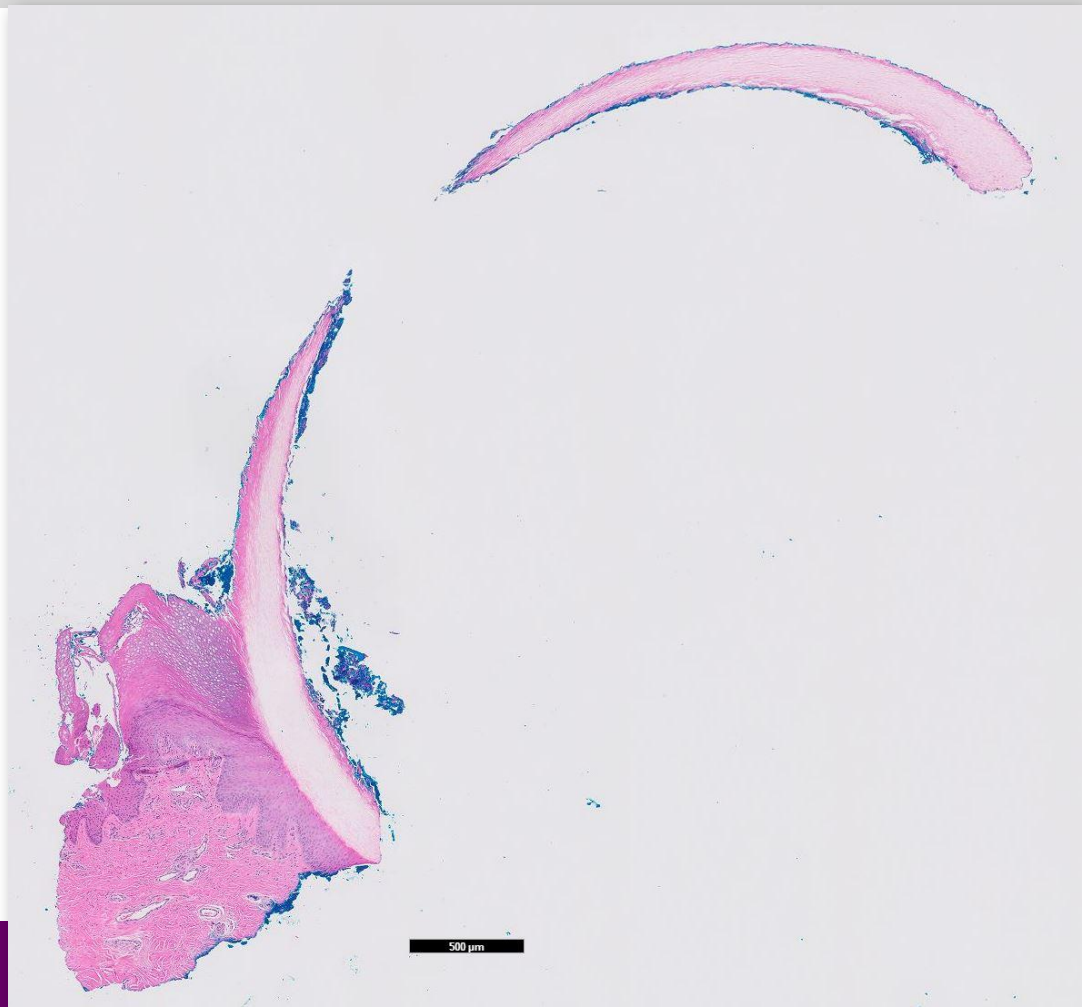
Histopathology of Common Nail Lesions

Curtis T. Thompson, M.D.
CTA Lab
and
Clinical Professor of Dermatology and Pathology
Oregon Health and Sciences University
Portland, Oregon, USA

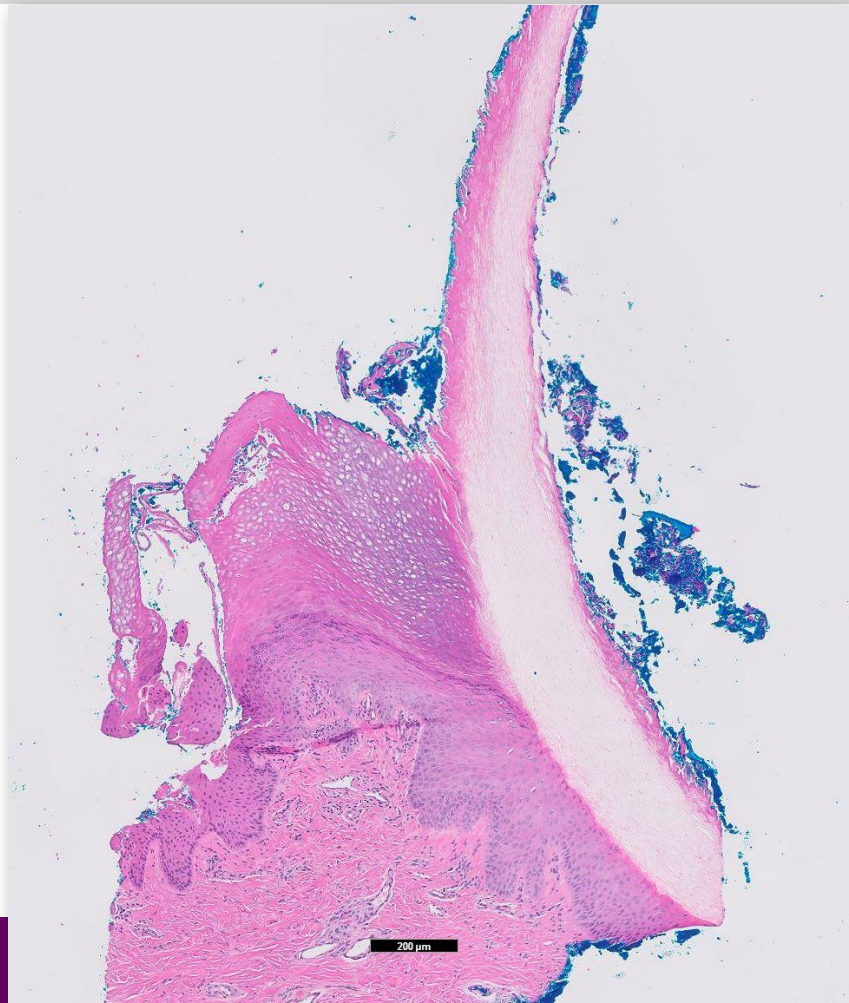
- Right index finger of 8 y/o male

8 y/o index

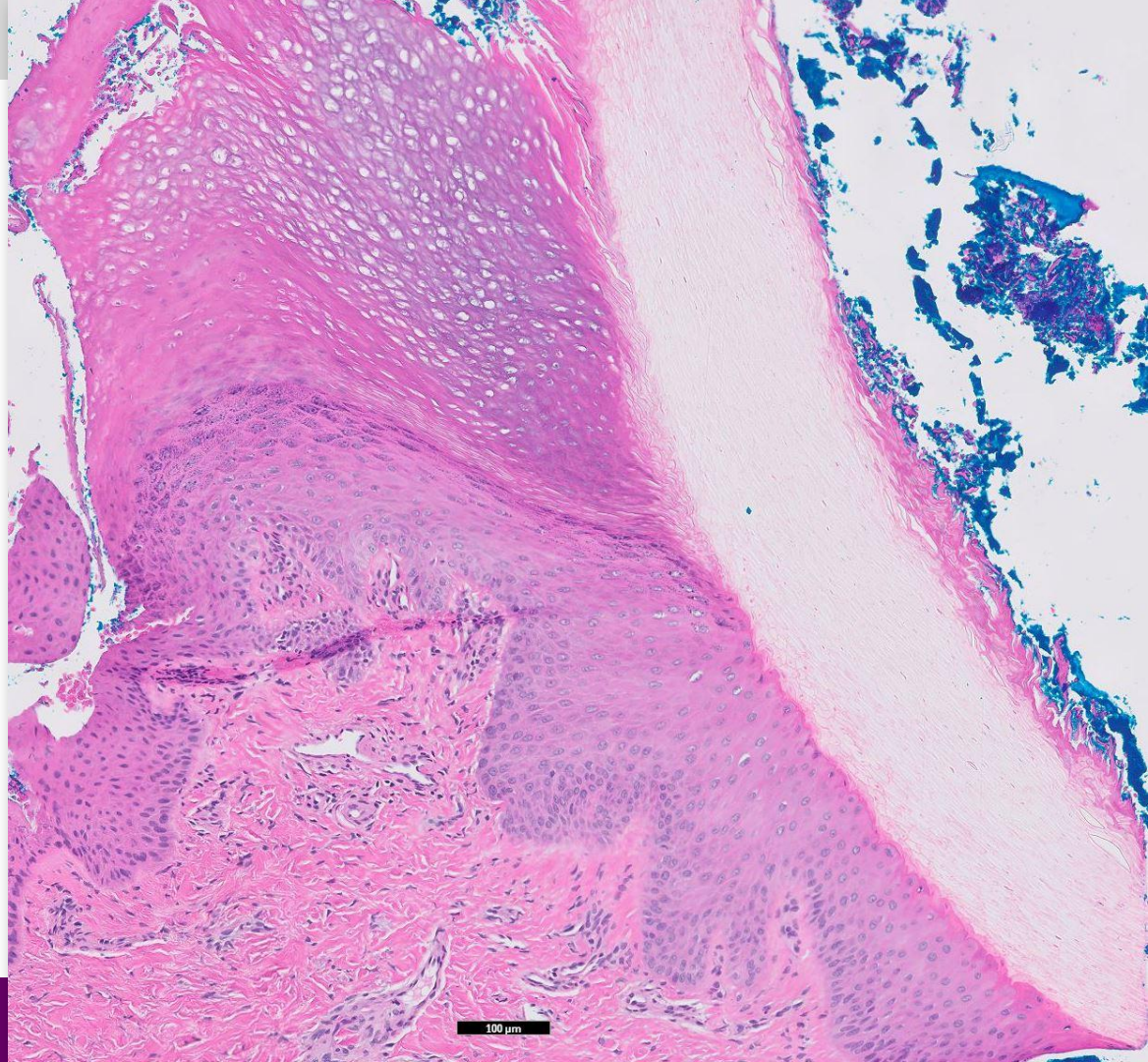
8 y/o index



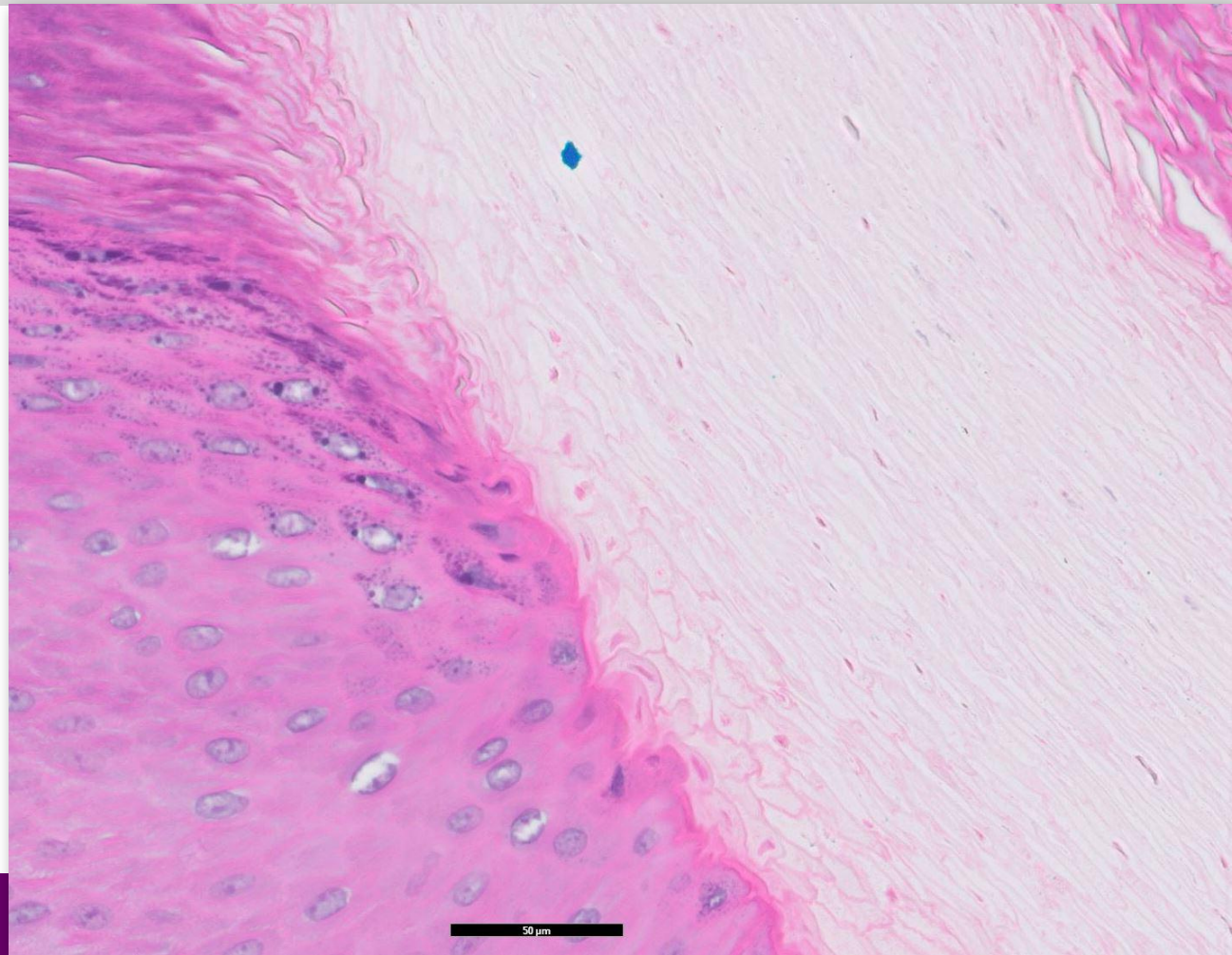
8 y/o index



8 y/o index



8 y/o index



Onychoheterotopia (Ectopic Nail)

- Nail is growth of nail unit tissue outside the usual anatomic area.
- Japan and India
- Congenital from syndromes such as Pierre-Robin Syndrome and Congenital Palmar Nail Syndrome.
- Trauma or chronic repetitive injury.

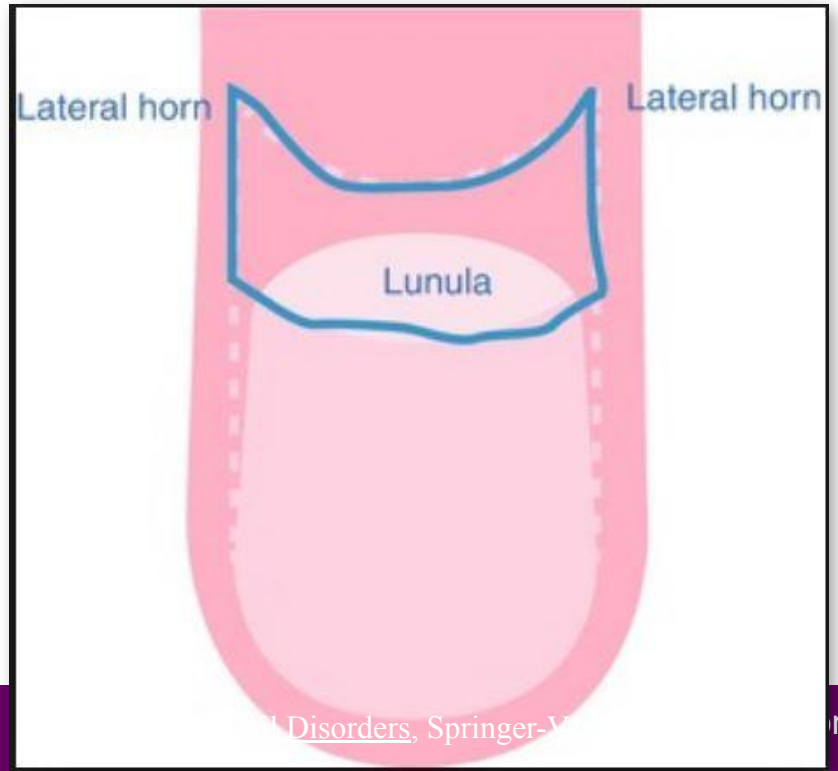
Onychoheterotopia (Ectopic Nail)

- Dorsal aspect of the hand.
- Osseous defects if matrix close to bone.

Traumatic ectopic nail

Çalişkan et al. Ann Dermatol, http://dx.doi.org/10.5021.ad.2014.26.6.768,

Matrix horns



Onychoheterotopia (Ectopic Nail)

- All component of nail unit
  - Matrix
  - Place
  - Bed
  - Nail Fold

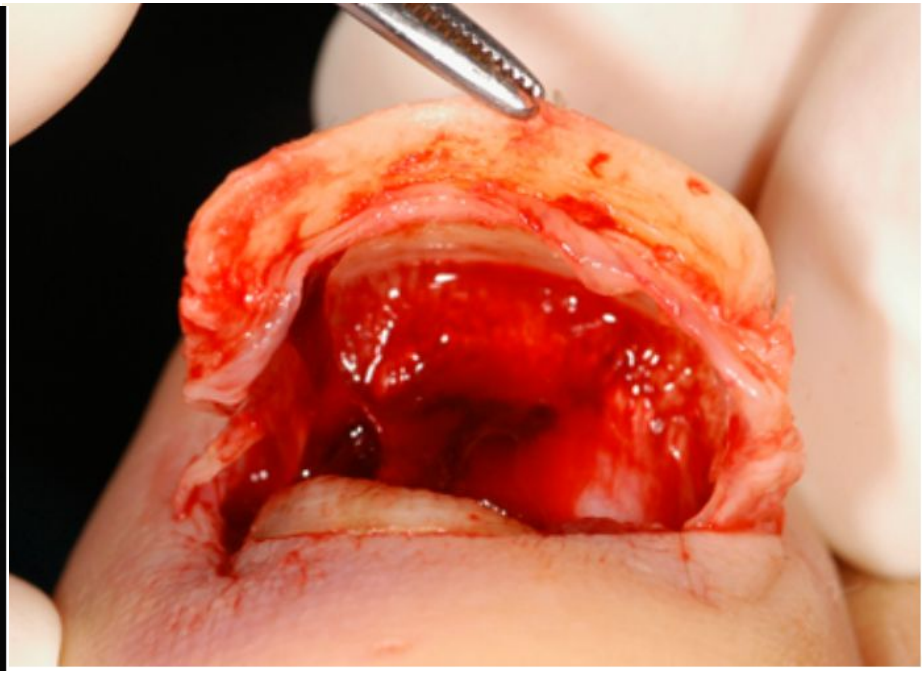
Onychoheterotopia (Ectopic Nail)

- Differential:
  - Retronychia
  - Squamous cell carcinoma in-situ (HPV)
  - Residual nail unit after incomplete excision

Retronychia

Courtesy of Dr. Bertrand Richert

Retronychia

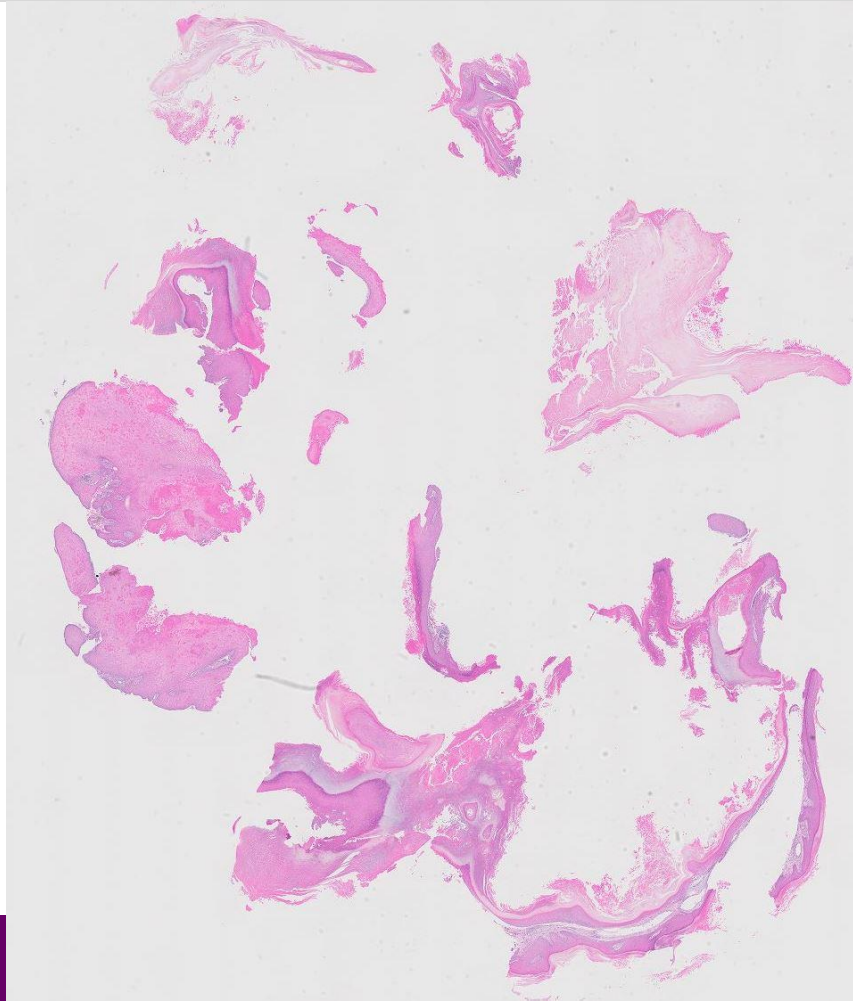


Baumgartner M and Haneke E. Retronychia: Diagnosis and Treatment. Dermatologic Surgery 36(10):1610-4, 2010

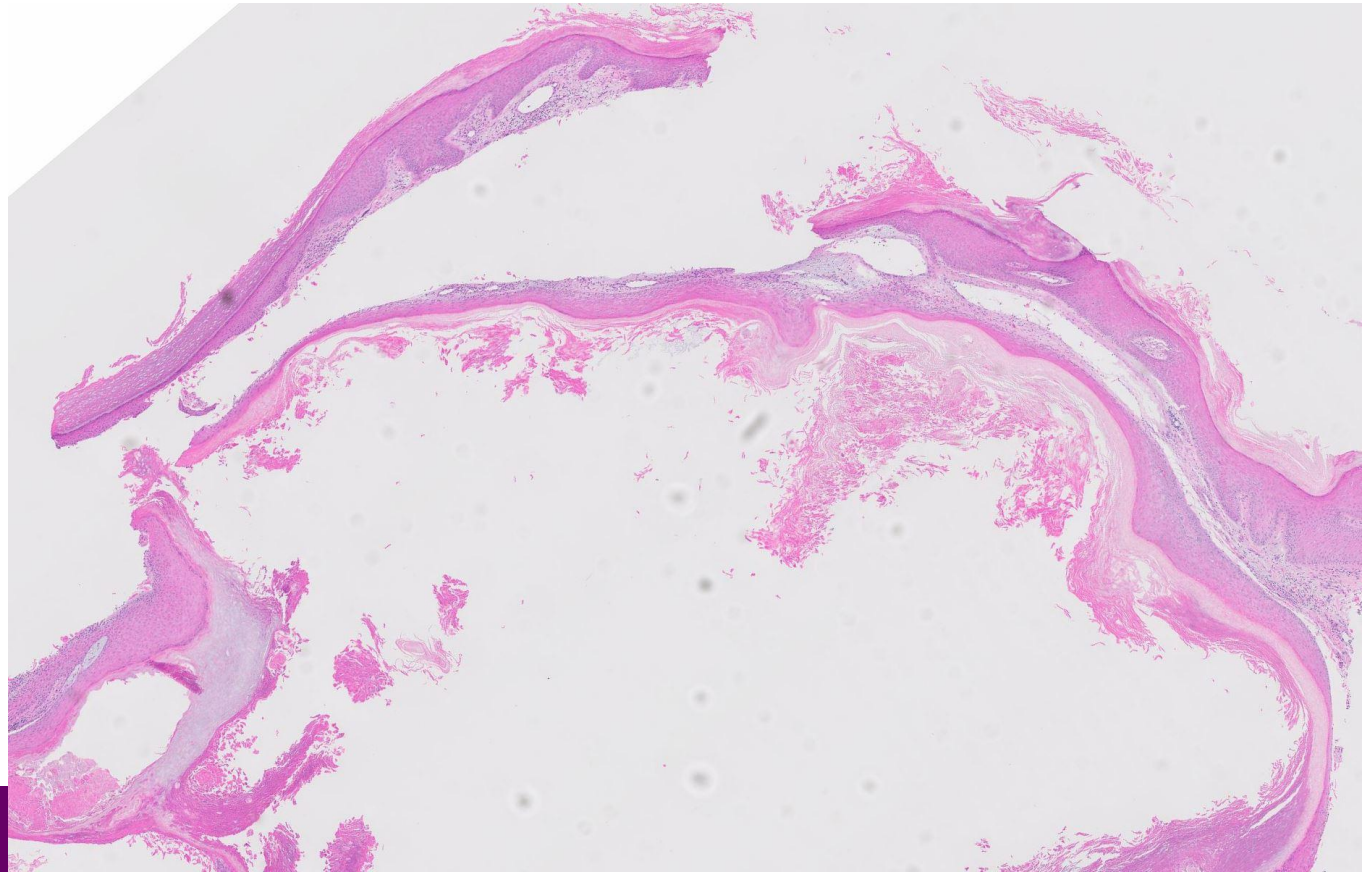
64 y/o male

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

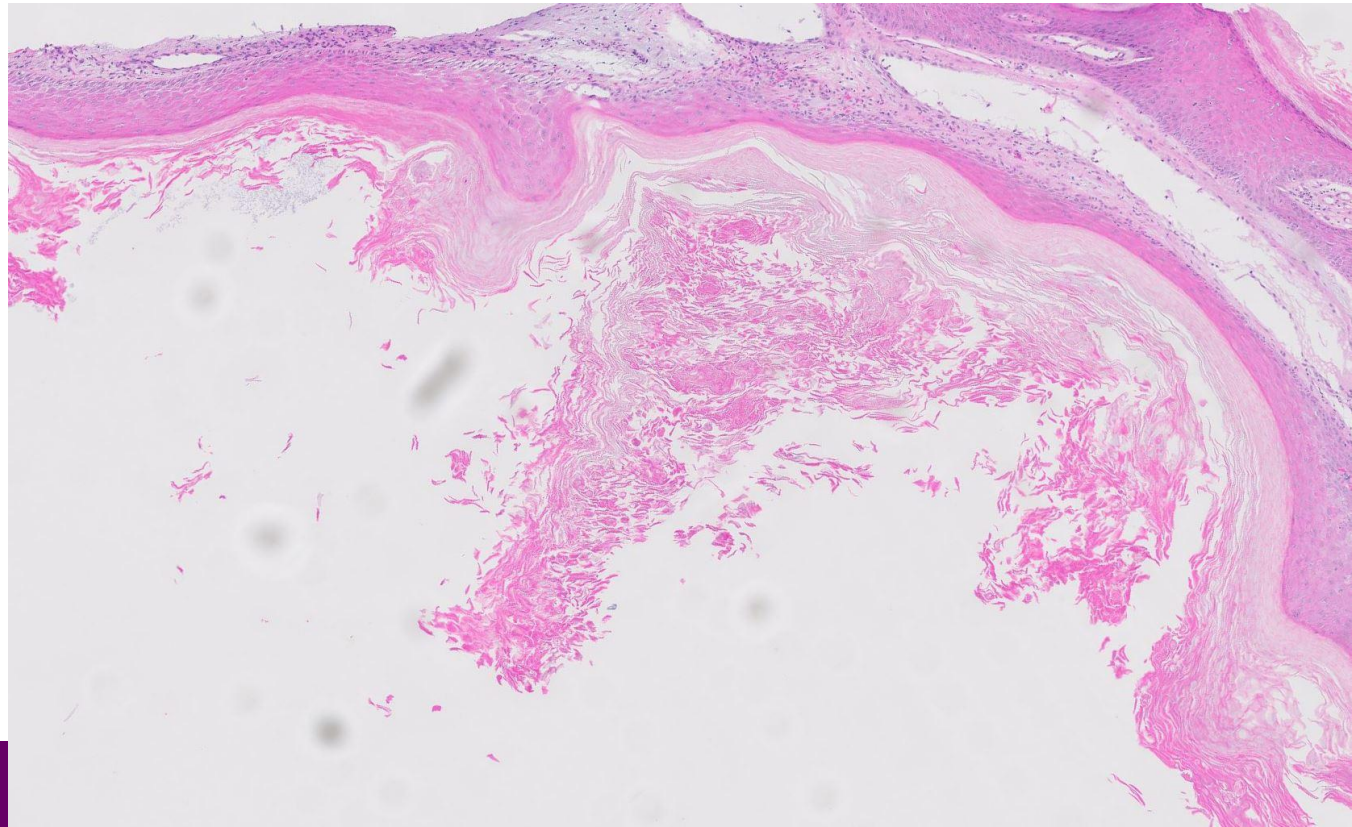
64 y/o male



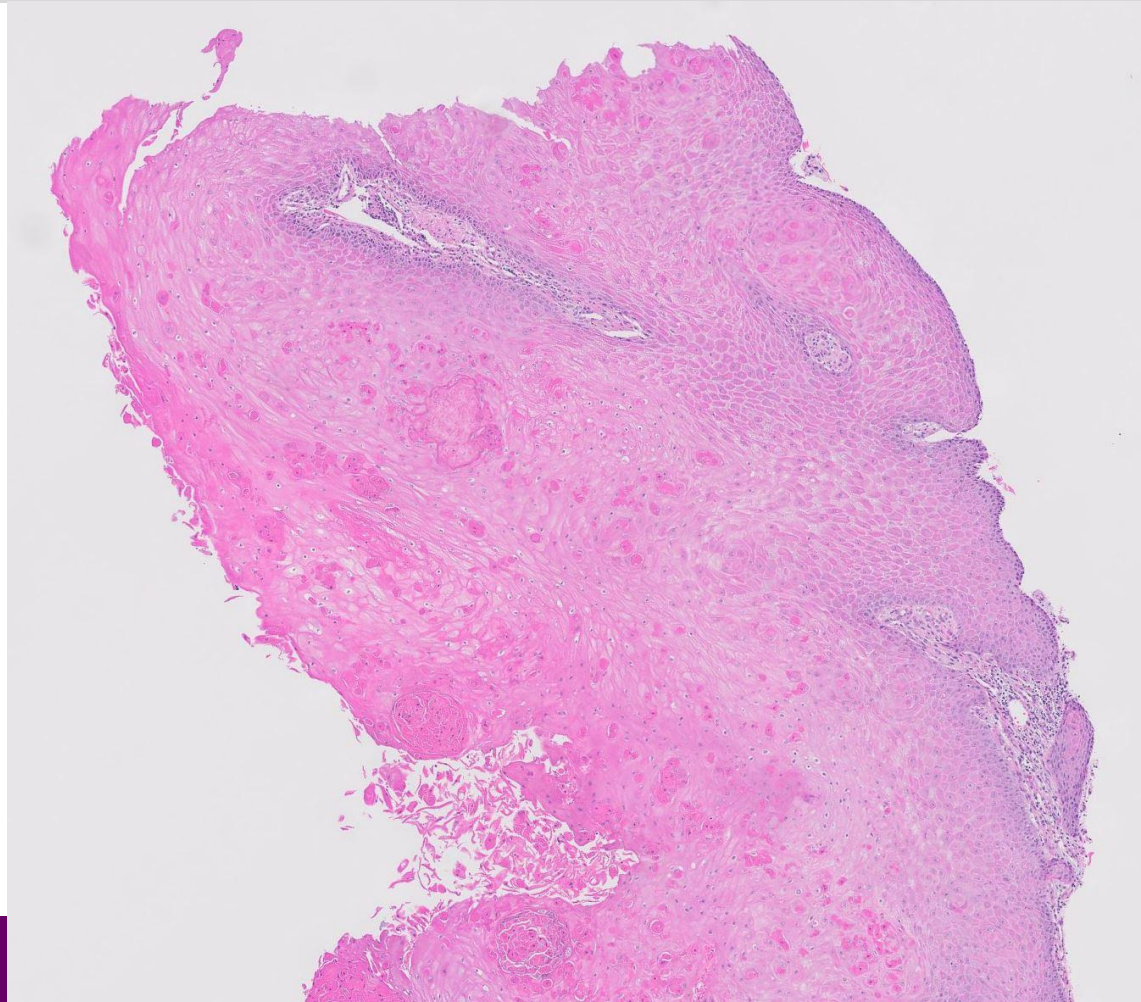
64 y/o male



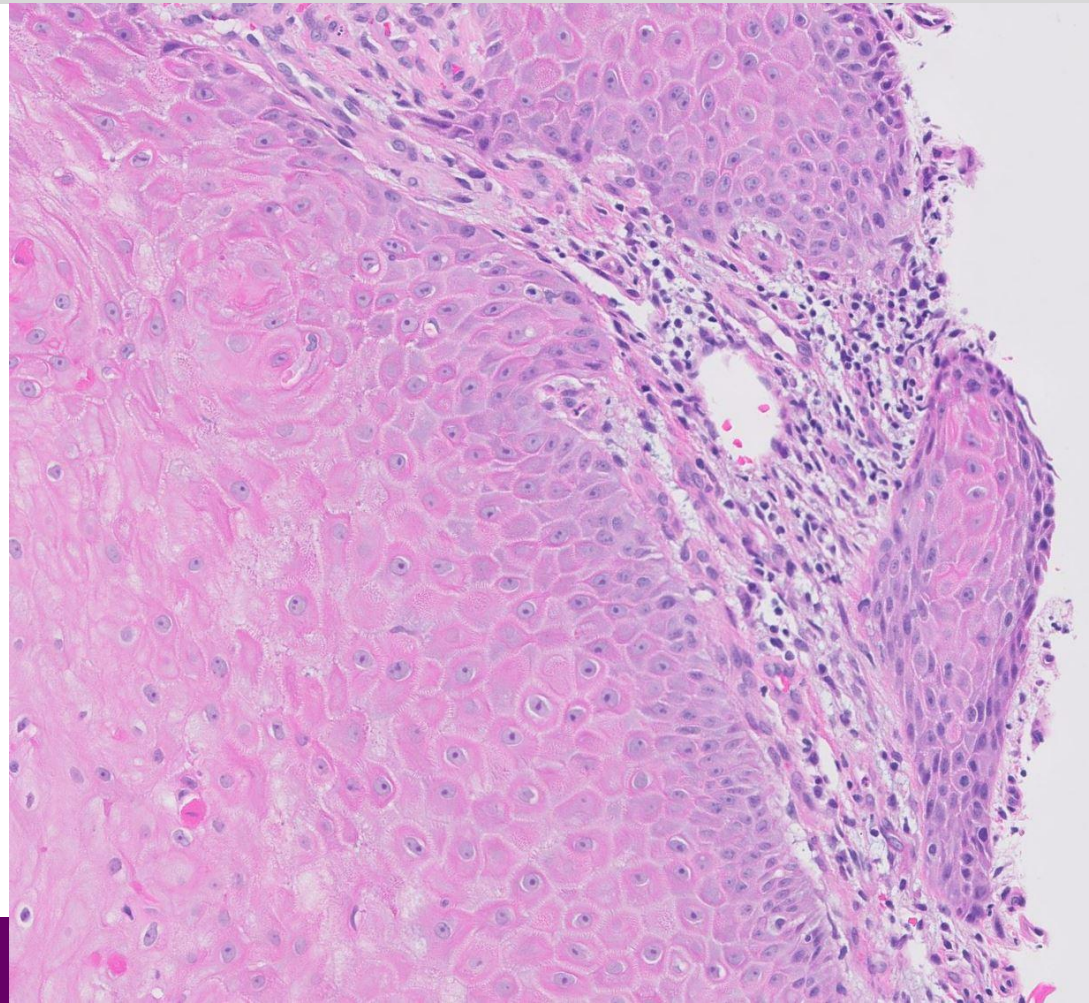
64 y/o male



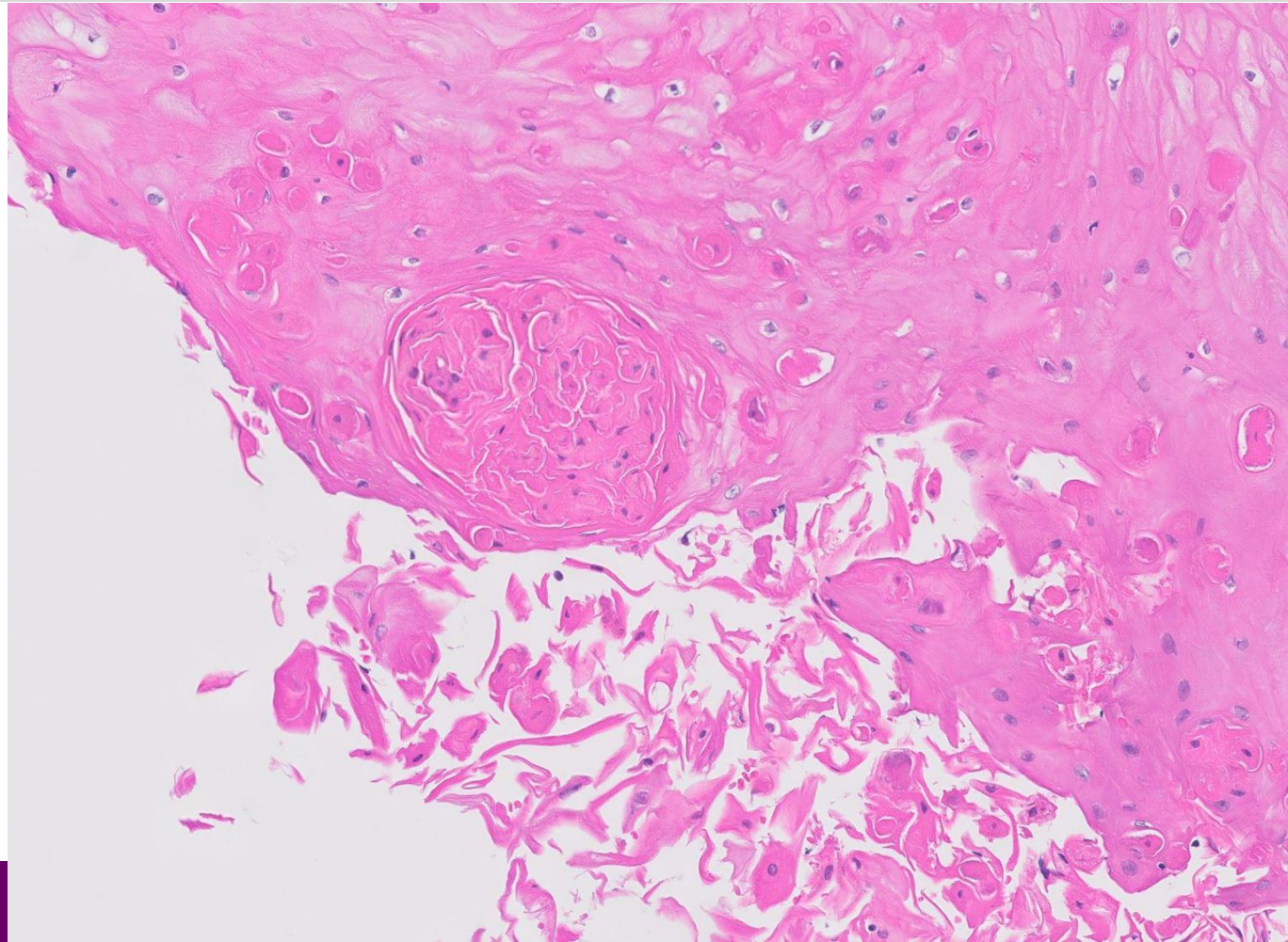
64 y/o male



64 y/o male



64 y/o male



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

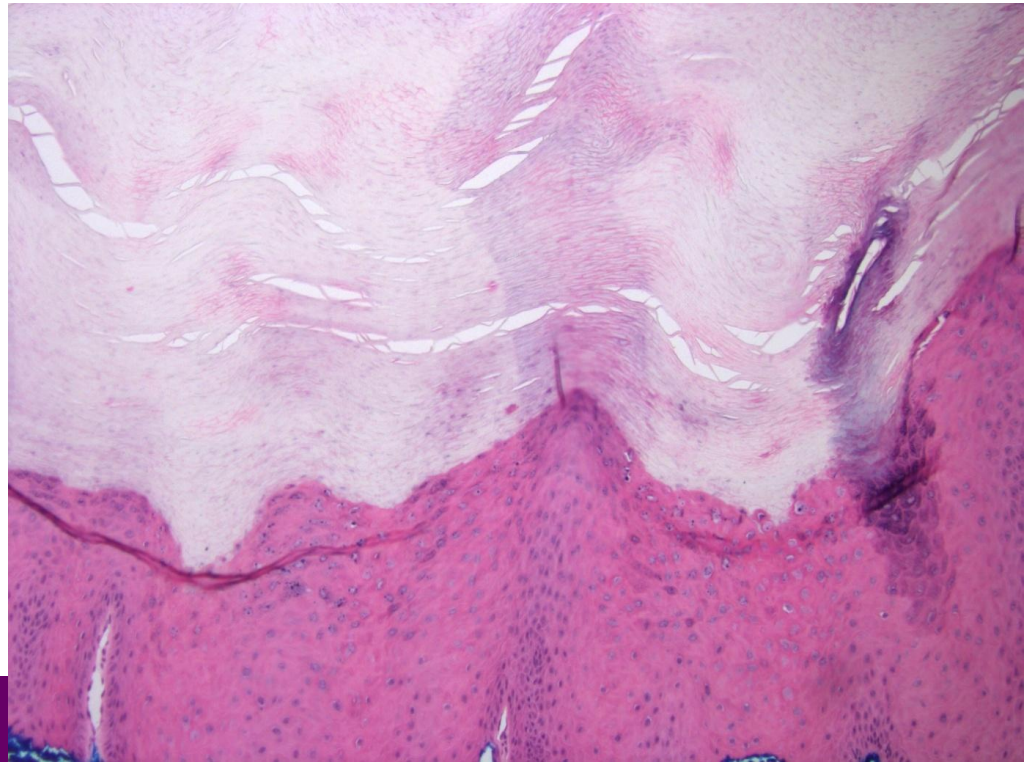
- Crateriform squamous proliferation with abundant keratin and parakeratotic foci
- Minimal keratinocytic atypia
- Variable mixed inflammatory cell infiltrate with intraepithelial neutrophils and surrounding lymphocytes, plasma cells and sometimes eosinophils

Subungual Keratoacanthoma

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

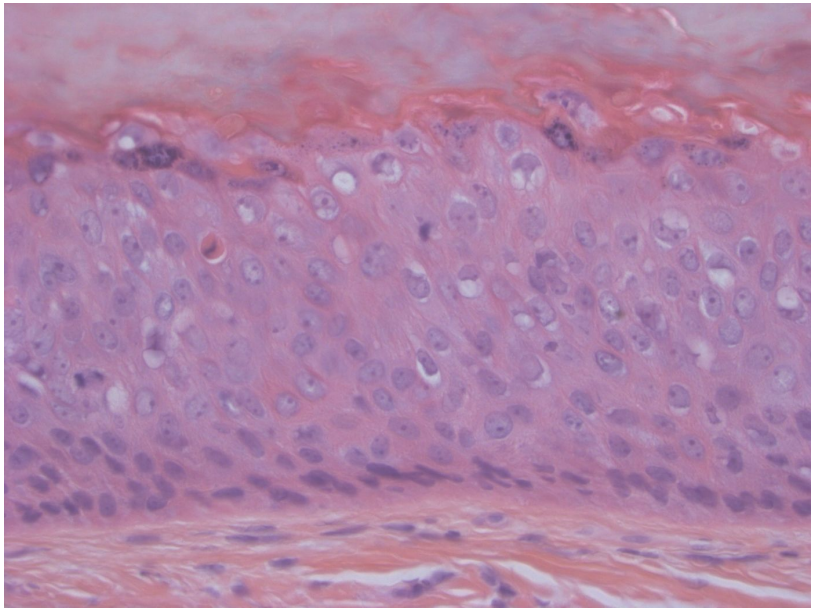
Subungual Keratoacanthoma Differential

- Verruca or SCC
  - Both HPV



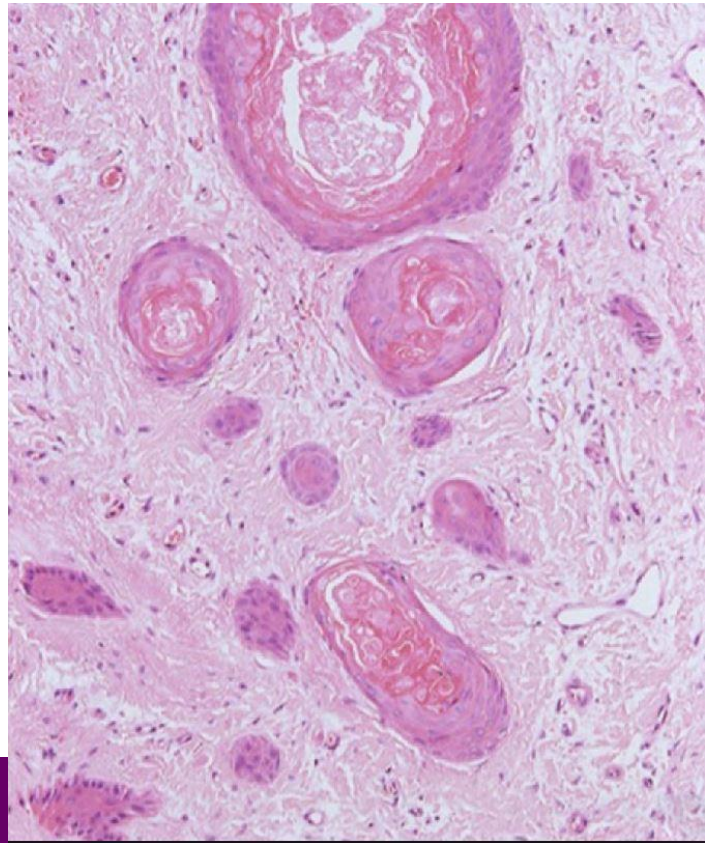
Subungual Keratoacanthoma Differential

- 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

Donati et al. Eur J Dermatol. 2009;19:243-7.

Confusing Nail Tumor Terminology

- Onychopapilloma
- Onychomatricoma
- Onychocytic matricoma
- Oncholemmal (cyst, horn tumor)

Onychopapilloma

Onychopapilloma

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

Onychopapilloma

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

Figure 1

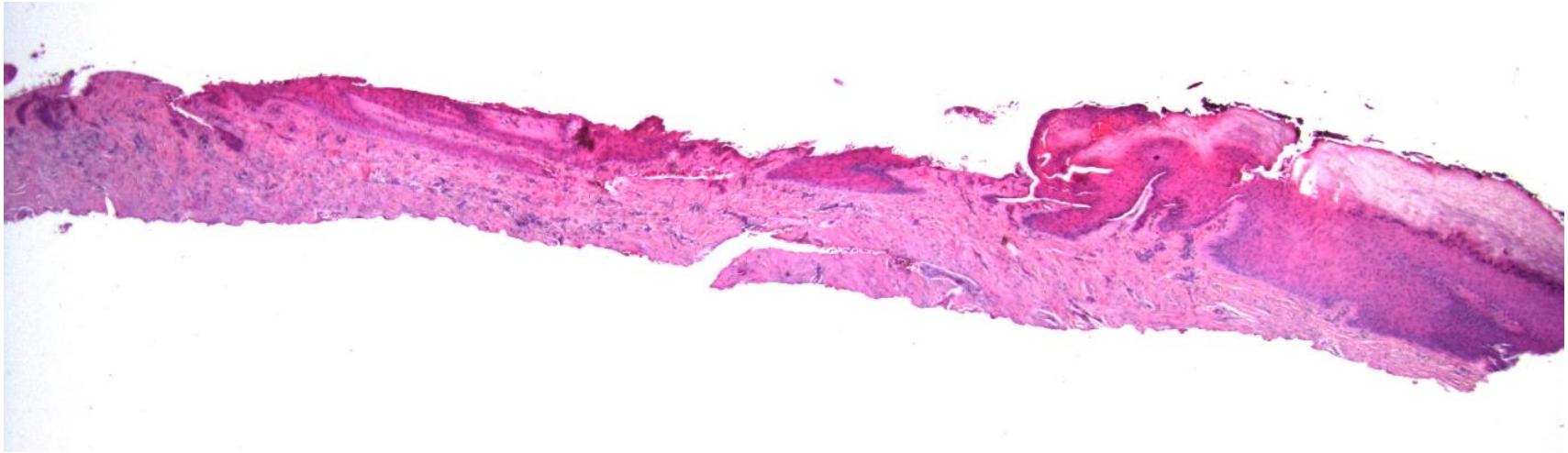
Onychopapilloma

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

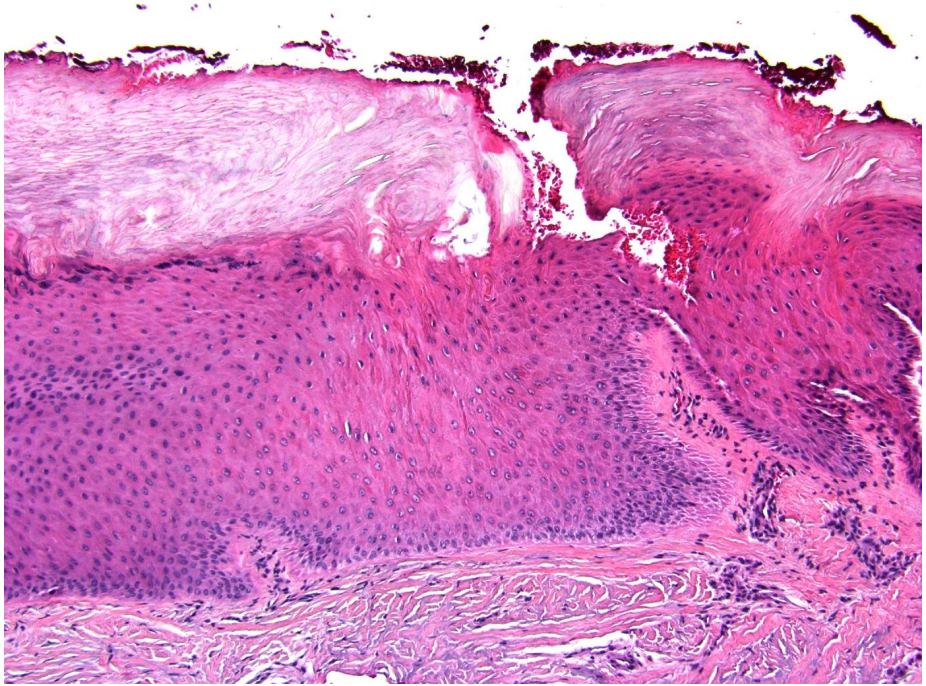
Embed proximal to distal

Figure 1

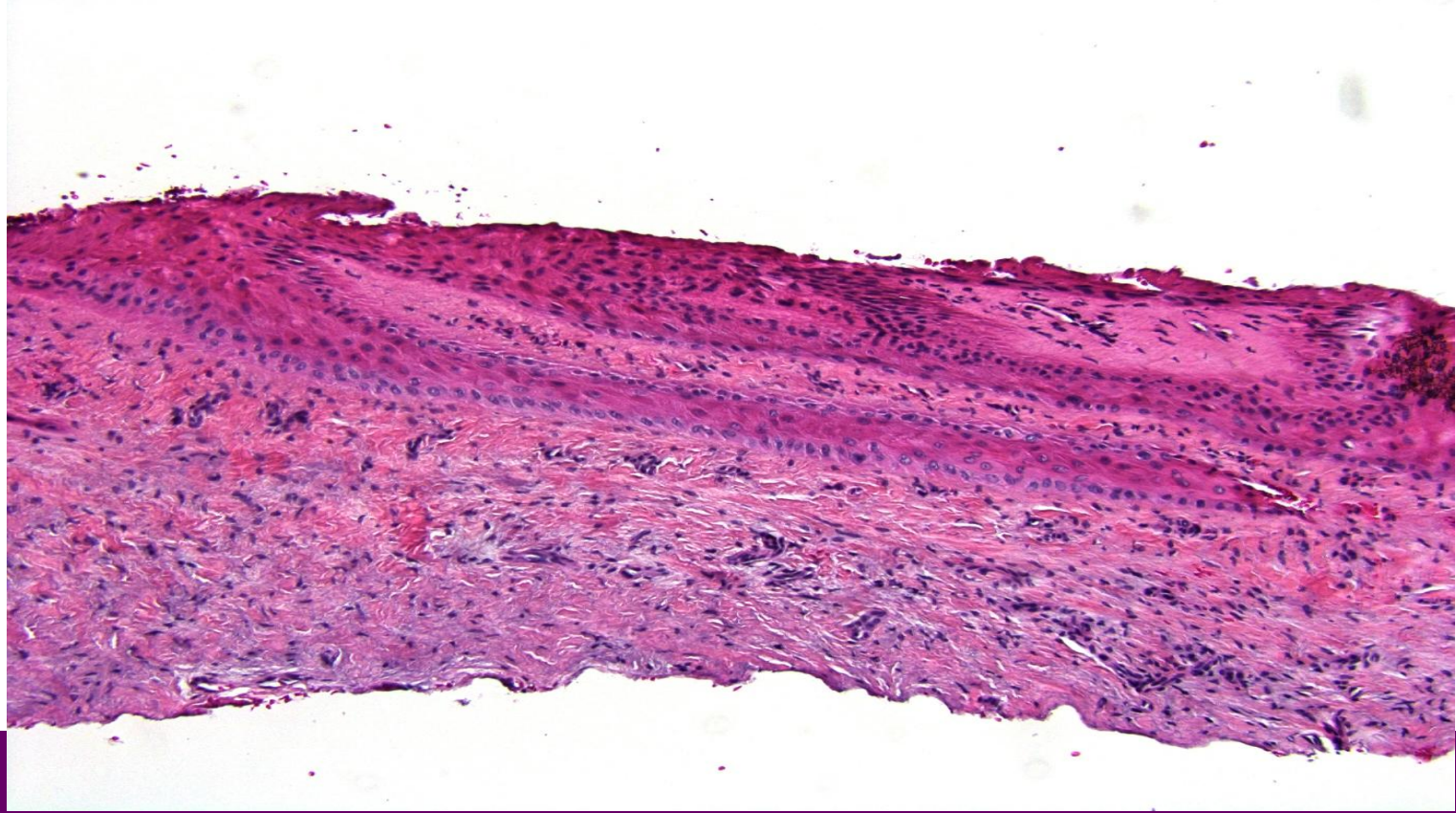
Onychopapilloma—Keratin Producing



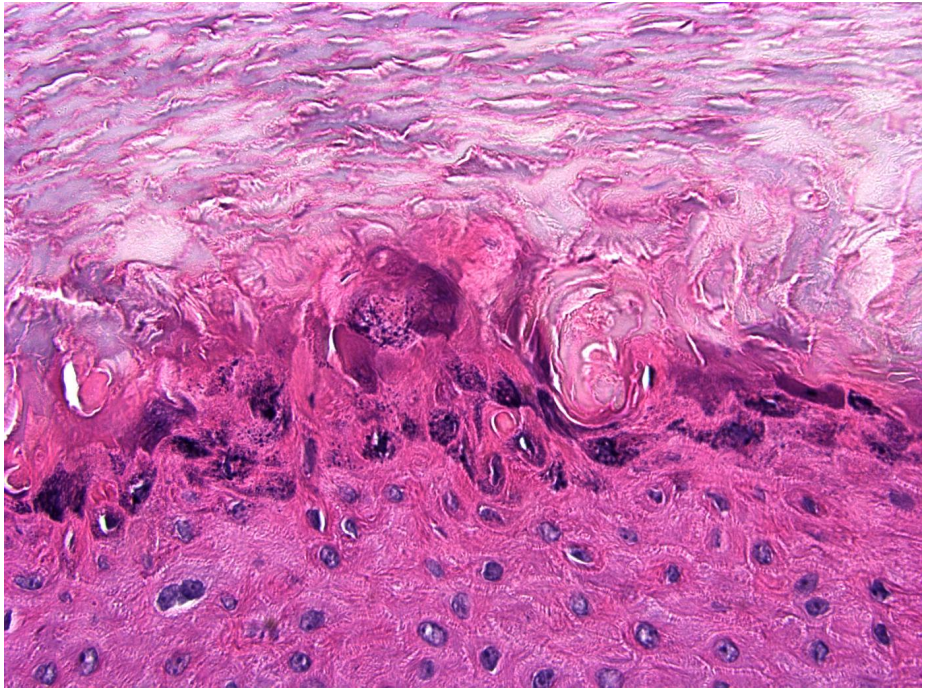
Onychopapilloma—Keratin Producing



Onychopapilloma



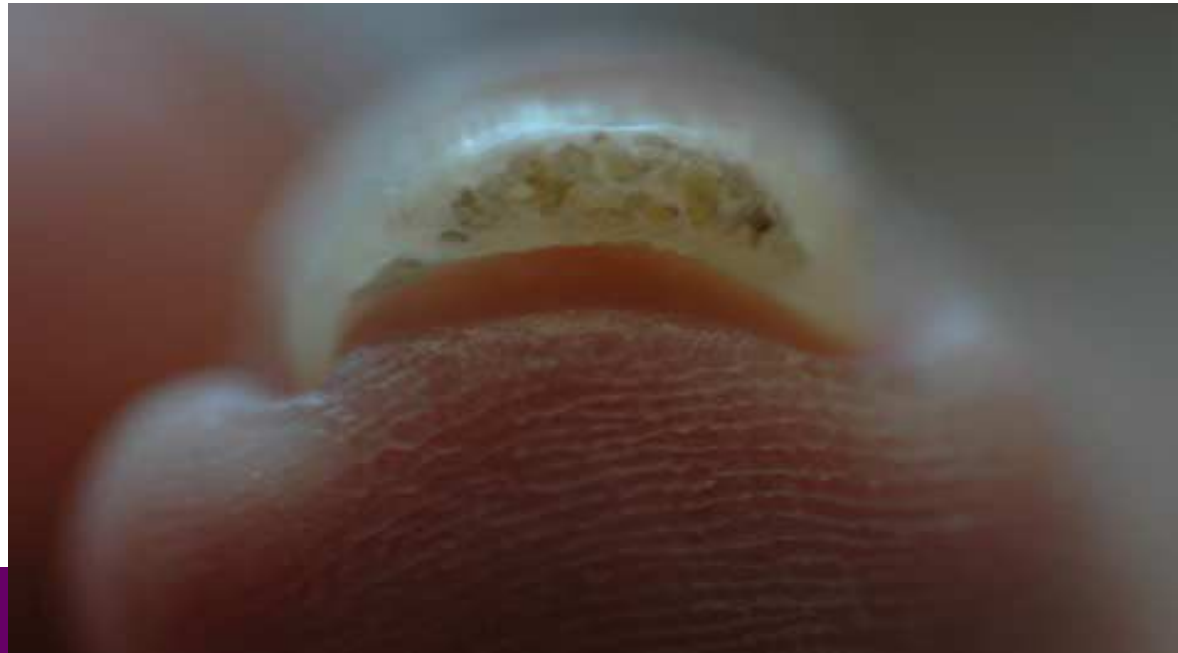
Onychopapilloma—Not a wart



Onycomatricoma

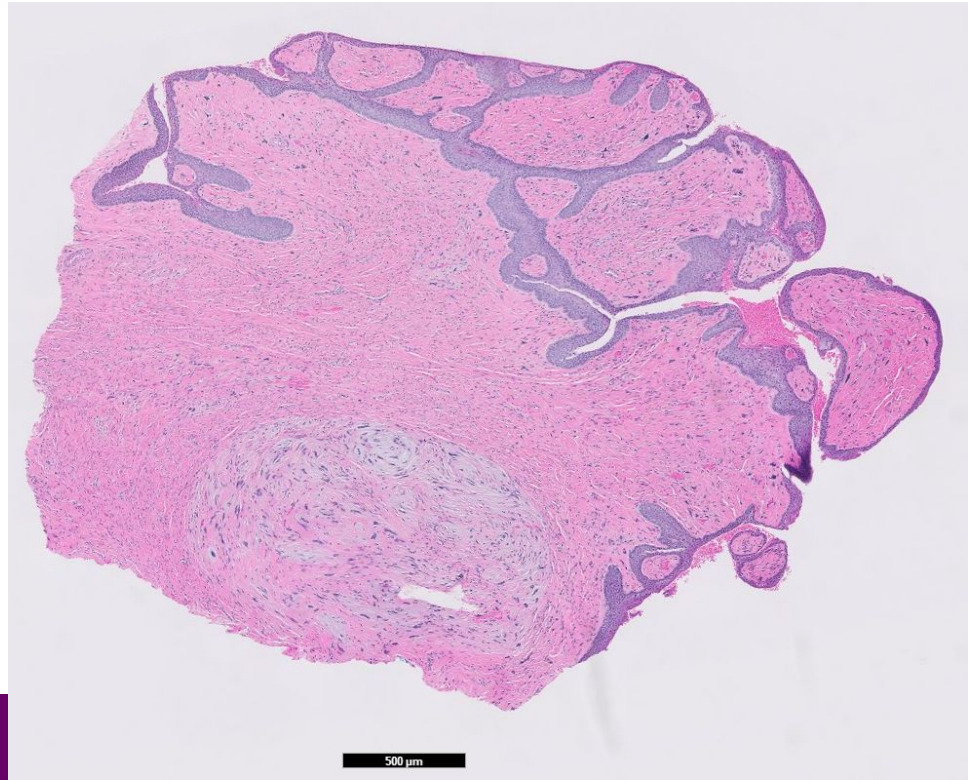
Onycomatricoma

- Examine nail for holes—Transverse sections of dystrophic nail

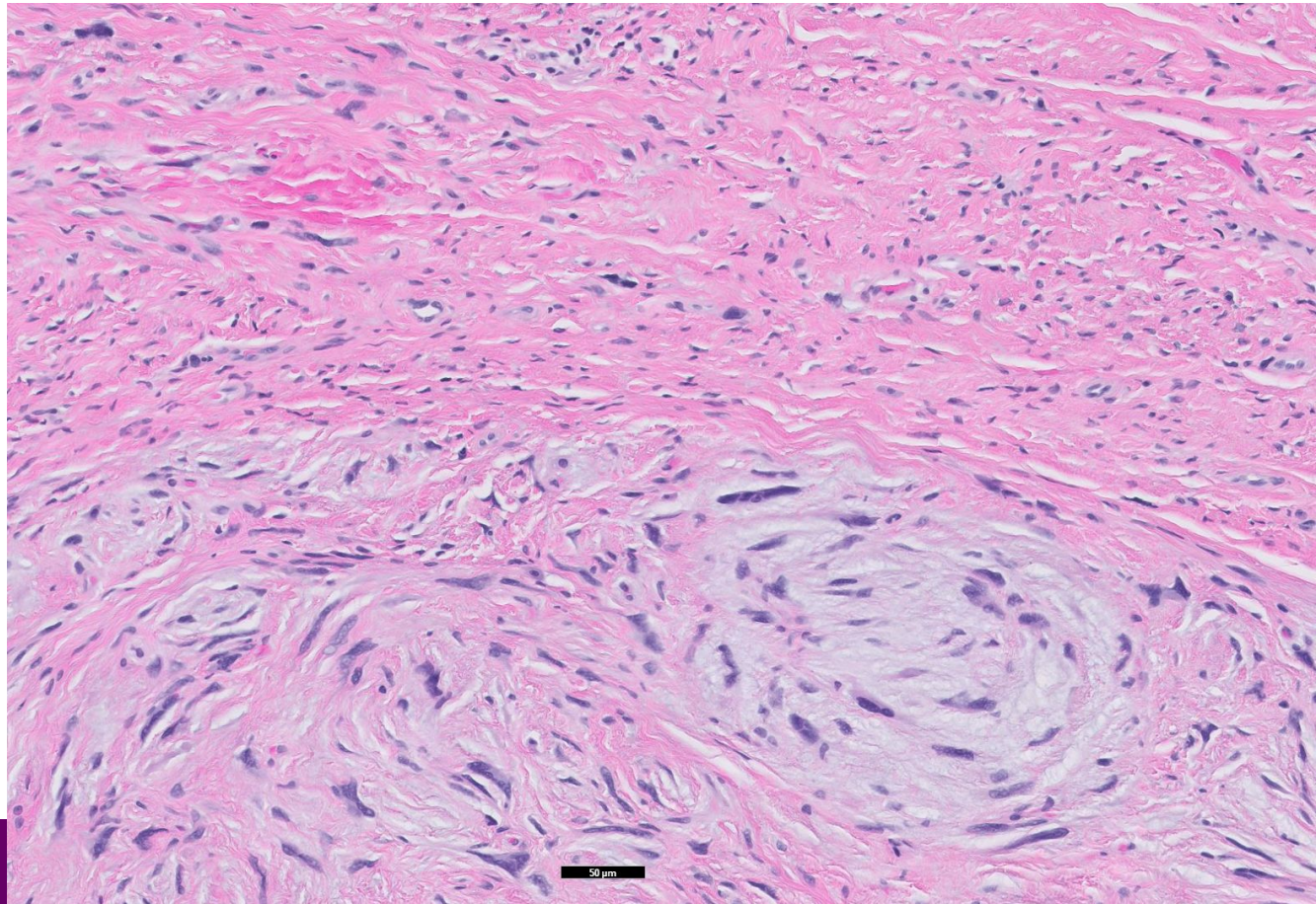


Onychomatricoma

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

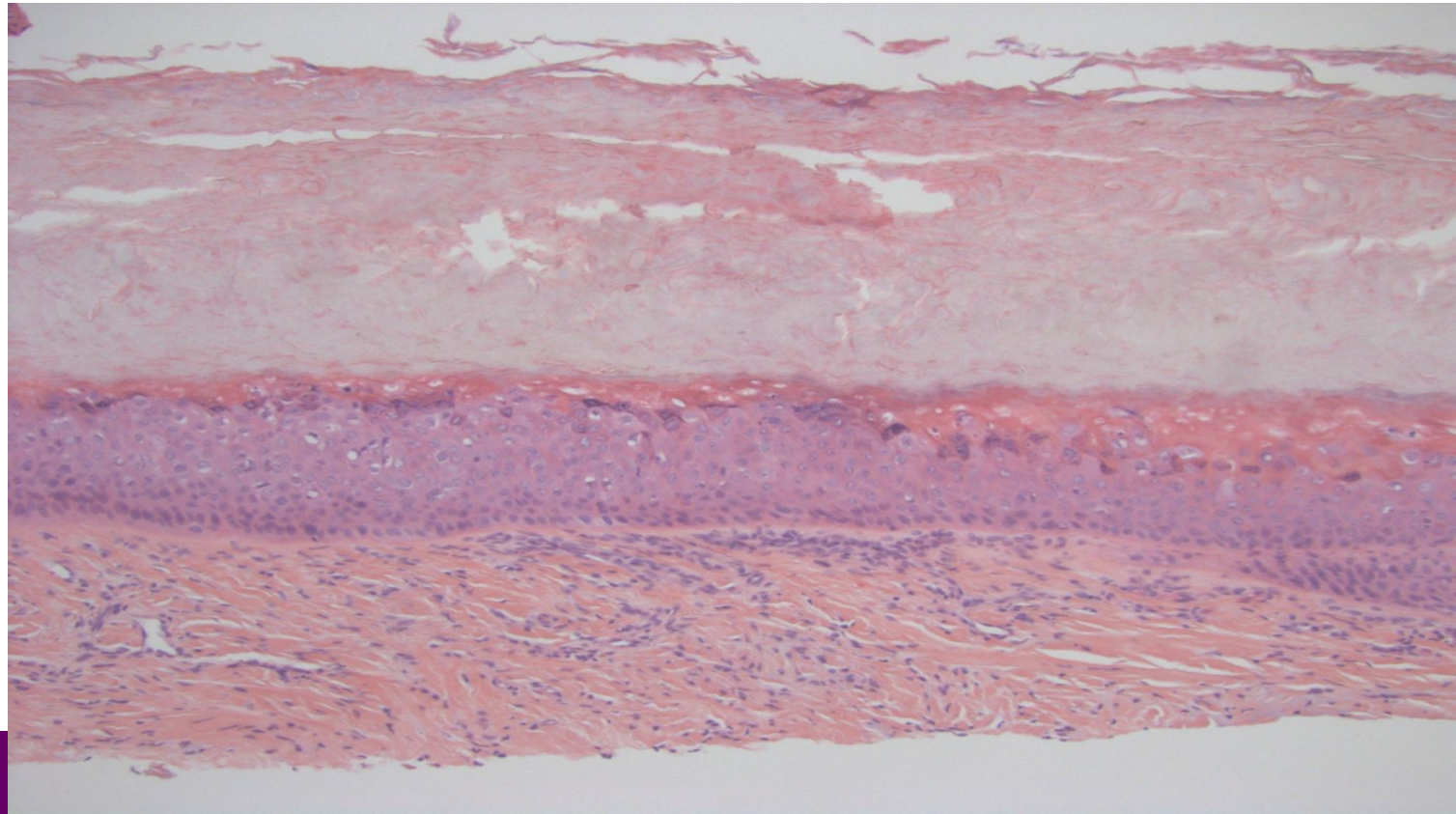


Onycomatricoma

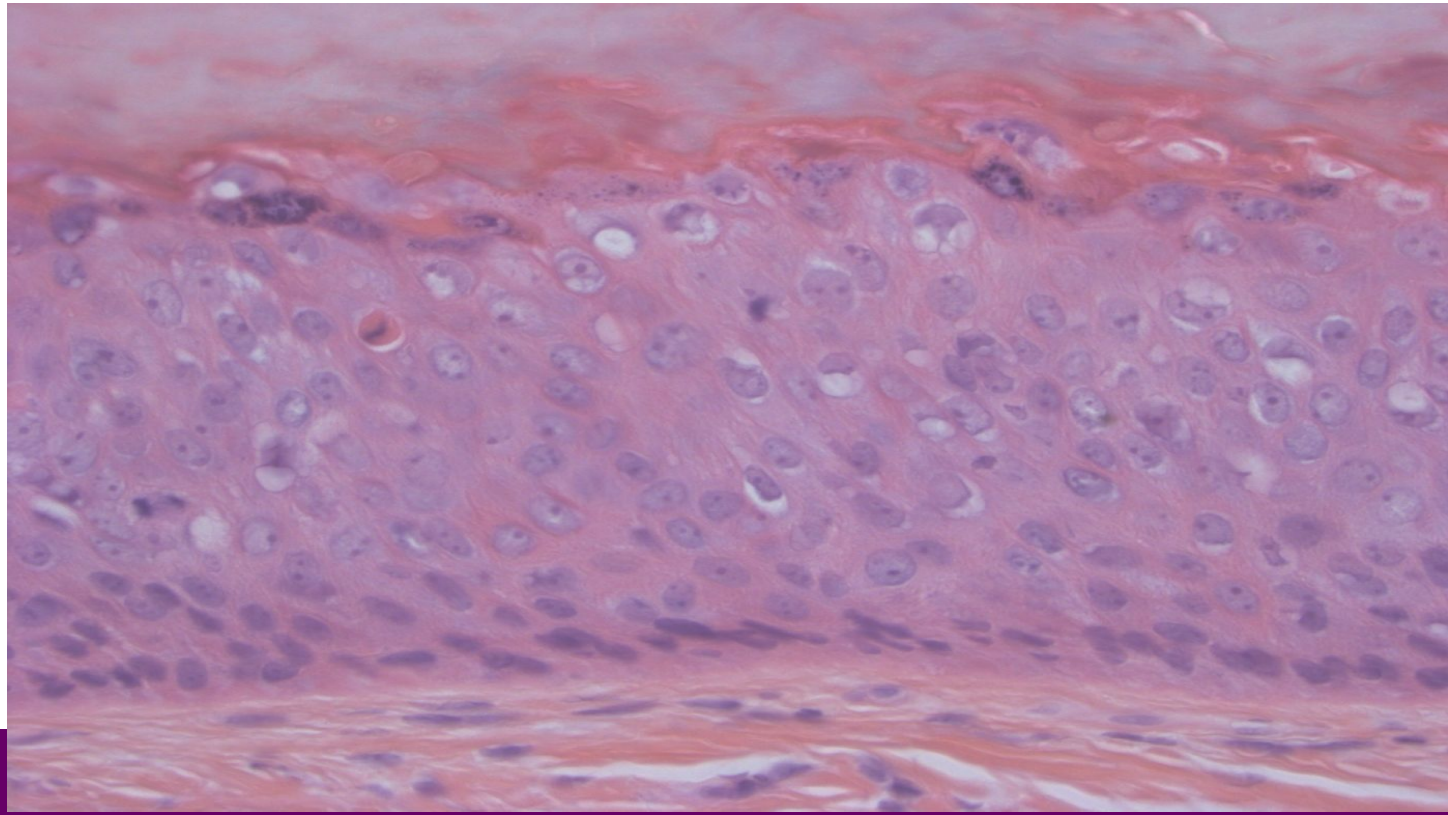


Squamous cell carcinoma

Squamous cell carcinoma

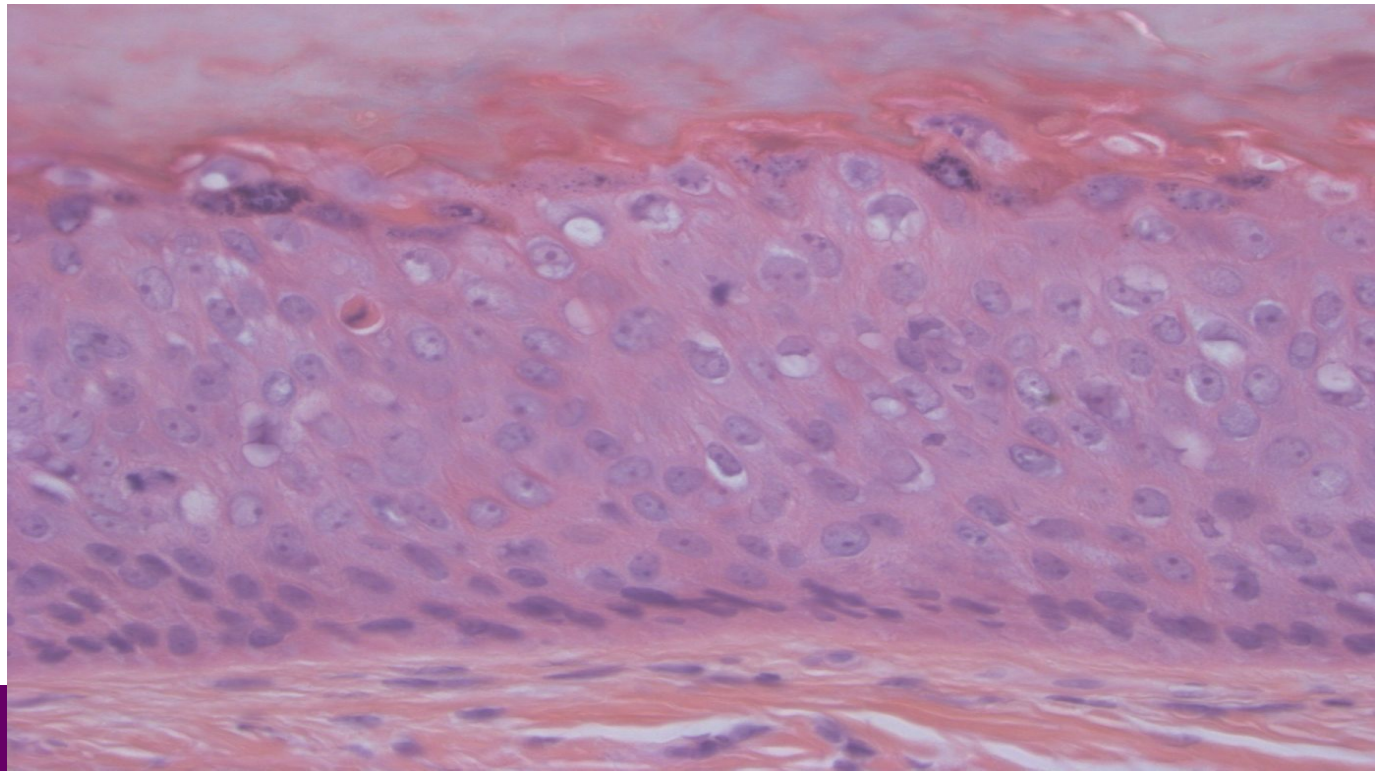


Squamous cell carcinoma in-situ

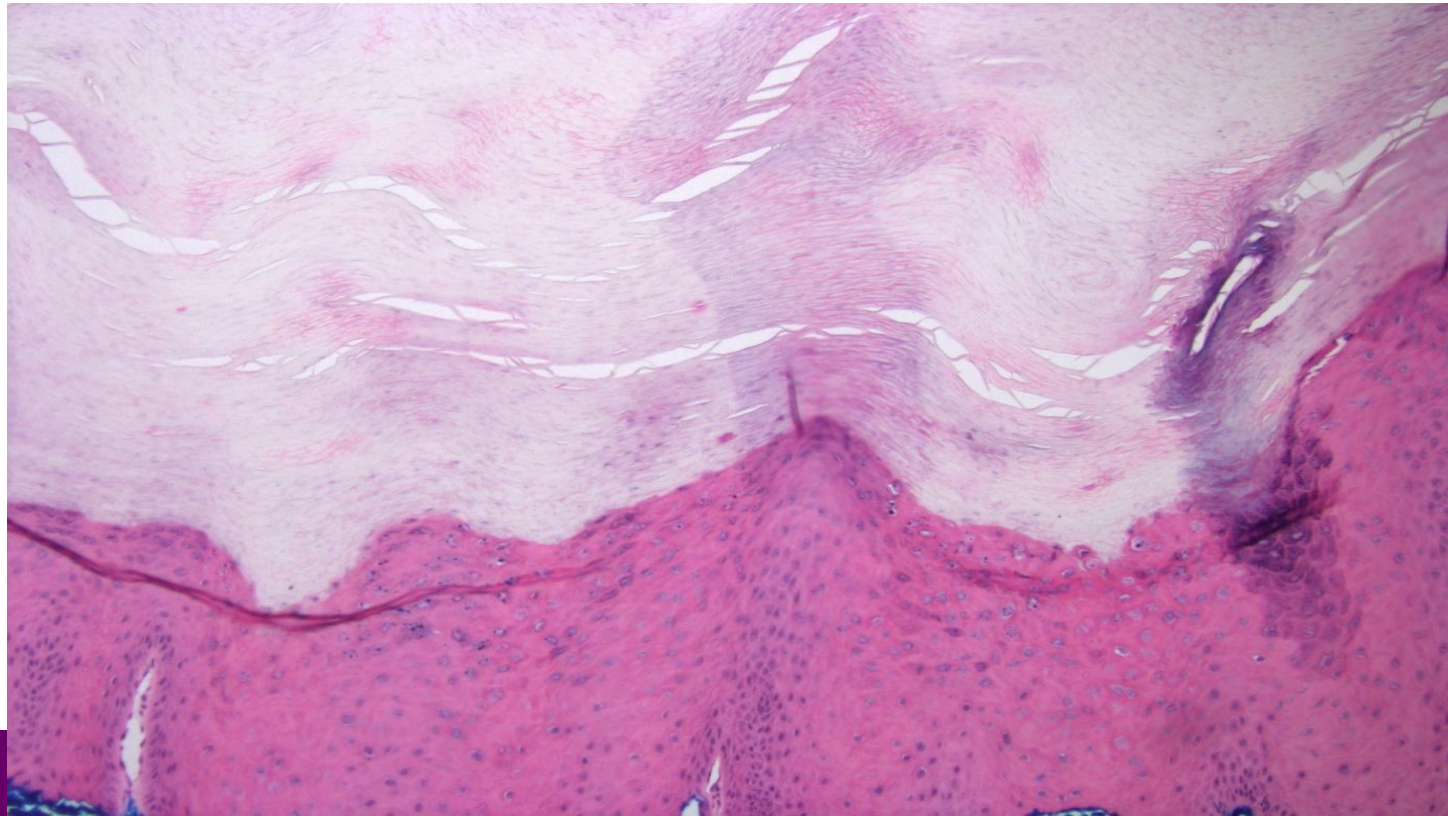


Squamous cell carcinoma in-situ

- Human Papillomavirus (HPV) features



SCC versus Wart/Verruca



SCC versus Wart/Verruca

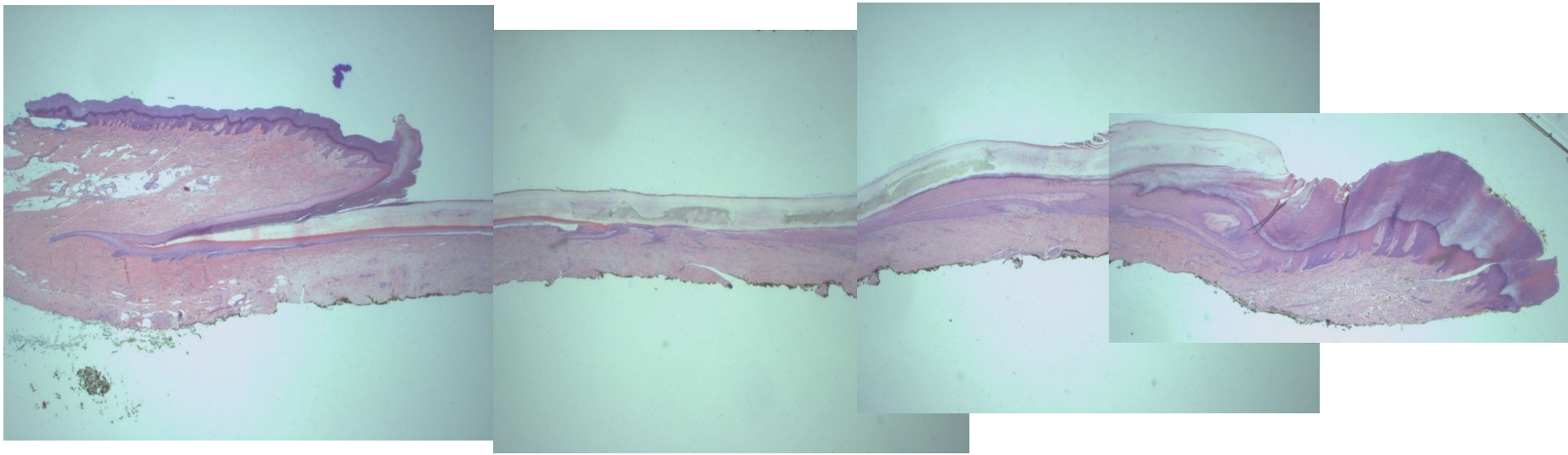
- Clinical correlation often necessary
  - Immunosuppression (esp HIV)
  - If it is destroying bone, it is not benign!
  - Sample more if suspicious

HPV In-situ Hybridization (ISH)

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

Hutchinson's Sign

Hutchinson's Sign



Hutchinson’s Sign

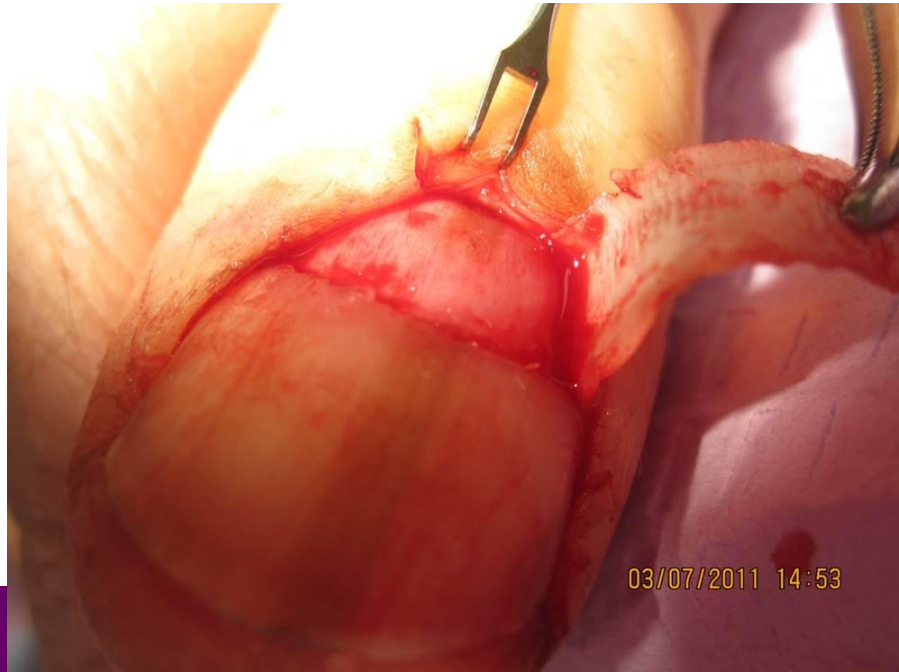
- J Am Acad Dermatol. 2001 Feb;44(2):305-7.
- **Two kinds of Hutchinson's sign, benign and malignant.**
- Kawabata YKawabata Y, Ohara KKawabata Y, Ohara K, Hino H, Tamaki K.
- Department of Dermatology, Faculty of Medicine, University of Tokyo, Japan. KAWABATA-der@h.u-tokyo.ac.jp
- We examined 6 subungual melanomas in situ and 18 melanocytic nevi and compared pigmentation of the nail plates and hyponychium with the use of a dermatoscope. Hutchinson's sign on the hyponychium was not always evidence of subungual melanoma because it can be seen in both diseases. However, there was a wide difference in their dermatoscopic features. We believe that observation of pigmentation on the hyponychium with the use of a dermatoscope contributes to the precise diagnosis of subungual melanoma.

Dr. Rich's Differential Diagnosis

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

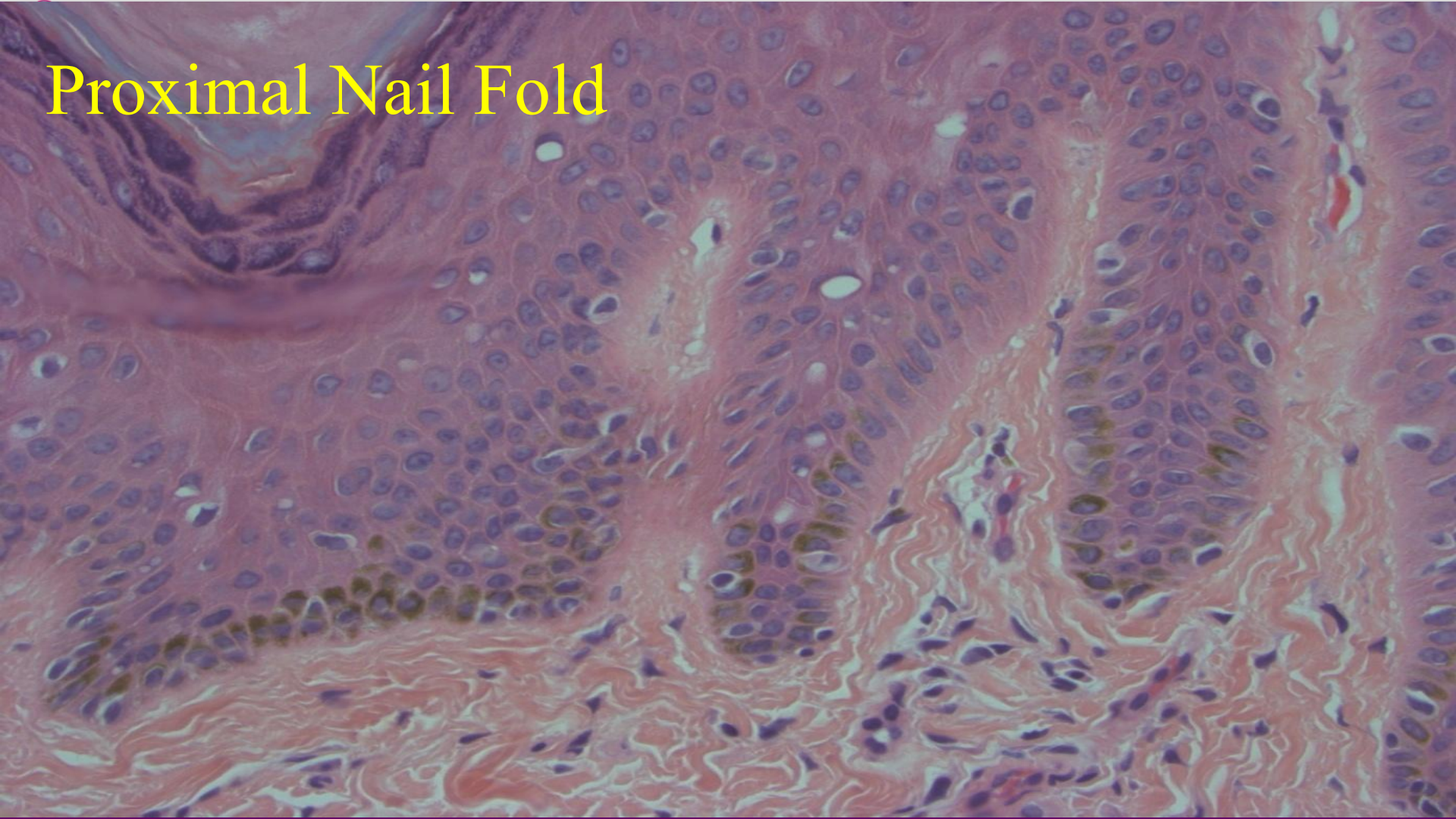
Biopsy

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

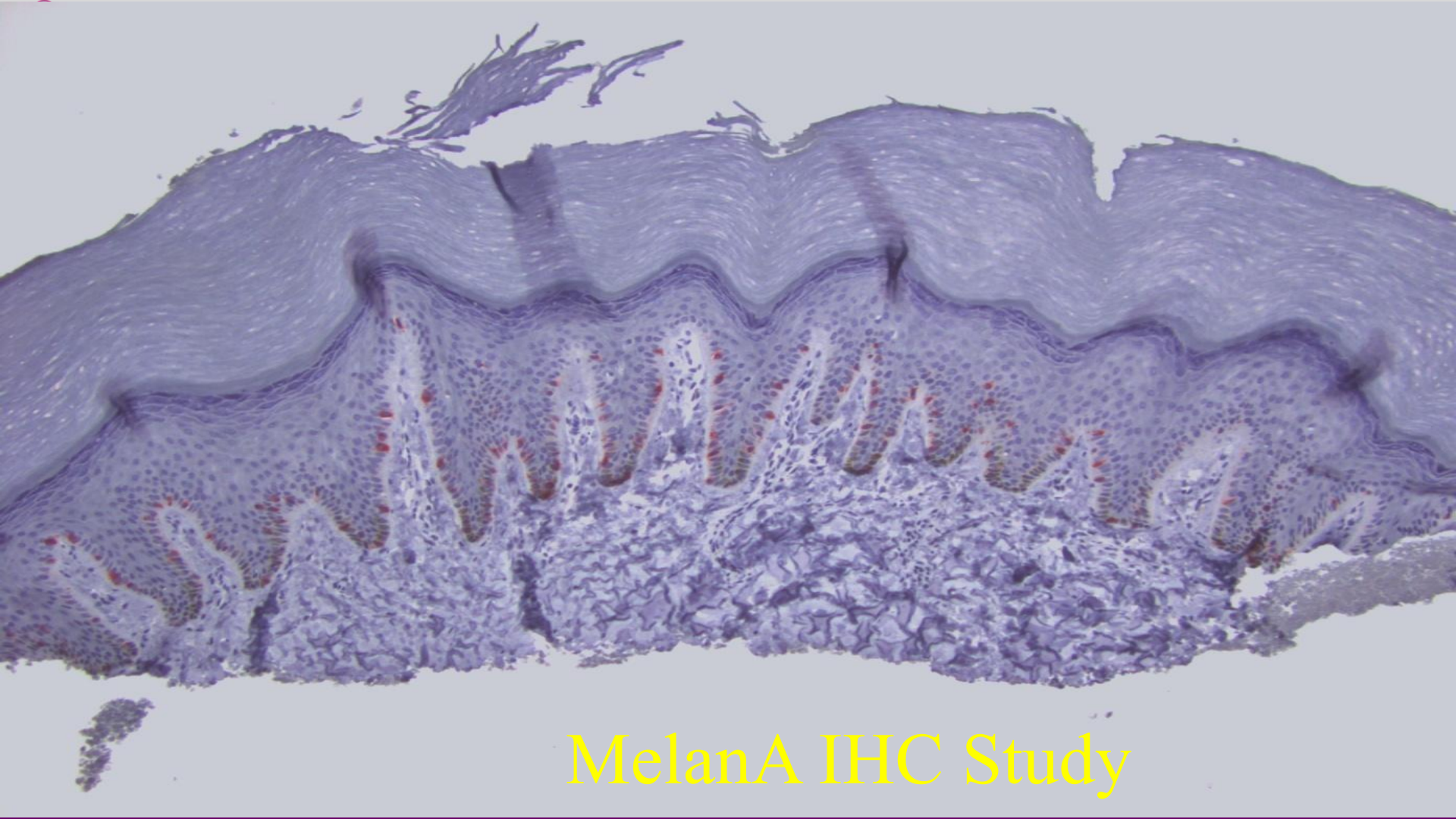


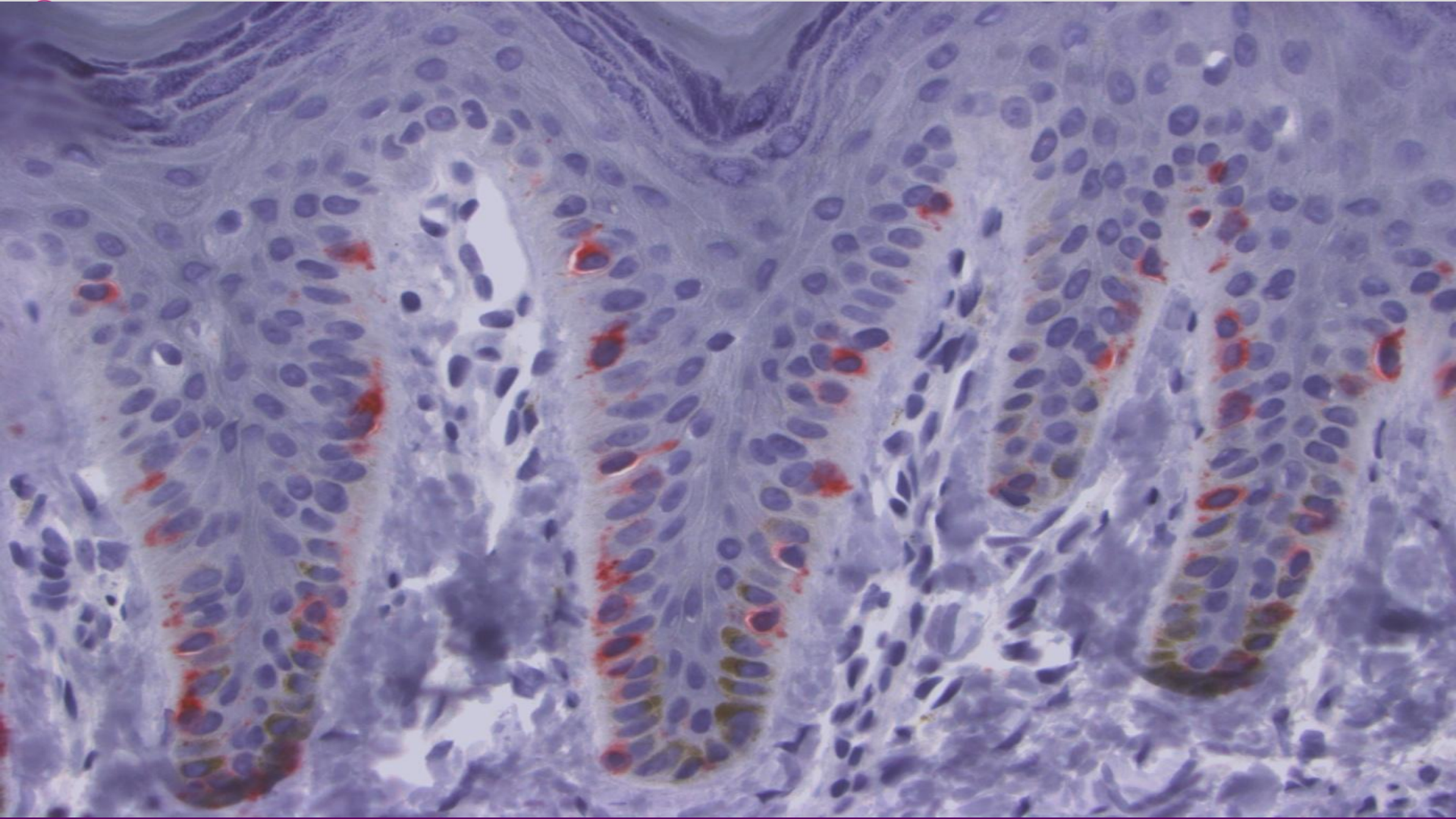
Proximal Nail Fold

Proximal Nail Fold

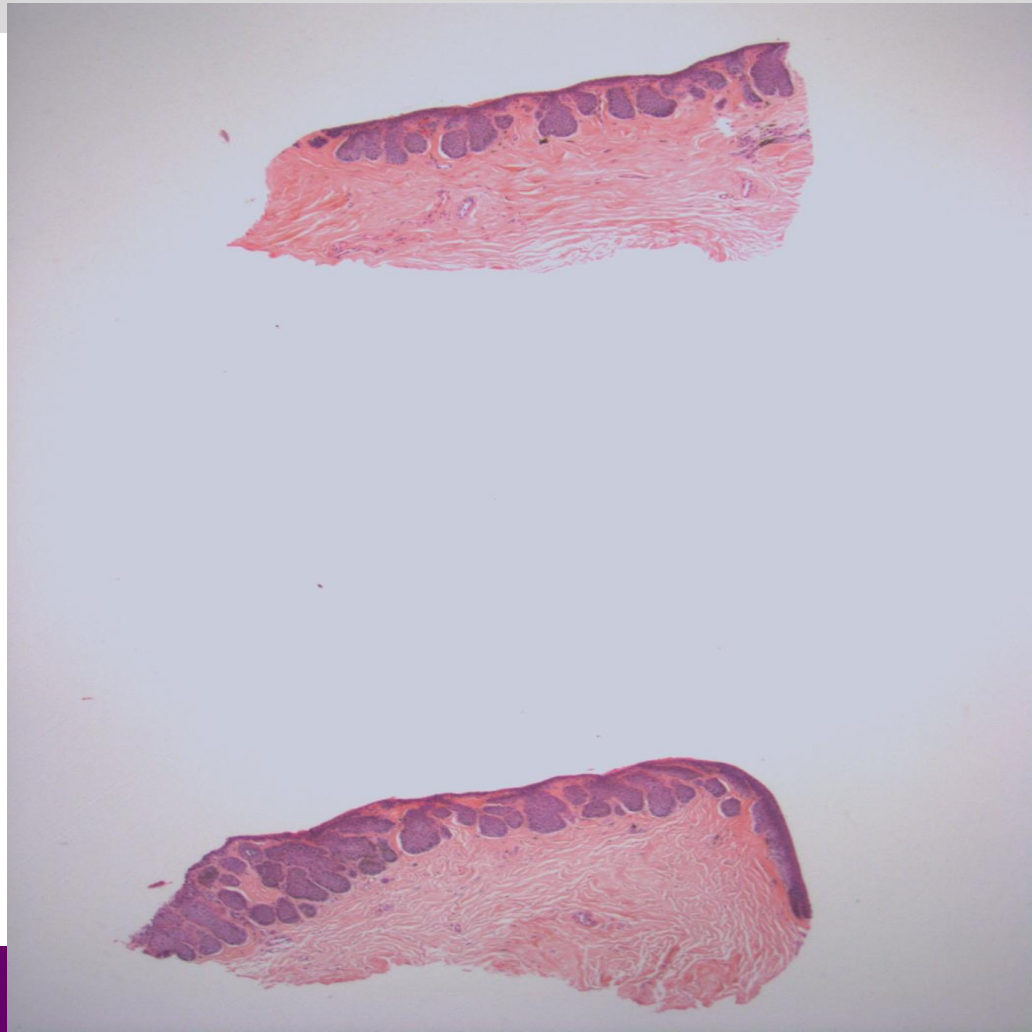


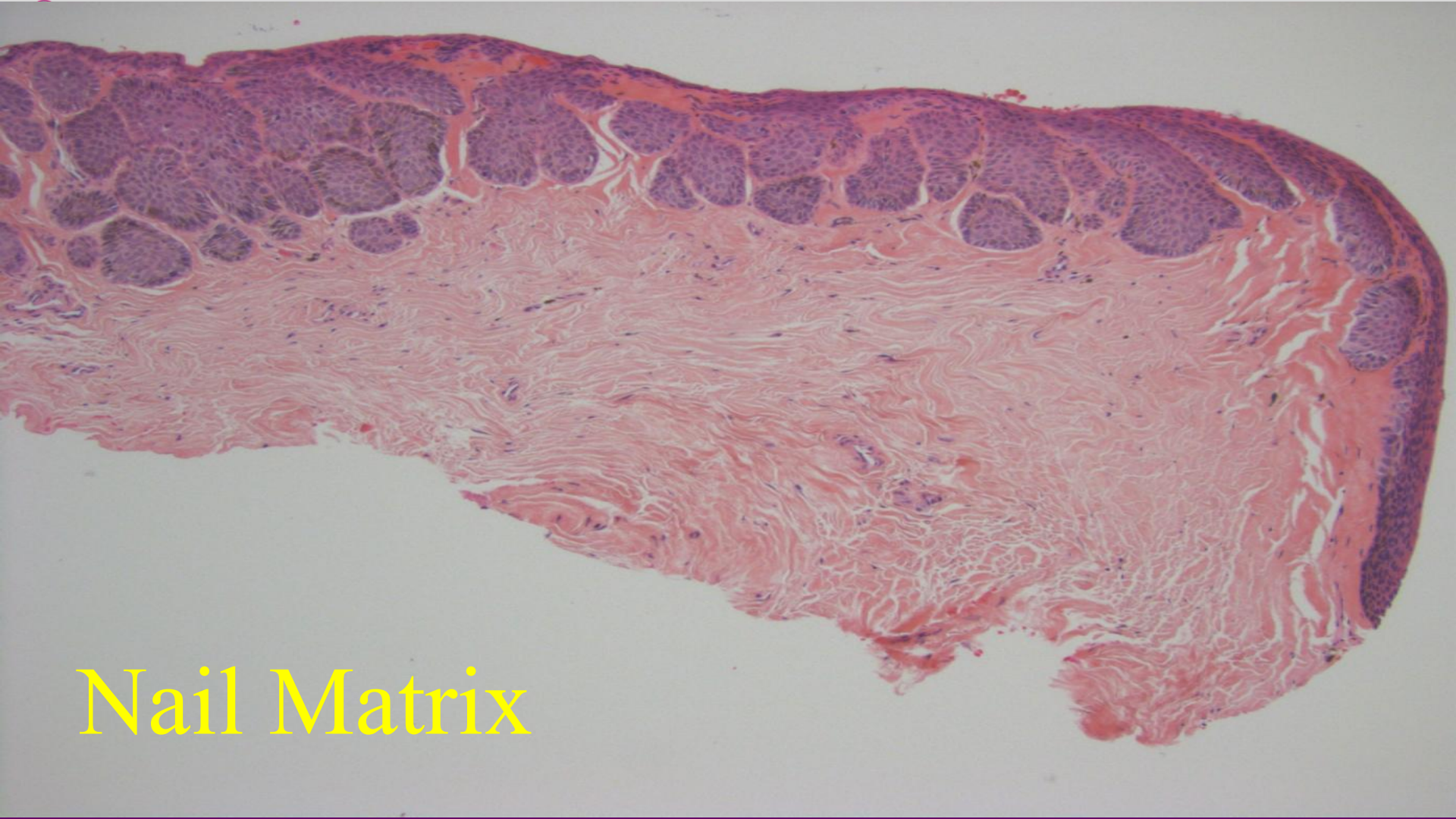

Fontana-Masson Stain


MelanA IHC Study

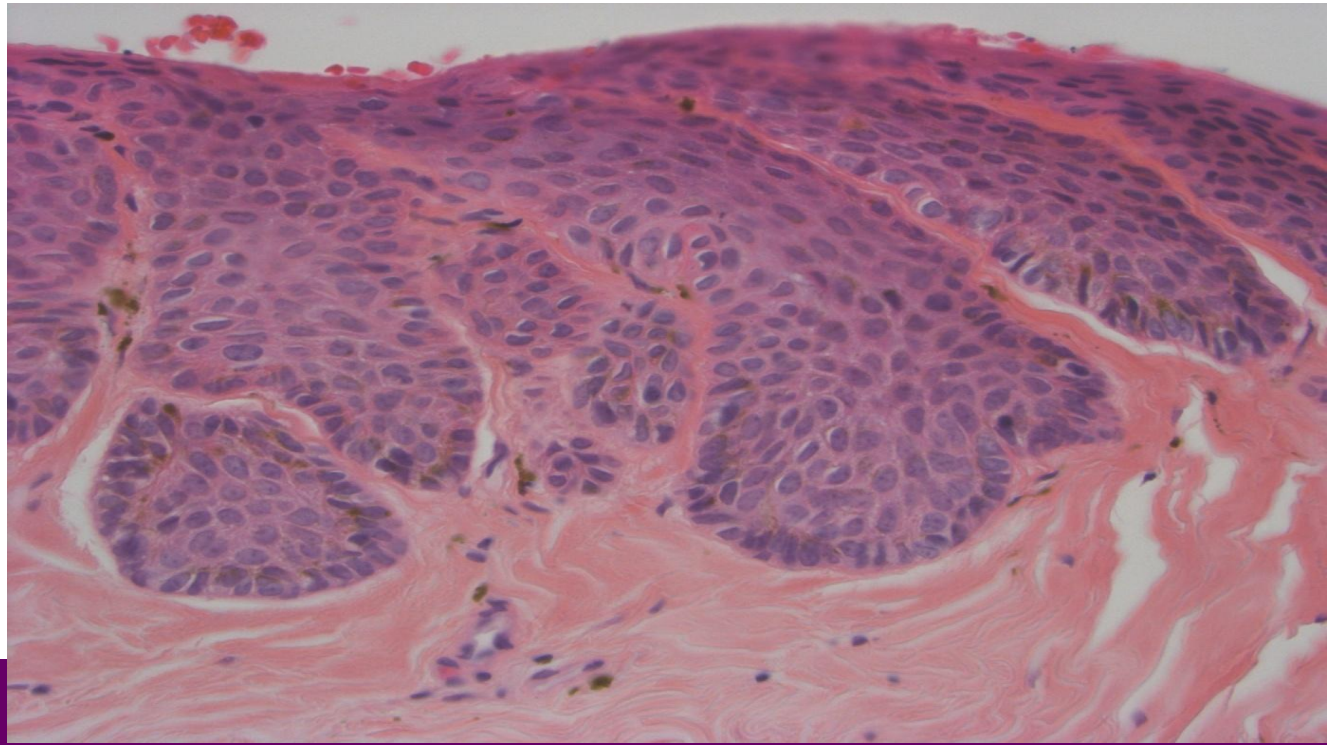


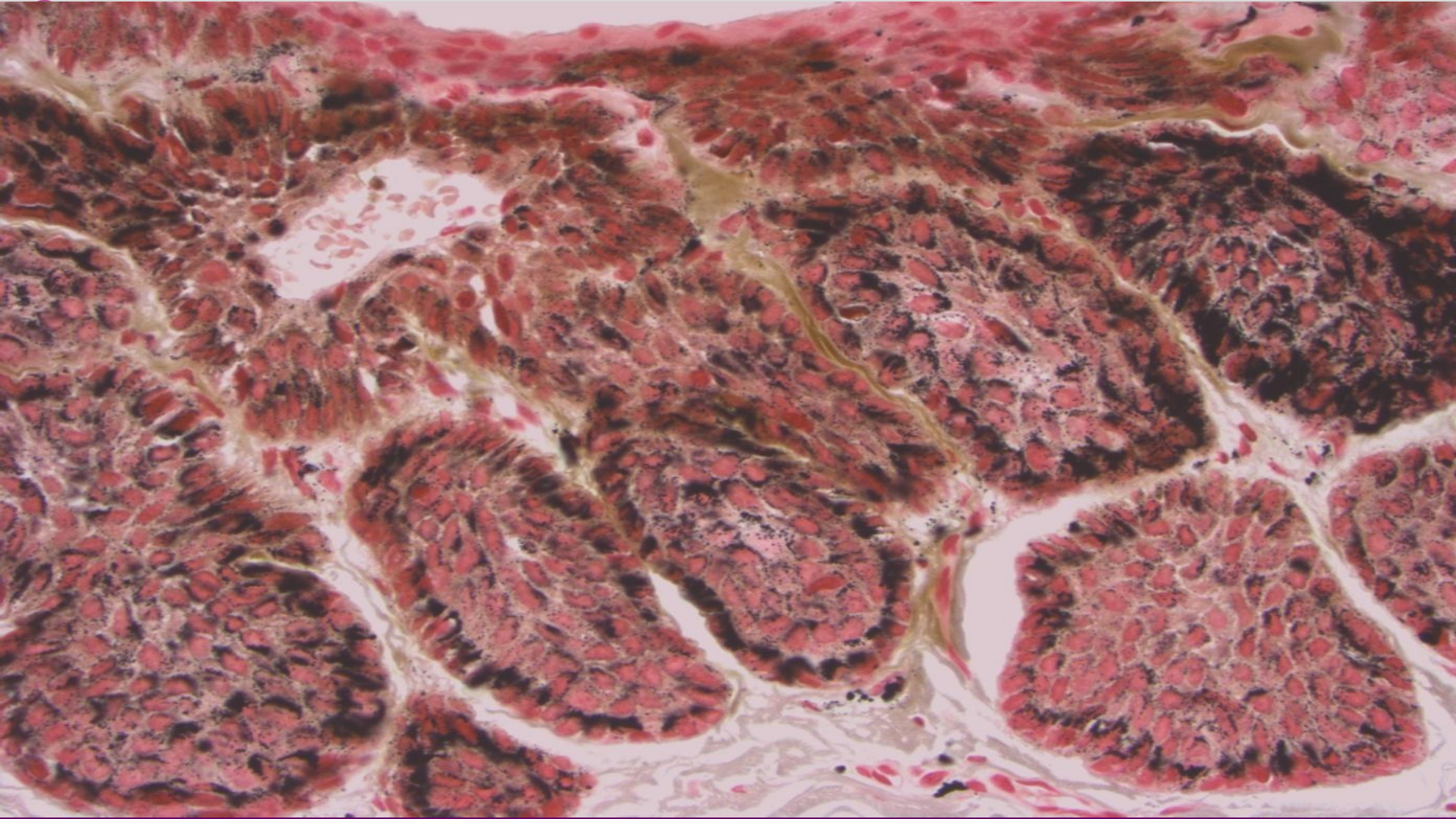
Nail Matrix

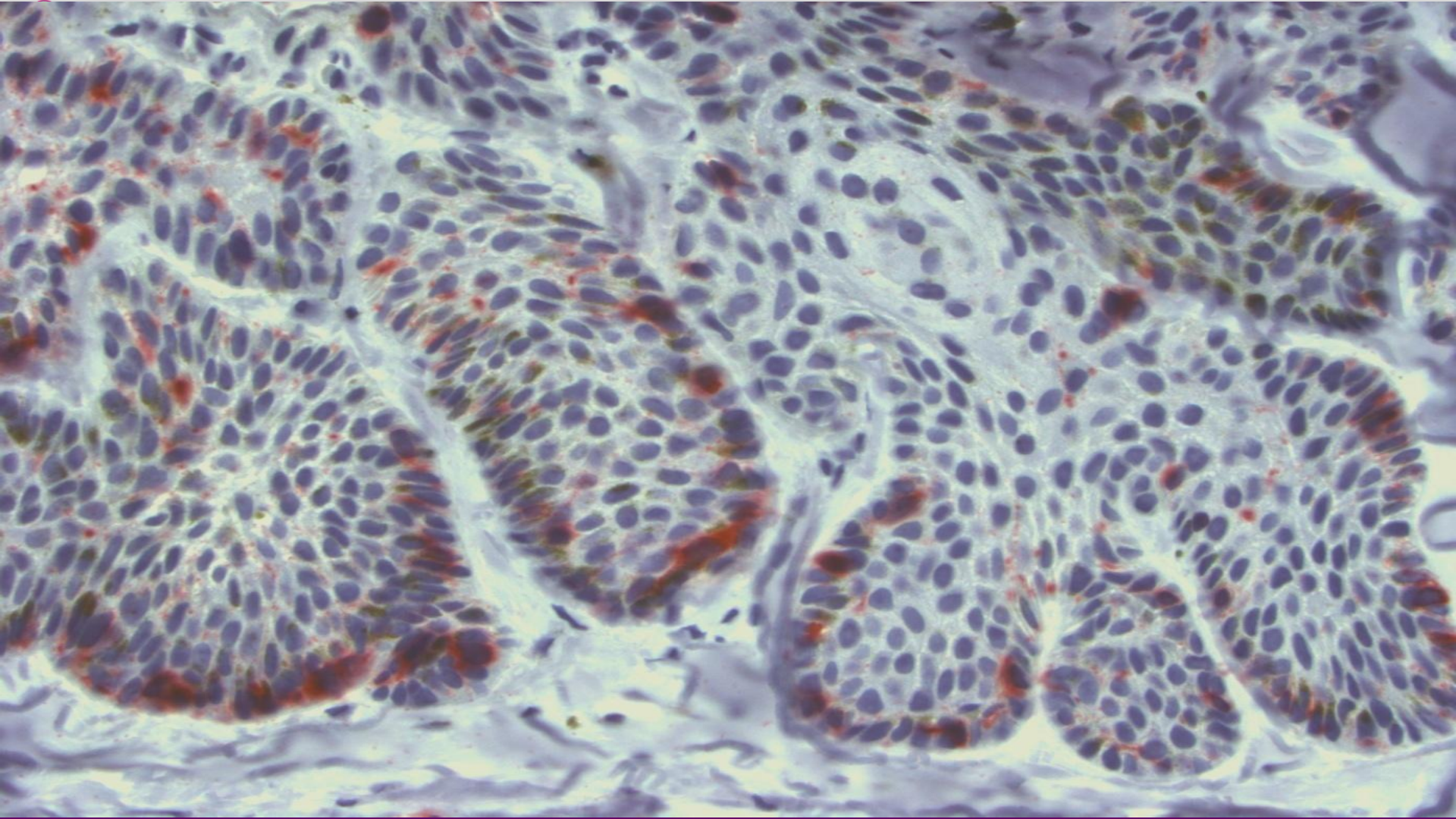


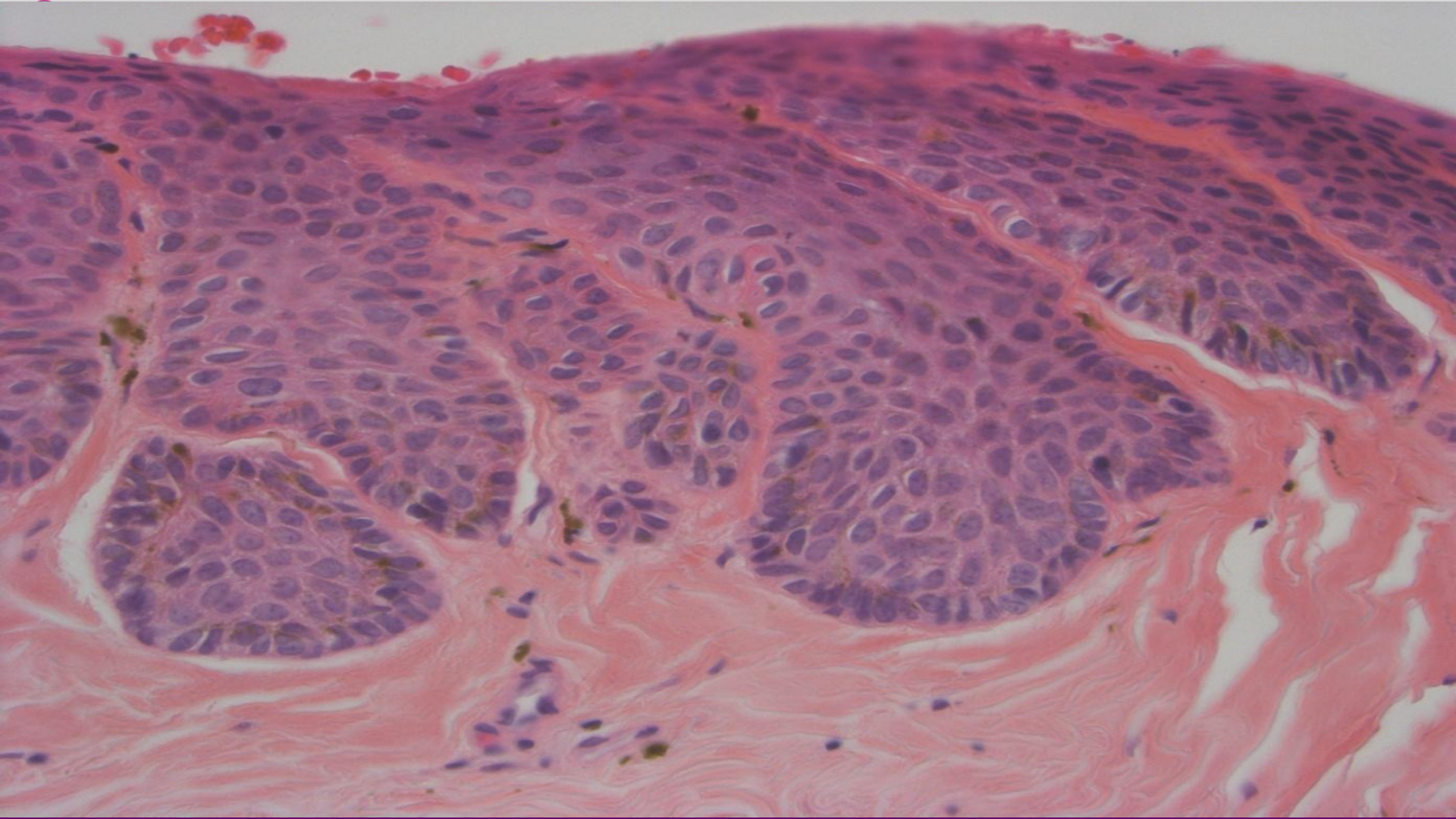

Nail Matrix

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 C[1], 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, MD[1]; Erika Reid, MD[1]; Adam I. Rubin, MD[1]

[1]Department 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 vs Nail unit seborrheic keratosis

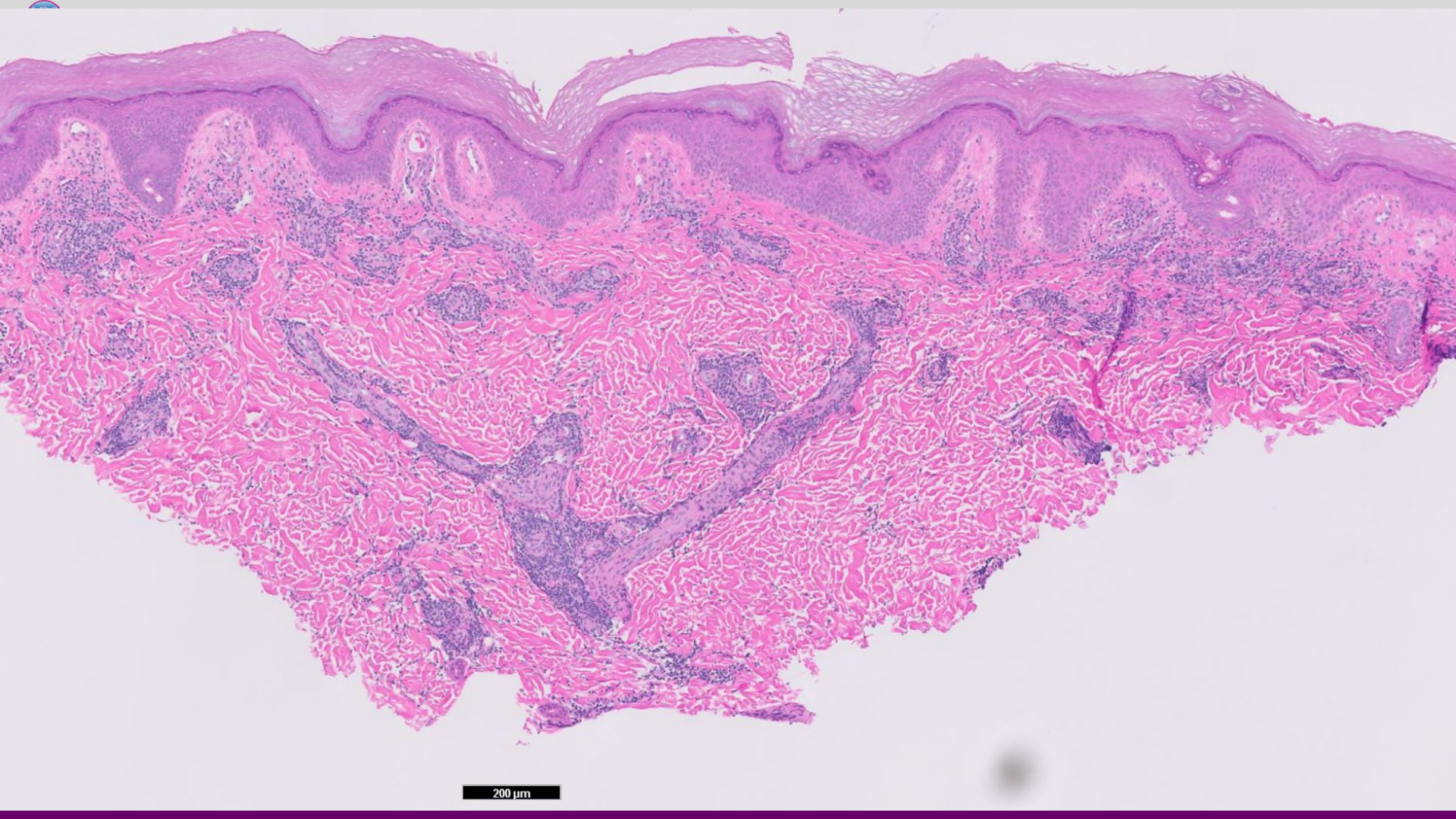
- Semantic difference
- Seborrheic keratosis is very common
- More important is to make sure this is not subtle, pigmented squamous cell carcinoma
- Onychocytic matricoma is a difficult name

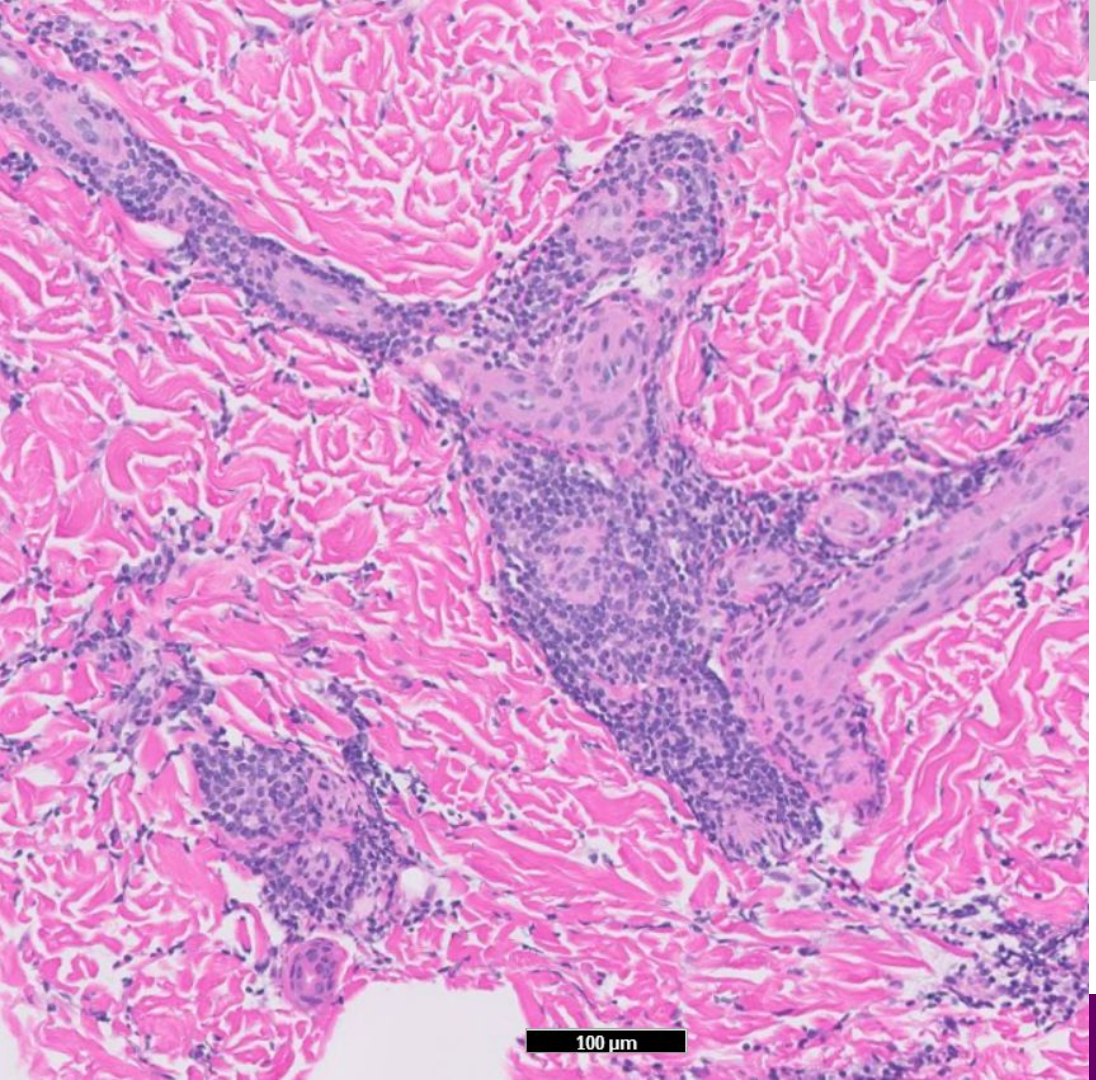
COVID-19

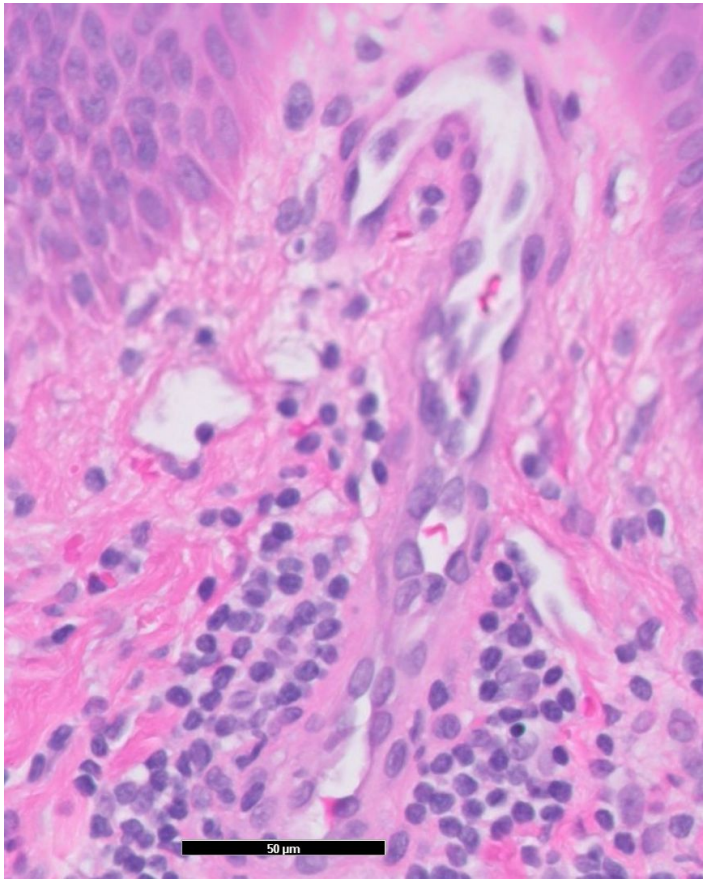
COVID-19

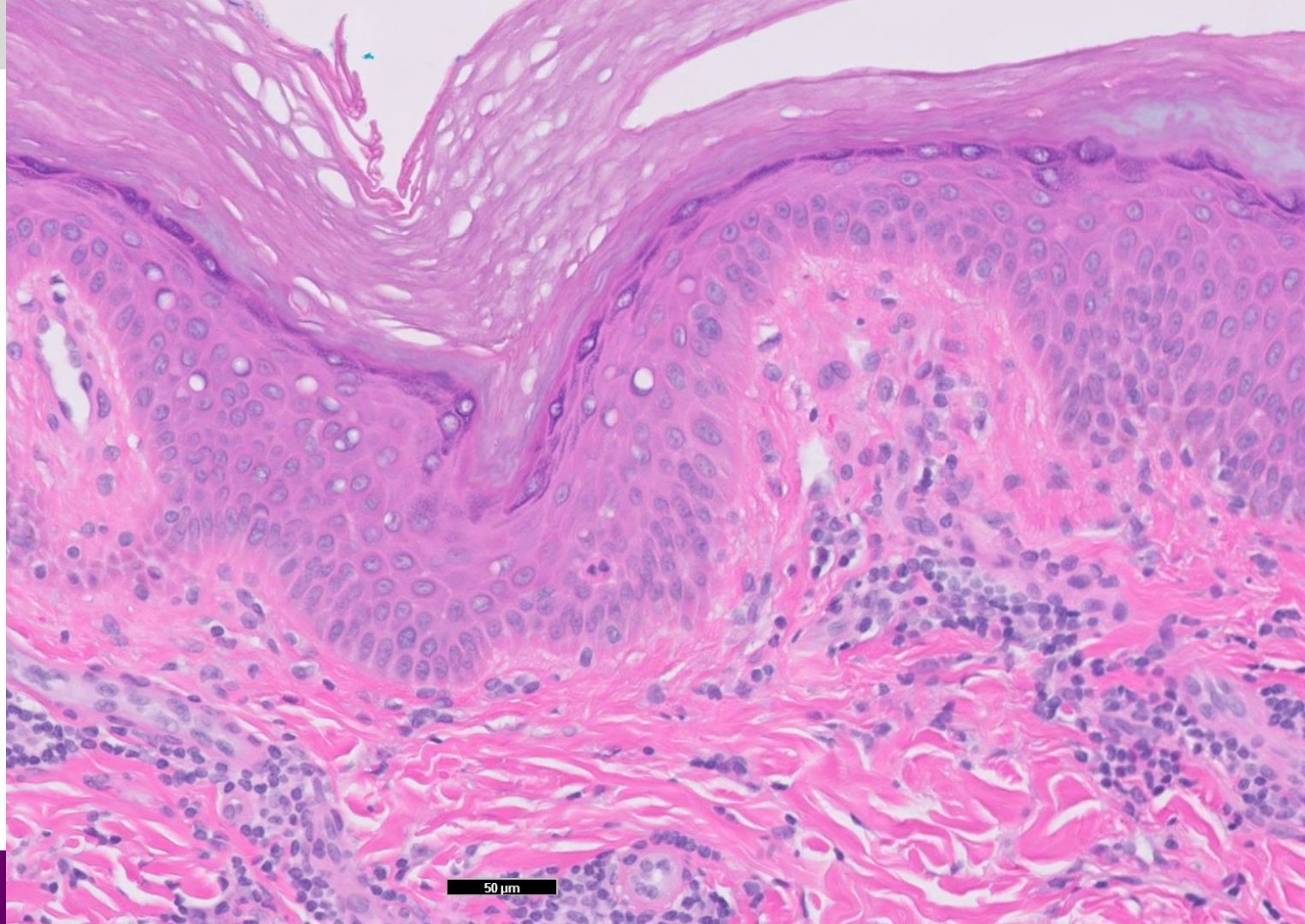
- Mee’s lines

31 y/o male with acute onset of toe papules


200 µm


100 µm


50 µm


50 µm

Nail and Periungual Changes Related to COVID-19 Infection: Histopathologic Features

Curtis T. Thompson, MD

Medical Director and Dermatopathologist, CTA Pathology

Affiliate Professor of Dermatology and Pathology, OHSU

C/What'sApp: 503.997.8920

curtisinportland@gmail.comcurtisinportland@gmail.com www.ctapathology.com

Nail and Periungual Changes Related to COVID-19 Infection: Histopathologic Features

Curtis T. Thompson, MD

Medical Director and Dermatopathologist, CTA Pathology

Affiliate Professor of Dermatology and Pathology, OHSU

C/What'sApp: 503.997.8920

curtisinportland@gmail.comcurtisinportland@gmail.com www.ctapathology.com

Nail and Periungual Changes Related to COVID-19 Infection: Histopathologic Features

No conflict of interest

Curtis T. Thompson, MD
Medical Director and Dermatopathologist, CTA Pathology
Affiliate Professor of Dermatology and Pathology, OHSU
C/What'sApp: 503.997.8920
curtisinportland@gmail.comcurtisinportland@gmail.com www.ctapathology.com

COVID-19 Nail Reported

- Mees and Beau's Lines and Red Half-Moon Sign
- Chilblains
- Thrombotic

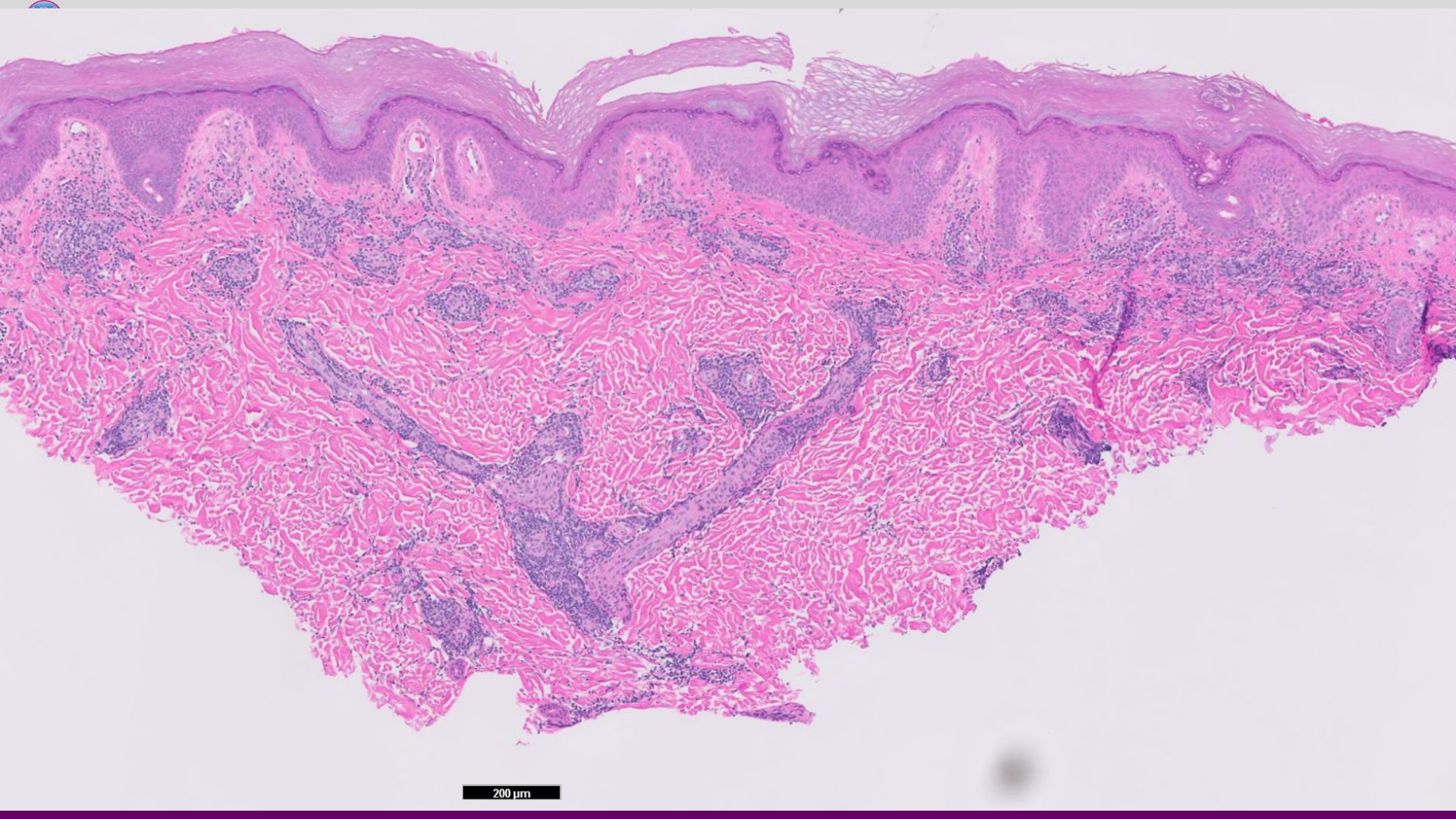
J Eur Acad Dermatol Venereol. 2020 Jun 29 : 10.1111/jdv.16747.
doi: 10.1111/jdv.16747 [Epub ahead of print]
PMCID: PMC7323324
PMID: 32535979

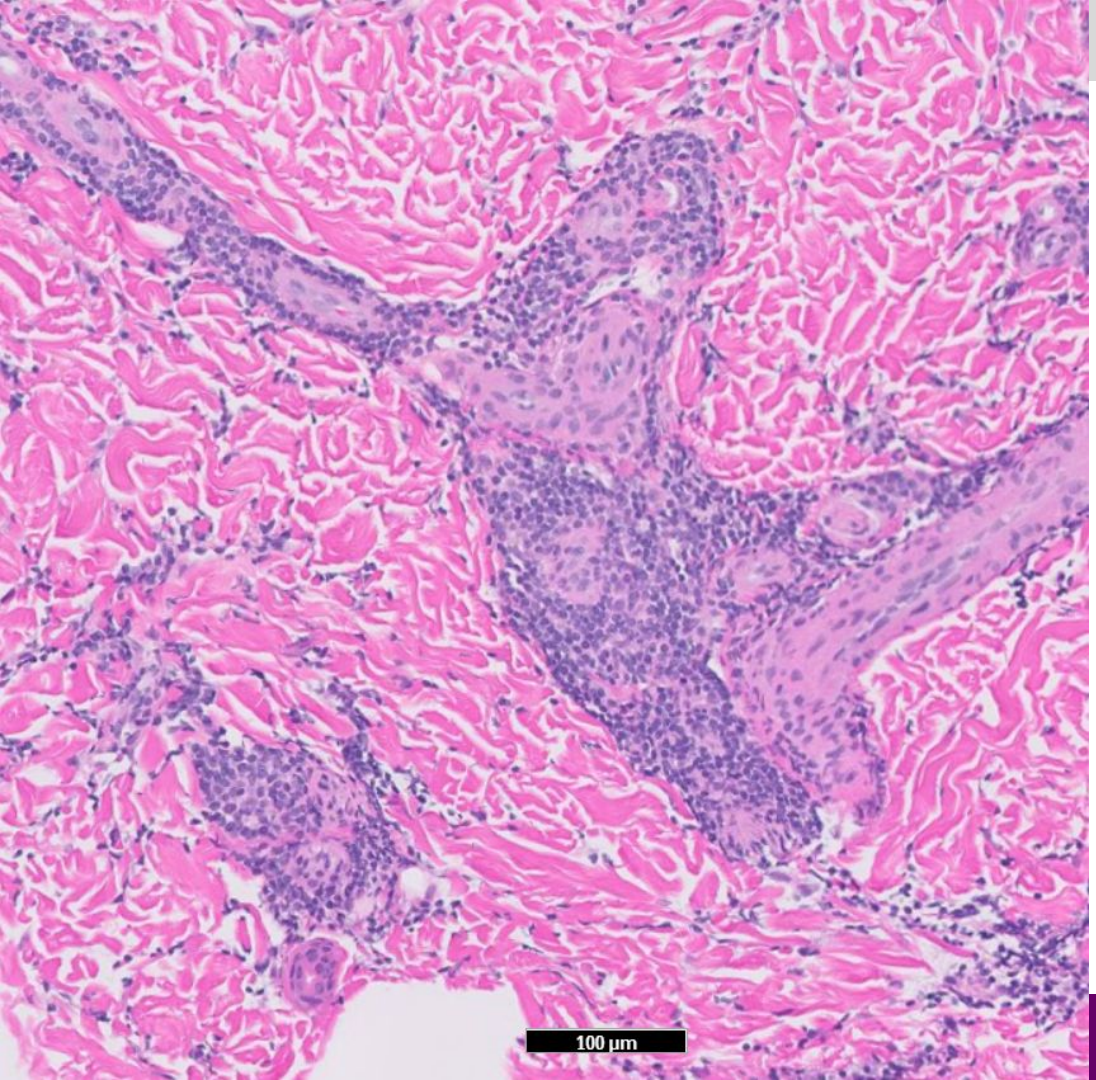
The red half-moon nail sign: a novel manifestation of coronavirus infection

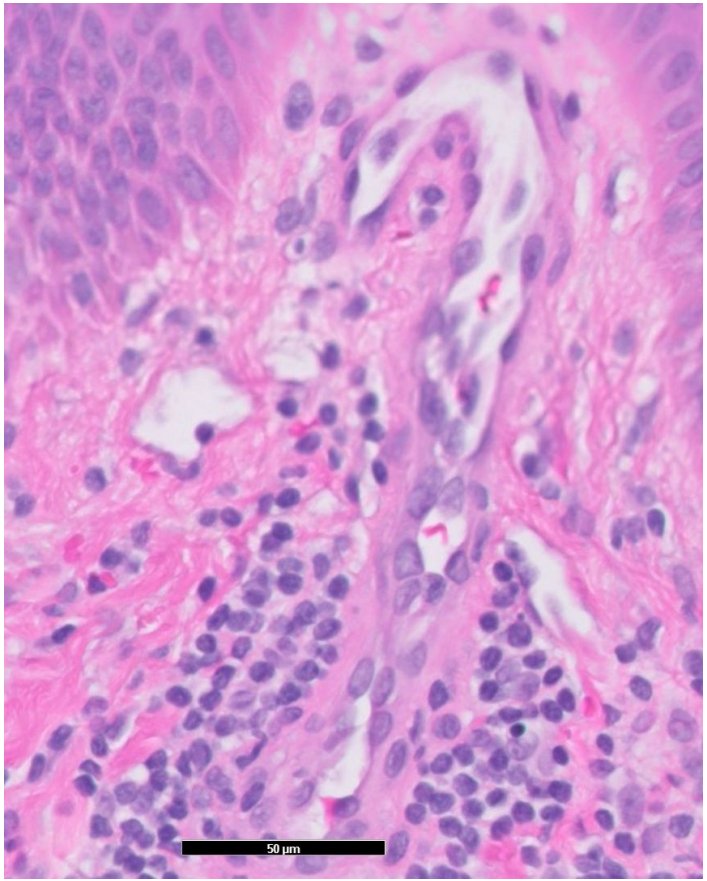
I. Neri, [1] A. Guglielmo, [1] A. Virdi, [1] V. Gaspari, [1] M. Starace, [1] and B.M. Piraccini [1]

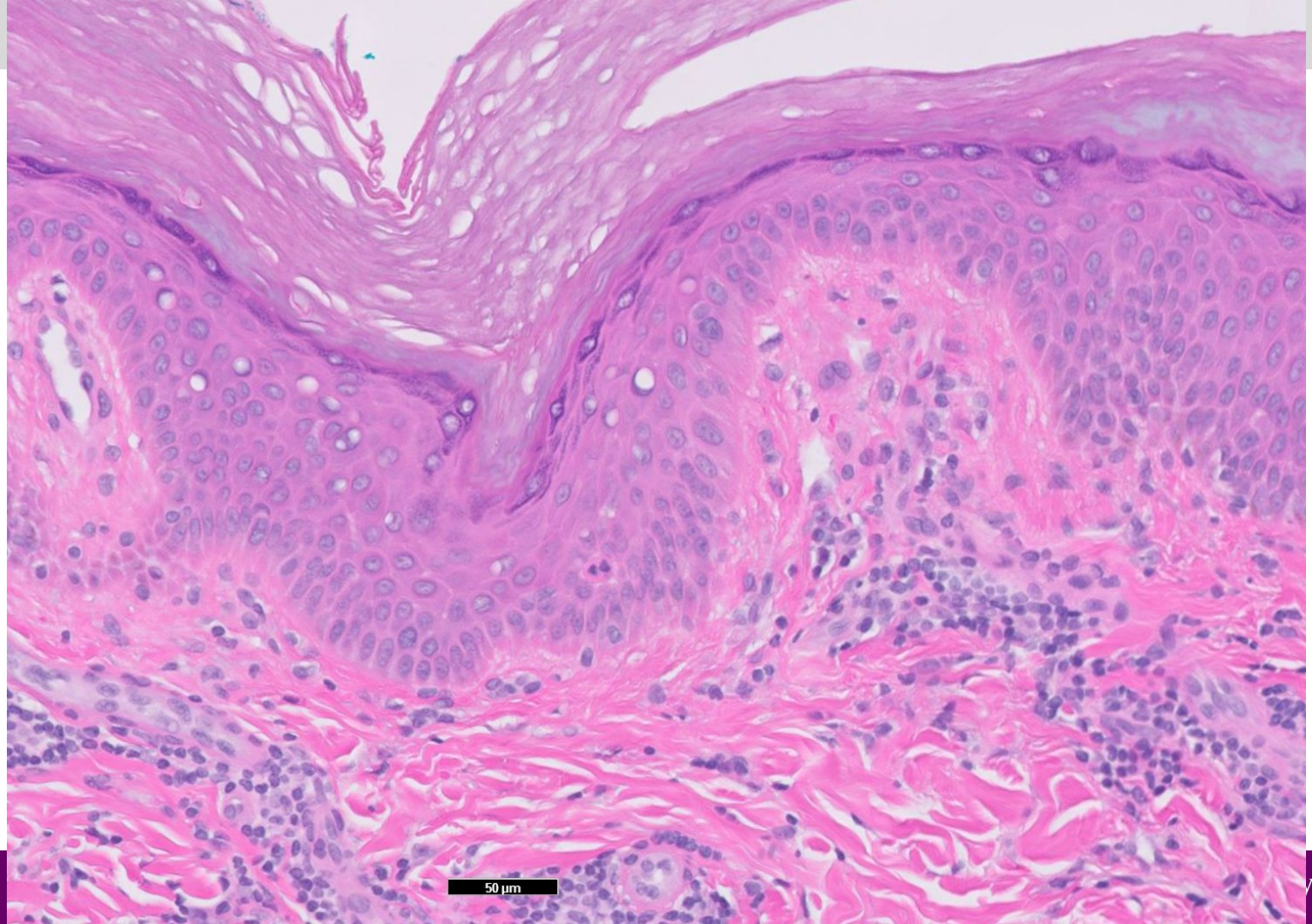
▸ Author information ▸ Article notes ▸ Copyright and License information Disclaimer

31 y/o male with acute onset of toe papules


200 µm


100 µm


50 µm


50 µm

Prospective Brussels Study—32 patients

- PCR nasopharyngeal—32 patients
- Thoracic CT—28 patients
- Blood and urine labs—31 patients
- Skin biopsy—24 patients
- Direct immunofluorescence studies—24 patients
- Electron microscopy—4 patients

Clinical lesions

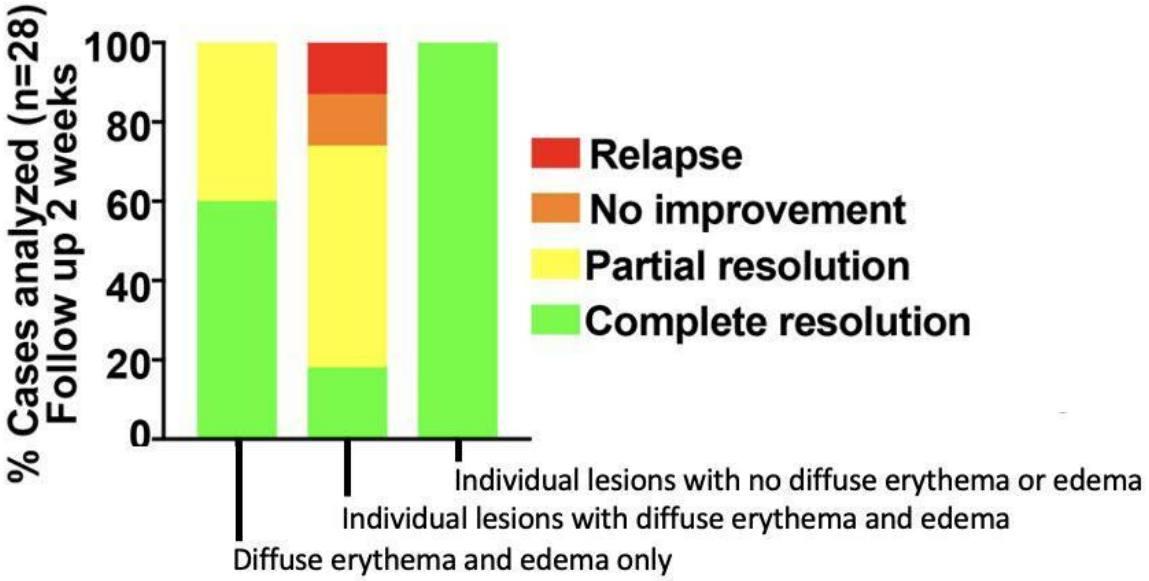
Clinical description of COVID-19 induced chilblains			Included patients	Patients after exclusion criteria
Diffuse erythema and edema	Location	Digits	30/32 (93.75%)	27/29 (93.10%)
		Lateral border of feet	2/32 (6.25%)	2/29 (6.89%)
		Soles	1/32 (3.12%)	1/29 (3.44%)
	Individual lesions with diffuse erythema and edema		22/32 (28.75%)	19/29 (65.61%)
	Diffuse erythema and edema only		10/32 (31.25%)	10/29 (34.48%)
Individual lesions	Location	Dorsal side of digits	30/32 (93.75%)	27/29 (93.10%)
		Ventral side of digits	2/32 (6.25%)	2/29 (6.89%)
		Lateral border of feet	2/32 (6.25%)	2/29 (6.89%)
		Soles	1/32 (3.12%)	1/29 (3.44%)
	Primary elementary lesions	Macules	2/32 (6.25%)	2/29 (6.89%)
		Papules and plaques	18/32 (56.25%)	15/29 (51.72%)
		Nodules	0/32	0/29
		Vesicles	0/32	0/29
		Bullae	1/32 (3.12%)	1/29 (3.44%)
	Secondary elementary lesions	Erosions/ulcerations and/or crusting	17/32 (53.12%)	15/29 (51.72%)
		Excoriations	0/32	0/29
		Violaceous color/purpuric	14/32 (43.75%)	13/29 (44.82%)
Associated findings		Distal digital necrosis	0/32	0/29
		Livedo racemosa	0/32	0/29
		Retiform purpura	0/32	0/29

Clinical Details

- No patient with autoimmune disease
- No evidence of thrombosis
- Cold exposure only 1/29
- Decreased physical activity 2/29
- Contact with COVID-19 in 3/29 (11%)
- PCR positive 1/29 (3.45%)

Clinical characteristics and complementary studies		Included patients		Patients after exclusion criteria	
Clinical history	Age (years)	See text			
	Gender	Female 19/32 (59.37%)	Male 13/32 (40.63%)	Female 16/29 (55.17%)	Male 13/29 (44.83%)
	Race/ethnicity	White 28/32 (87.5%), North African 4/32 (12.5%)		White 26/29 (89.65%), North African 3/29 (10.35%)	
	Raynaud	5/32 (15.62%)		3/29 (10.71%)	
	Smoking	3/32 (9.37%)		2/29 (7.14%)	
	Photosensitivity	0/32		0/29	
	Arthralgia/arthritis	0/32		0/29	
	Lupus, systemic sclerosis or other auto-immune disease	0/32		0/29	
	Thrombosis	0/32		0/29	
	Exposure to cold	1/32 (3.12%)		1/29 (3.57%)	
	Decrease of physical activities during lockdown	3/32 (9.37%)		2/29 (7.14%)	
	Contact with hospital, nursing home, assisted living facility	1/32 (3.12%)		1/29 (3.57%)	
	Contact with patient suspected of COVID-19 infection	13/32 (40.62%)		10/29 (35.71%)	
	Contact with confirmed COVID19 infected patient	4/32 (12.5%)		3/29 (10.71%)	
	Delay between general symptoms and chilblains	See text			
	Delay between chilblains and baseline visit	19.69 days in 32 patients		16.92 days in 29 patients	
	Symptomatic chilblains (pain and/or pruritus)	24/32 (75%)		21/29 (72.41%)	
Clinical examination	Temperature	37.47°C in 31 patients (35.6°C – 37.3°C)		36.51°C in 28 patients (35.6°C – 37.3°C)	
	Oxygen saturation	97.83% in 30 patients (95%-100%)		97.77 in 27 patients (95%-100%)	
	Heart rate	84.64/min in 31 patients (60-118/min)		85.07/min in 28 patients (60-118/min)	
	Respiration rate	17.72/min in 11 patients (15-19/min)		17.72 in 11 patients (15-19/min)	
Clinical evolution	Complete resolution without recurrence and total duration	After 2 weeks: 14/31 (45.16%) Total duration: 32.42 days	After 6 weeks: 15/24 (62.5%)	After 2 weeks: 11/28 (39.28%) Total duration: 32.75 days	After 6 weeks: 12/21 (57.14%)
	Partial resolution without recurrence	After 2 weeks: 12/31 (38.70%)	After 6 weeks: 5/24 (20.84%)	After 2 weeks: 12/28 (42.85%)	After 6 weeks: 5/21 (23.8%)
	No improvement	After 2 weeks: 2/31 (6.46%)	After 6 weeks: 2/24 (8.33%)	After 2 weeks: 2/28 (7.15%)	After 6 weeks: 2/21 (9.53%)
	Recurrence	After 2 weeks: 3/31 (9.68%)	After 6 weeks: 2/24 (8.33%)	After 2 weeks: 3/28 (10.72%)	After 6 weeks: 2/21 (9.53%)
Other studies	Positive COVID-19 PCR of nasopharyngeal swab	2/32 (6.25%)		1/29 (3.45%)	
	Abnormal findings on CT-Scan	0/28		0/25	
	Abnormal laboratory tests: Positive COVID-19 serology	6/31 (19.35%)		6/31 (19.35%)	
	Abnormal laboratory tests: Other abnormal findings	See text			

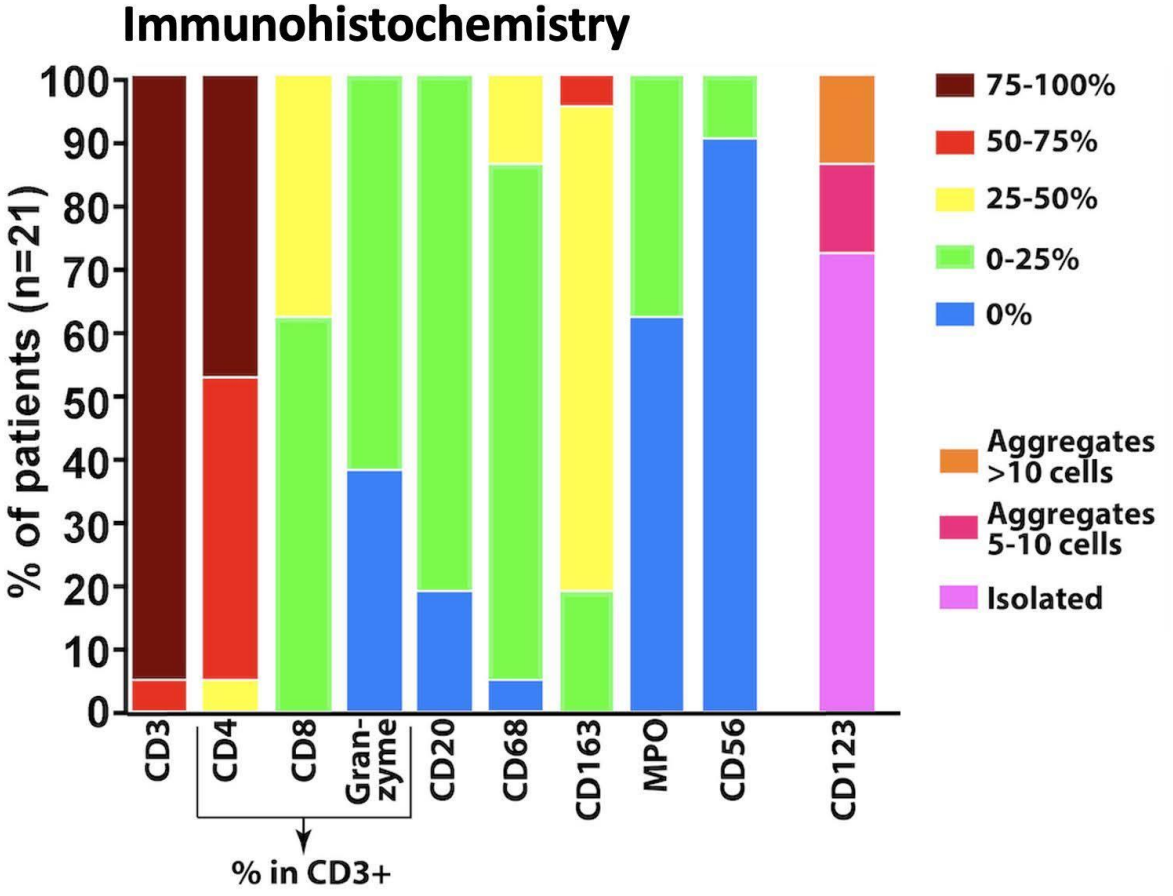
Clinical Course



Histopathologic findings:

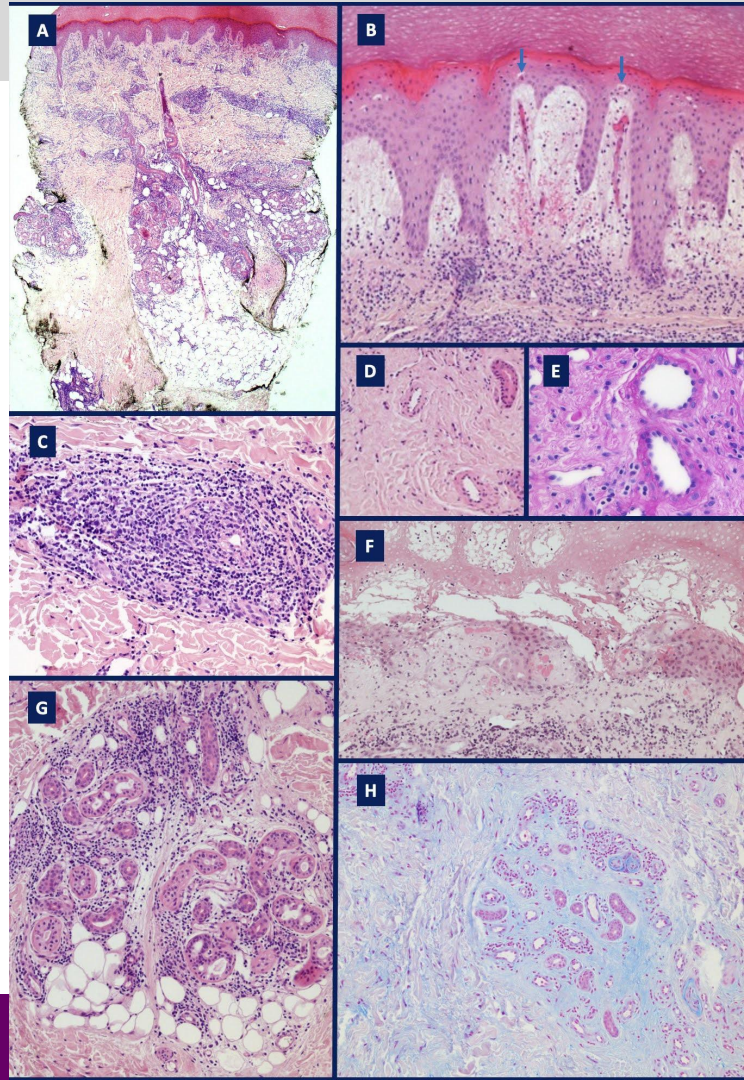
- Interface with apoptotic keratinocytes in 100%
- Red cell extravasation in 76%.
- Lymphocytes in venule walls in 86%.
- Vessel wall thickening in 86%.
- Deep dermal lymphocytes 95%
- Peri-eccrine lymphocytes in 94%
- Peri-eccrine mucin in 95%

Histopathological findings		% of patients (n=21) with this finding present or absent	
		Present	Absent
Epidermal changes	Acanthosis	86	14
	Hyperkeratosis	100	0
	Parakeratosis	14 (upper) 43 (lower)	43
	Humid parakeratosis	38 (humid) 19 (dry)	43
	Spongiosis	33	67
	Exocytosis	48	52
Interface dermatitis	Vacuolar interface	62 (focal) 19 (Diffuse) 19 (Continuous)	0
	Number of apoptotic keratinocytes (x20)	48 (1 keratinocyte) 38 (2-3 keratinocytes) 14 (≥4 keratinocytes)	0
	Basal membrane thickening	48 (focal) 10 (diffuse)	42
	Lichenoid infiltrate	0	100
	Pigmentary incontinence	5 (focal)	95
Papillary dermal changes	Papillary dermal edema	28	72
	Red cell extravasation	76	24
	Fibrin deposition	14	86
Lymphocytic vasculitis	Peri-vascular lymphocytic infiltrate	14 (discrete) 43 (moderate) 43 (intense)	0
	Post-capillary venule wall infiltration	86	14
	Swollen endothelial cells	57	43
	Vessel wall thickening	86	14
	Fibrin deposition	5 (focal)	95
	Red cell extravasation	43	57
	Intraluminal thrombi formation	5 (focal)	95
Lymphocytic infiltrate	Superficial infiltrate	95	5
	Deep infiltrate	95	5
	Distribution	21 (top heavy) 5 (bottom heavy)	74 (no difference)
	Perivascular	14 (discrete) 43 (moderate) 43 (intense)	0
	Interstitial	48 (discrete) 24 (moderate) 10 (intense)	18
	Peri-eccrine	42 (discrete) 26 (moderate) 26 (intense)	6
Other	Interstitial mucin deposition	71 (focal) 29 (diffuse)	0
	Peri-eccrine mucin deposition	25 (focal) 71 (diffuse) 25 (intense)	5
	Collagen necrobiosis	0	100
	Subcutaneous infiltration	31 (discrete) 31 (moderate) 7 (intense)	31

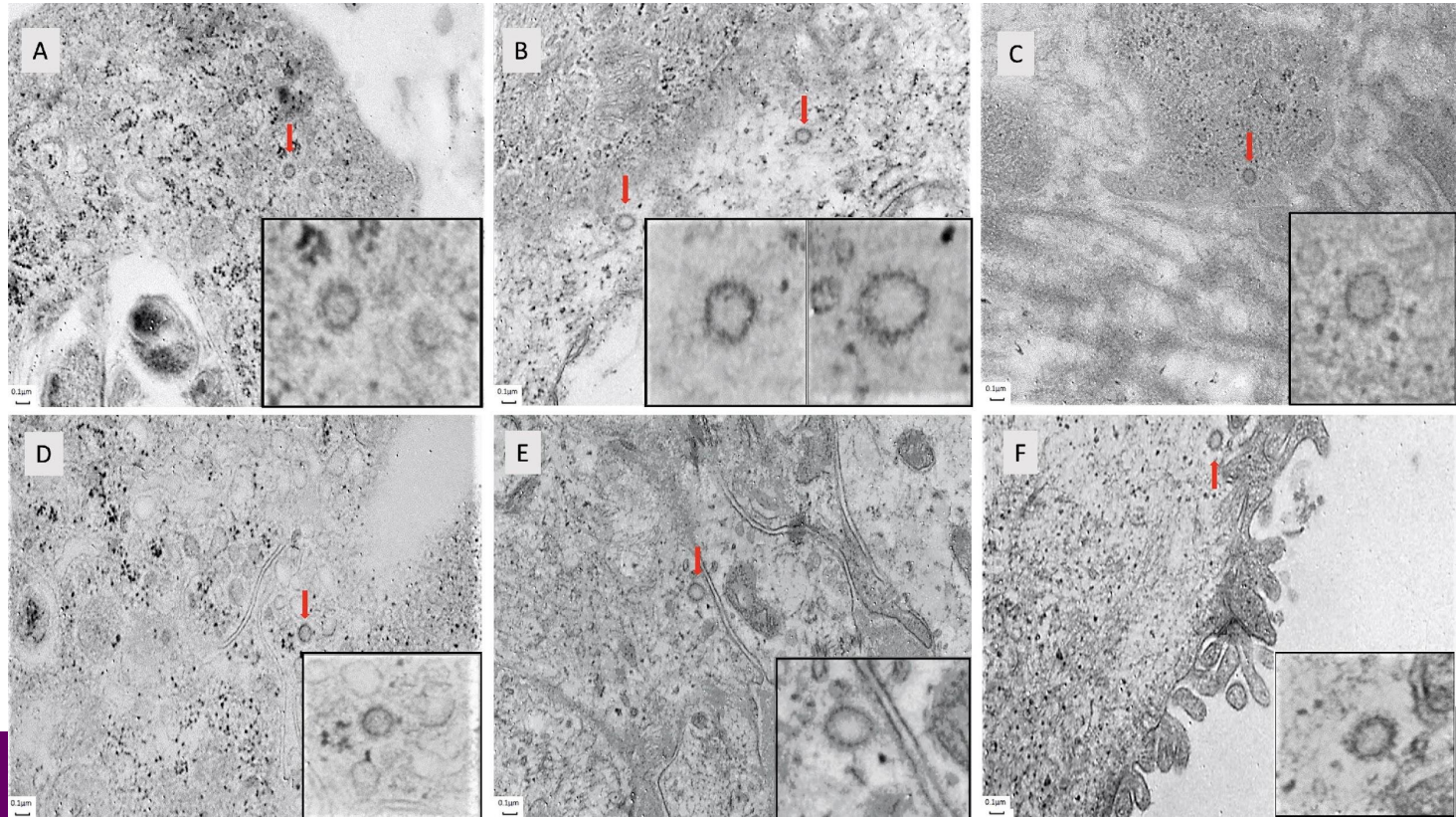

Immunohistochemistry
% of patients (n=21)
100
90
80
70
60
50
40
30
20
10
0
CD3
CD4
CD8
Gran-zyme
CD20
CD68
CD163
MPO
CD56
CD123
% in CD3+
75-100%
50-75%
25-50%
0-25%
0%
Aggregates >10 cells
Aggregates 5-10 cells
Isolated

Direct immunofluorescence (DIF)		% of patients (n=21) with positive DIF				
		IgG	IgA	IgM	C3	Fibrinogen
Blood vessel walls	Superficial dermis	0	0	23 (focal)	23 (focal)	35 (focal) 35 (moderate)
	Deep dermis	0	0	23 (focal)	0	35 (focal) 8 (moderate)
Dermo-epidermal junction		0	0	0	8 (granular)	4 (linear continuous) 4 (linear discontinuous)

Histopathology identical to chilblains from other causes



Probable viral particles 120-133µm



Chilblains vs Chilblain lupus erythematosus

- Chilblain LE is a manifestation of chronic cutaneous LE (CCLE)
  - Discoid lesions on hands/fingers and feet/toes
  - Subungual (nail bed) hyperkeratosis
  - Atropic digital ulcers similar to those seen in systemic sclerosis
  - Proximal nail fold capillary alterations (dermoscopic)
  - Histopathology—Interface dermatitis

- Chilblains—digits are normal
  - Swelling = Papillary dermal edema
  - No interface dermatitis

Parvovirus B19 simulating SLE

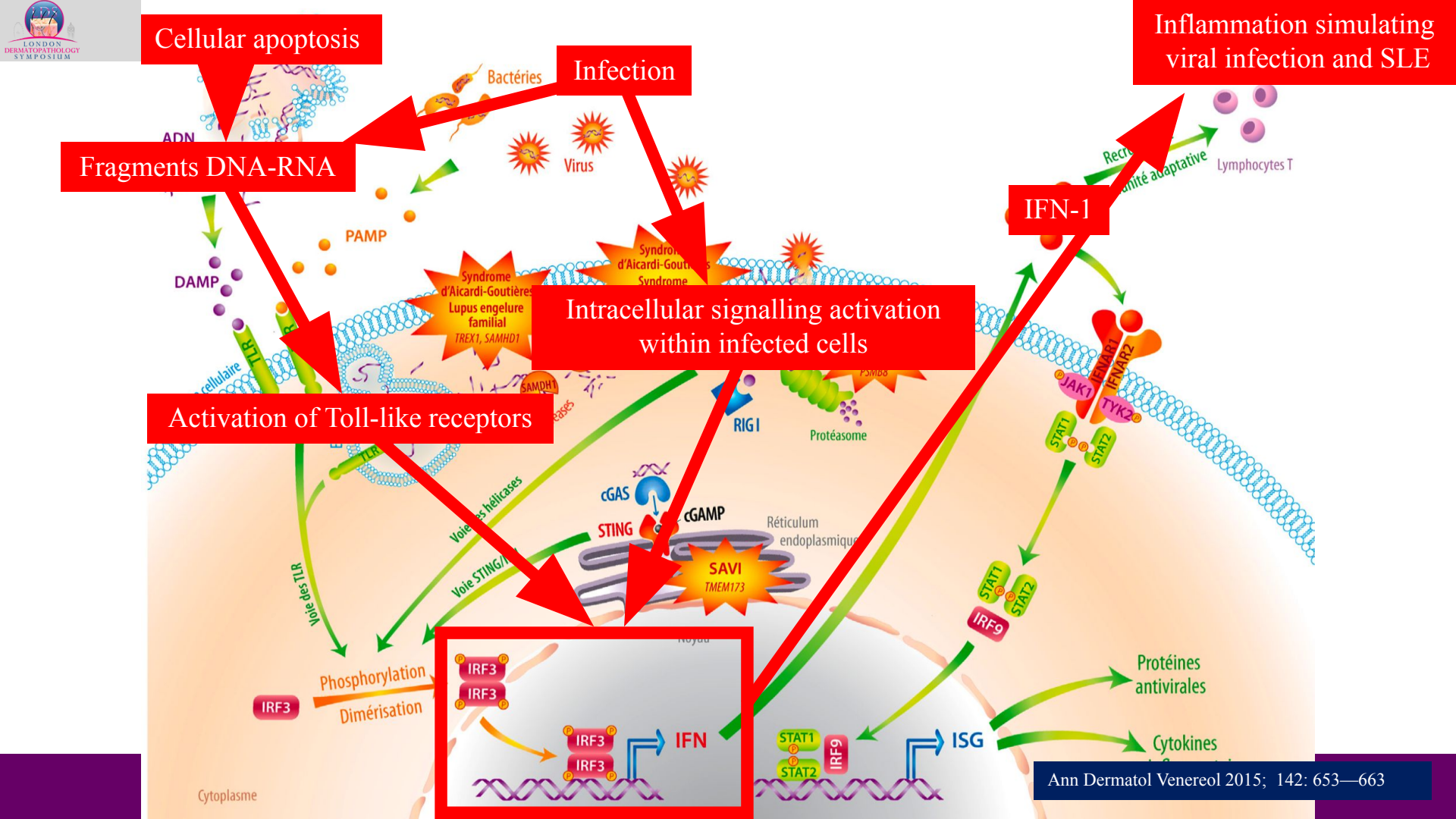
- Accumulation of nucleic acids after apoptosis

- Transient ANA titer and other serologies
  - RF, anti-DS-DNA, anti-phospholipids,
  - Ribonucleoprotein, Sjögren syndrome A/B
  - Topoisomerase scl-70

- When the ANA is positive, the patient is no longer considered to be infectious.

Parvovirus B19 simulating SLE

Clinical feature	Parvovirus B19 infection	Lupus
Course	Self-limiting	Persistent
Severity	Mild	Mild to severe
Persistent fevers	Rare	May be present
Anemia	Secondary to bone marrow suppression	Secondary to autoimmune hemolysis
Reticulocyte count	Low in presence of bone marrow suppression	Normal to high in presence of evidence of hemolysis
Splenomegaly	Rare	May be present
Discoid lesions, alopecia	Absent	May be present
Oral ulcers	Rare	May be present
Raynaud phenomenon	Absent	May be present
Neurologic (seizures, psychosis, chorea) and ocular symptoms	Rare	May be present
Gastrointestinal involvement (peritonitis, pancreatitis, obstruction/pseudo-obstruction)	Rare	May be present
Cardiac involvement	Rare	May be present
Renal involvement	Rare	May be present



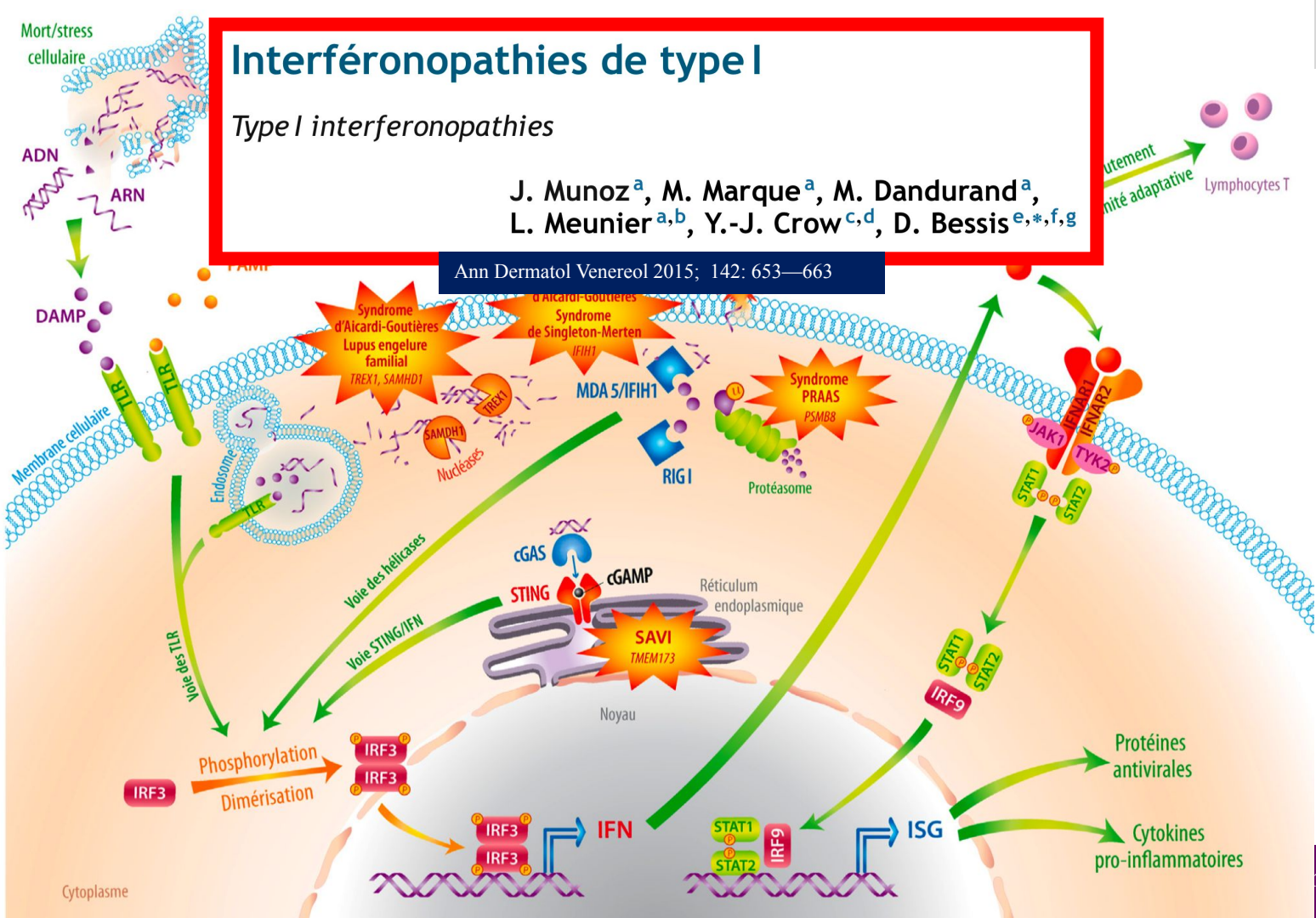
Ann Dermatol Venereol 2015; 142: 653—663

Interféronopathies de type I

Type I interferonopathies

J. Munoz[a], M. Marque[a], M. Dandurand[a],
L. Meunier[a,b], Y.-J. Crow[c,d], D. Bessis[e,*,f,g]

Ann Dermatol Venereol 2015; 142: 653—663



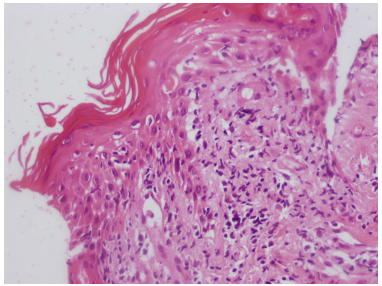
Type I Interferonopathy	Major cutaneous findings	Major extra-cutaneous findings	SLE-like
Aicardi-Goutières syndrome (AGS)	Chillblains, digital amputations, ear tissue loss, panniculitis	Severe neurological disease with developmental delay and intracranial calcification	+++
Familial chillblain lupus (FCL)	Chillblains, digital amputations, ear tissue loss	-	+
Spondylenchodrodysplasia (SPENCD)	Chillblains, digital amputations	Skeletal dysplasia, neurological developmental delay with intracranial calcification	+++
Stimulator of interferon genes (STING) - associated vasculopathy with onset in the infancy (SAVI)	Chillblains, digital amputations, ear tissue loss	Interstitial lung disease	+++

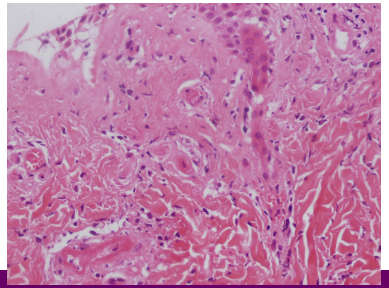
Cutaneous histopathological findings of Aicardi–Goutières syndrome, overlap with chilblain lupus

Athanassios Kolivras[1], Alec Aeby[2], Yanick J. Crow[3], Gillian I. Rice[3], Ursula Sass[1] and Josette André[1]

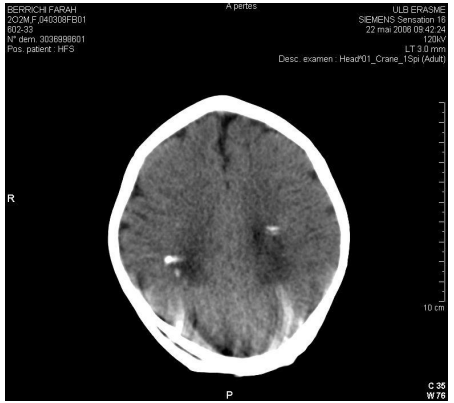
J Cutan Pathol 2008; 35: 774–778

+





+



= Aicardi-Goutières syndrome

Familial chilblain lupus and Aicardi-Goutières syndrome are allelic phenotypes of the same disease

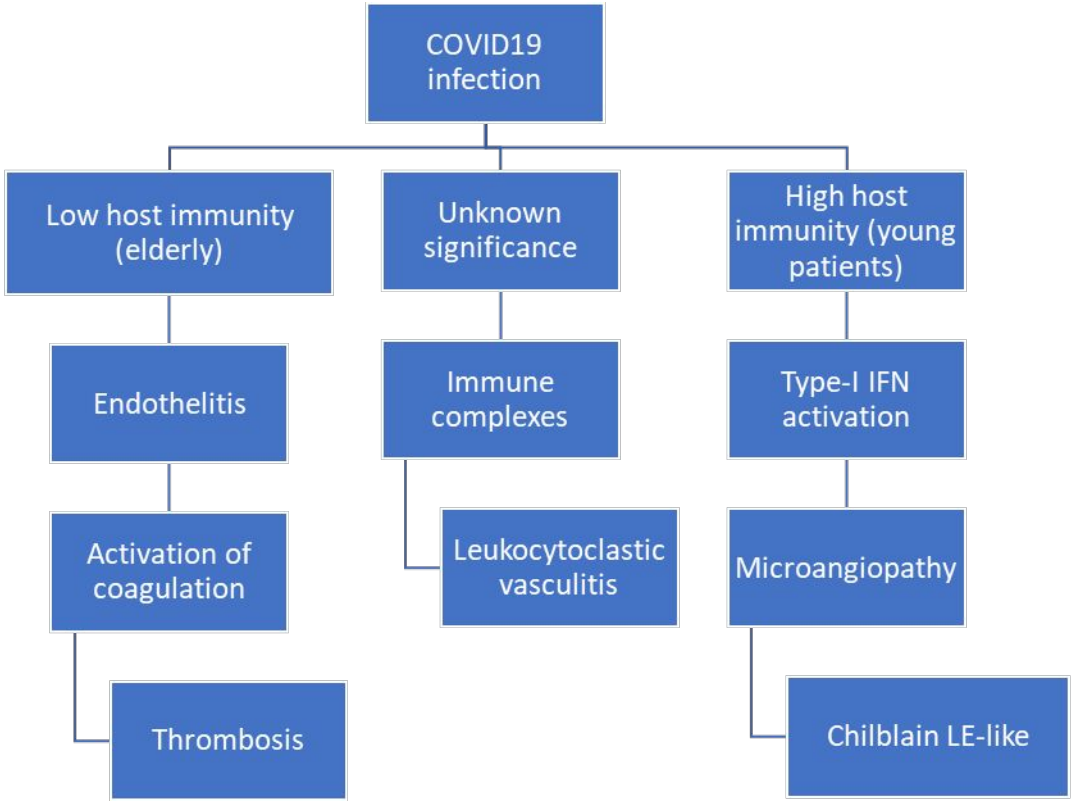
Aicardi-Goutières syndrome

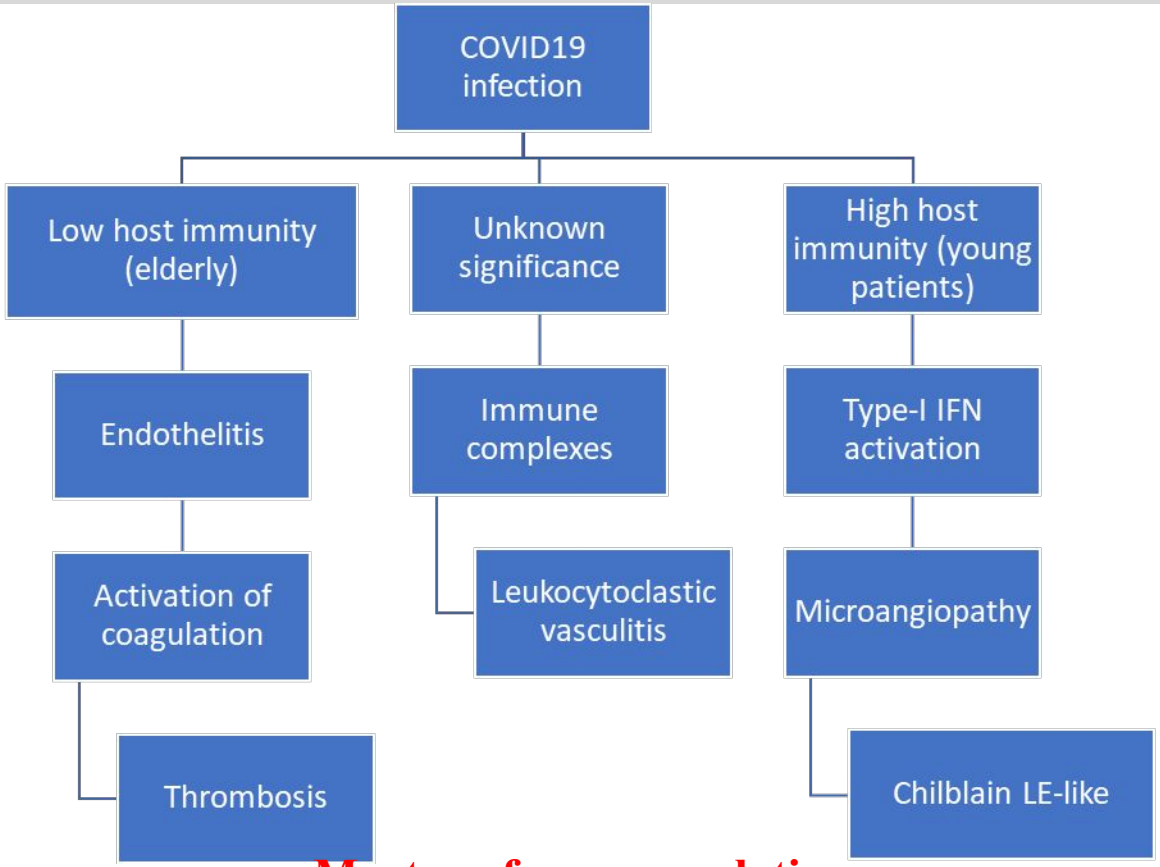
Familial chilblain lupus

Ann Dermatol Venereol 2015; 142: 653—663

Summary of COVID-19 Toes

- Stronger evidence that COVID-19 may cause chilblains, especially in young people;
- COVID-19-induced chilblains are histologically identical to chilblains resulting from the many other primary and secondary causes;
- No patients showed evidence for a systemic coagulopathy or a genetic susceptibility for a hypercoagulable state;
- Negative PCR and antibody tests do not rule-out COVID-19 causality;
- COVID-toes signal a good prognosis usually in asymptomatic patients.


COVID19 infection
Low host immunity (elderly)
Unknown significance
High host immunity (young patients)
Endothelitis
Immune complexes
Type-I IFN activation
Activation of coagulation
Leukocytoclastic vasculitis
Microangiopathy
Thrombosis
Chilblain LE-like



Must perform coagulation Studies (D-dimers)

Thanks!

curtisinportland@gmail.com