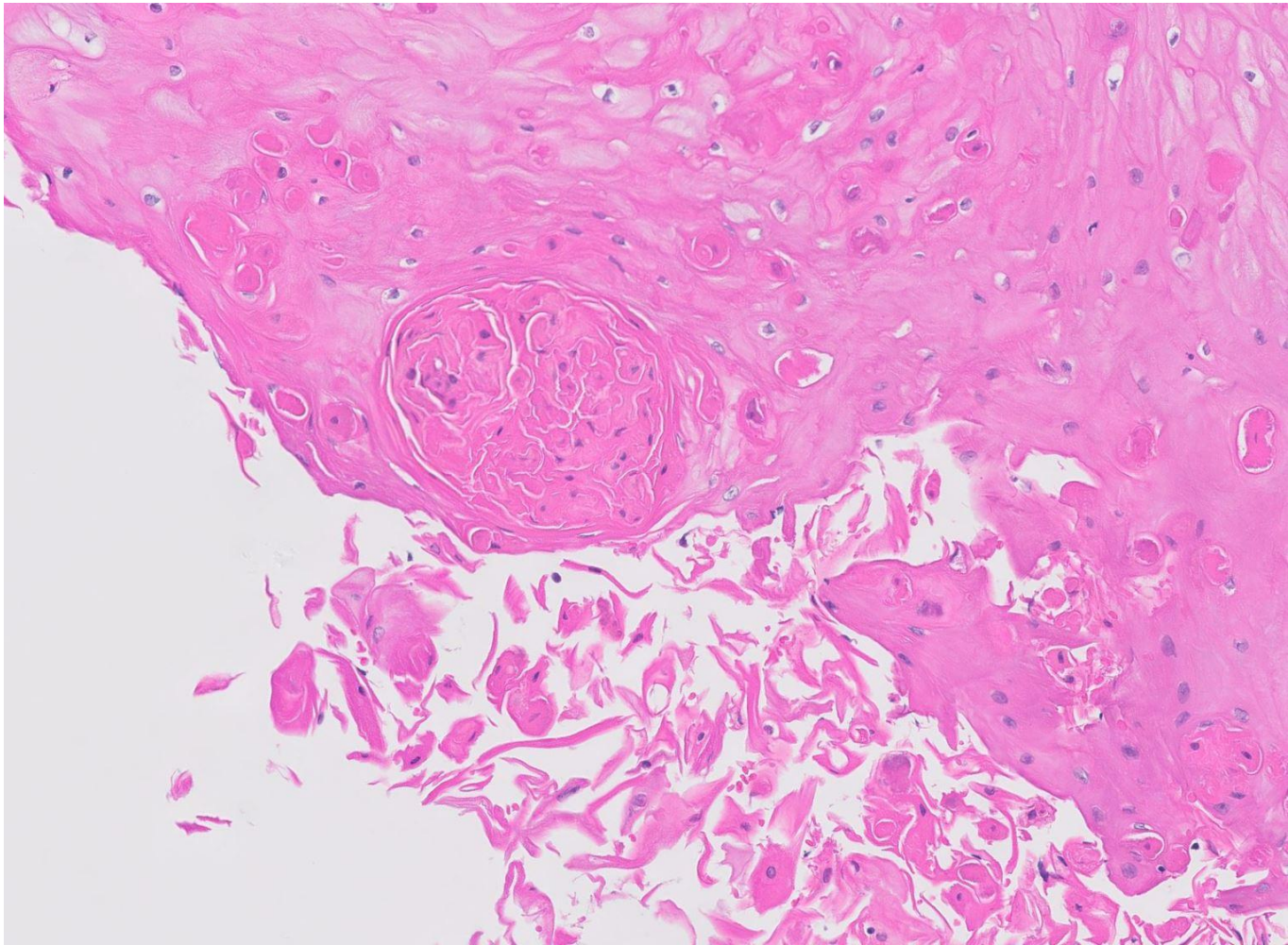
64 y/o male



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Subungual Keratoacanthoma

- Similar to the keratoacanthoma-type of SCC elsewhere
- Destroys bone and does not regress but otherwise not aggressive
- Biopsy is curative

Subungual Keratoacanthoma

- Initial biopsy is curative

- Calling squamous cell carcinoma often leads to an unnecessary amputation

Subungual Keratoacanthoma

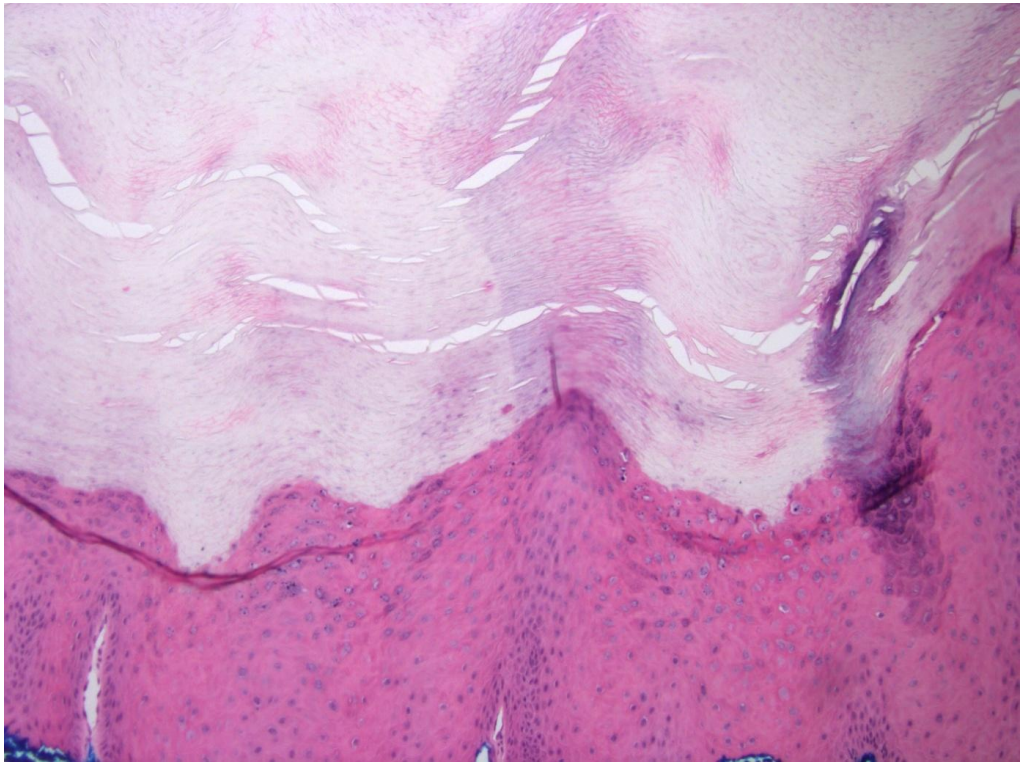
- Crateriform squamous proliferation with abundant keratin and parakeratotic foci
- Minimal keratinocytic atypia
- Variable mixed inflammatory cell infiltrate with intraepithelial neutrophils and surrounding lymphocytes, plasma cells and sometimes eosinophils

Subungual Keratoacanthoma

- Differential
  - Verruca
  - Squamous cell carcinoma of the nail unit
  - Nail bed inclusions
  - Onycholemmal cyst
  - Subungual tumor of incontinentia pigmenti

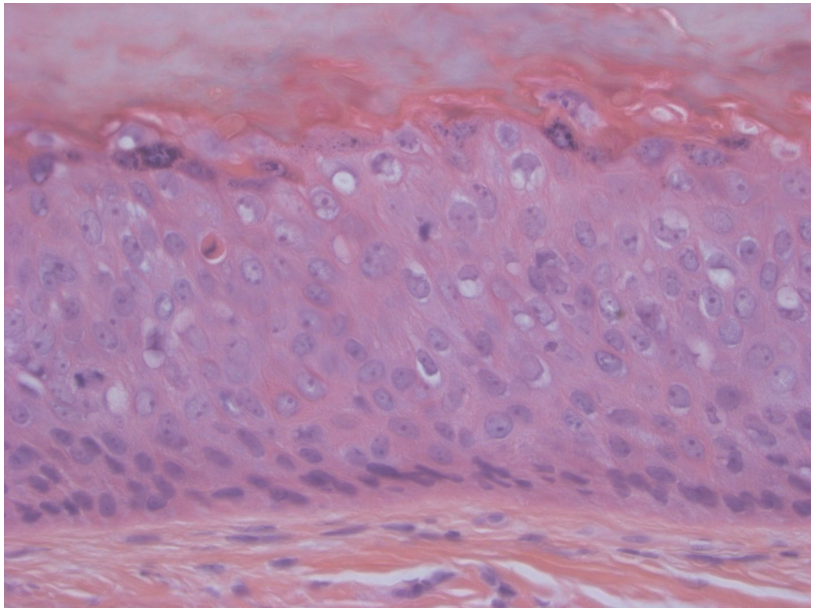
Subungual Keratoacanthoma Differential

- Verruca or SCC
  - Both HPV



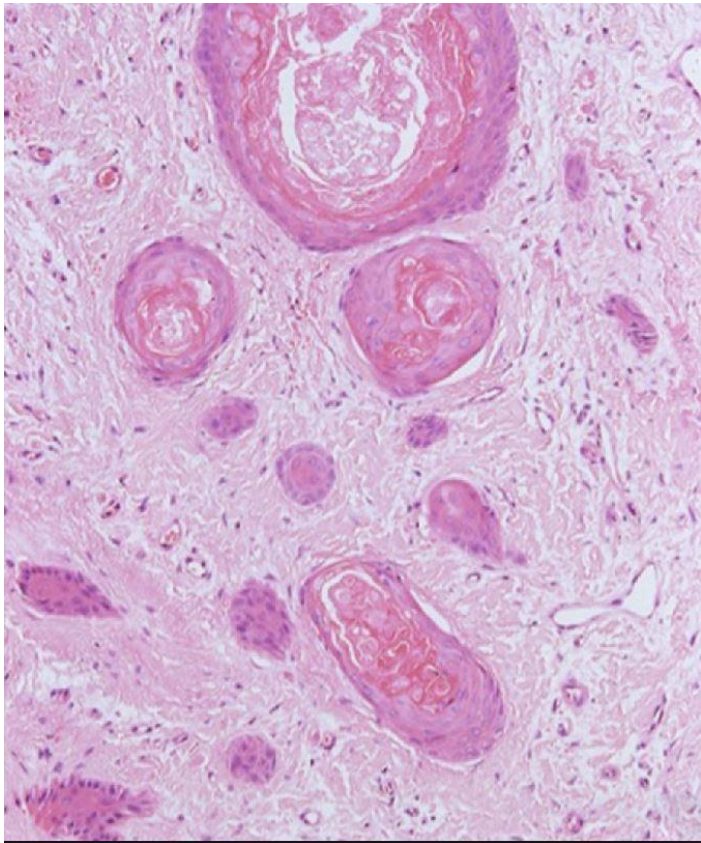
Subungual Keratoacanthoma Differential

- Verruca or SCC
  - Both HPV
  - Sampling important



Subungual Keratoacanthoma Differential

- Nail bed inclusions
- Onycholemmal cyst
  - Likely result of trauma



Martin B. Nail histopathology. Actas Dermosifiliogr 104:564-78, 2013

Subungual Keratoacanthoma Differential

- Subungual tumor of incontinentia pigmenti (IP)
  - Suspect if young female
  - May be first presentation

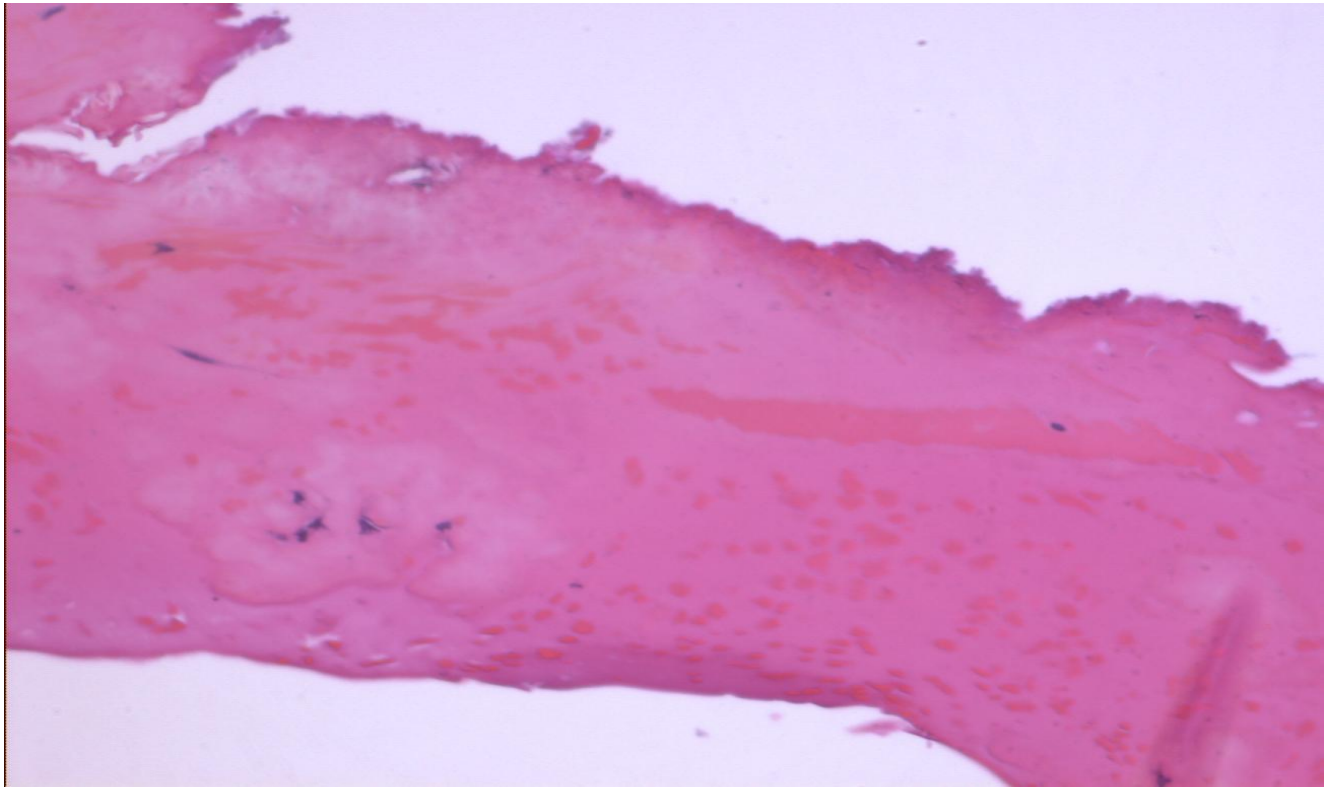
of IP in mosaic cases

What is the source of the pigment?

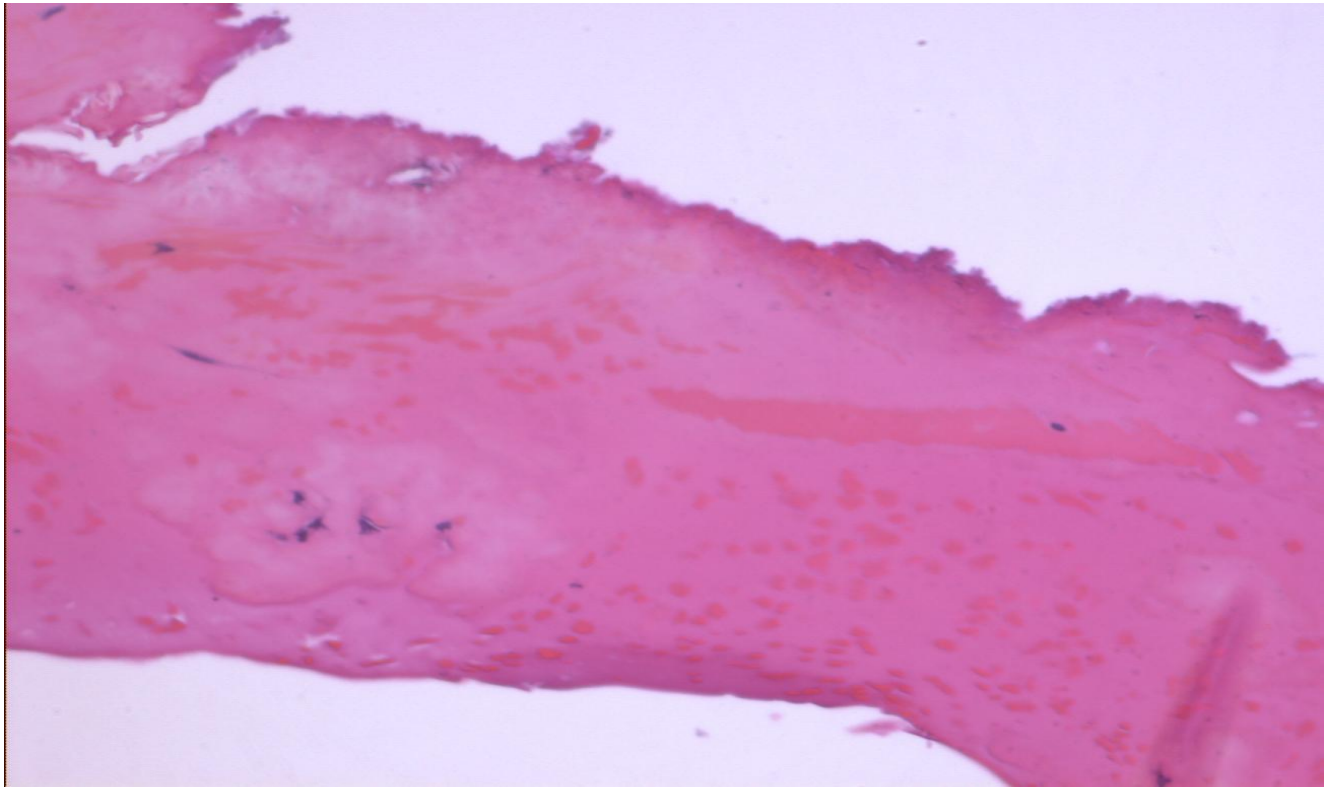
What is the source of the pigment?

- Melanocytic neoplasm
  - Benign
  - Malignant
- Melanocyte ‘activation’

Blood in nail plate



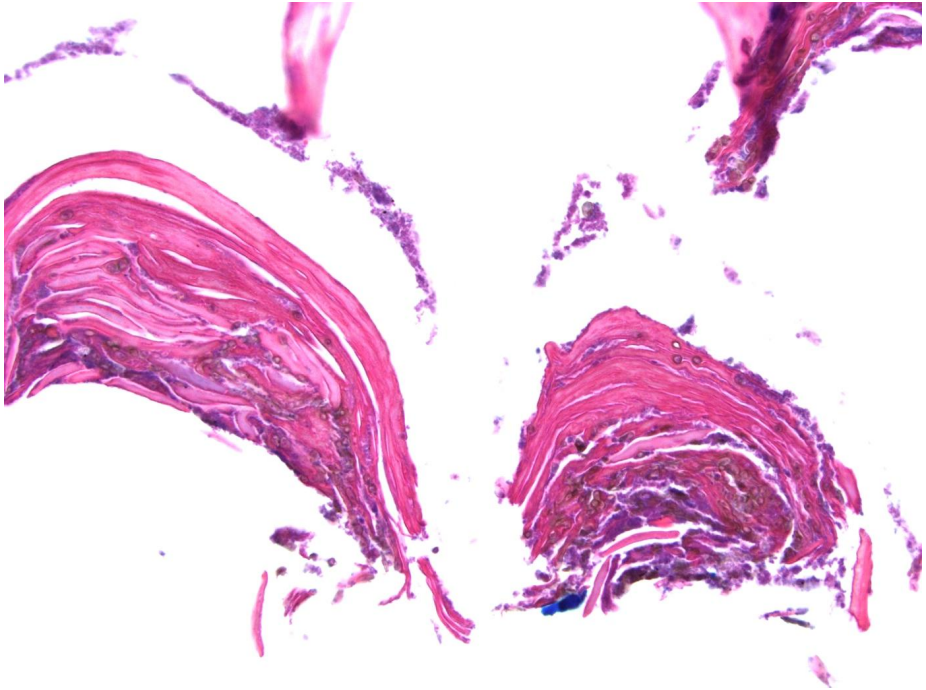
Perl’s iron stain does not work.



What is the source of the pigment?

- Non-melanocytic
  - Trauma—blood

Pigmented fungus



What is the source of the pigment?

- Non-melanocytic
  - Trauma—blood
  - Infection
    - Pigmented fungus

What is the source of the pigment?

Pseudomonas *aeruginosa*

What is the source of the pigment?

- Non-melanocytic
  - Trauma—blood
  - Infection
    - Pigmented fungus
    - Bacteria (Pseudomonas)

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Drug deposition

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Drug deposition

- Multiple nails
- Iron and melanin may be present

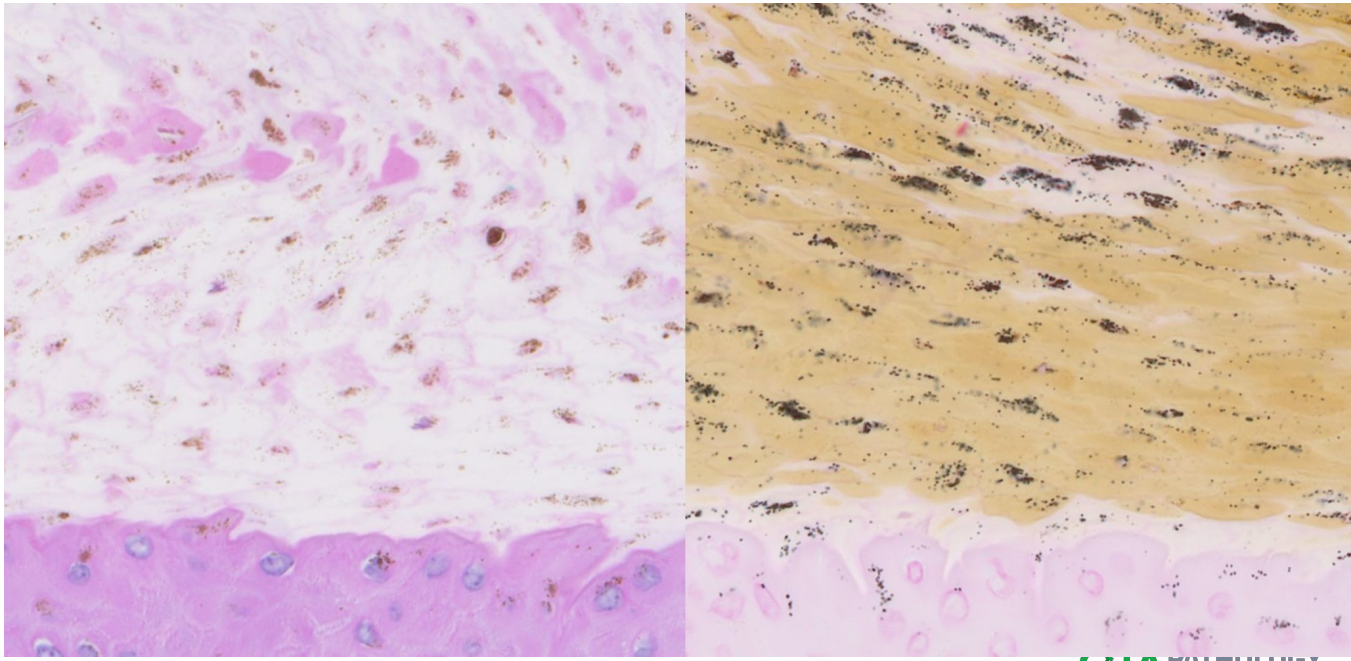
Drug Deposition

- Deposition
- Change in growth rate of nail
- Hemorrhage

Drug Deposition

- Deposition
- Change in growth rate of nail
- Hemorrhage (splinter or subungual)
  - Anticoagulants and antiplatelet agents
  - Taxanes
  - Tetracyclines
  - EGFR inhibitors (imatinib, etc)

Nail plate pigment—melanin or other



Cutaneous diseases also present in nails.

- Dermatitides
  - Psoriasis, lichen (planus, aureus, niditus, striatus), PRP, eczema, AA, EM, KLC, GA, EED, DM, LE, PV, PF, BP, scleroderma, vasculitis, PG, ILVEN . . .
  - Infection (viral, bacteria, myco, treponeme, mycosis, protozoa, leishmaniasis, scabies, parasite)

What is the source of the pigment?

- Non-melanocytic
  - Trauma—blood
  - Infection
    - Pigmented fungus
    - Bacteria (Pseudomonas)
  - Drug

What is the source of the pigment?

- Melanocytic neoplasm
  - Benign
  - Malignant
- Melanocyte ‘activation’

What is the source of the pigment?

- Melanocytic neoplasm
  - Benign
  - Malignant
- Melanocyte ‘activation’

Longitudinal melanonychia

Challenge

- Identifying source of clinical pigmentation

Finding the pigment

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

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How to find the pigment

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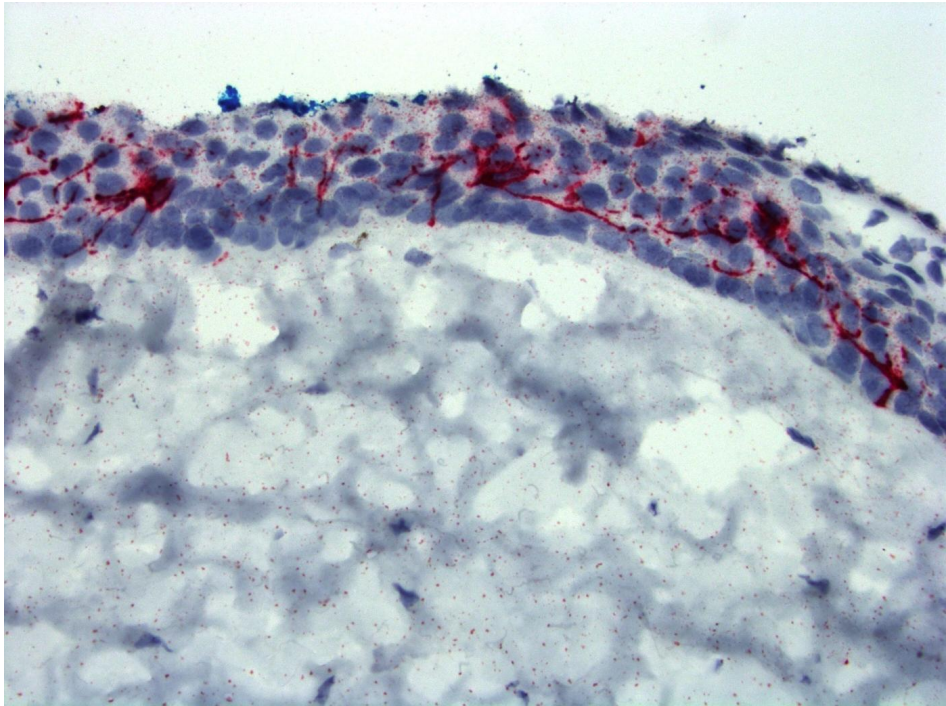
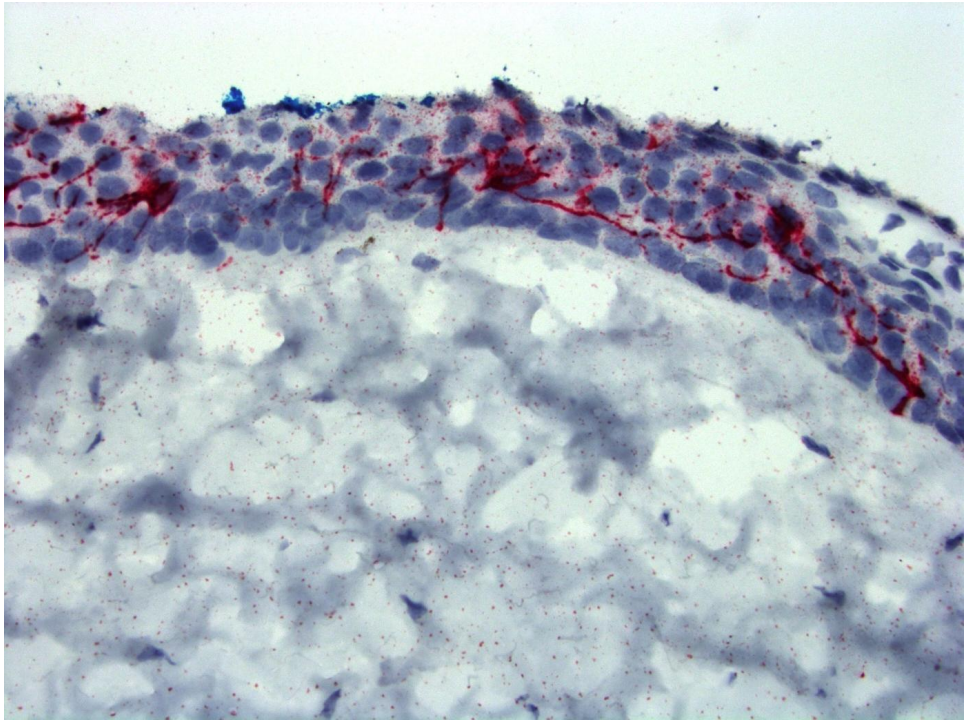
MelanA/Mart1

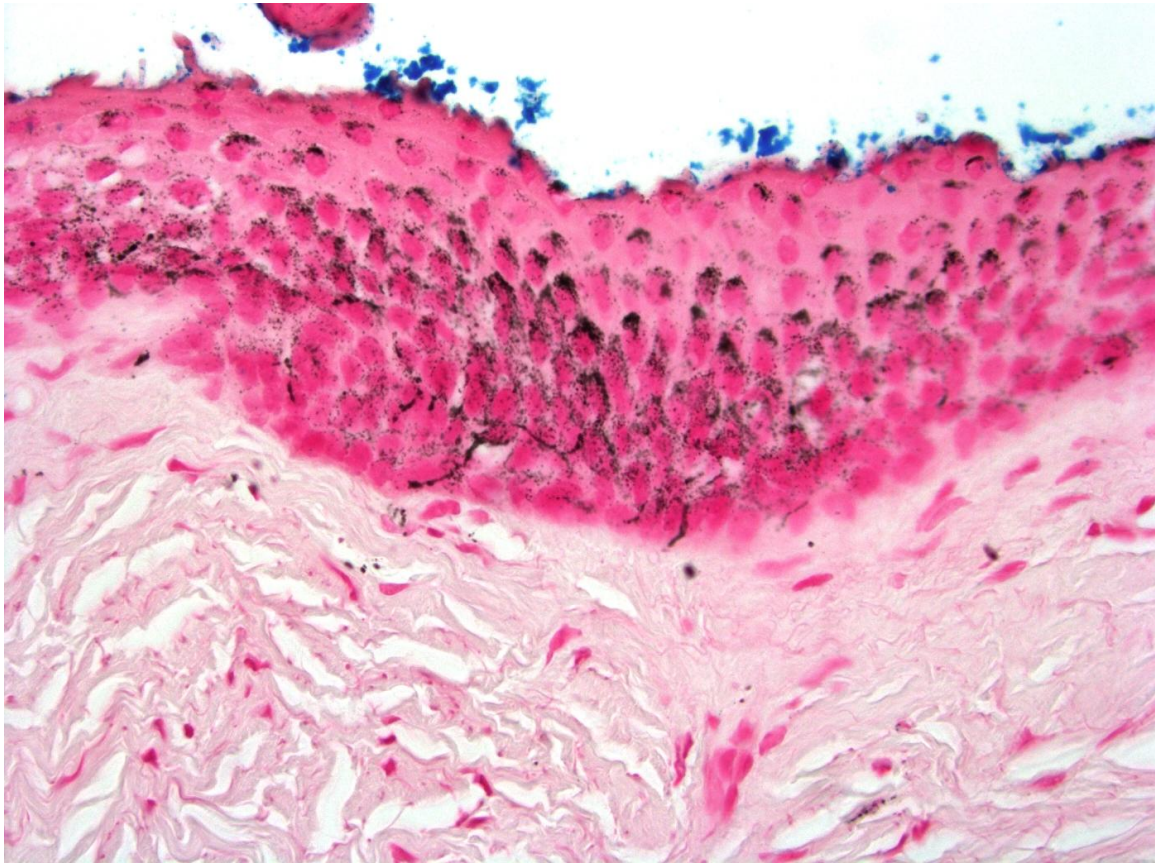
- Melanocyte density
- Red chromogen



melanA/Mart-1 is better than SOX-10



Fontana-Masson Stain



Special stains for pigment do not work in nail plate

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Fontana-Masson—must dilute

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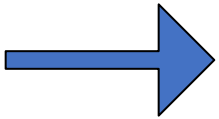
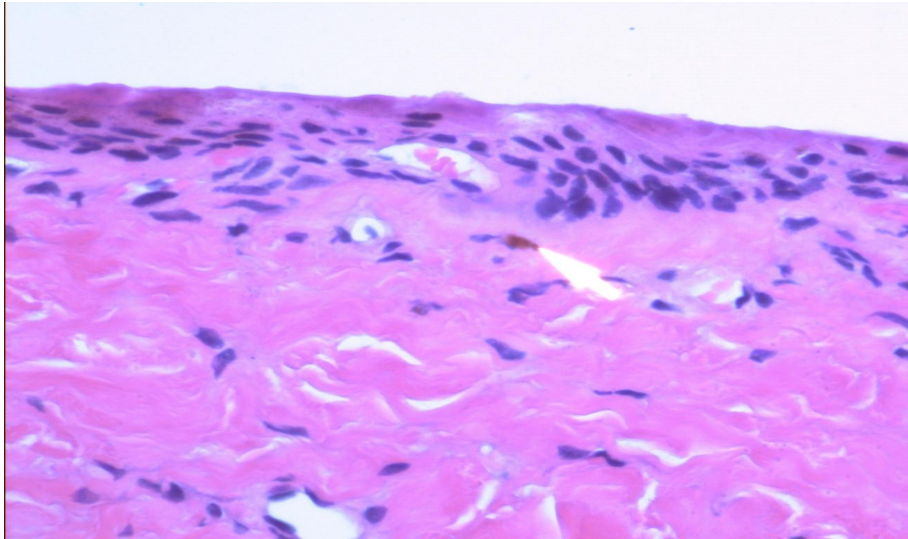
Finding subtle pigment





Benign Activation of Junctional Melanocytes

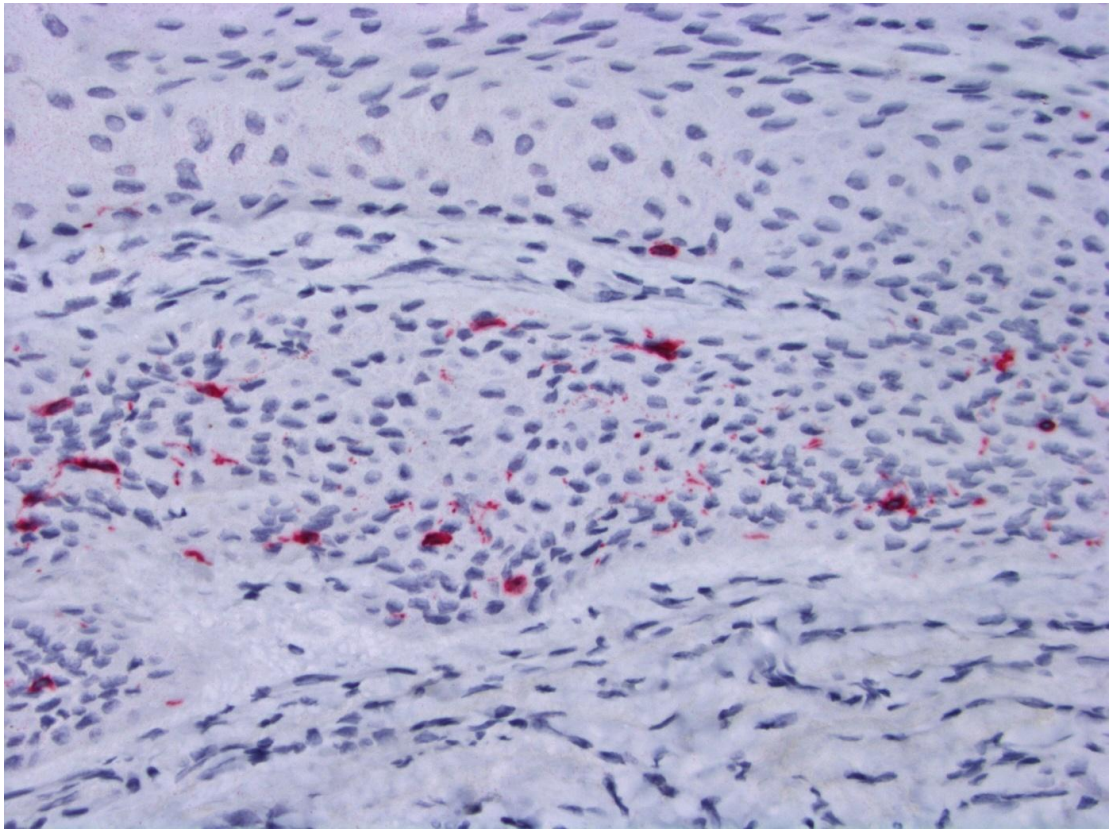
- Synonyms
  - Melanotic macule of the nail
  - Nail unit lentigo

Benign Activation of Junctional Melanocytes

- Similar to benign solar lentigo

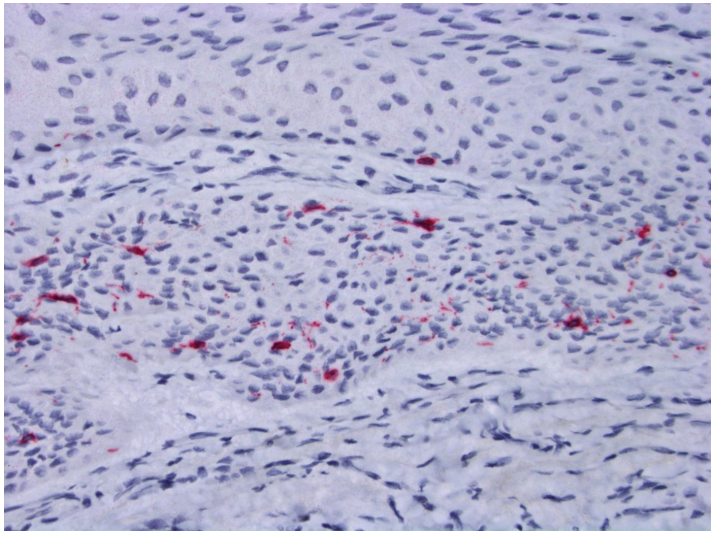
=

Density of melanocytes

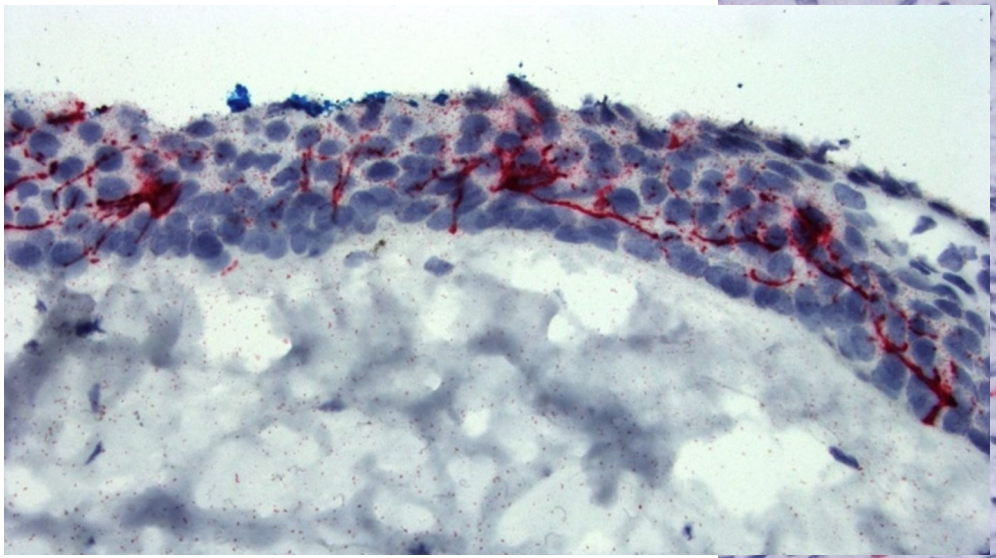


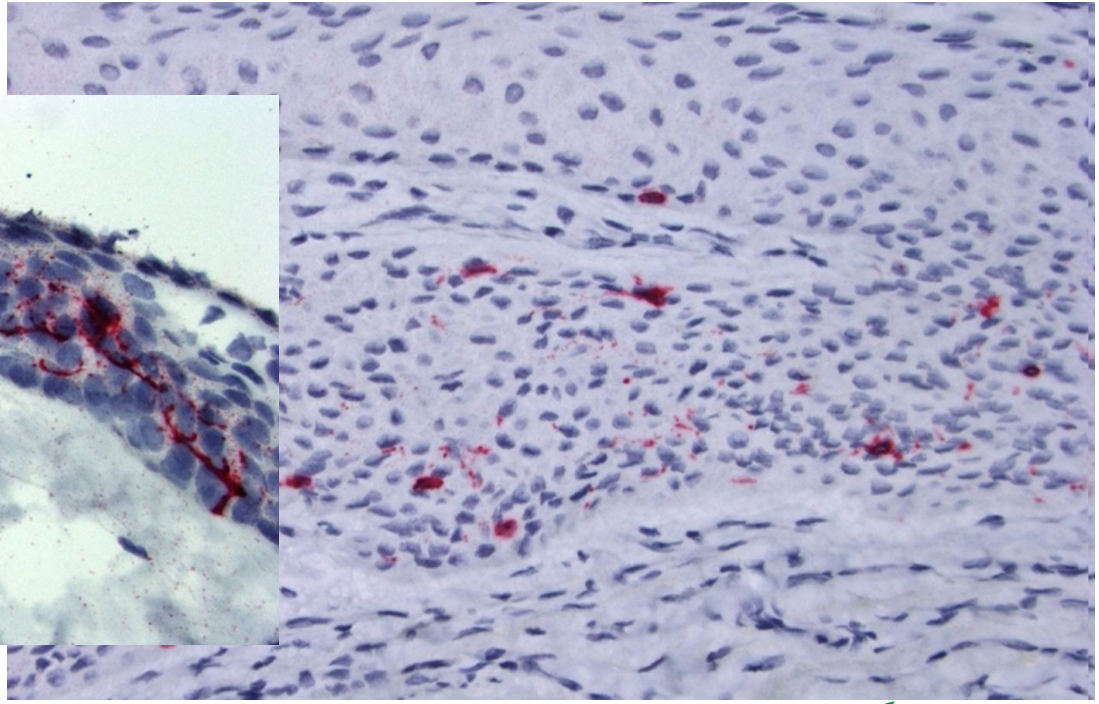
Density of melanocytes

- Depends upon skin type



Nail pigmentation varies with skin type

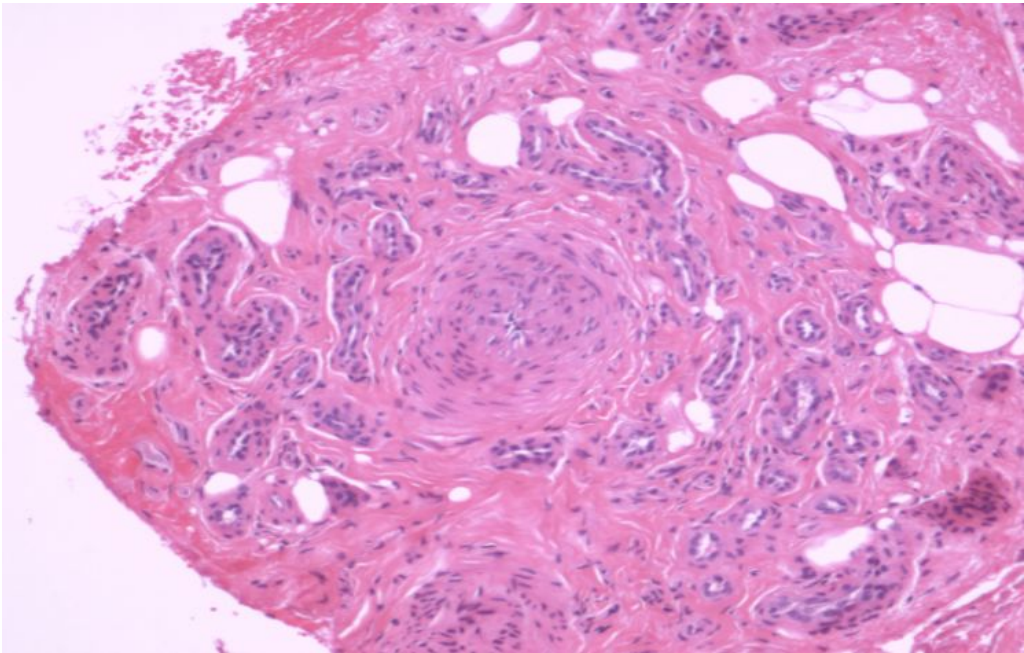




Neoplasms

- Squamous
  - HPV-related
  - Benign and malignant “Onycho”
- Melanocytic
- Soft tissue
  - Vascular
  - Spindle cells

Pitfall: Normal vasculature
Don’t overdiagnose as hemangioma



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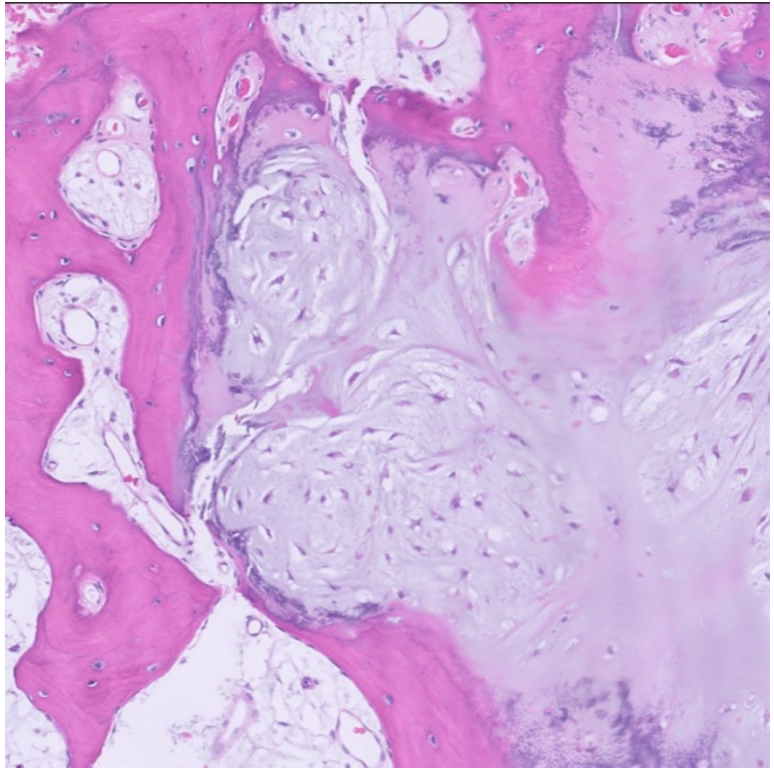
glomus

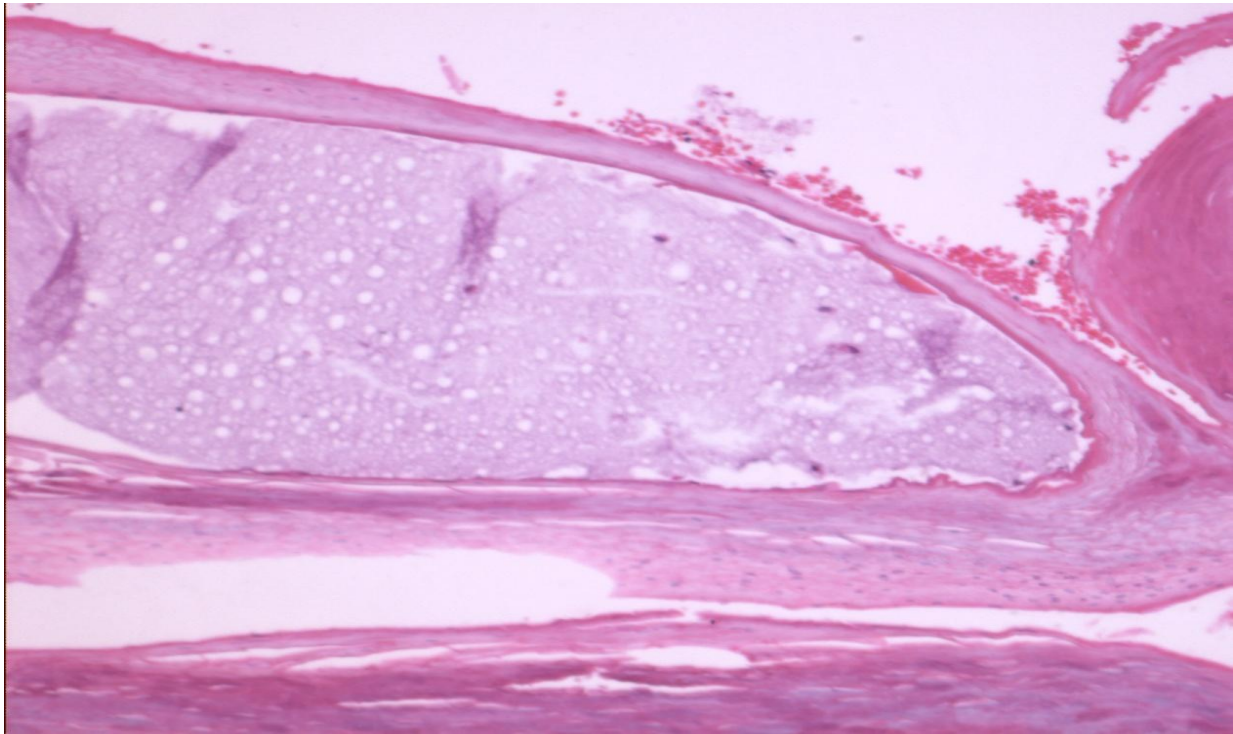
Deeper mass?
Remember to image



Digital Myxoid/Mucous Cyst

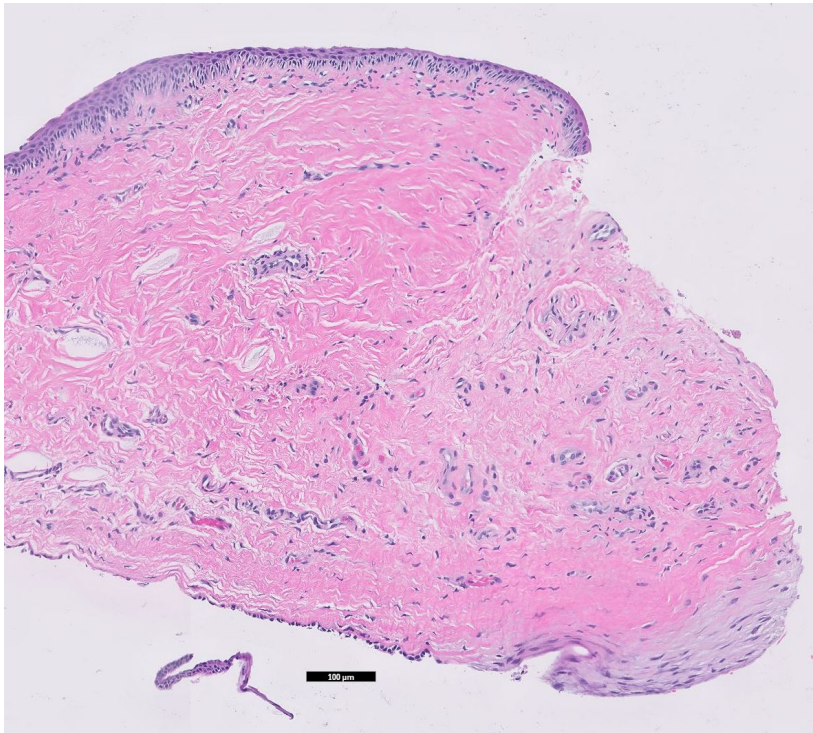
Digital Myxoid/Mucous Cyst

Mucin may be anywhere

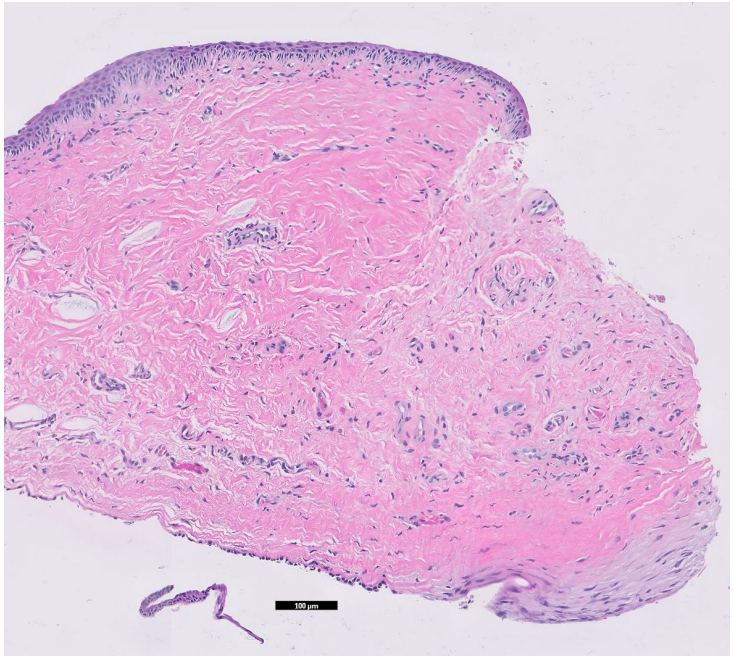


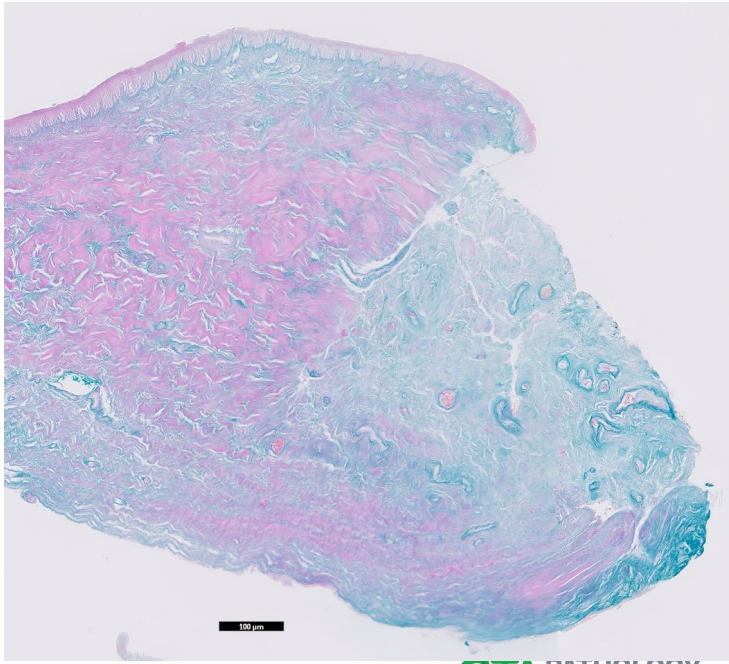
Digital Myxoid Cyst

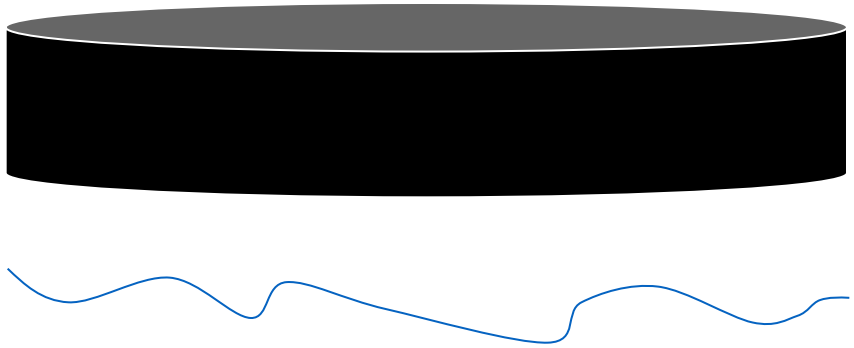
- Often don’t see mucin
  - Scar
  - Reactive changes



Mucin stain often required






10% formalin
Nail Fragments

Continuous growth observable

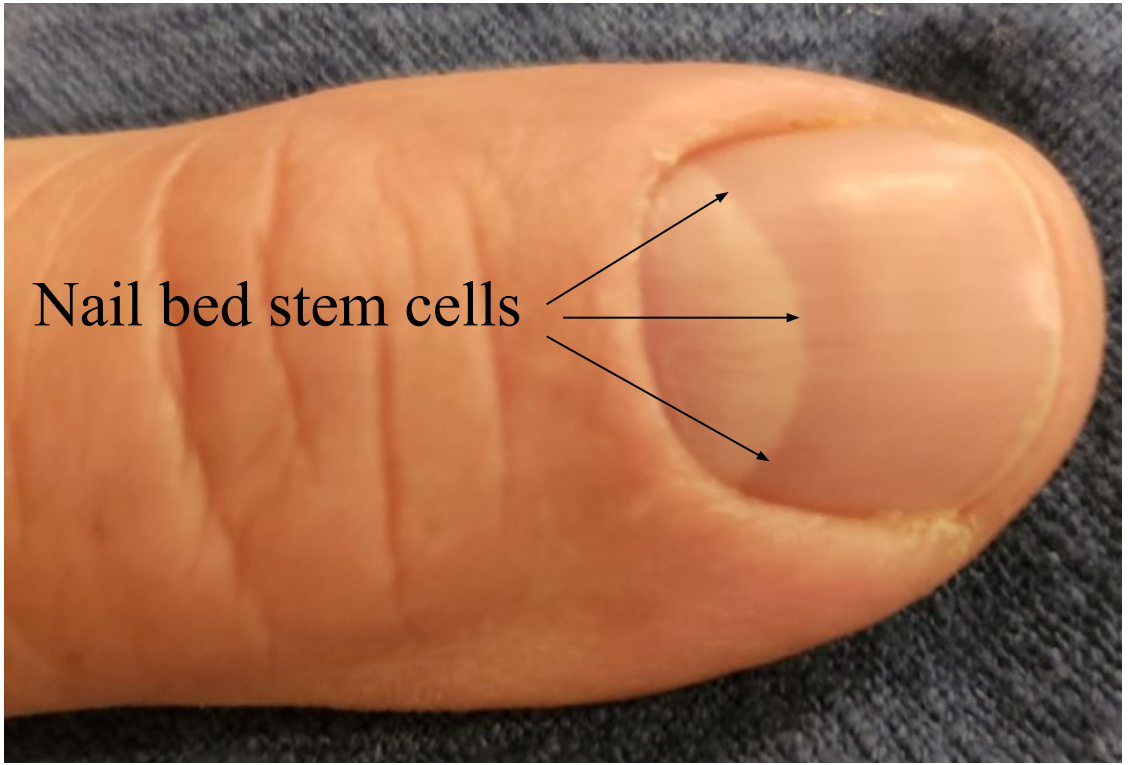
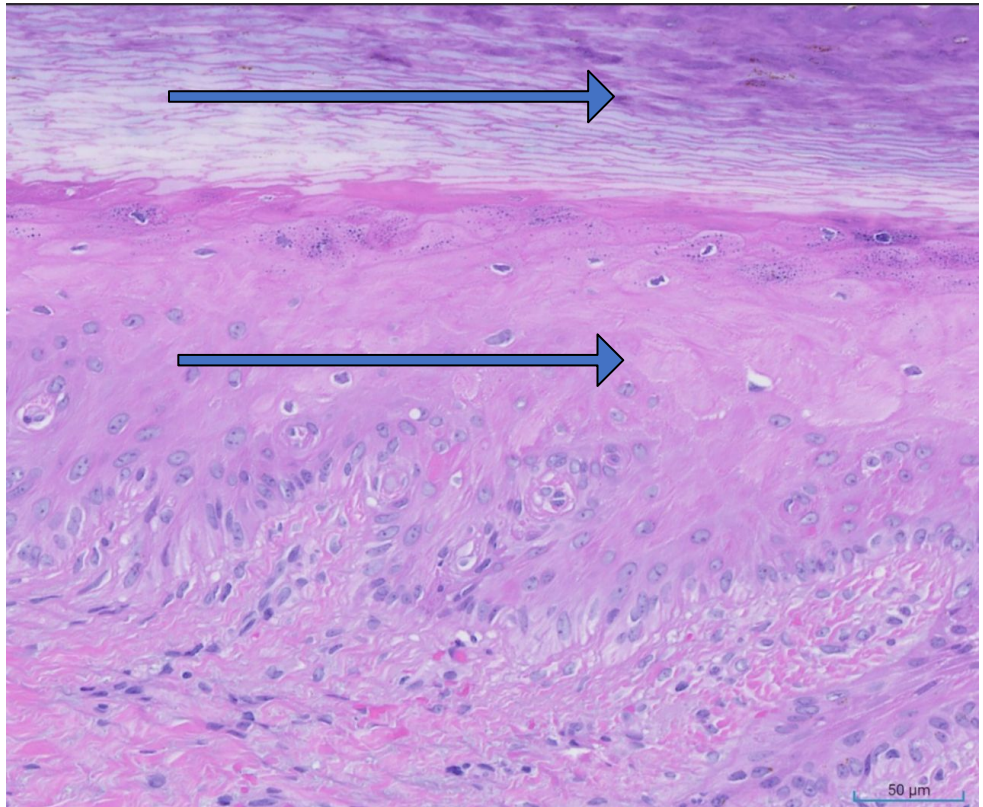


Plate and epithelium move



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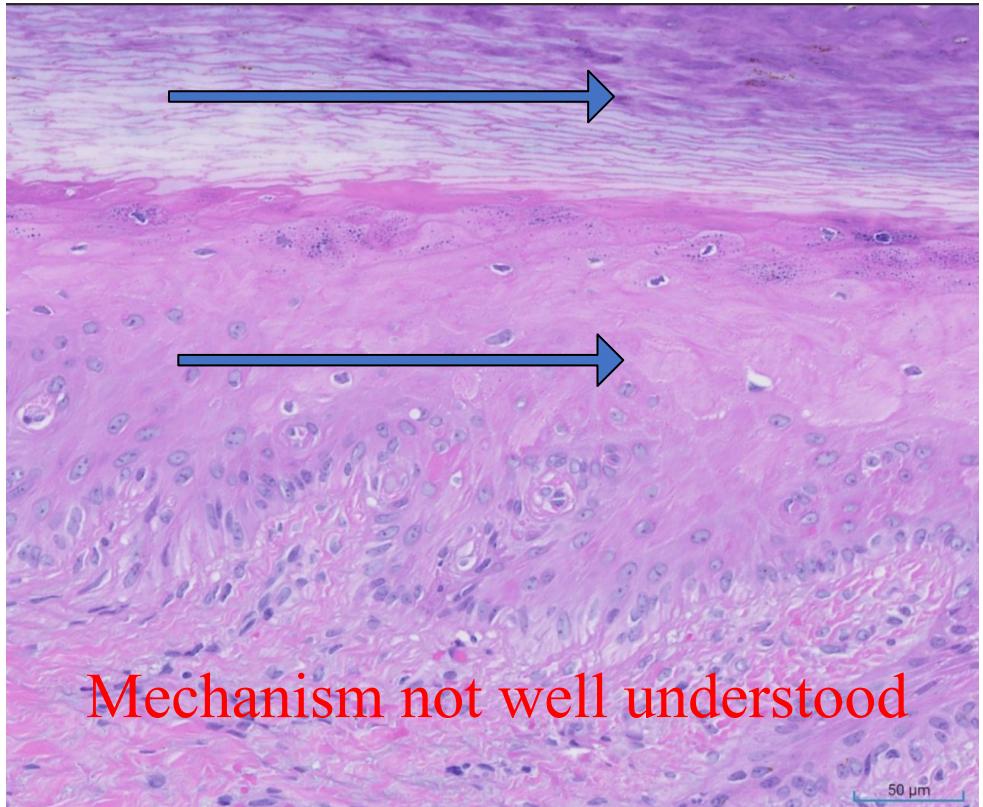
SKIN, HAIR AND NAIL EXPERTS

Plate and epithelium move together



Death by ‘Onycho’pathology

Onychocytic acanthoma, onychopapilloma, onycholemmal horn, proliferating onycholemmal tumor, proliferating oncholemmal cyst, onychomatricoma, onychocytic carcinoma, onycholemmal carcinoma, onychocytic matricoma

Onychopapilloma

Onychopapilloma

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

Onychopapilloma

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

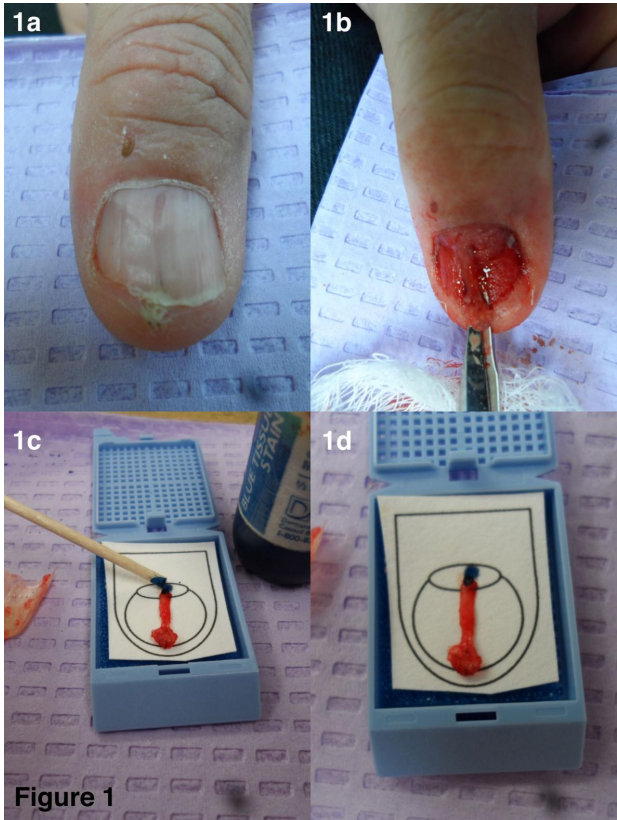
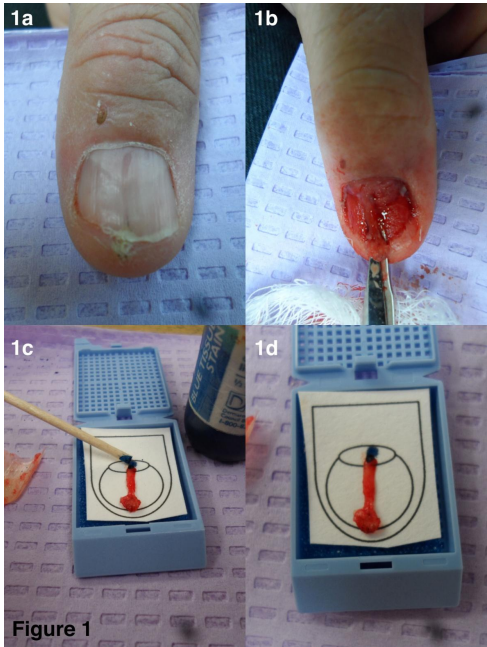


Figure 1

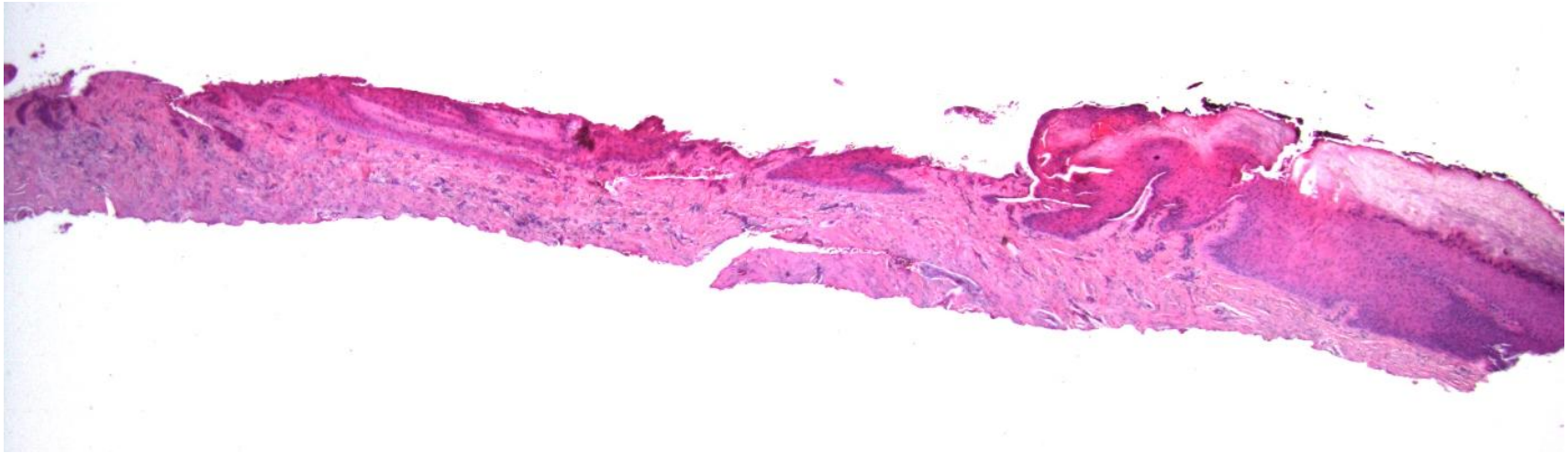
Onychopapilloma

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

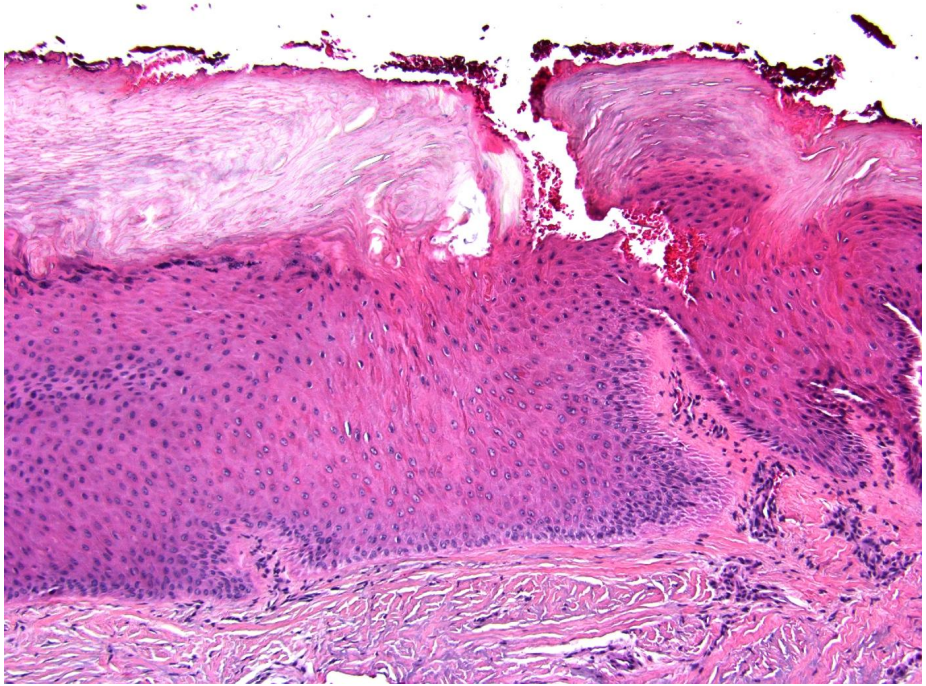
Embed proximal to distal



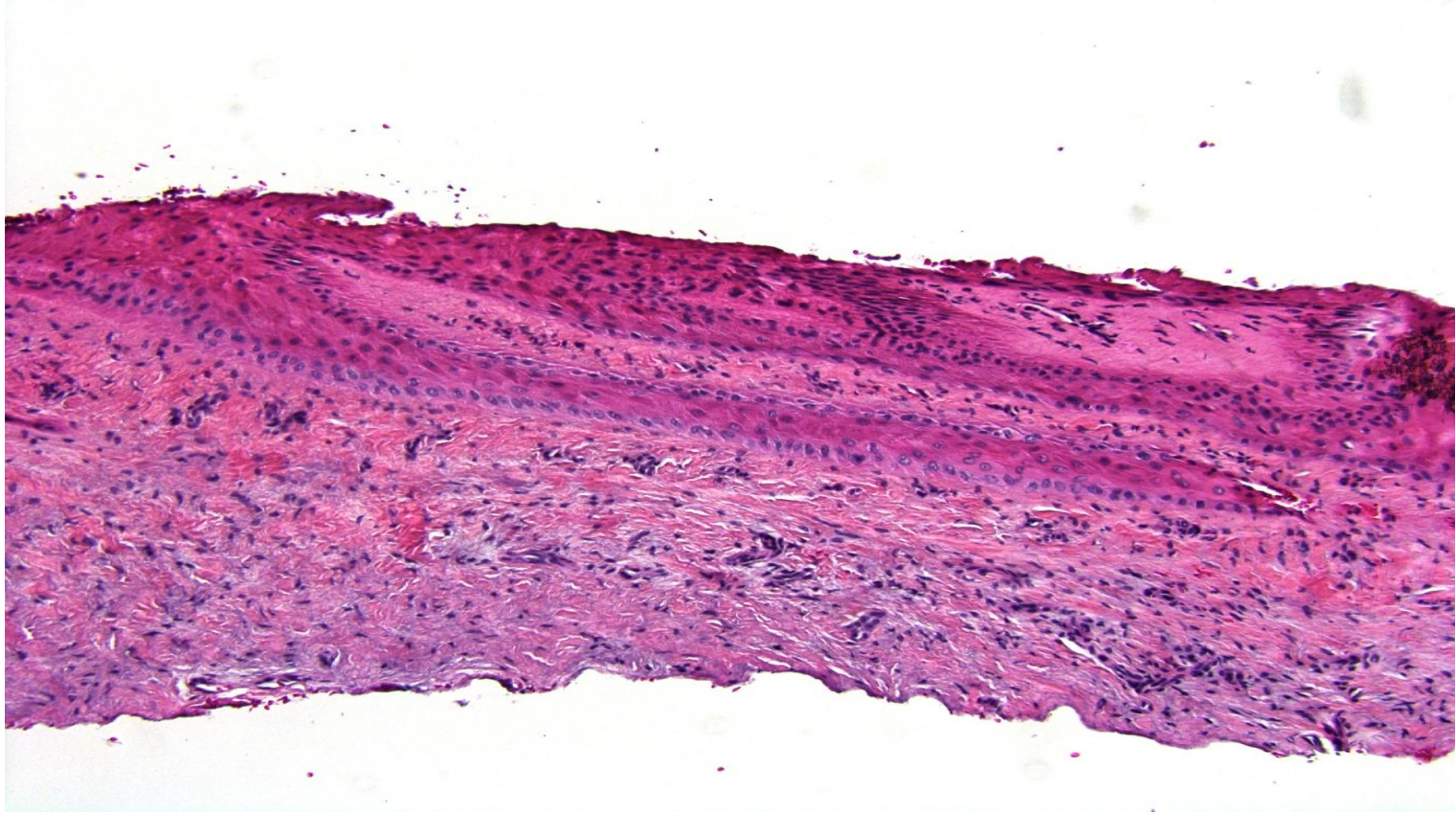
Onychopapilloma—Keratin Producing



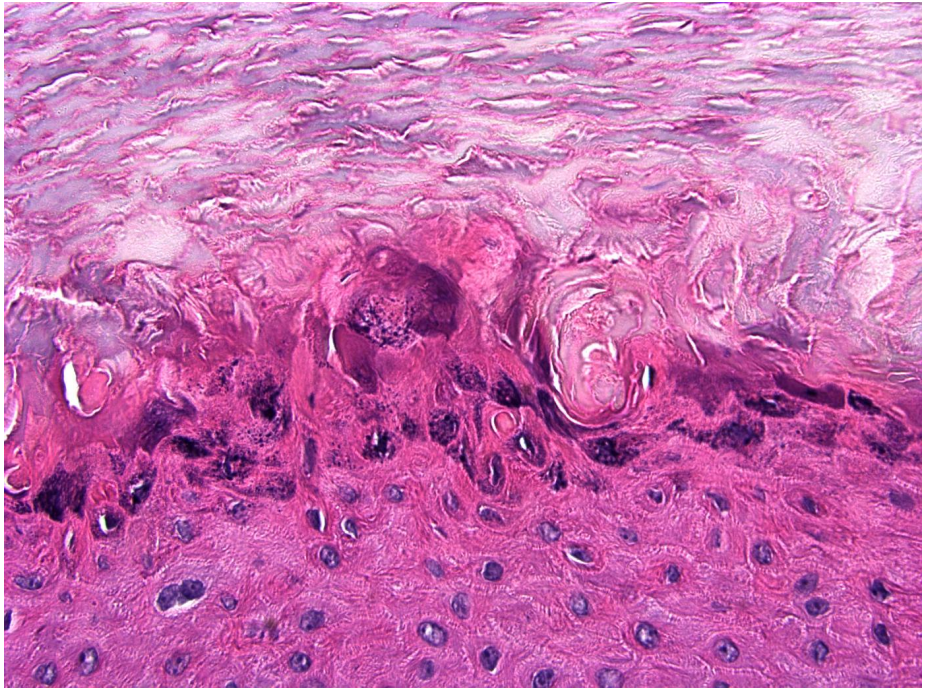
Onychopapilloma—Keratin Producing



Onychopapilloma



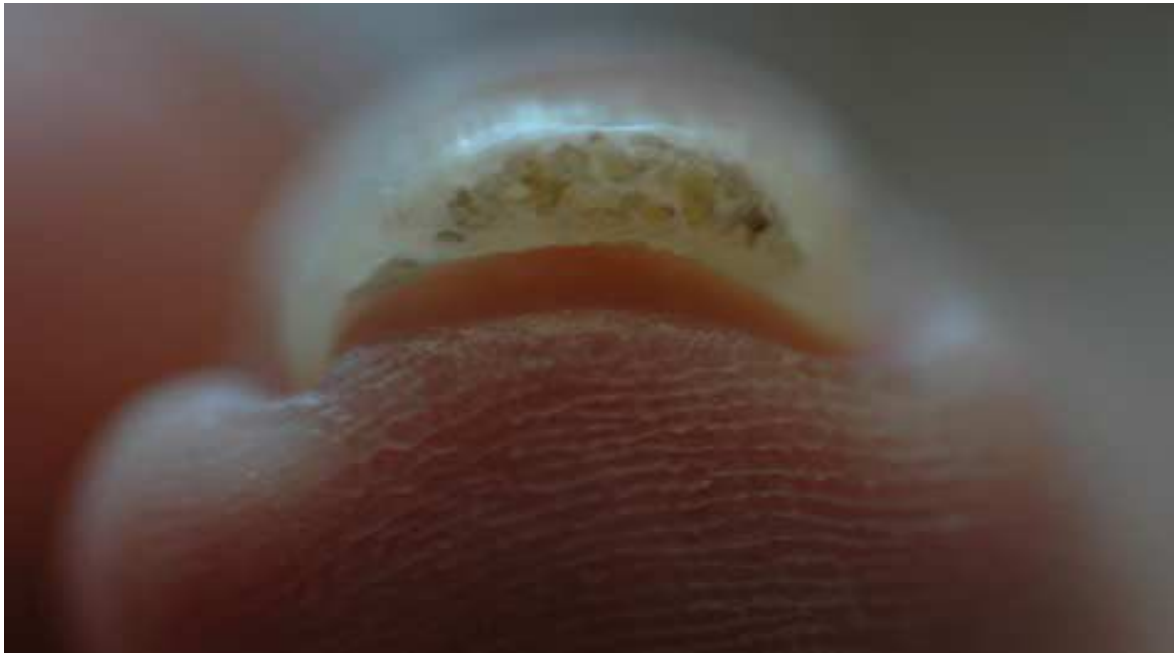
Onychopapilloma—Not a wart



Onycomatricoma

Onycomatricoma

- Examine nail for holes—Transverse sections of dystrophic nail

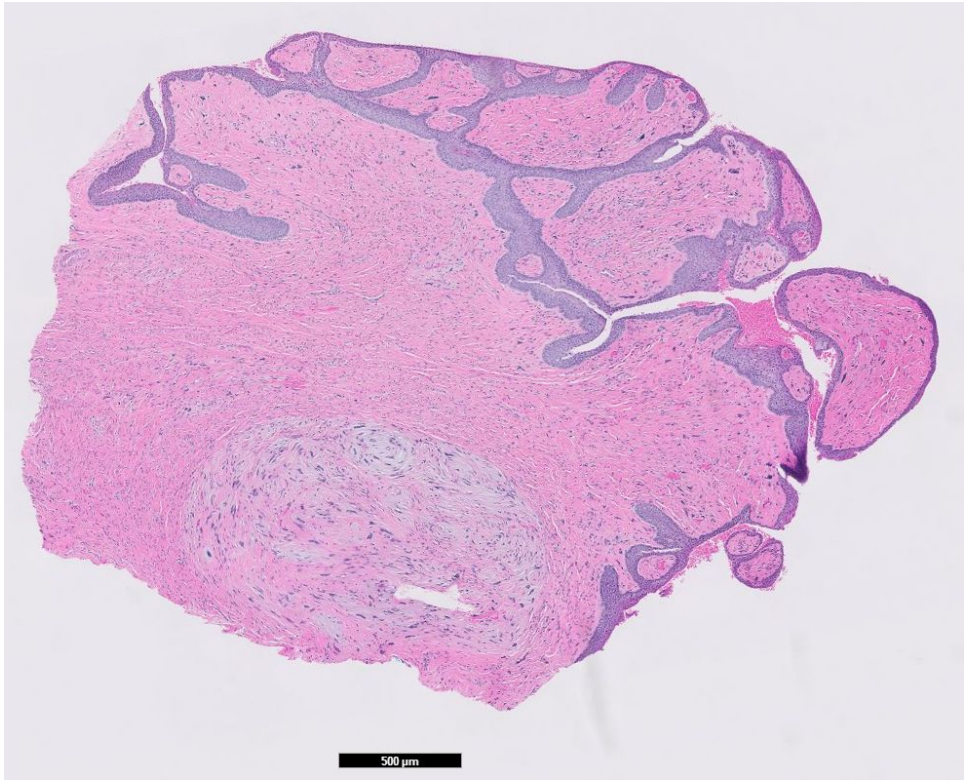


Onycomatricoma

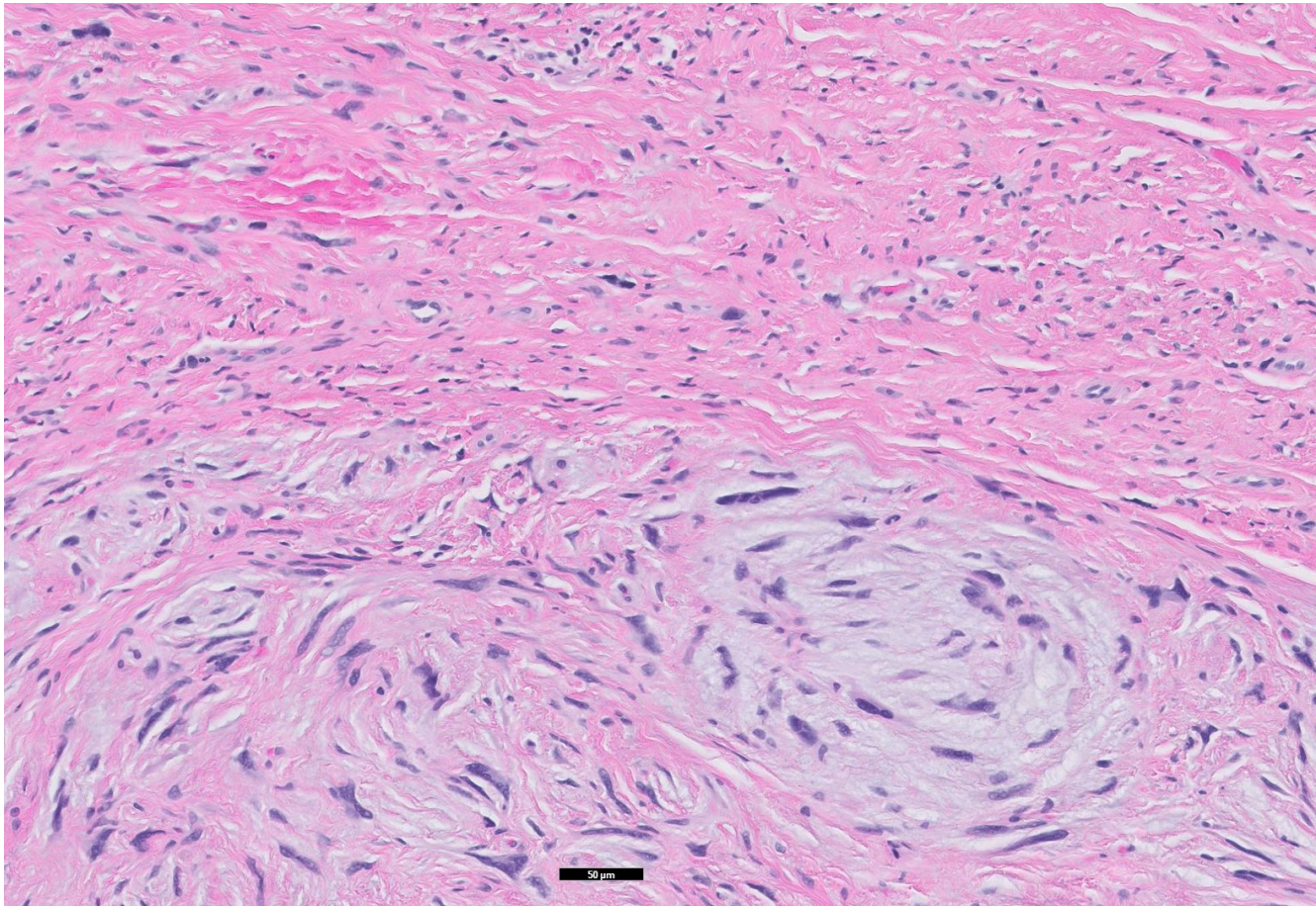
- Examine nail for holes—Transverse sections of dystrophic nail

Onychomatricoma

- Two components
  - Epithelial (?reactive)
  - Dermal spindle
    - (May be myxoid)



Onycomatricoma



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Nail Fungus Diagnostics

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Mold

PCR replacing culture

Patient ID : CT20-27456

Test result	Result
Dermatophyte	**Multiple infection**
Yeast/Mould	**Fusarium solani**

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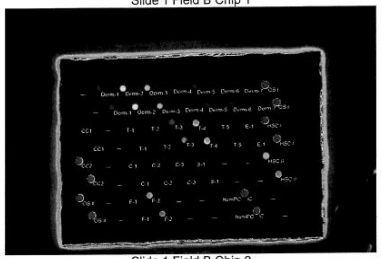
Patient ID : CT20-27456 **Protocol :** 1/6/21 AL

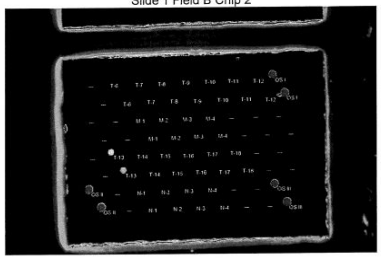
Page : 1

Partial result	Result
Cross contamination control	valid
Internal Control	valid
DNA positive control	**not detected**
Hybridisation specificity control	valid
Dermatophyte (universal)	**DETECTED**
Trichophyton equinum	not detected
Trichophyton tonsurans	not detected
Trichophyton interdigitale	**DETECTED**
Trichophyton mentagrophytes	not detected
T. interdigitale/mentagrophytes	not detected
Trichophyton quinckeanum	not detected
Trichophyton schoenleinii	not detected
Trichophyton simii	not detected
T. quinckeanum/schoenleinii/simii	**DETECTED**
Trichophyton benhamiae(white/afr.)	not detected
Trichophyton benhamiae (yellow)	not detected
T. bullosum/benhamiae (afr.)	not detected
T. concentricum/erinacei	not detected
Trichophyton erinacei	not detected
T. verrucosum/eriotrephon	not detected
Trichophyton rubrum	**DETECTED**
Trichophyton violaceum	not detected
Epidermophyton floccosum	not detected
Nannizzia fulva	not detected
Nannizzia gypsea	not detected
Nannizzia incurvata	not detected
Nannizzia persicolor	not detected
Microsporum canis	not detected
Microsporum ferrugineum	not detected
Microsporum audouinii	not detected
M. canis/audouinii	not detected
Candida parapsilosis	not detected
Candida guilliermondii	not detected
Candida albicans	not detected
Fusarium solani	**DETECTED**
Fusarium oxysporum	not detected
Scopulariopsis brevicaulis	not detected

Slide 1 Field B Chip 1



Slide 1 Field B Chip 2



PAS vs PCR Study

- 99 samples PAS and PCR
  - PCR+ 61%
  - PAS+ 35%
- 22 samples PCR+ and PAS-
- 2 samples PAS+ and PCR-

PAS vs PCR Study

- 10% samples were a mold
  - 4% were mixed (2 tinea; 2 candida)

22 cases PAS- PCR+

- 36% were a mold
- 14% were a yeast

- 50% of PAS- PCR+ were a yeast or mold
- PAS staining appears to miss some mold and yeast

Thanks!

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