The journey of a skin biopsy: from the patient to the lab and back

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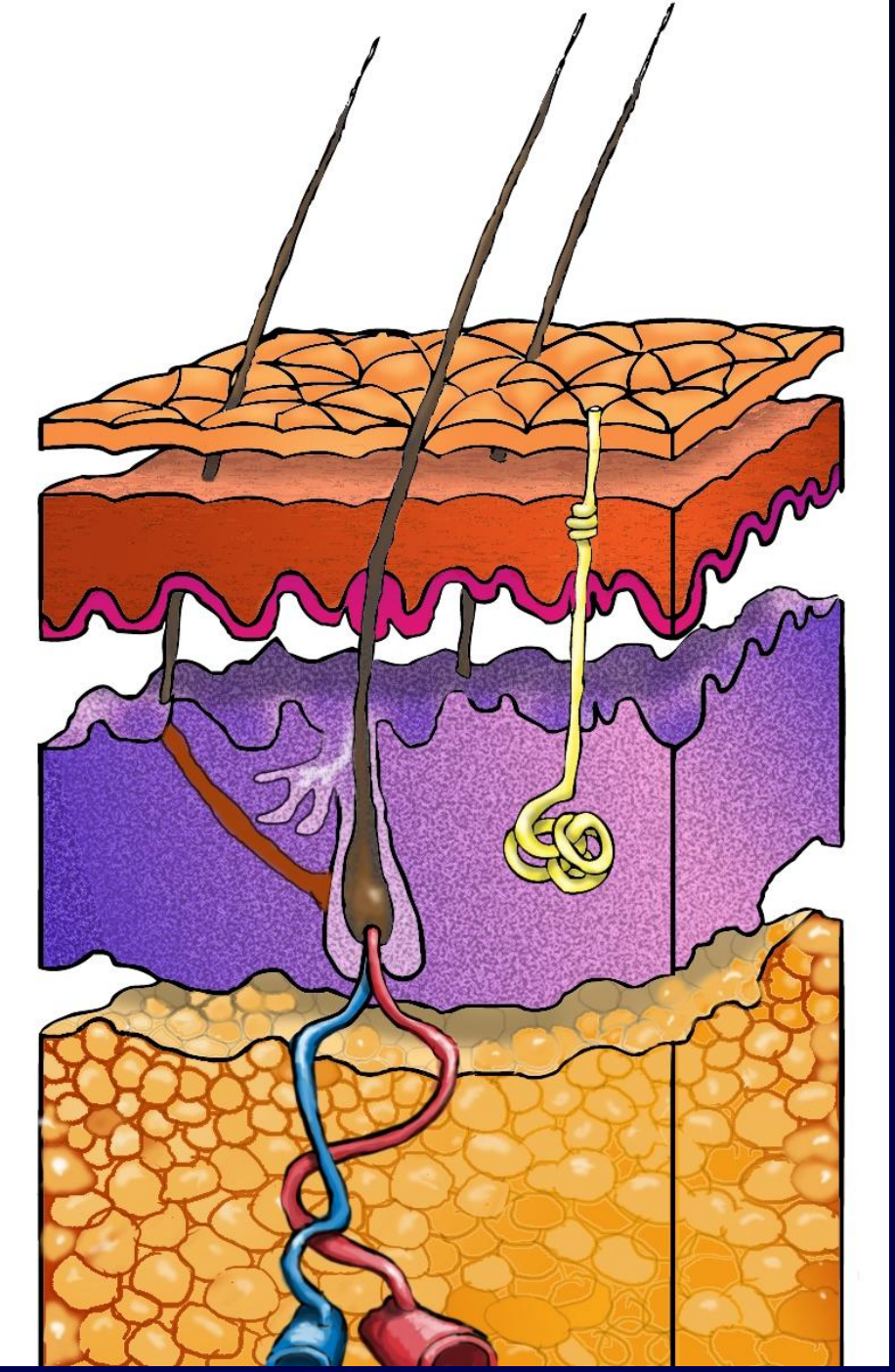
Part 1

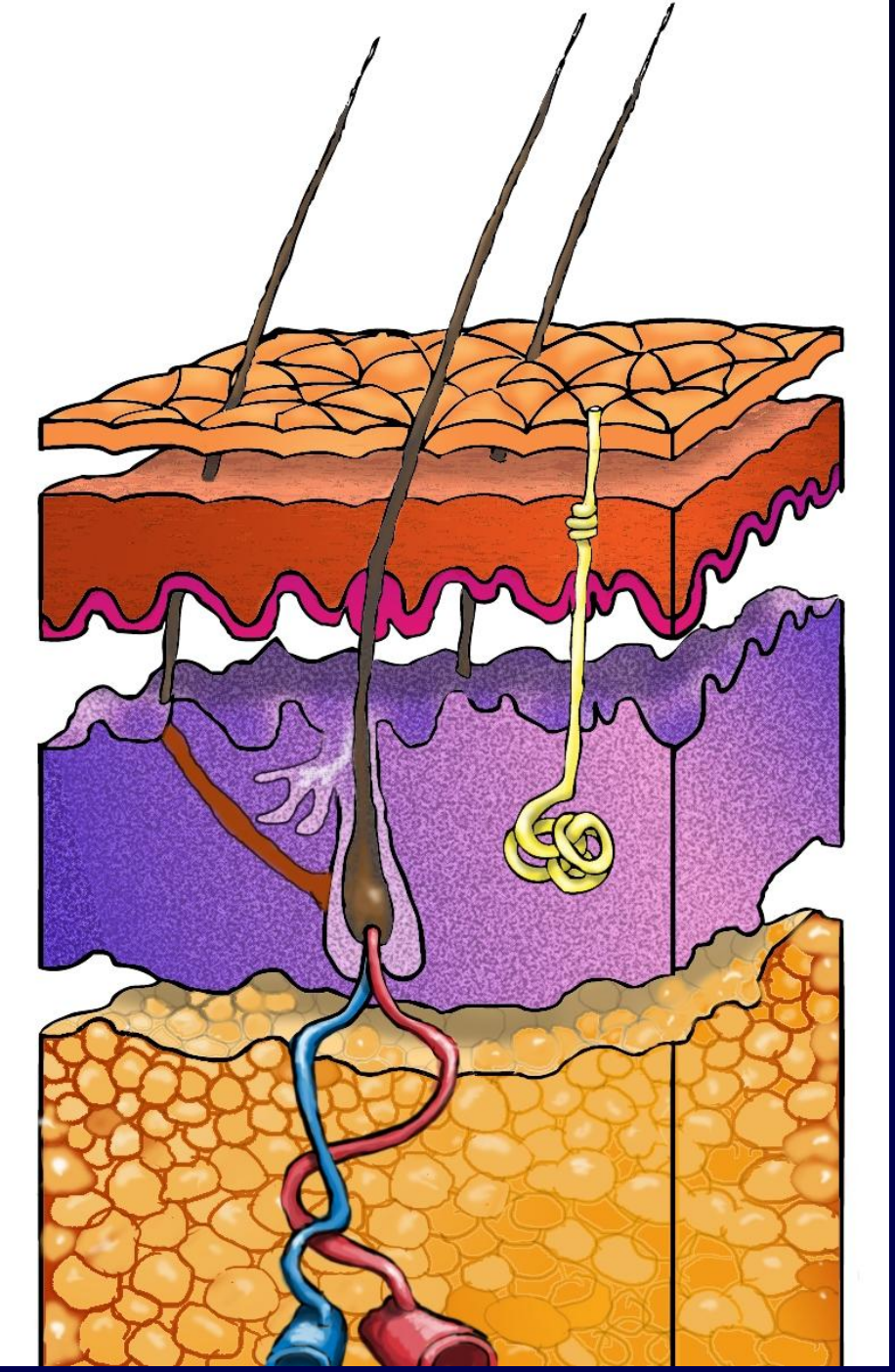
Microscopic anatomy of the skin



Epidermis

Dermis

Subcutaneous tissue



Epidermis

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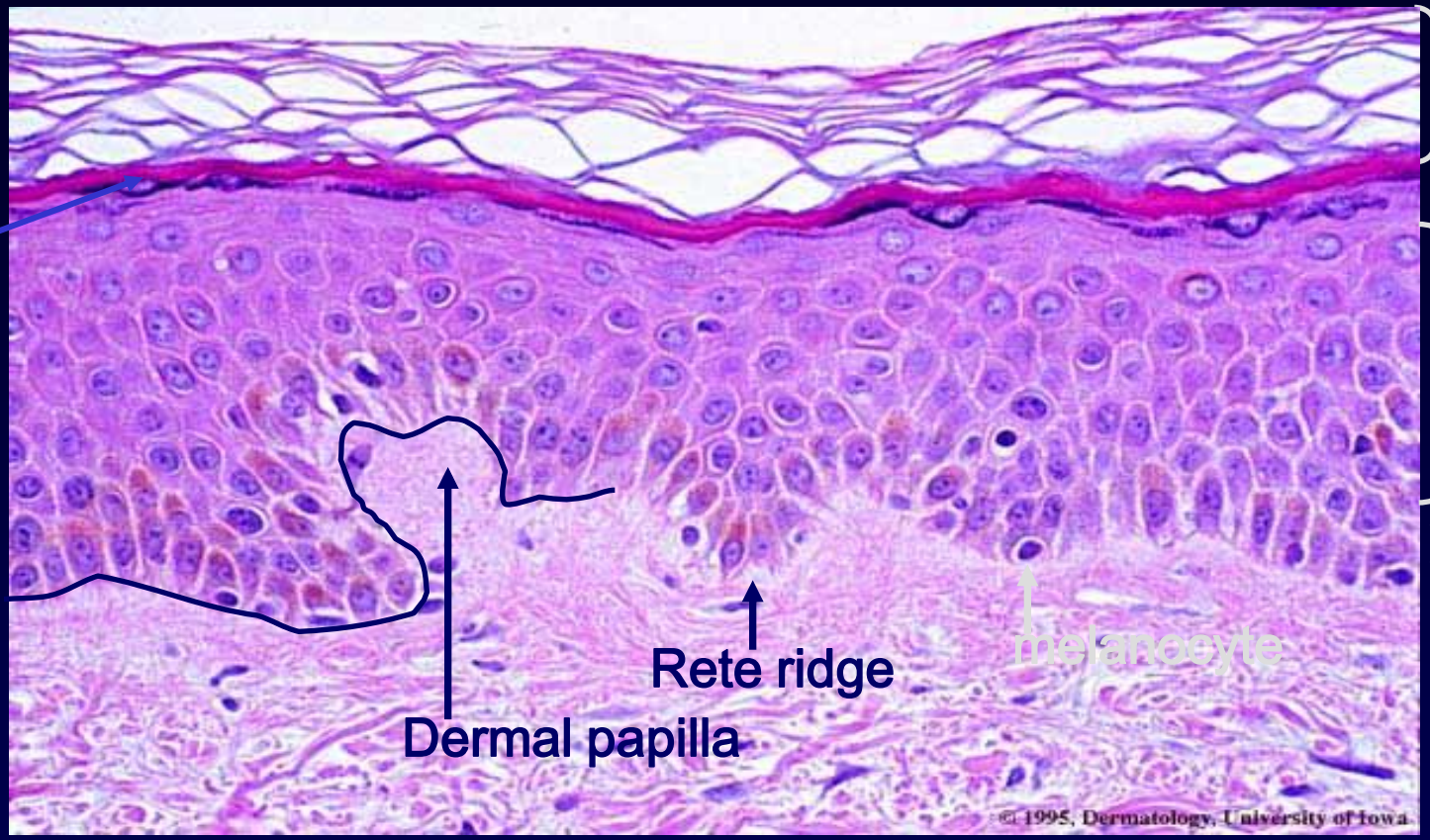
Subcutaneous tissue

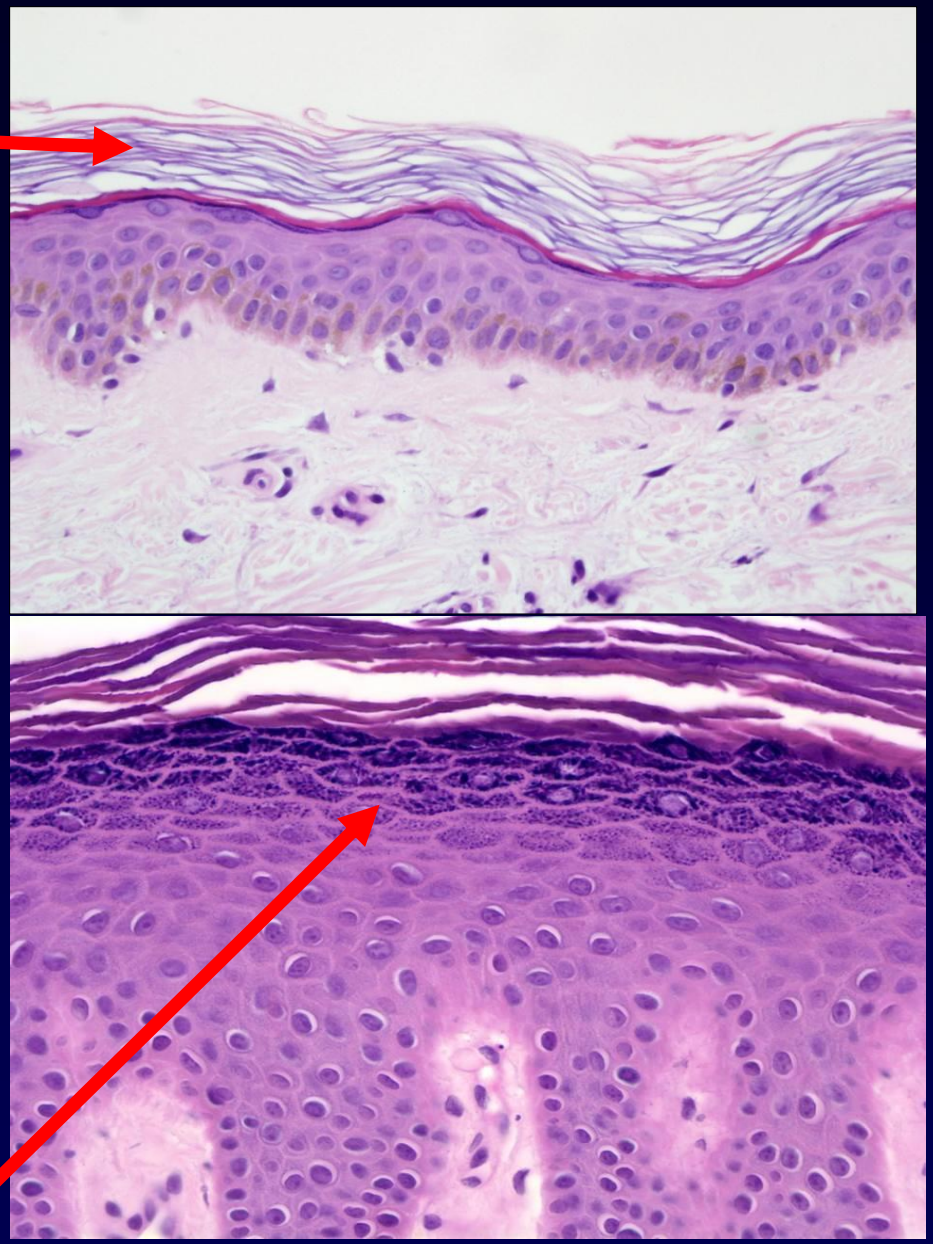
Epidermis



Normal Skin, high power

Cornified layer

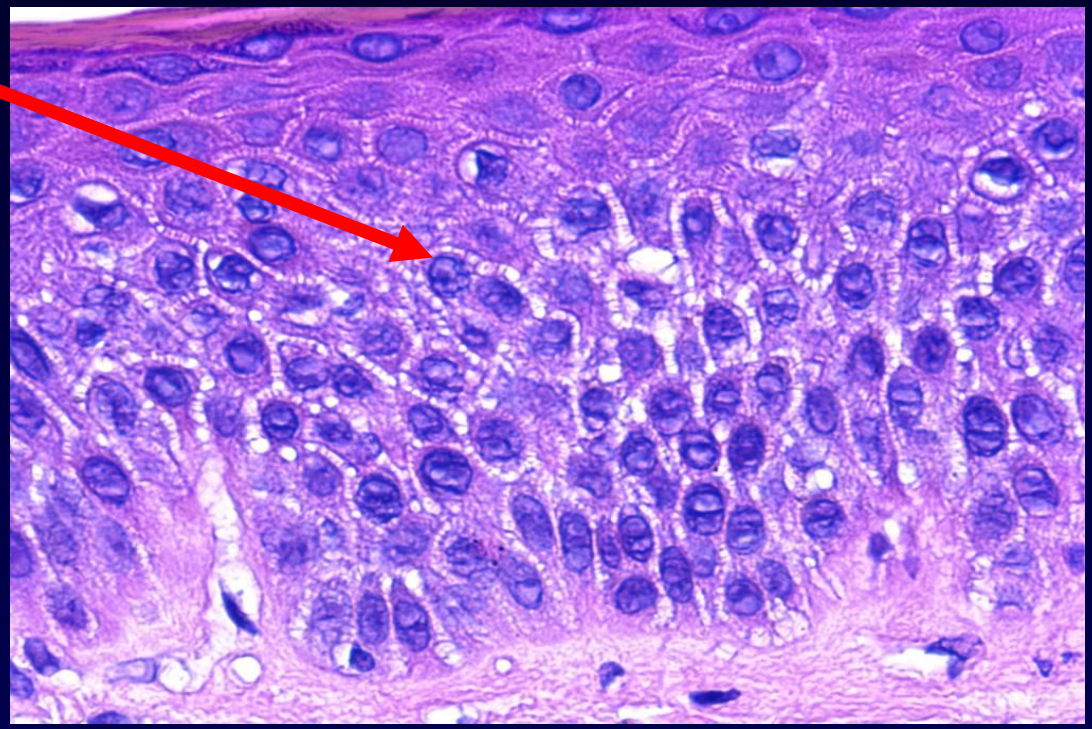
Granular cell layer: The contents of the keratohyalin granules, which give this layer its granular appearance, combine with the intermediate filament keratin to form an intracellular scaffold to strengthen the cohesion of the keratinocytes. In addition, the lipid rich, intracellular lamellar bodies discharge their contents into the intercellular space, increasing the barrier function. Cornified layer: The polyhedral cells of this layer lack nuclei or organelles and lose the scaffold as they ascend and eventually slough.

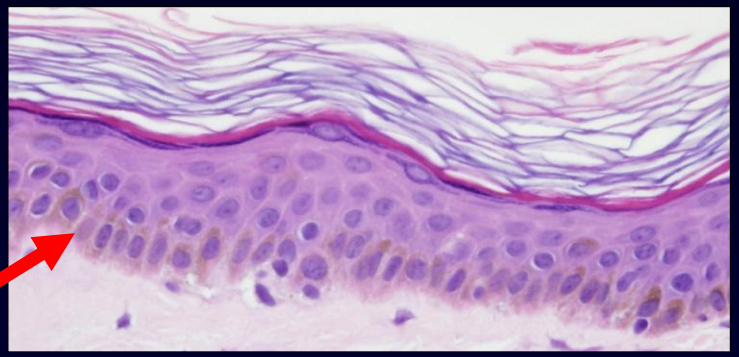


Granular cell layer

The spinous layer

The spinous layer consists of polygonal keratinocytes with numerous spiny projections called desmosomes spanning their intercellular spaces, attaching them to neighboring keratinocytes.

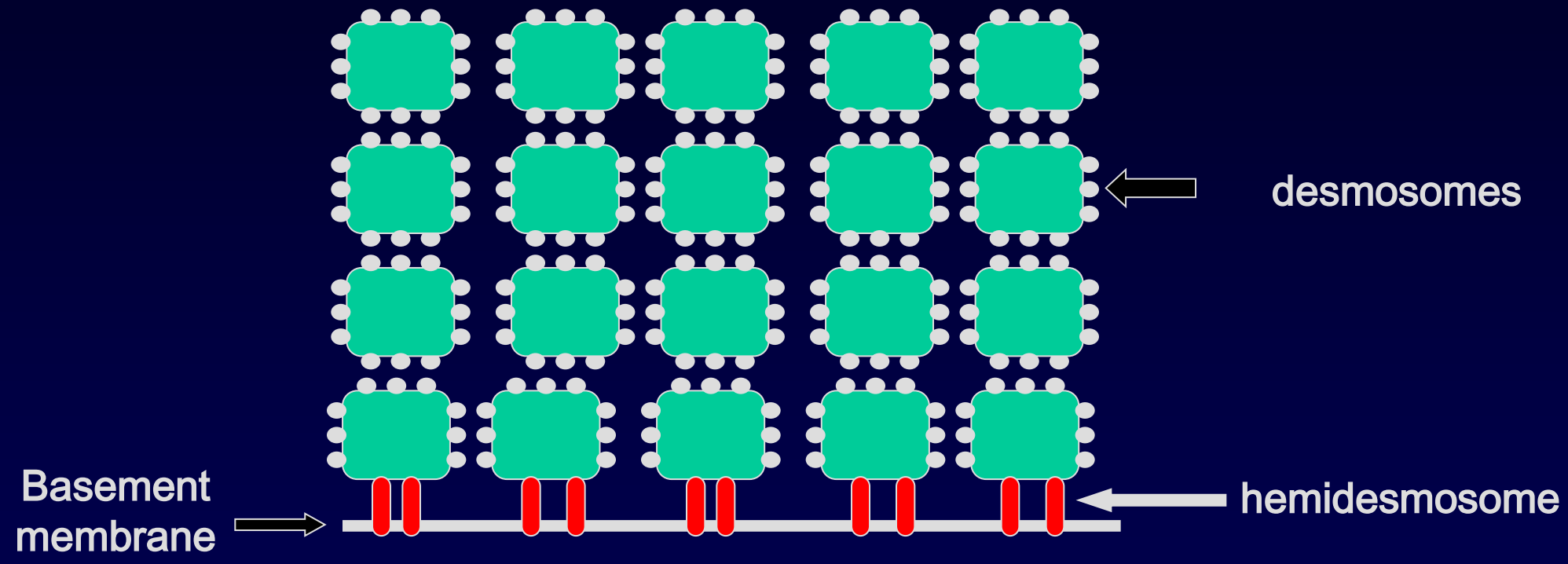




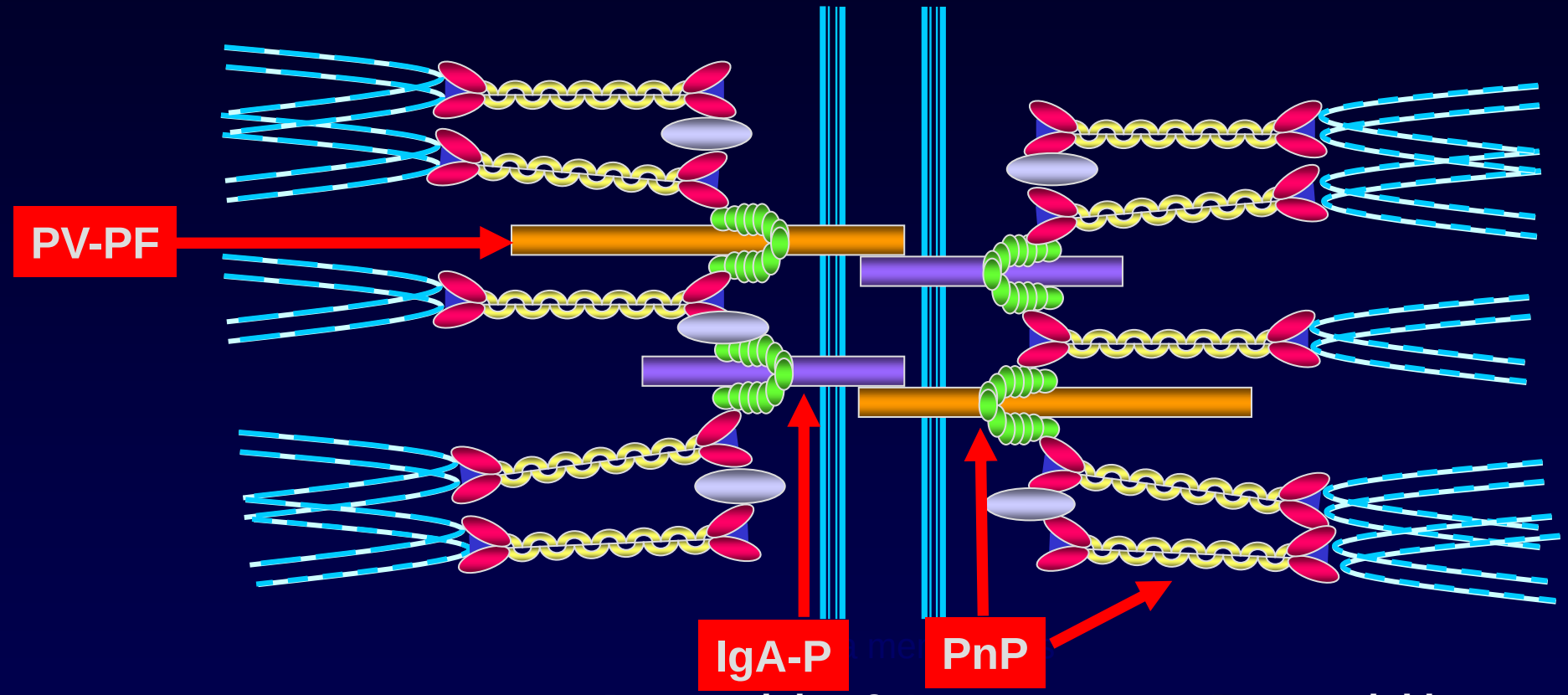
The basal layer

- Consists of cuboidal or columnar keratinocytes 1-3 cells thick. The basal layer is the main proliferative compartment of the epidermis, producing keratinocytes that eventually replace the terminally differentiated cells that are continuously shed from the skin surface.
- The epidermis completely renews itself every 12-14 days.
- The basal keratinocytes adhere to the basement membrane and dermis through hemidesmosomes.

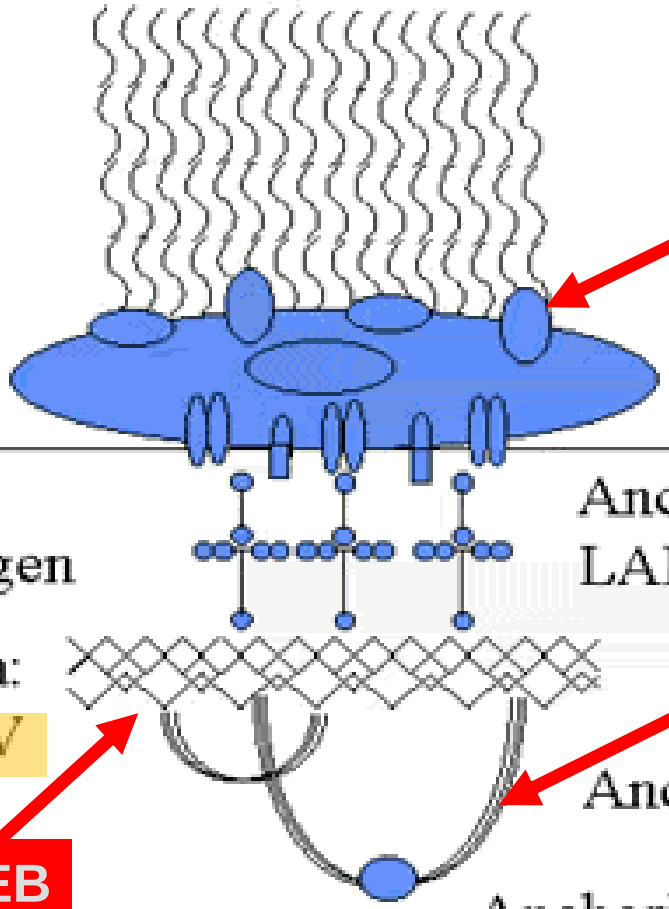
Schematic of Hemidesmosome and Desmosomes in the Epidermis



Desmosomes


PV-PF
IgA-P
PnP
Desmogleins 3-1
Desmocollin
Keratin filaments
Desmoplakin
Plakoglobin
Plakophilin

The dermal-epidermal basement membrane



Intermediate filaments: keratins 4, 15

BP

Hemidesmosome: 200 kD protein, BP180, $\alpha 6\beta 4$ integrin, BP230, HD1

Plasma Membrane

Lamina Lucida: laminin-1, nidogen

Anchoring filaments: laminin-5, laminin-6, LAD-1. uncein, LH39 antigen

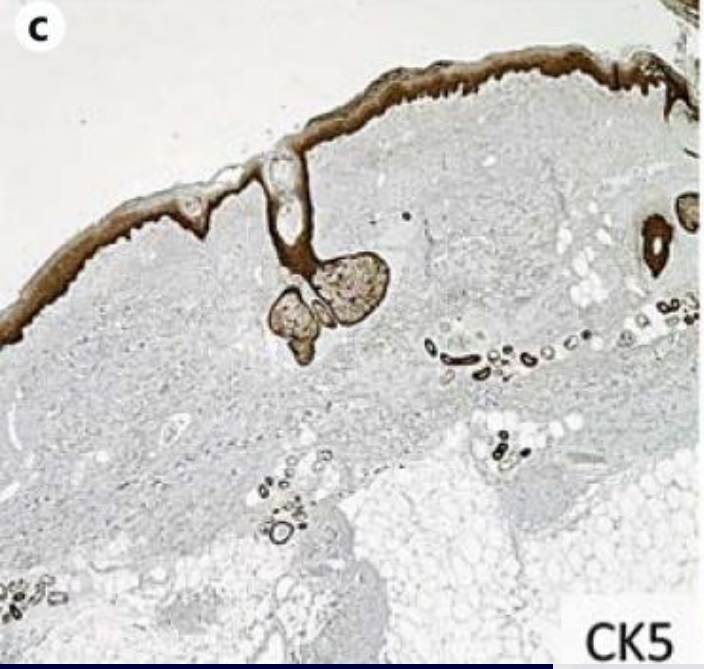
Lamina Densa: HSPG, type IV collagen

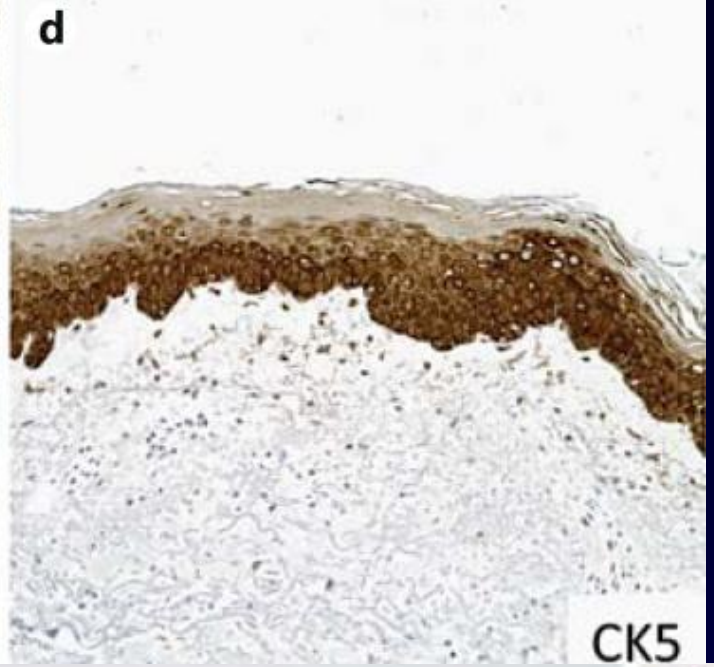
DysEB-EBA

Anchoring fibrils: type VII collagen

JEB

Anchoring plaques: type IV collagen


c
CK5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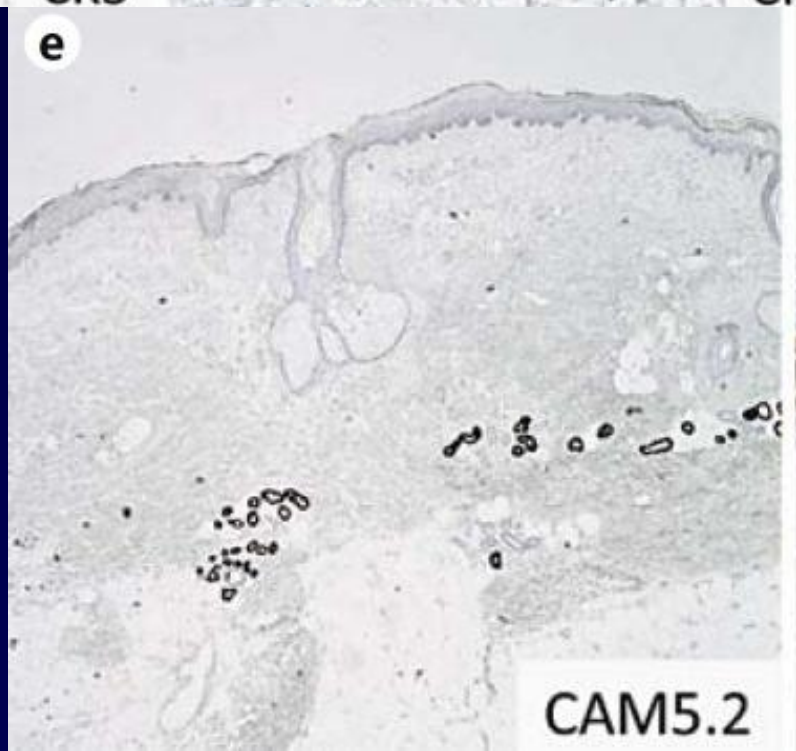
CK5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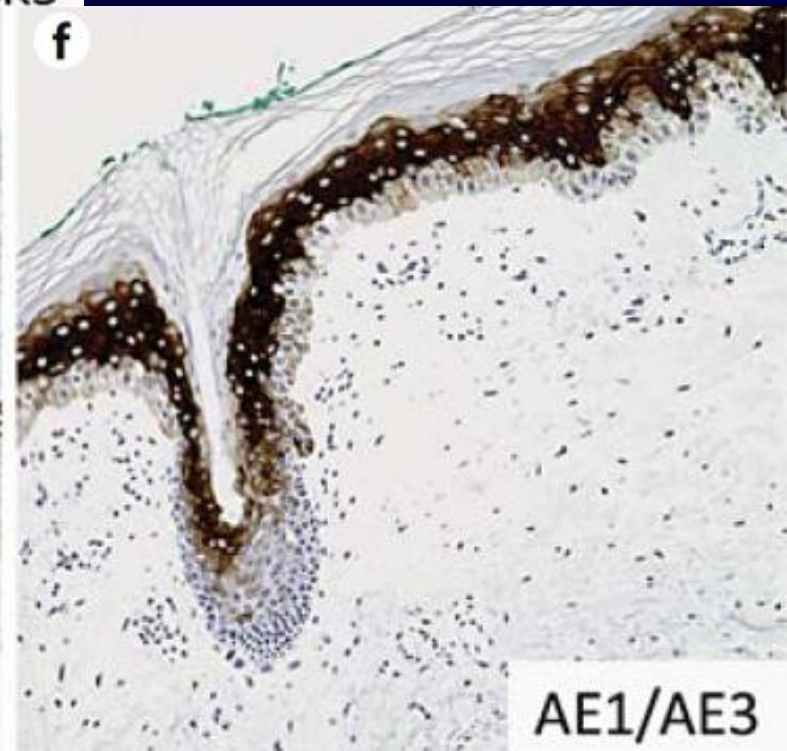
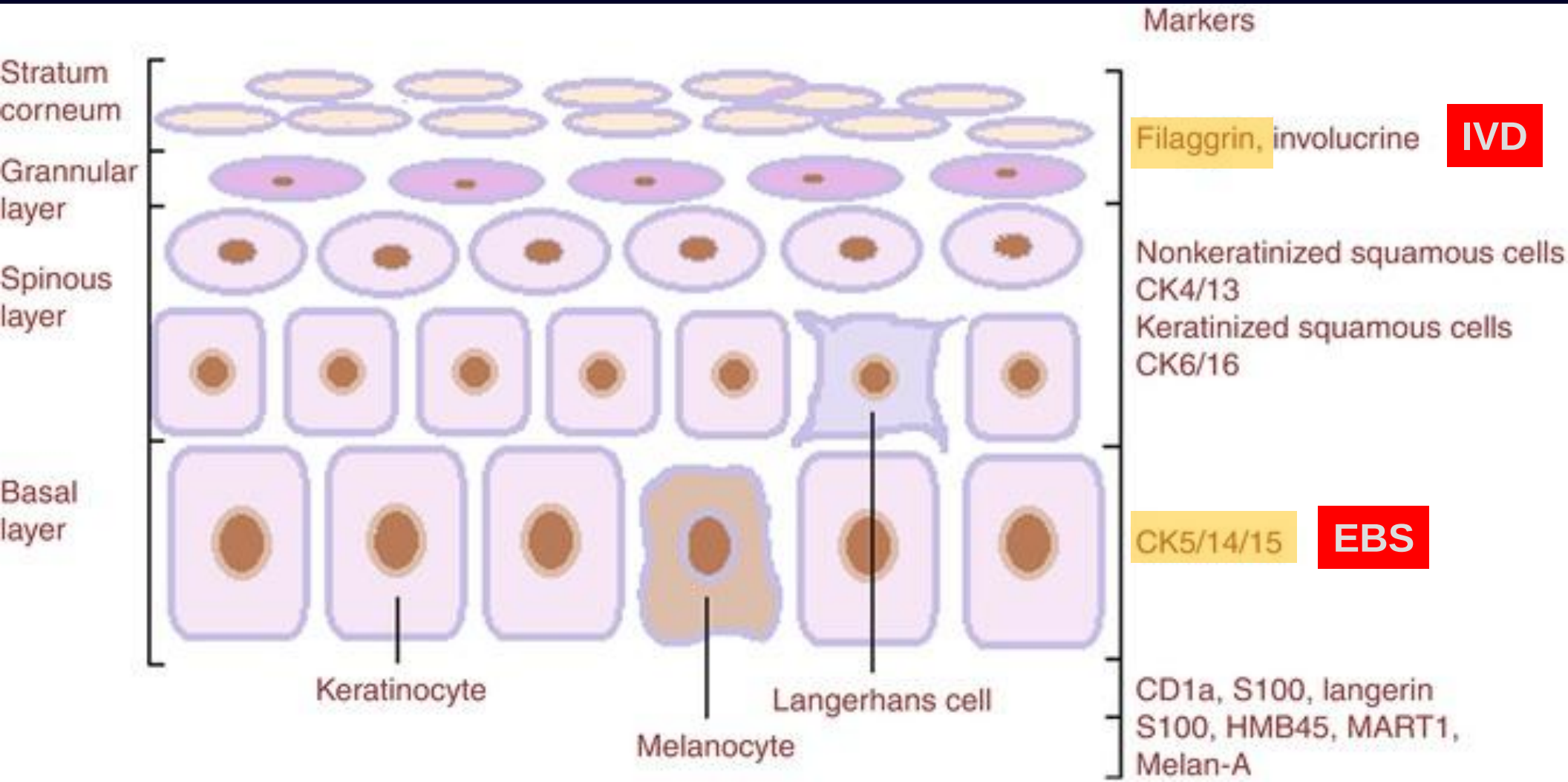
CAM5.2


f
AE1/AE3


Markers
Stratum corneum
Granular layer
Spinous layer
Basal layer
Filaggrin, involucrine
IVD
Nonkeratinized squamous cells
CK4/13
Keratinized squamous cells
CK6/16
CK5/14/15
EBS
Keratinocyte
Melanocyte
Langerhans cell
CD1a, S100, langerin
S100, HMB45, MART1,
Melan-A

The common ichthyoses are:

- Ichthyosis vulgaris (95% of all ichthyosis cases) *FLG* (filaggrin is a structural protein)
- Recessive X-linked ichthyosis *STS*

Autosomal recessive congenital ichthyosis

- Harlequin ichthyosis *ABCA12*
- Lamellar ichthyosis *TGM1* (transglutaminase 1 is an enzyme) and others
- Congenital ichthyosiform erythroderma *ALOXE3* and others

Keratinopathic ichthyoses

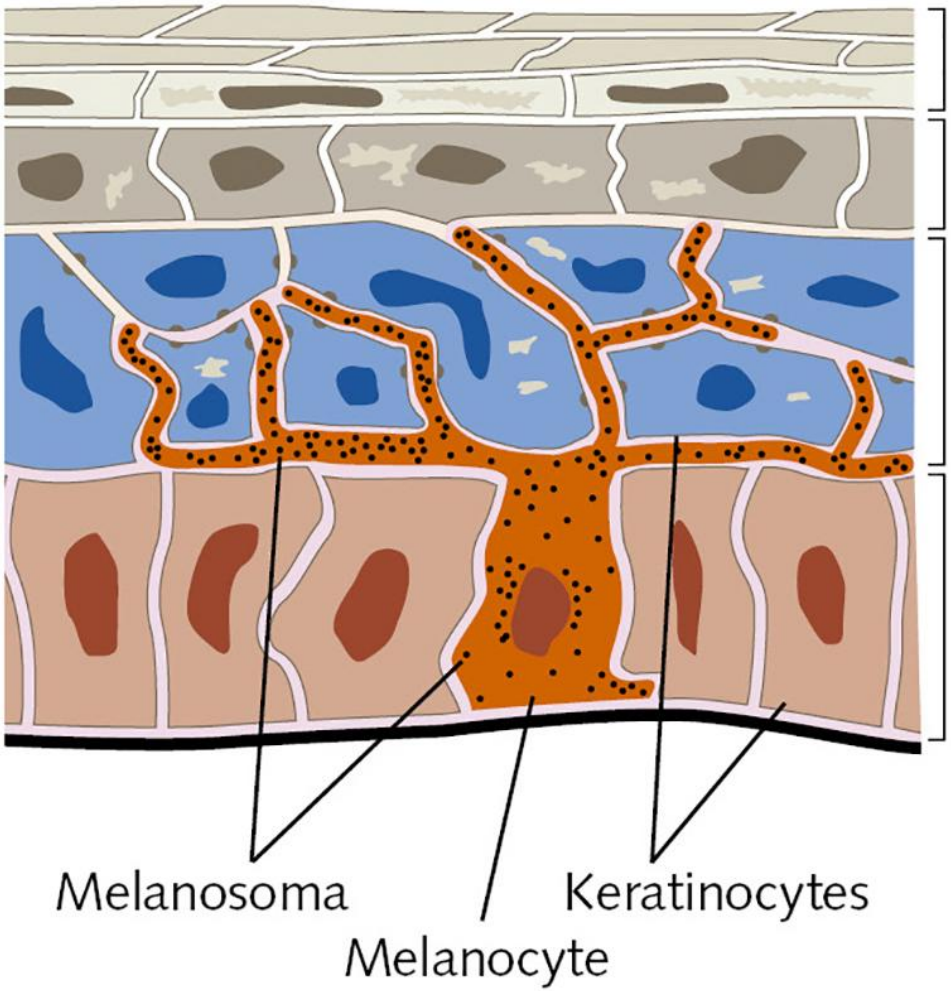
This group has keratin mutations. The main types of keratinopathic ichthyoses are:

- Epidermolytic ichthyosis* *KRT1, KRT10*
- Superficial epidermolytic ichthyosis¶ *KRT2*
- Ichthyosis Curth-Macklin§ *KRT1*
- Congenital reticular ichthyosiform erythroderma

* Previously called epidermolytic hyperkeratosis or bullous ichthyosiform erythroderma
¶ Previously called ichthyosis bullosa Siemens
§ Previously called ichthyosis hystrix

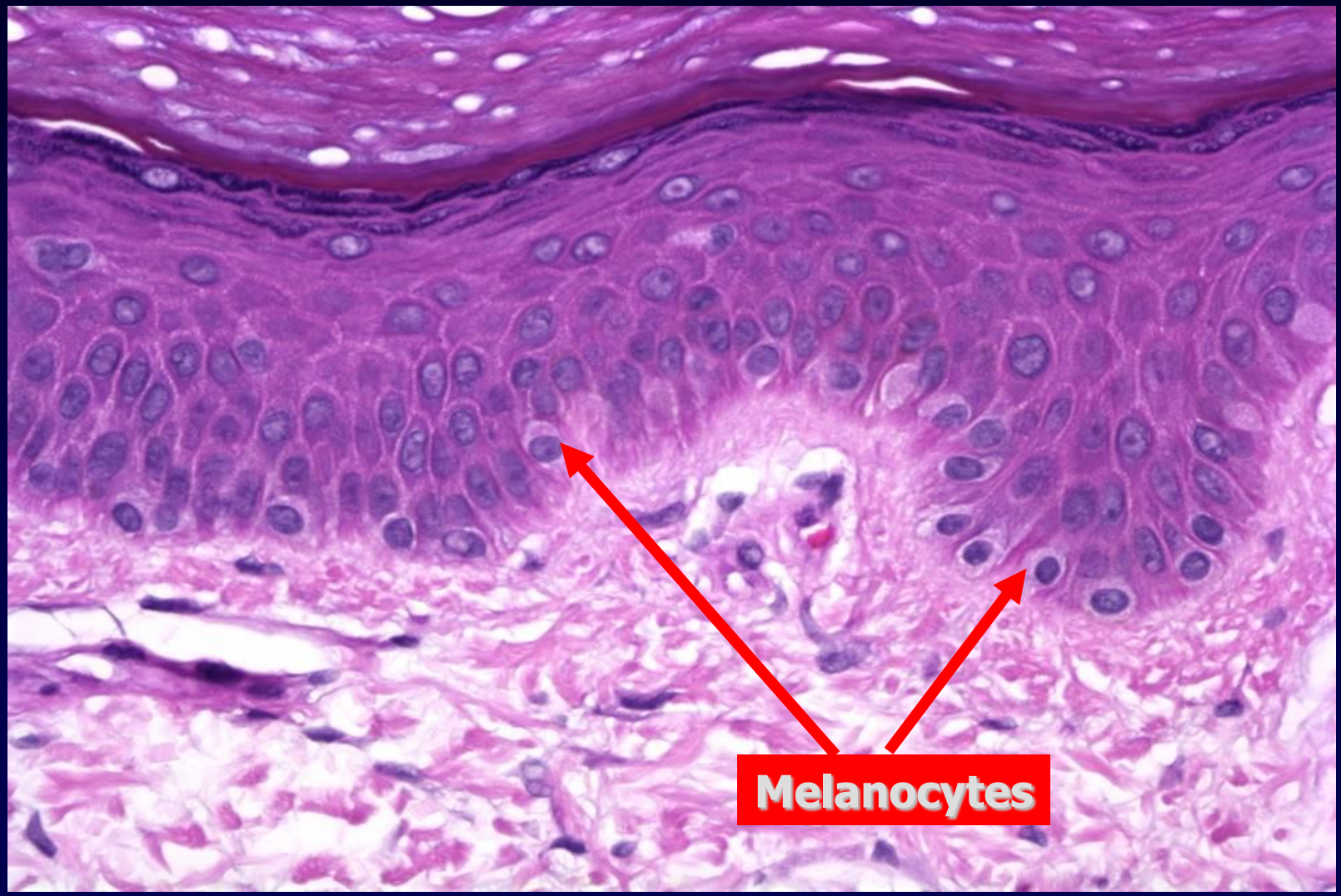
EB subtypes	Targeted gene product(s)
Plakophilin deficiency	plakophilin-1
Lethal acantholytic EBS	desmoplakin
EBS superficialis	unknown
Localized EBS	keratins 5 & 14
EBS, Dowling–Meara	keratins 5 & 14
EBS, generalized other	keratins 5 & 14
EBS, autosomal recessive	keratin 14
EBS with mottled hyperpigmentation	keratin 5
EBS with muscular dystrophy	plectin
EBS, Ogna	plectin
EBS, migratory circinate	keratin 5
EBS with pyloric atresia	α6β4 integrin, plectin

Melanocytes



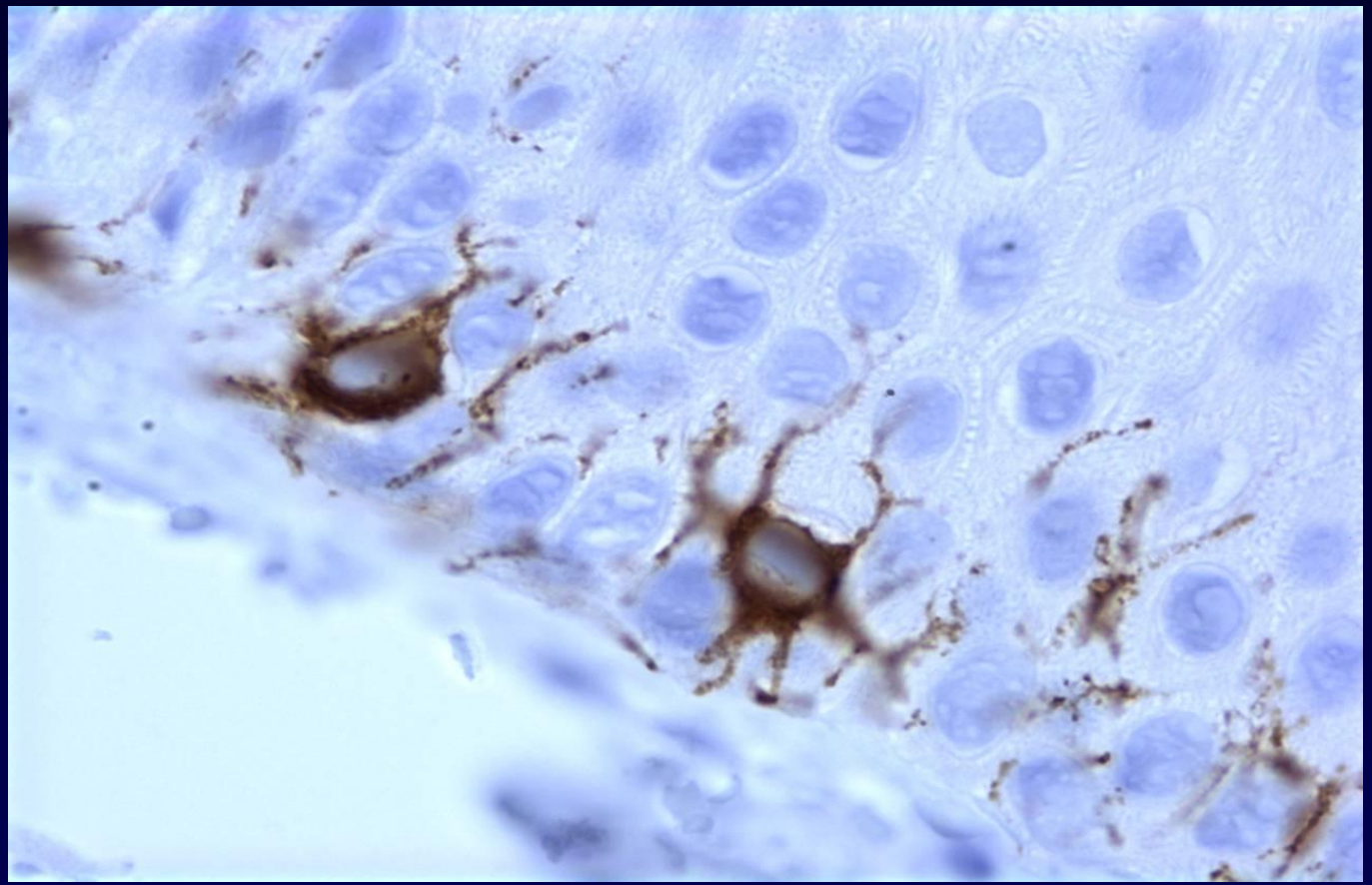
- 1:5/1:10 keratinocytes
- S100
- MelanA/MART1
- Tirosinasi
- Sox10
- MITF
- NKI.C3
- HMB45 (act)
- p16/p21 (sen)

Melanocytes

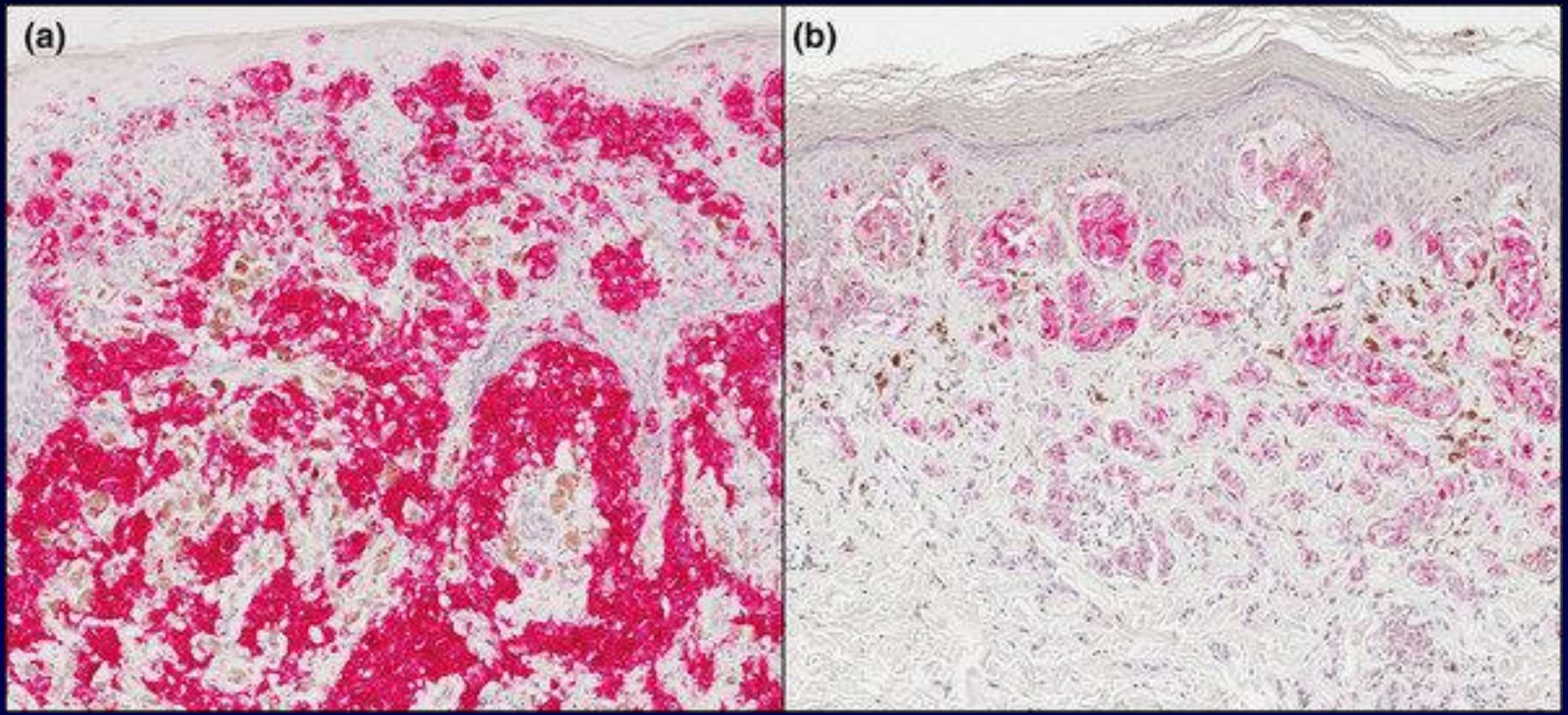


Melanocytes

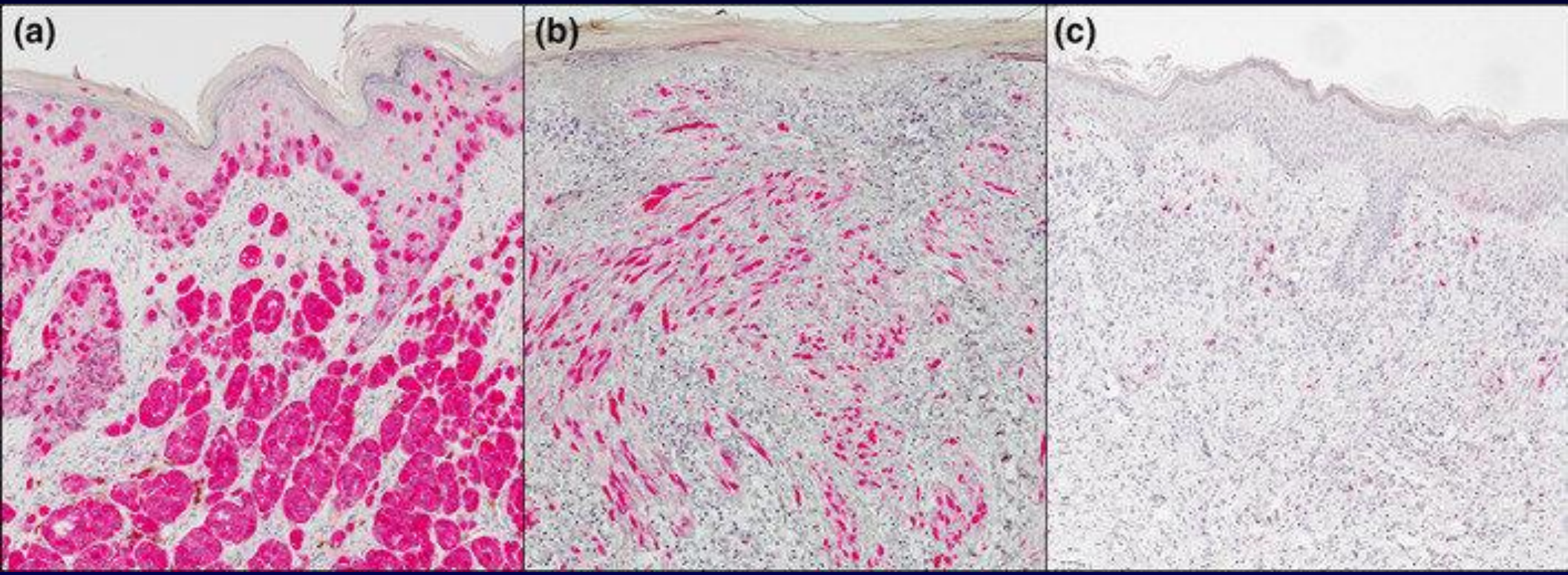
Mart-1 Immunoperoxidase shows dendritic processes of melanocytes



HMB45



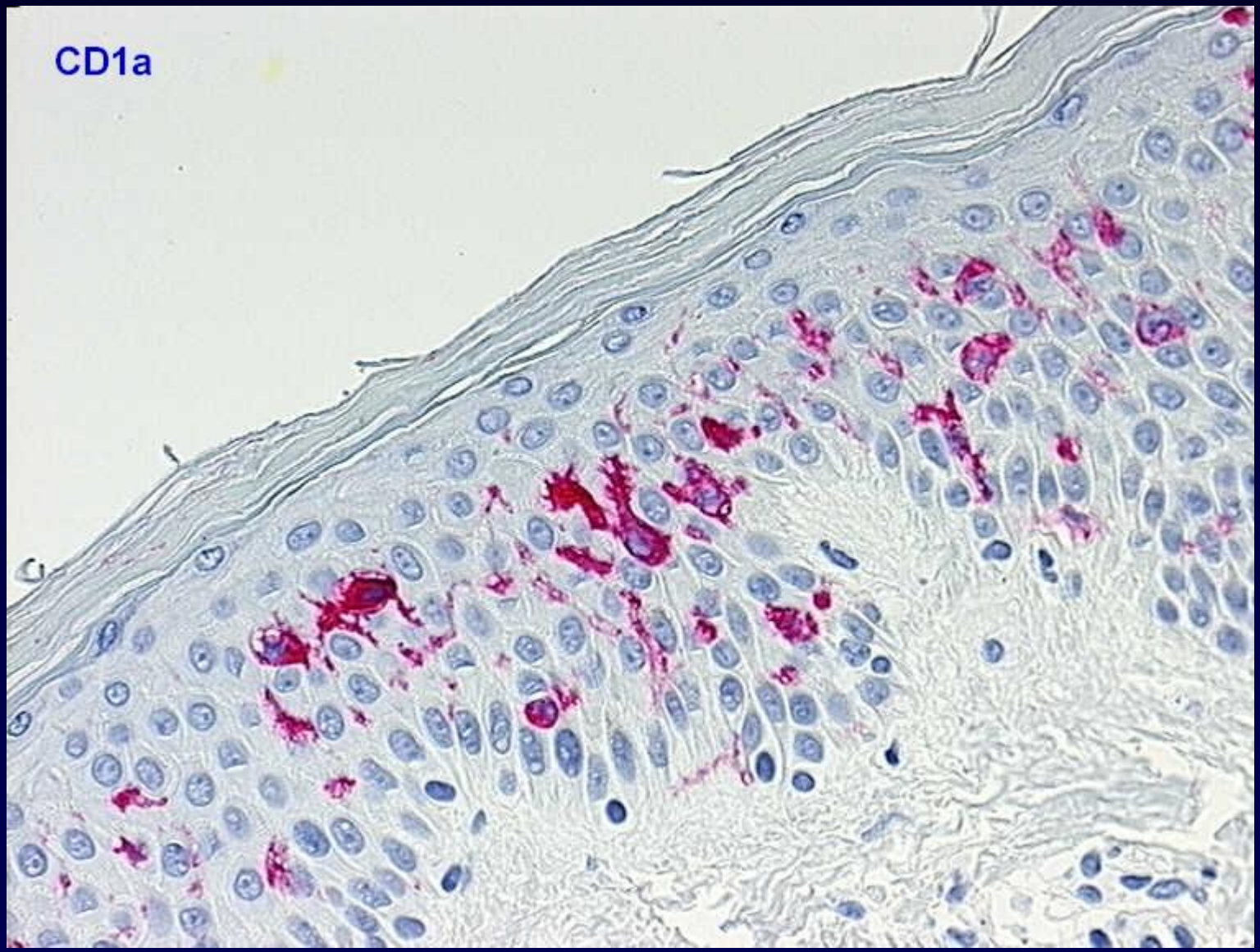
p16



Embriogenesis

- Melanoblast (melanocyte precursor) dorsolateral and ventral migration starting at the VIII wk
- Early melaninization at the X wk
- In fetal skin: melanocytes within the dermis as well as within the epidermis (basally and suprabasally)
- Disappearance of dermal active (dendritic) melanocytes (apoptosis? Migration toward the epidermis?) except in:
  - The head-neck district
  - The dorsal aspects of hands and feet
  - The presacral area

Langerhans cells



- Single units, spinous l.
- Antigen-presenting
- S100
- CD1a
- Langerin (CD207)
- Also: CD4, CD68, CD163

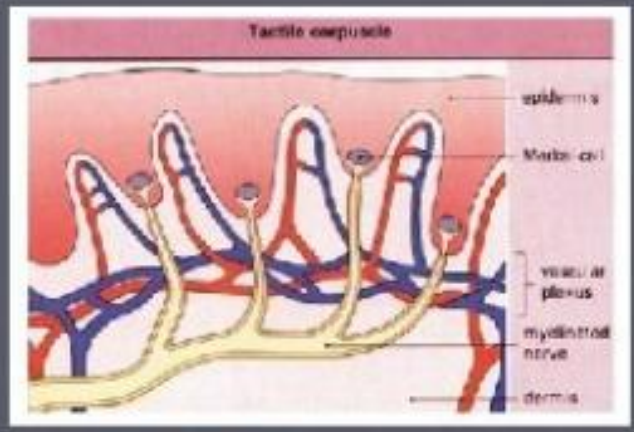
Sensory Perception in Dermis

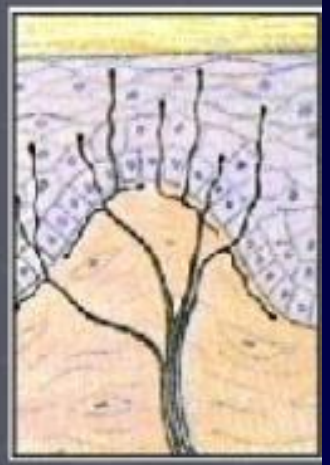
Merkel cells: deep layers of epidermis
- superficial touch

Free Nerve Endings: superficial dermis
- pain and temperature

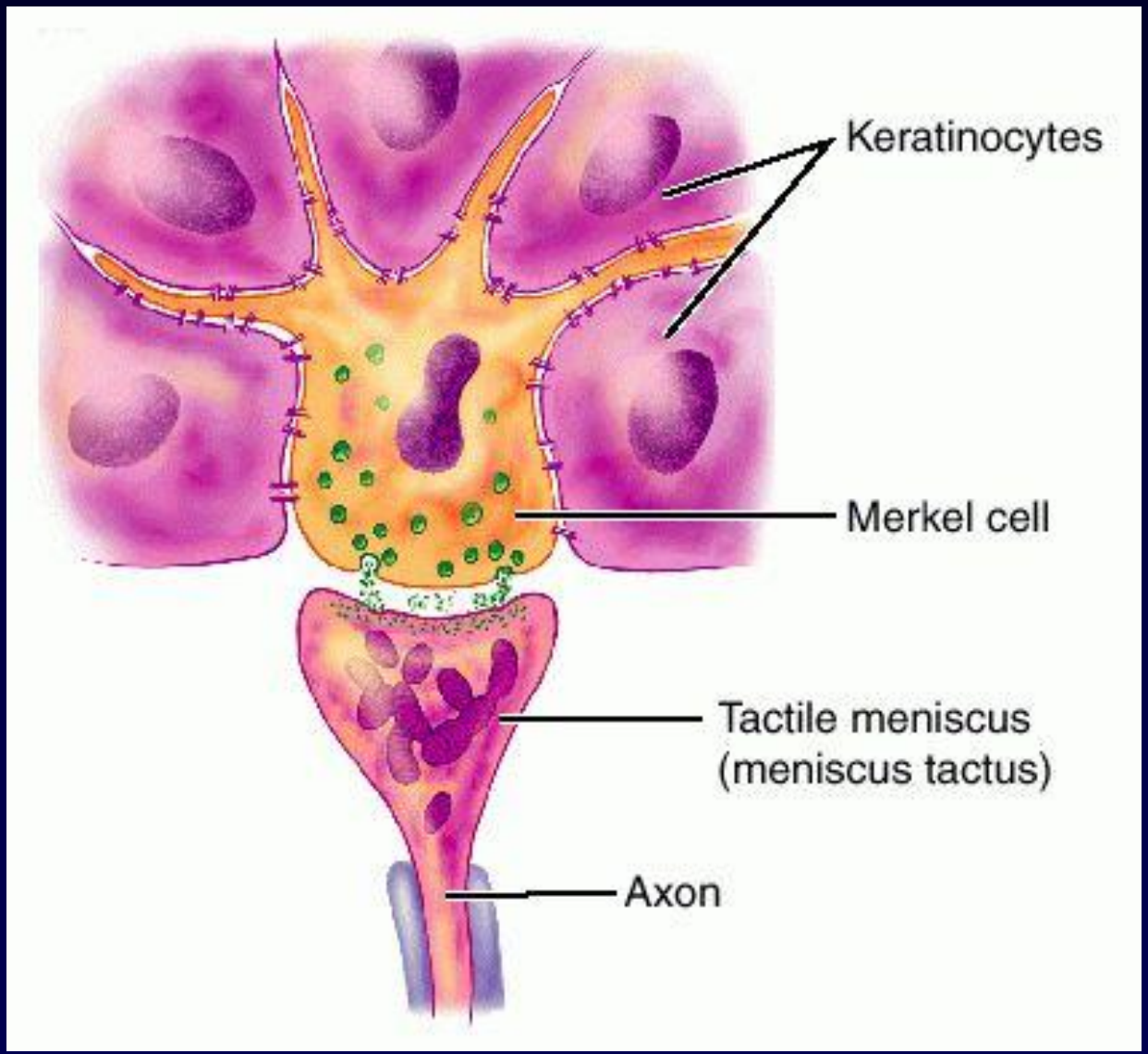
Meissner's Corpuscles: superficial dermis
- light touch

Pacinian Corpuscles: deep dermis
- pressure and vibrations

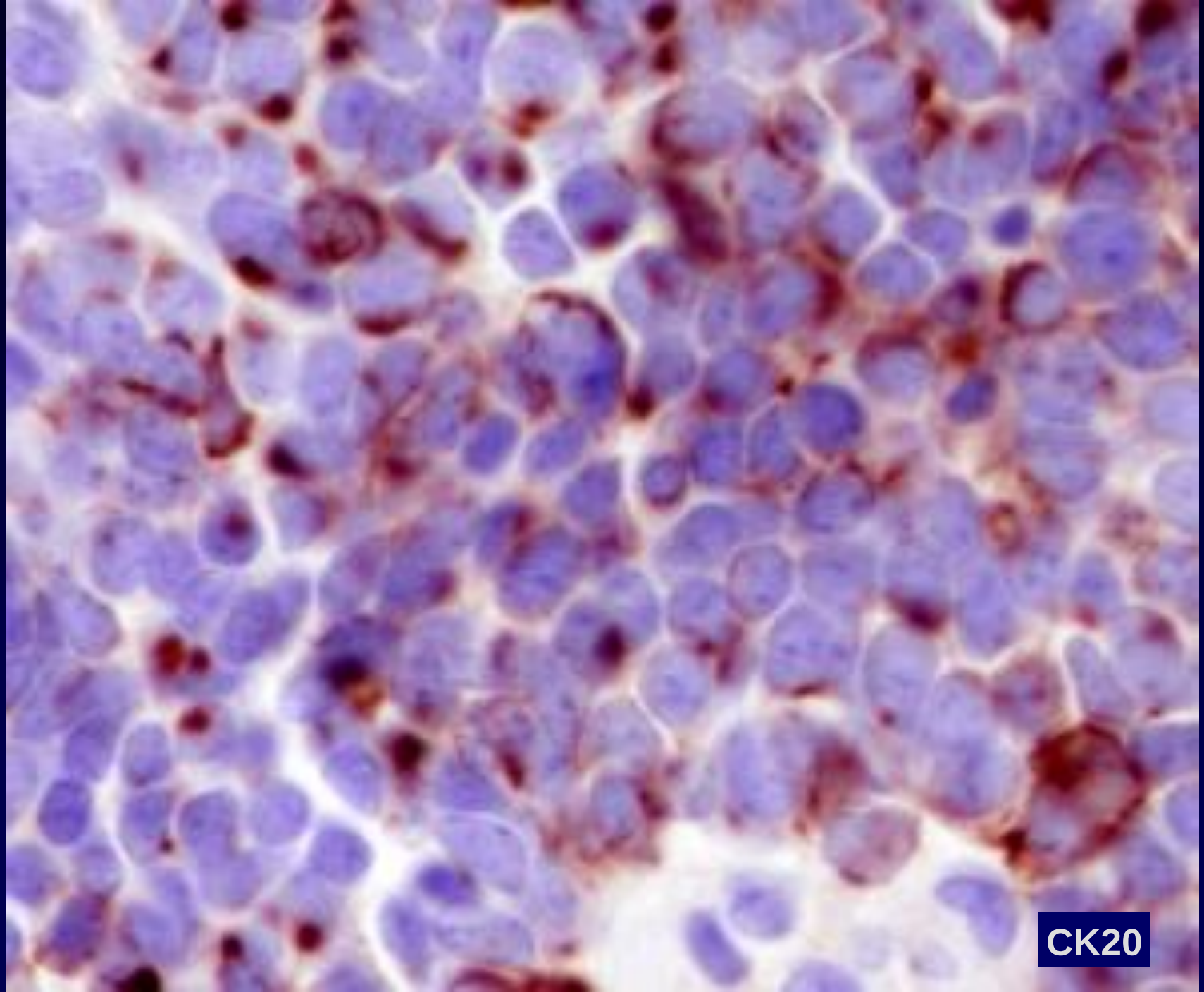


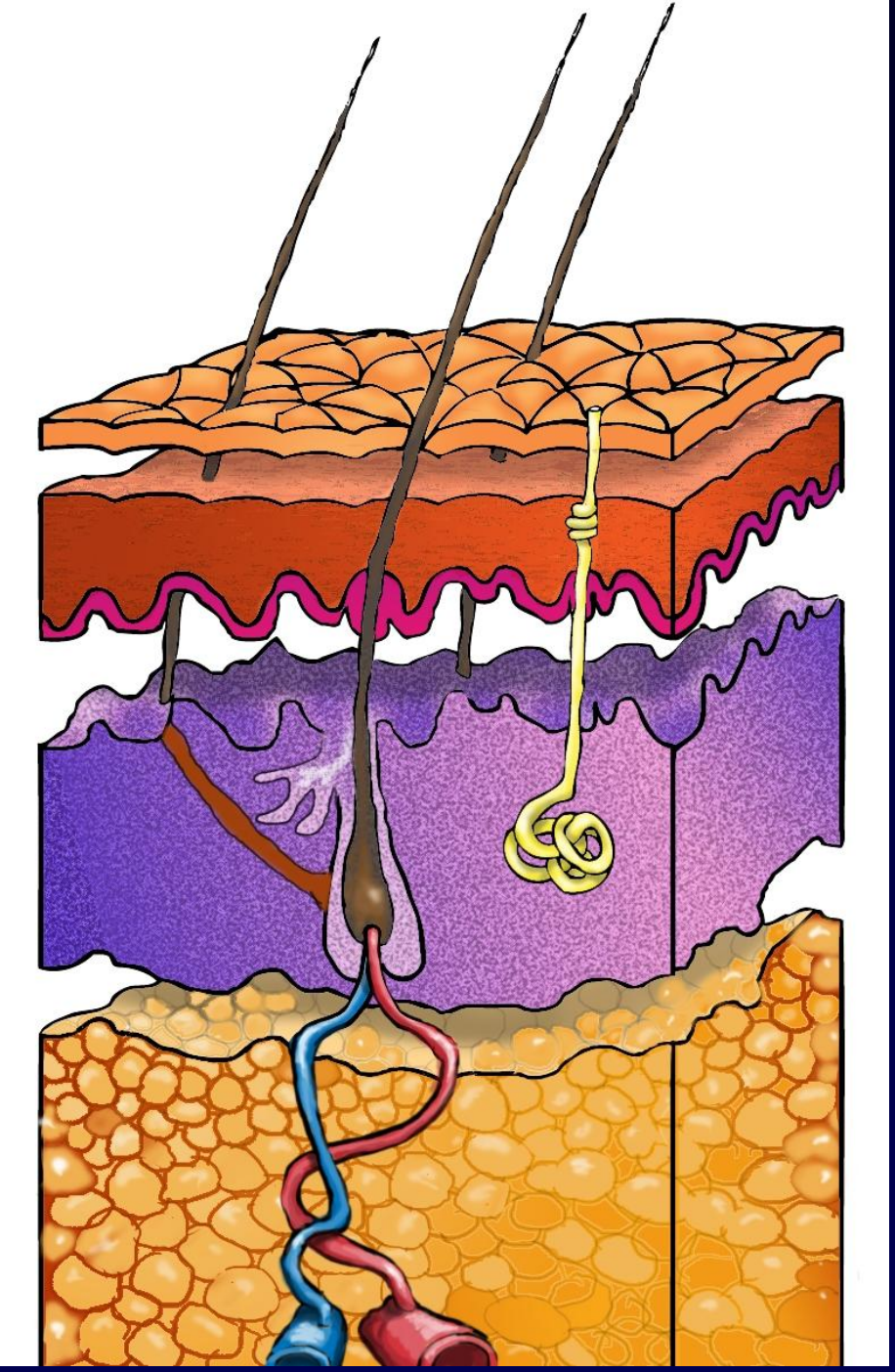


Merkel cells



- CK AE1/AE3
- CK 8/18
- CK 19
- CK20
- Neurofilaments
- Chromogranin A
- Sinaptophisin
- CD56
- PGP9.5

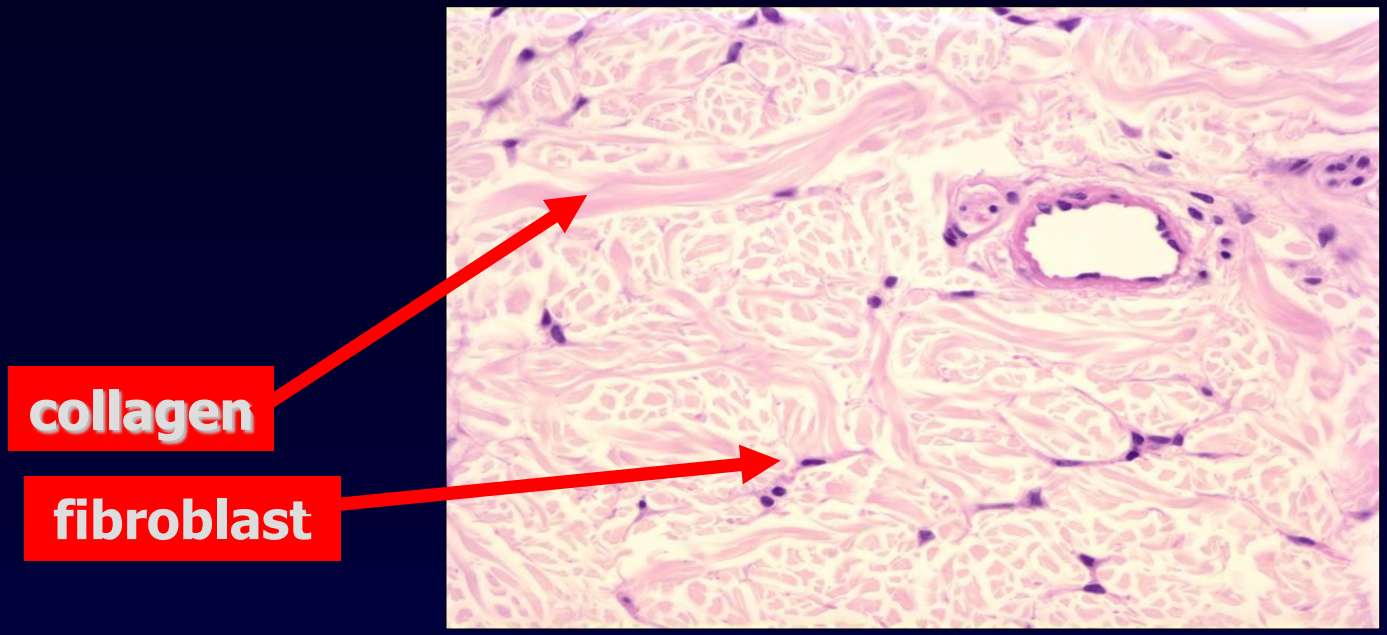

CK20



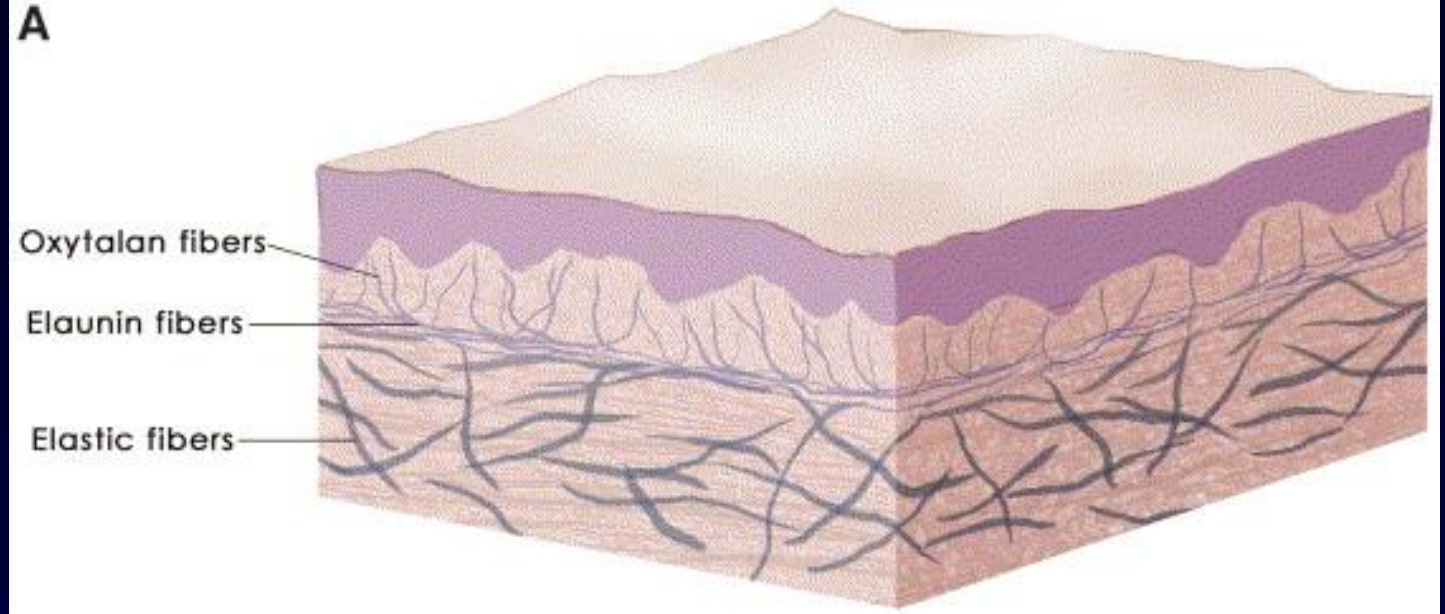
Epidermis

Dermis

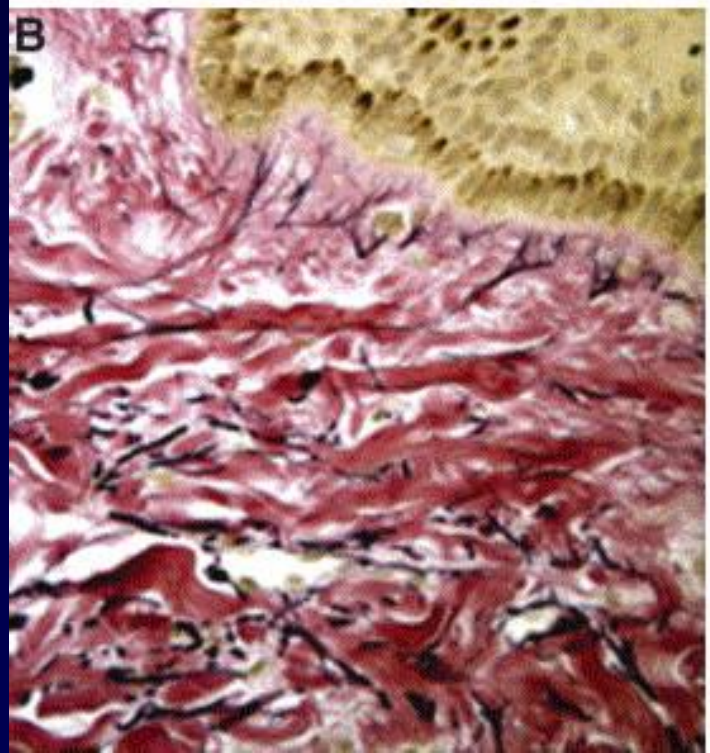
Subcutaneous tissue

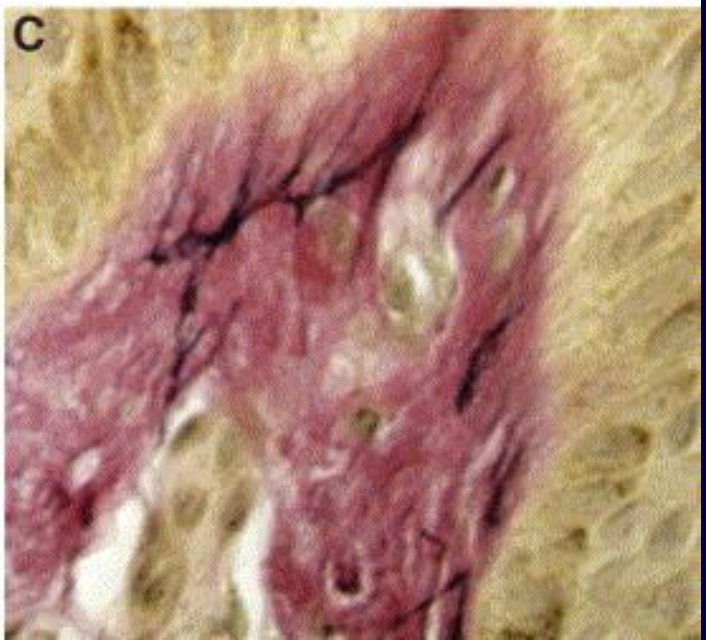


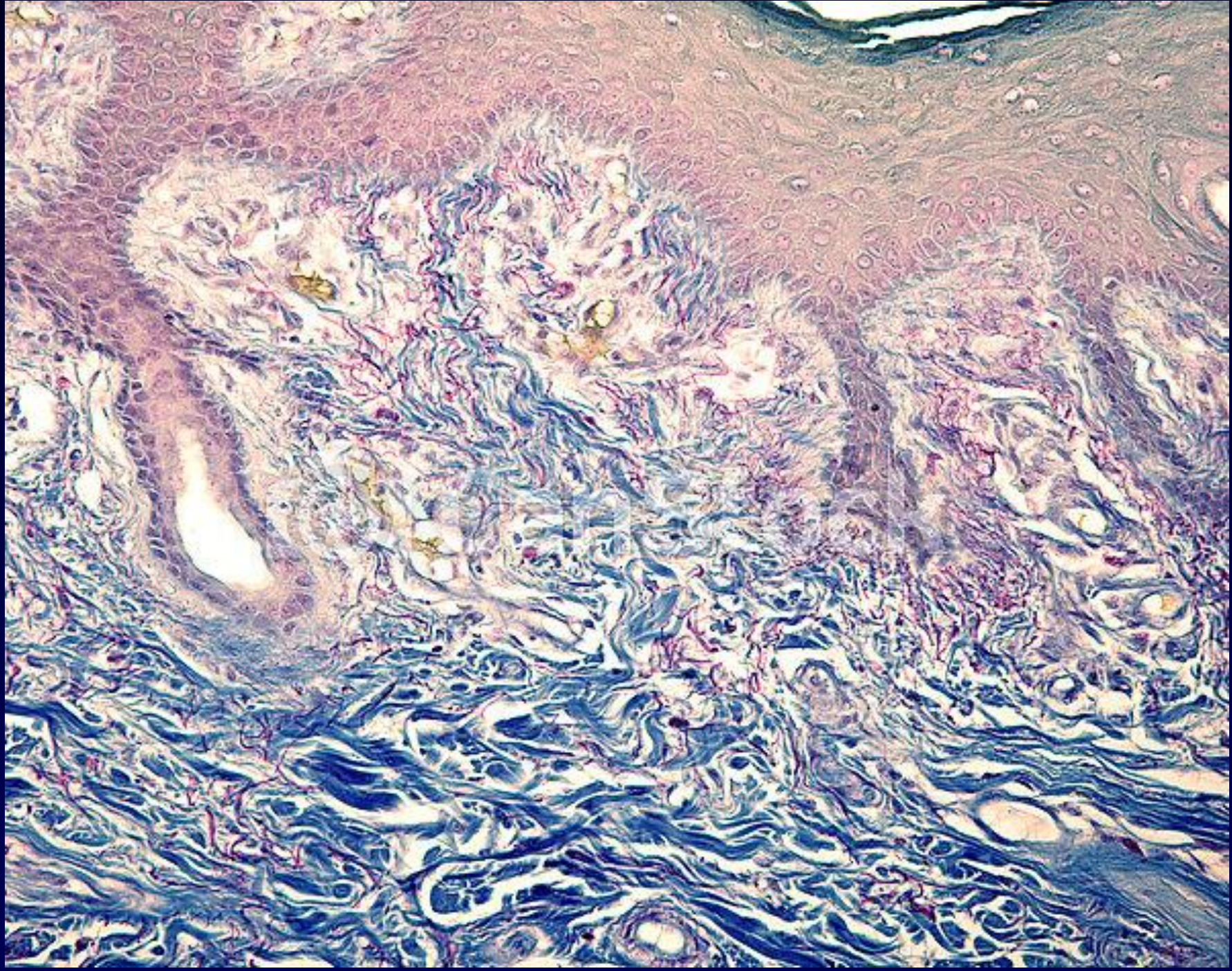
- The dermis is composed predominantly of connective tissue; collagen, elastic tissue, and ground substance. The major function of the dermis is to protect against trauma and envelop the body in a strong and flexible wrap.
- Collagen comprises the majority of the dermis, especially type I collagen, which accounts for 80% of the total collagen in skin. This provides the tensile strength of the skin.
- Ground substance (connective tissue mucin) is the amorphous material that fills spaces between the cellular and fibrillar components of the dermis. It is composed of proteoglycans.



3% of the dry weight of the skin



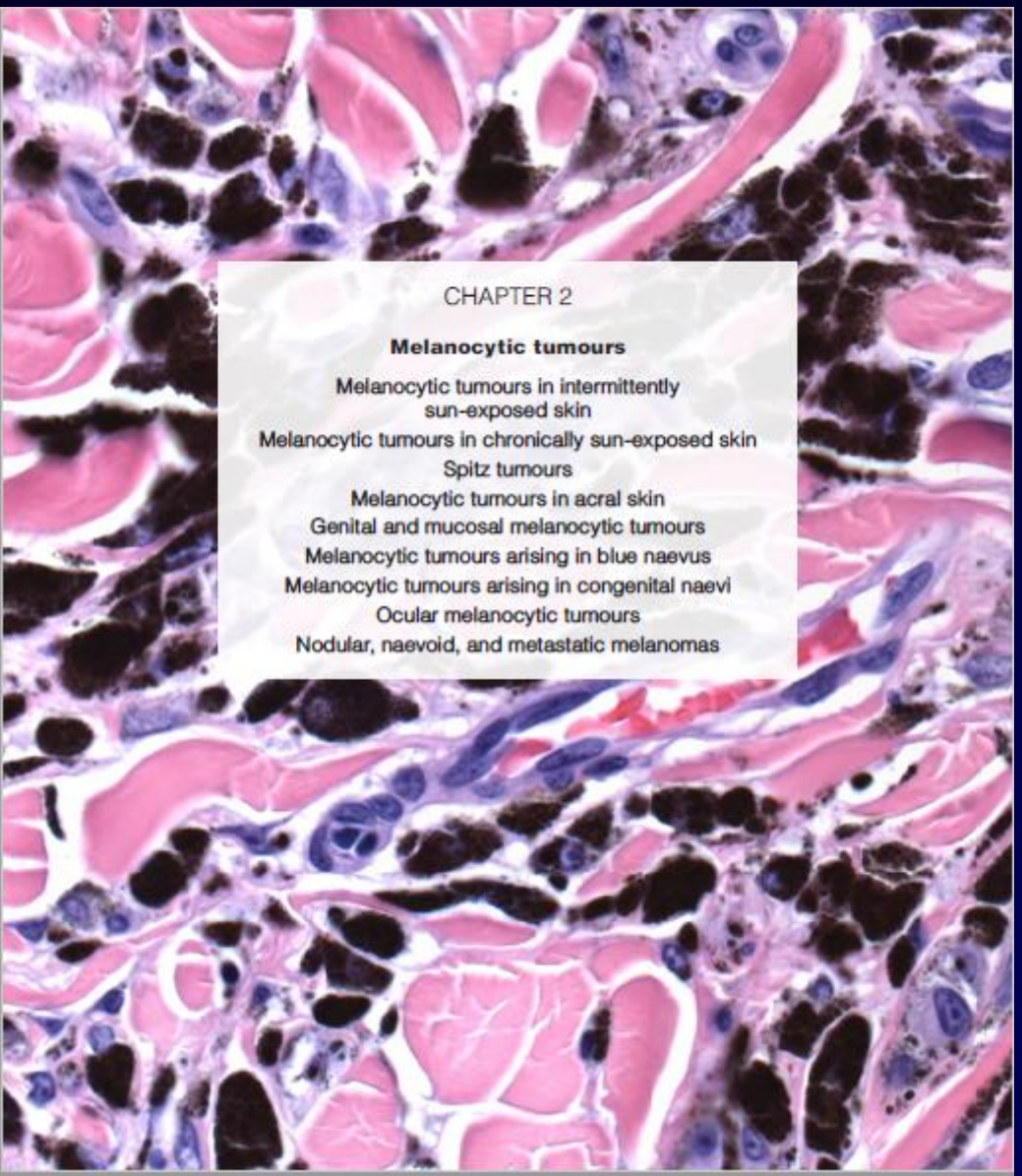




Aging skin


Smoother skin
Epidermis
Oxytalan
Elastin
Collagen
Deep wrinkle
Hyaluronan and water
Fibroblast
Capillary vessel
YOUNGER SKIN
OLDER SKIN

WHO, 2018



CHAPTER 2

Melanocytic tumours

Melanocytic tumours in intermittently sun-exposed skin

Melanocytic tumours in chronically sun-exposed skin

Spitz tumours

Melanocytic tumours in acral skin

Genital and mucosal melanocytic tumours

Melanocytic tumours arising in blue naevus

Melanocytic tumours arising in congenital naevi

Ocular melanocytic tumours

Nodular, naevoid, and metastatic melanomas

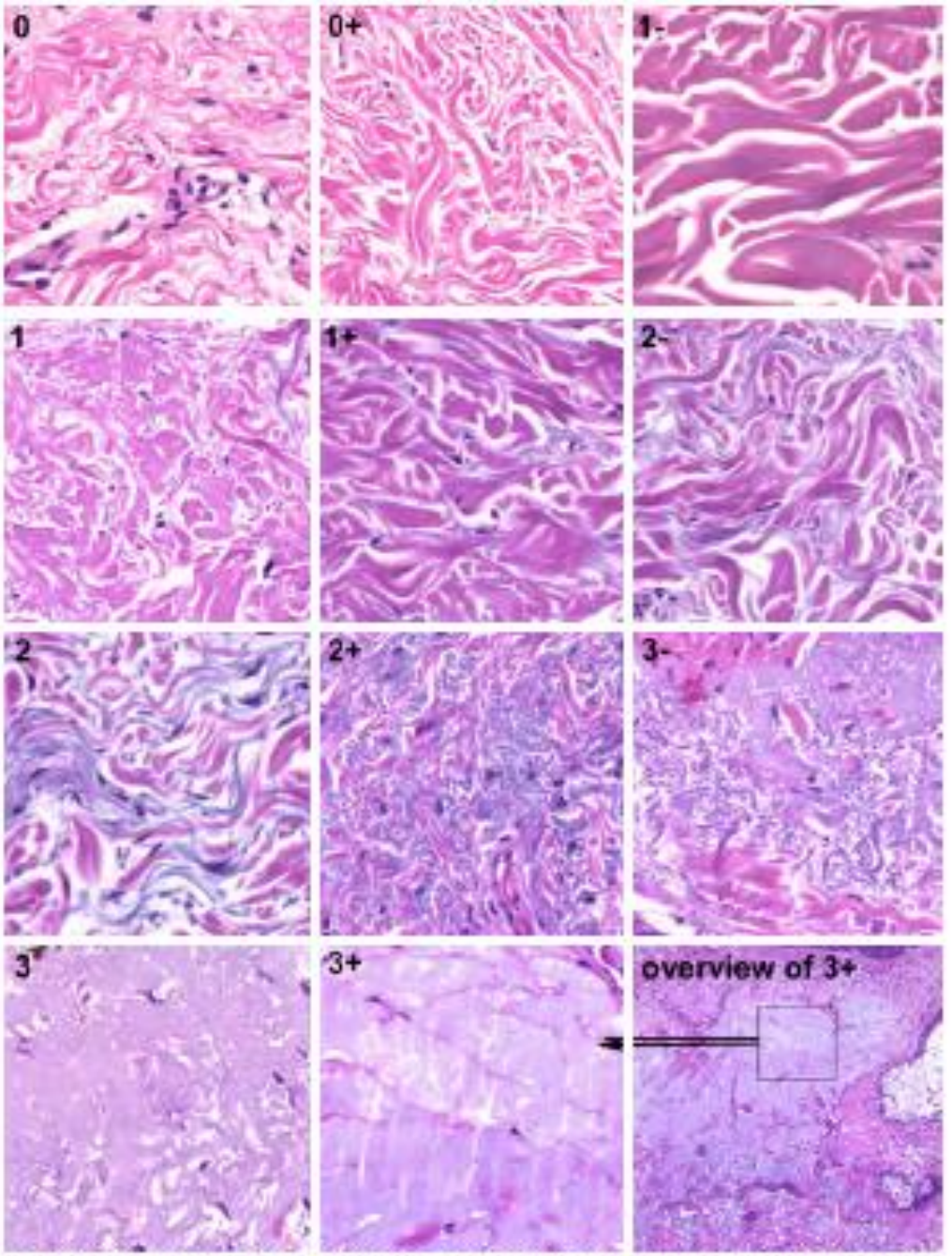


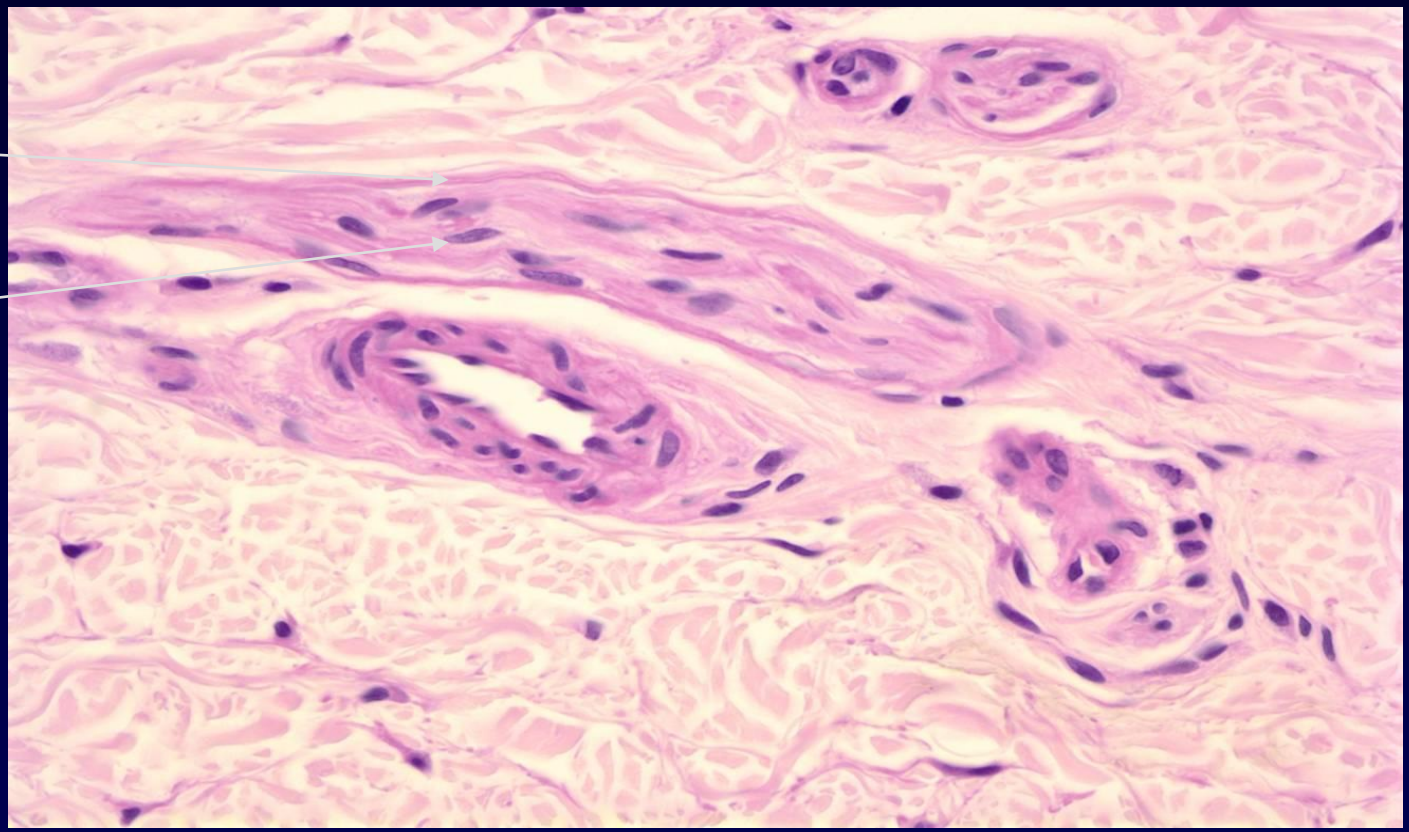
Fig. 7650 Grades of solar elastosis. Grade 1 is distinguished by the presence of single elastic fibres, grade 2 by bunches of fibres, and grade 3 by basophilic material that has lost its fibrillary texture.

Neurovascular Bundle

perineurium

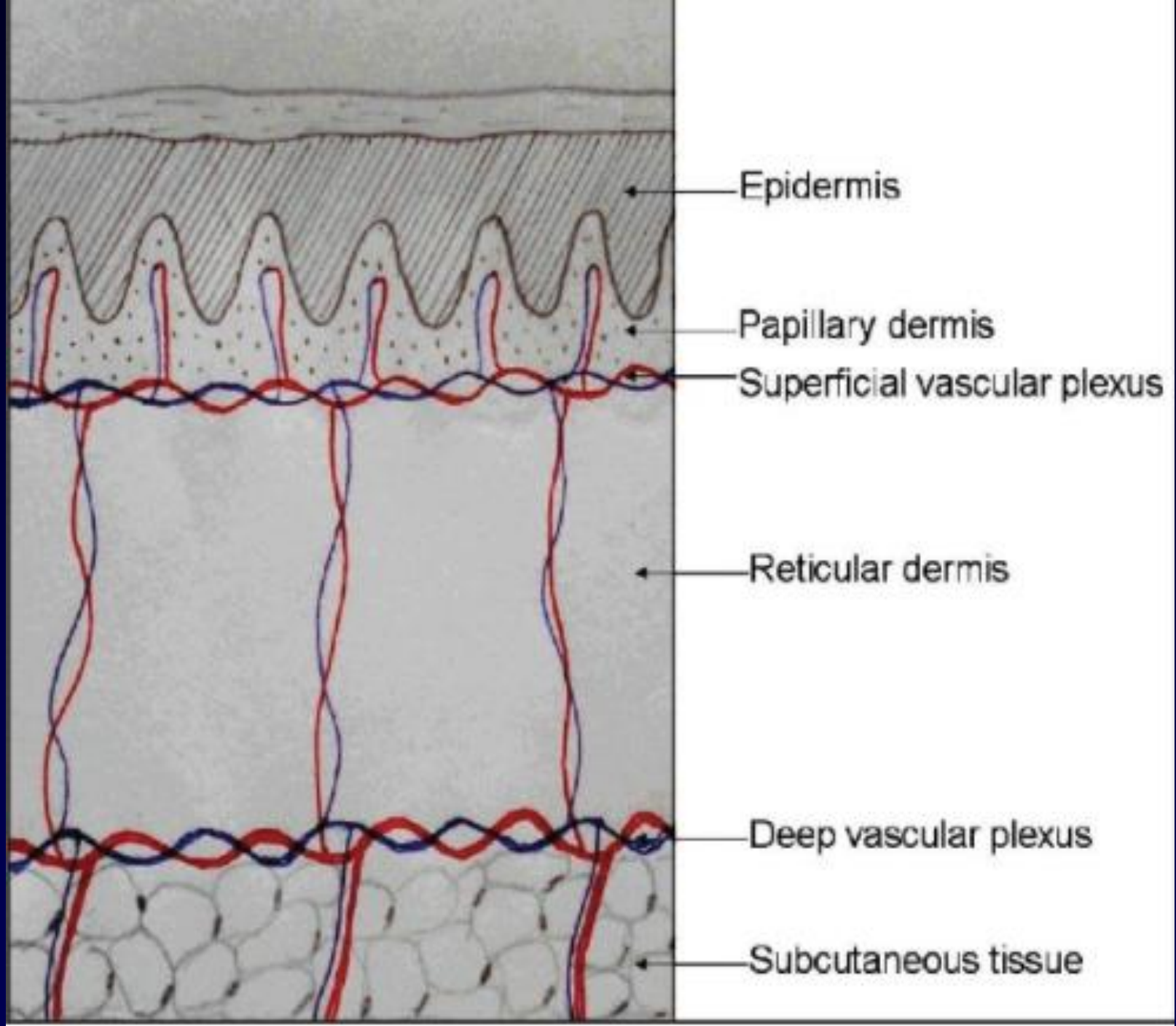
Wavy nuclei of Schwann cells

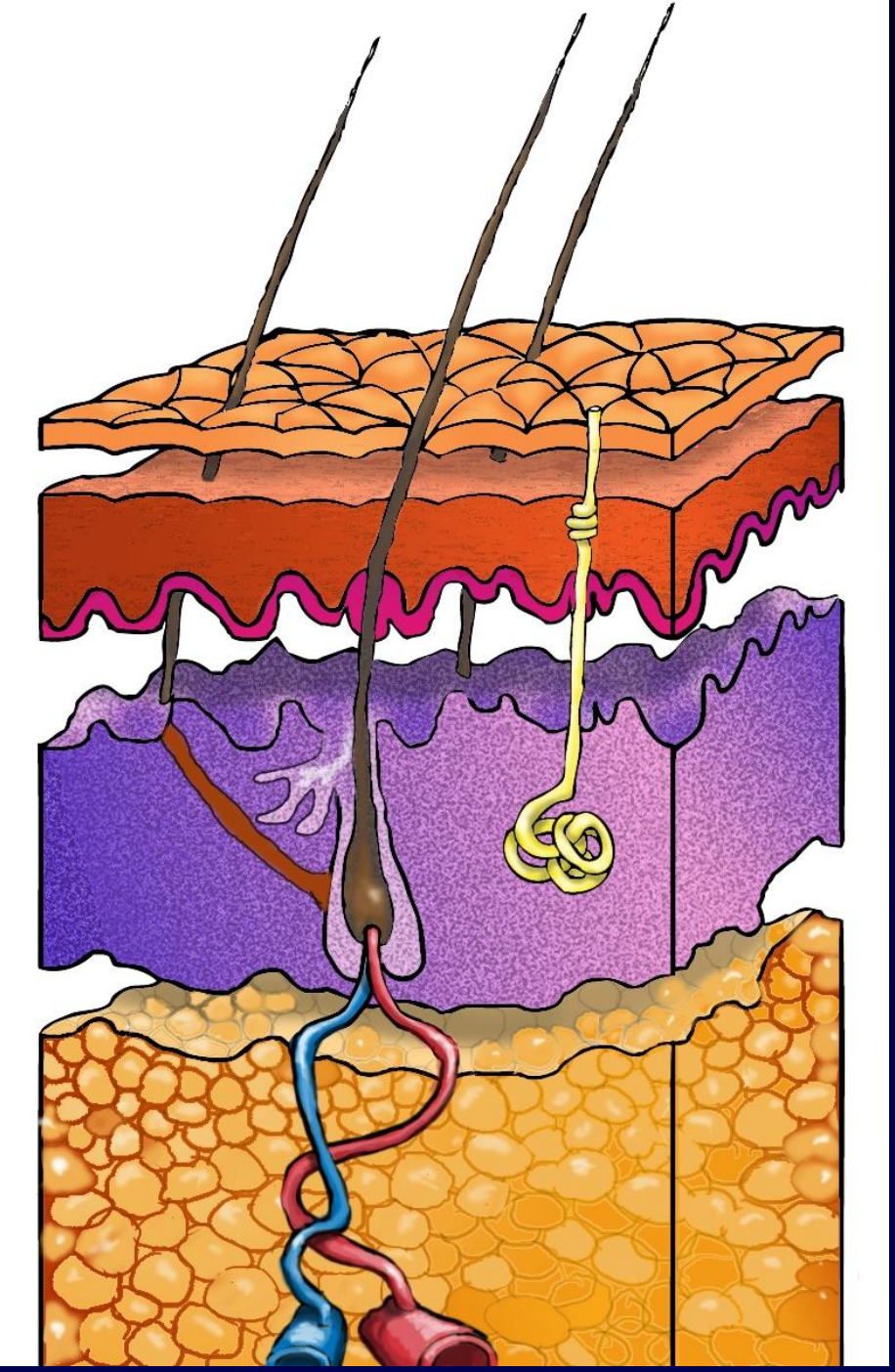
Nerve fibers are zig-zag to permit stretching



Caveats

- There are two vascular plexuses in the skin; one at the junction of papillary dermis and reticular dermis and another at the junction of reticular dermis and subcutaneous tissue. These plexuses are interconnected by few vertically traversing vessels
- When a biopsy ends at the mid-reticular level, the residual dermis is at risk of necrosis due to reduced vascularity. This increases the chances of secondary infection and scarring. Hence, while performing biopsy, it is important to go subcutaneous tissue deep.


Epidermis
Papillary dermis
Superficial vascular plexus
Reticular dermis
Deep vascular plexus
Subcutaneous tissue



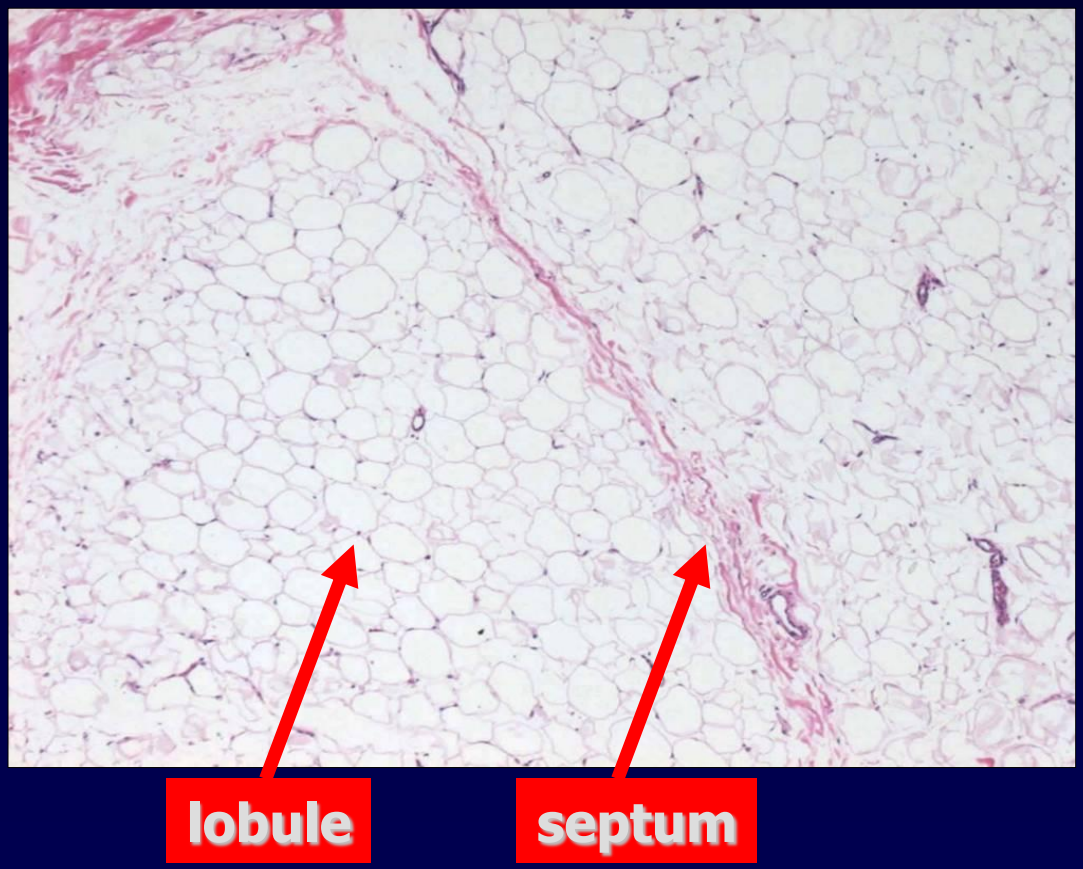
Epidermis

Dermis

Subcutaneous tissue

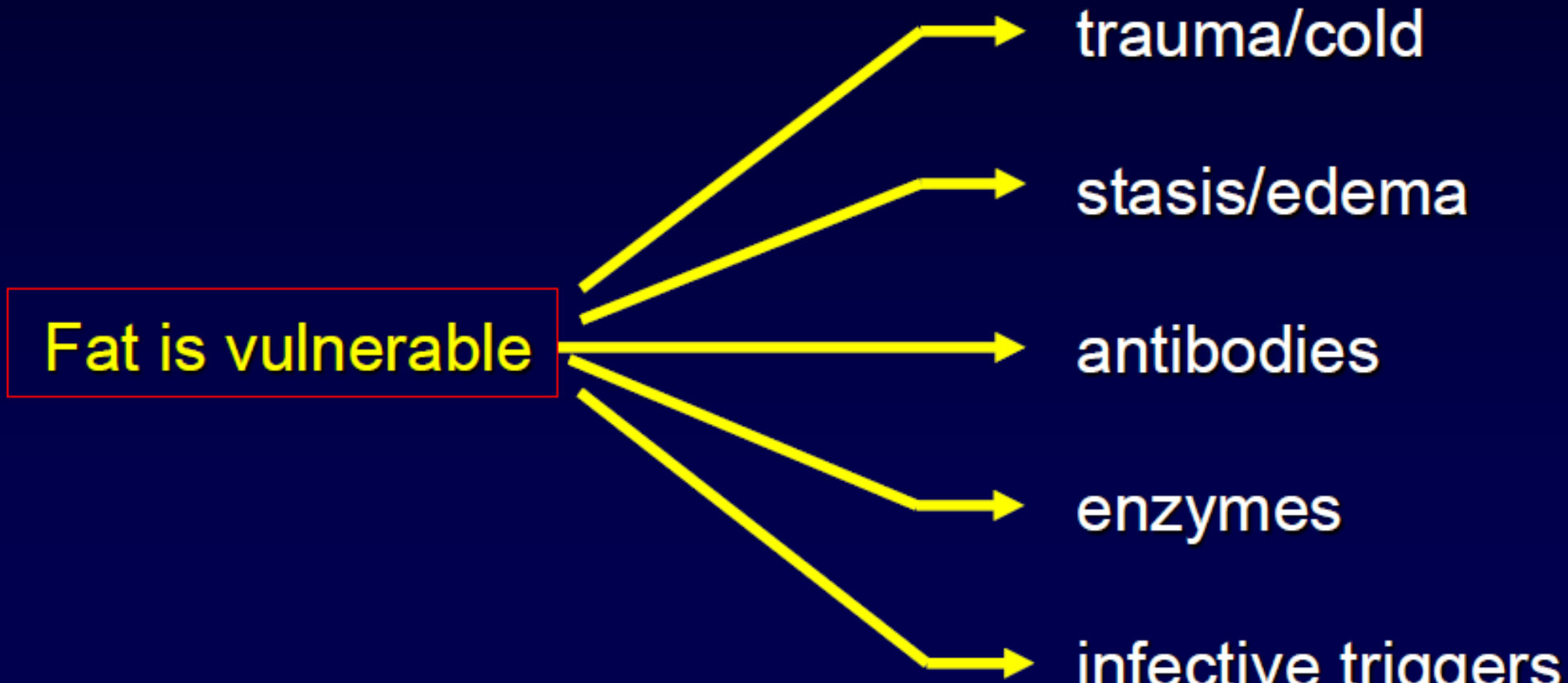
Subcutaneous fat

The subcutaneous fat is composed of lobules of adipocytes separated by fibrous septae containing nerves, blood vessels, and lymphatics. The fibrous septae connect the overlying dermis to the underlying fascia. The subcutis serves as a shock absorber, insulator, and energy store.

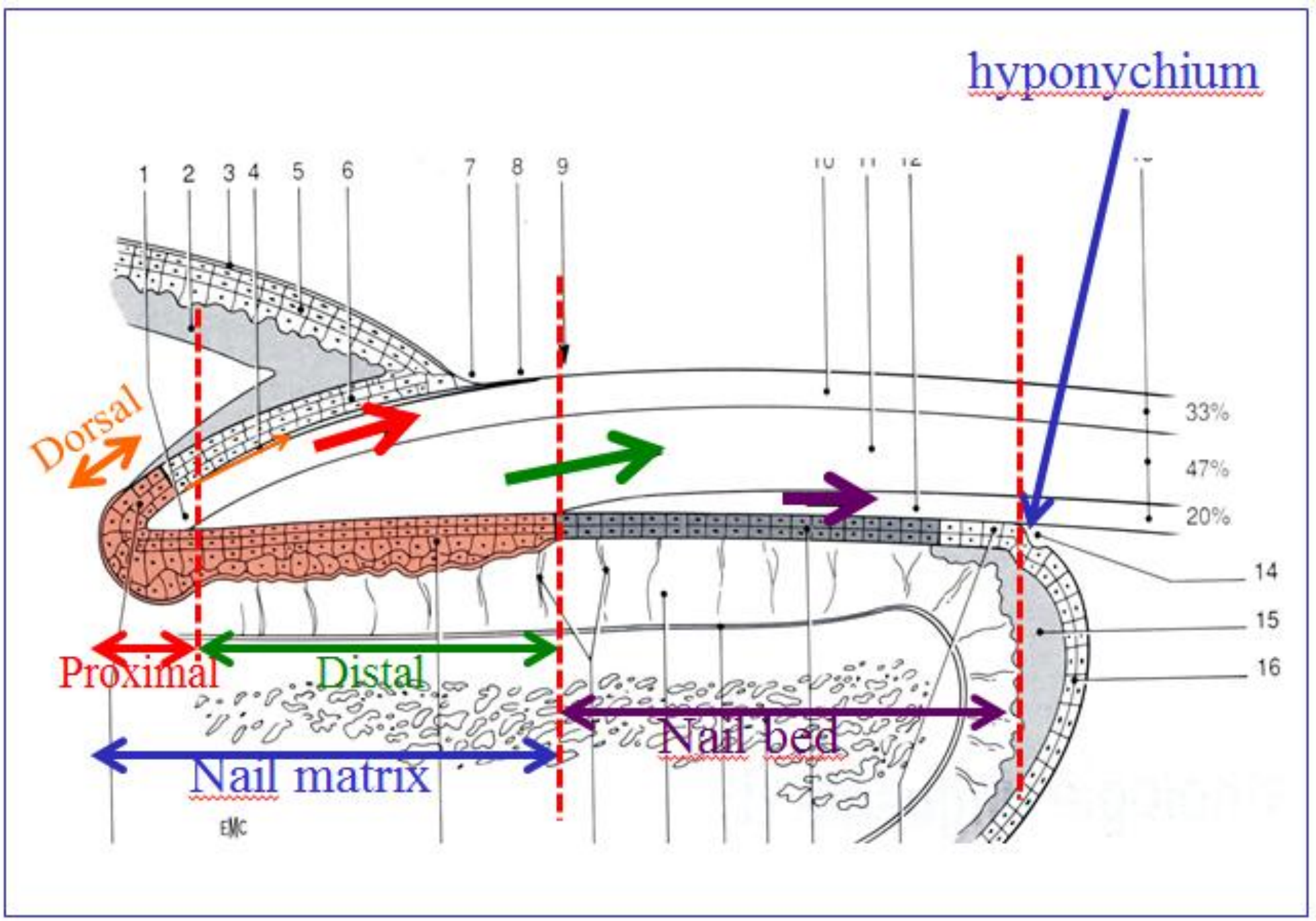


Panniculitis: pathogenesis

Vascular supply is rich but SLOW FLOWING



Cutaneous adnexa

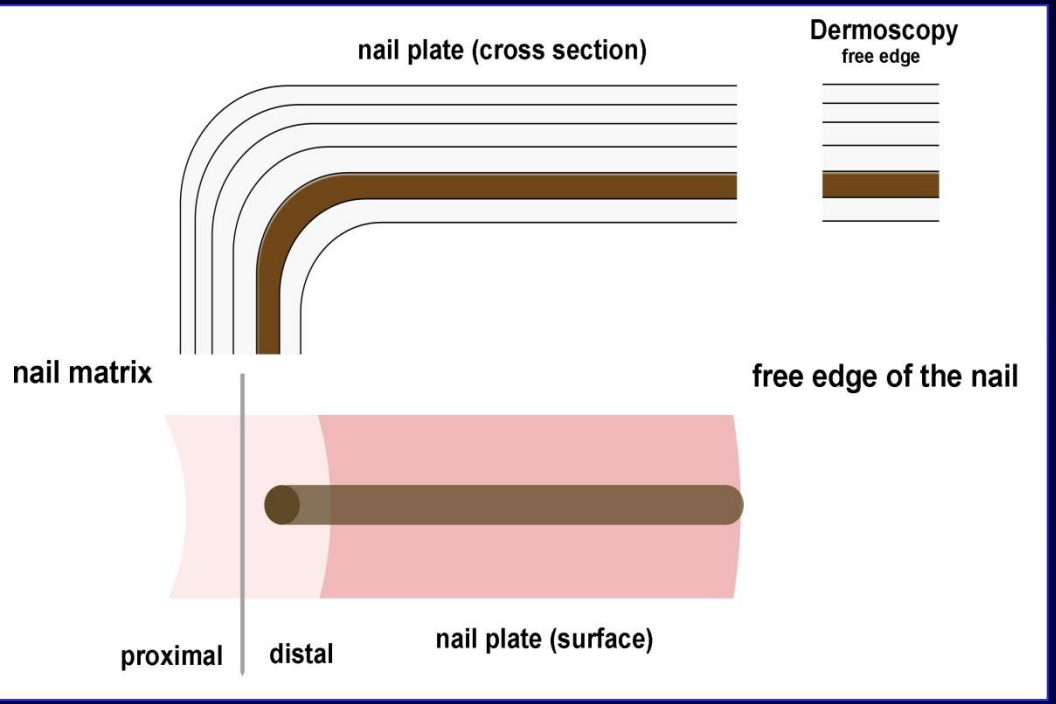

hyponychium
1
2
3
4
5
6
7
8
9
33%
47%
20%
14
15
16
Dorsal
Proximal
Distal
Nail bed
Nail matrix
EMC

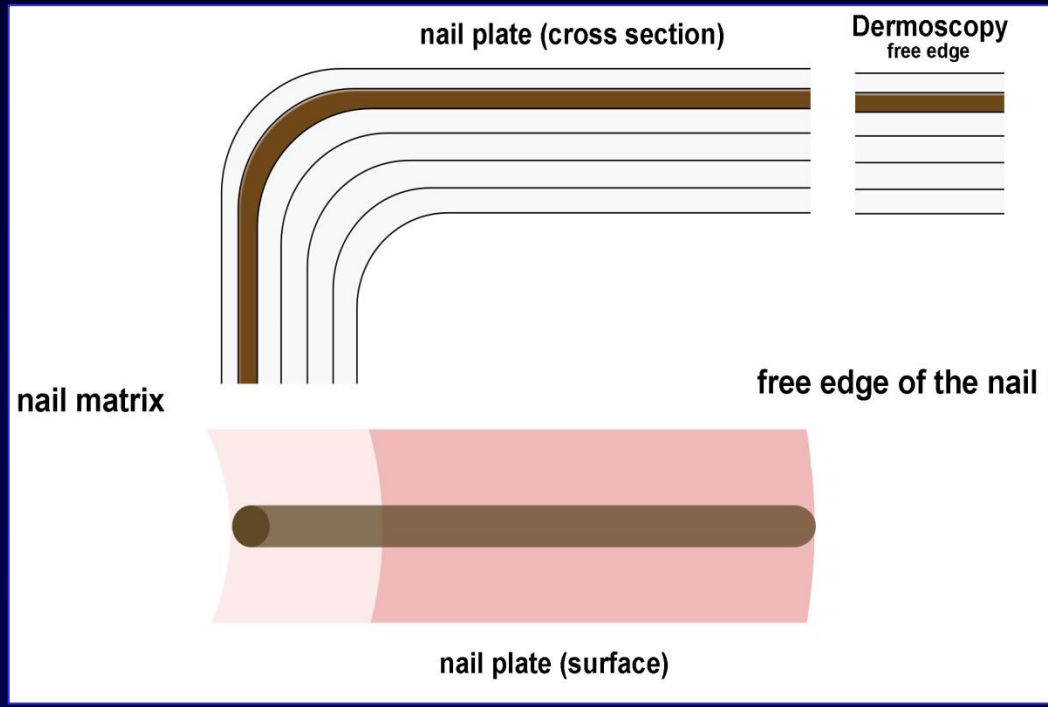
3. Nail dermoscopy

- Free-edge dermoscopy

3. Nail dermoscopy

- Free-edge dermoscopy

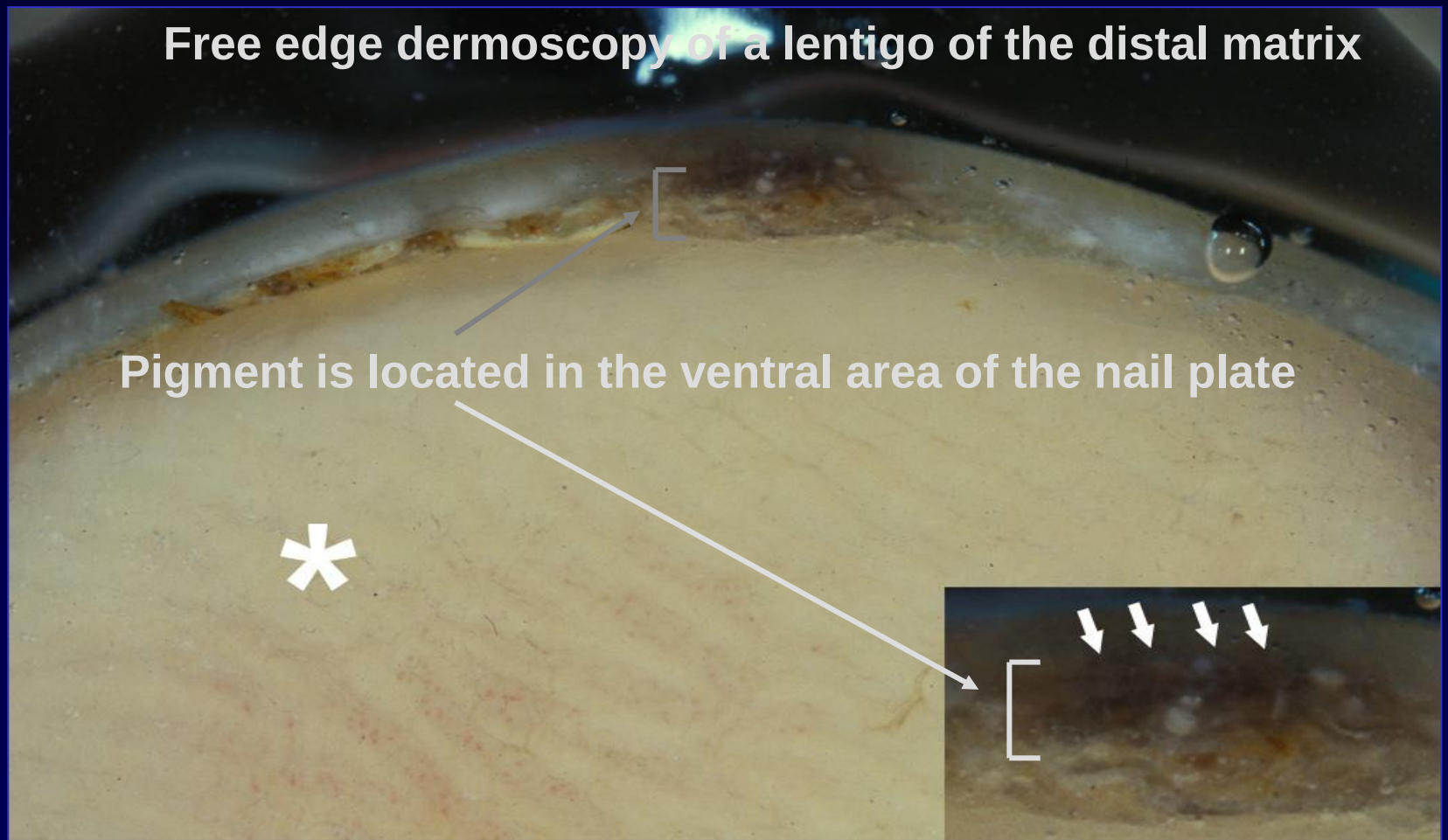




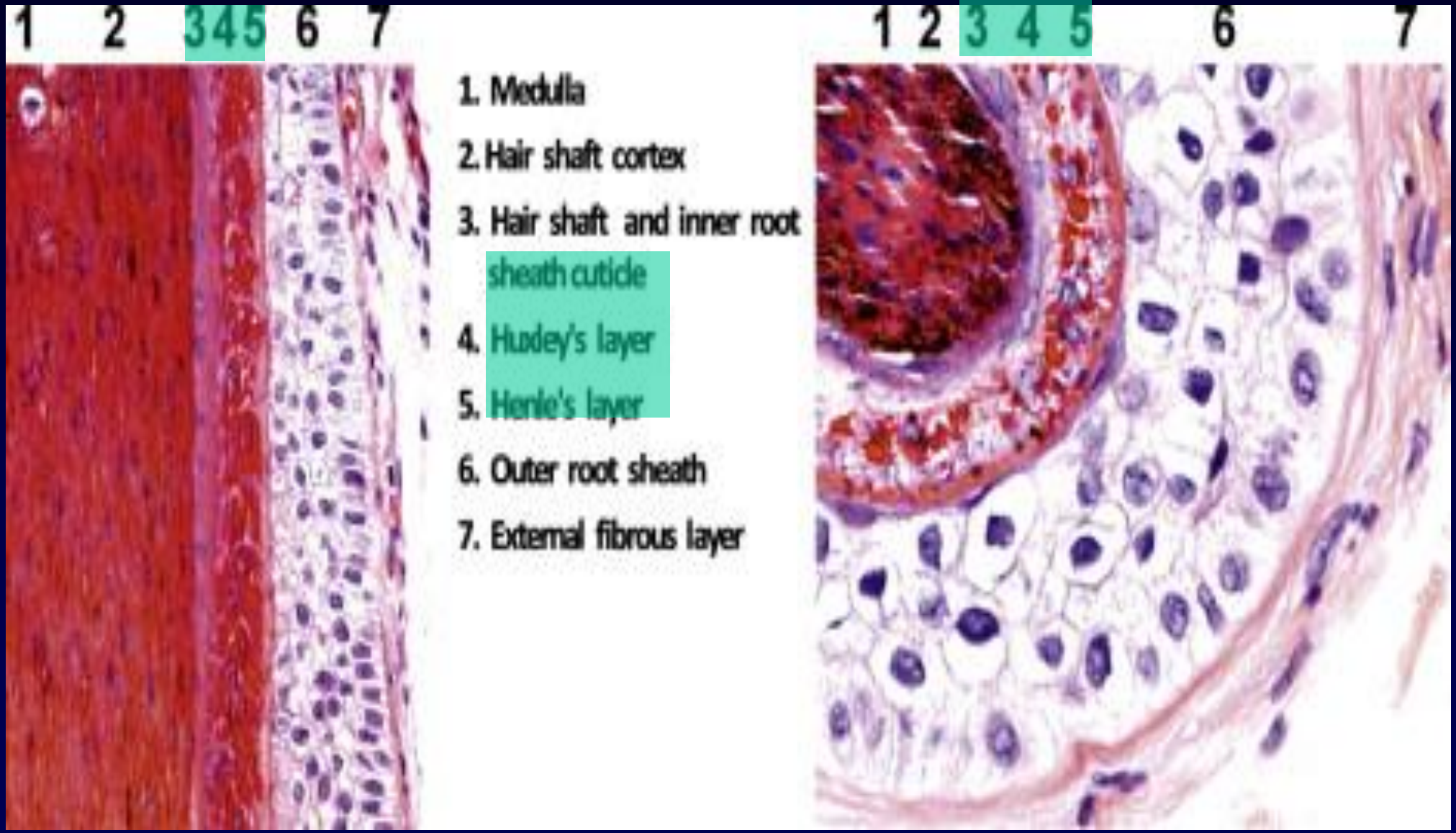
The location of the pigment (observed at the free edge) can predict the location of the causative pigmentary lesion
Up : proximal matrix / Down : distal matrix

Nail dermoscopy

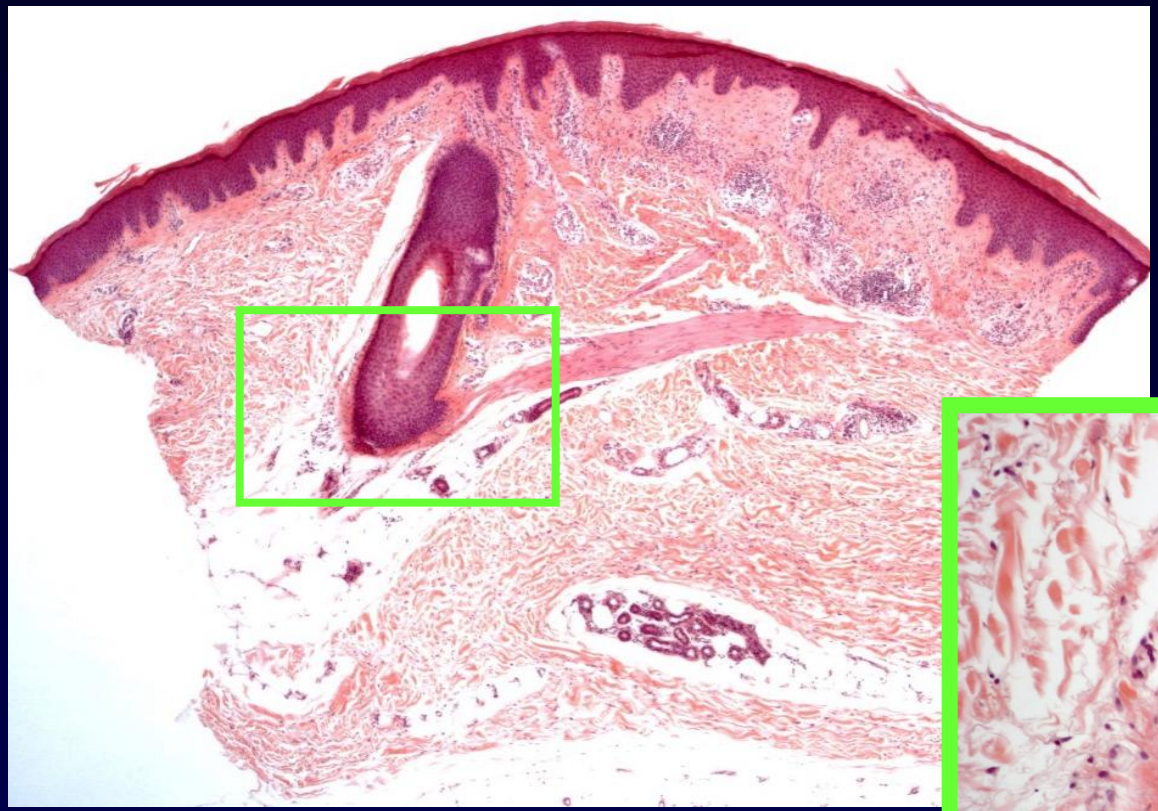
- Free-edge dermoscopy

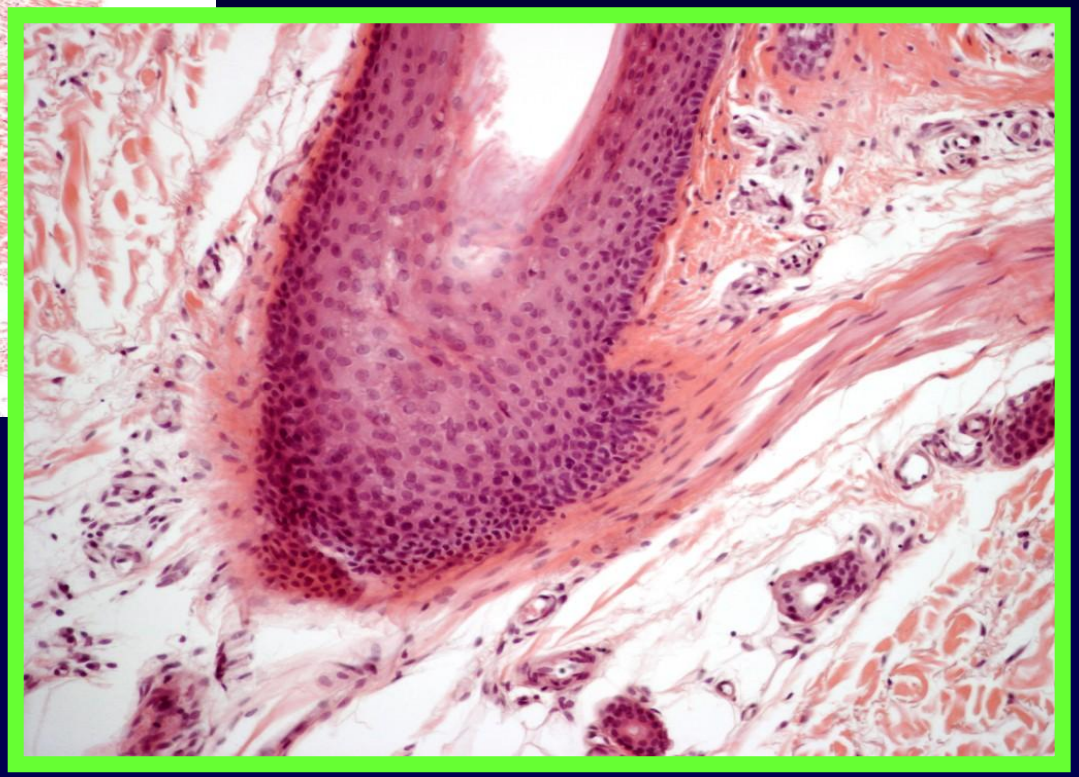


Hair follicles

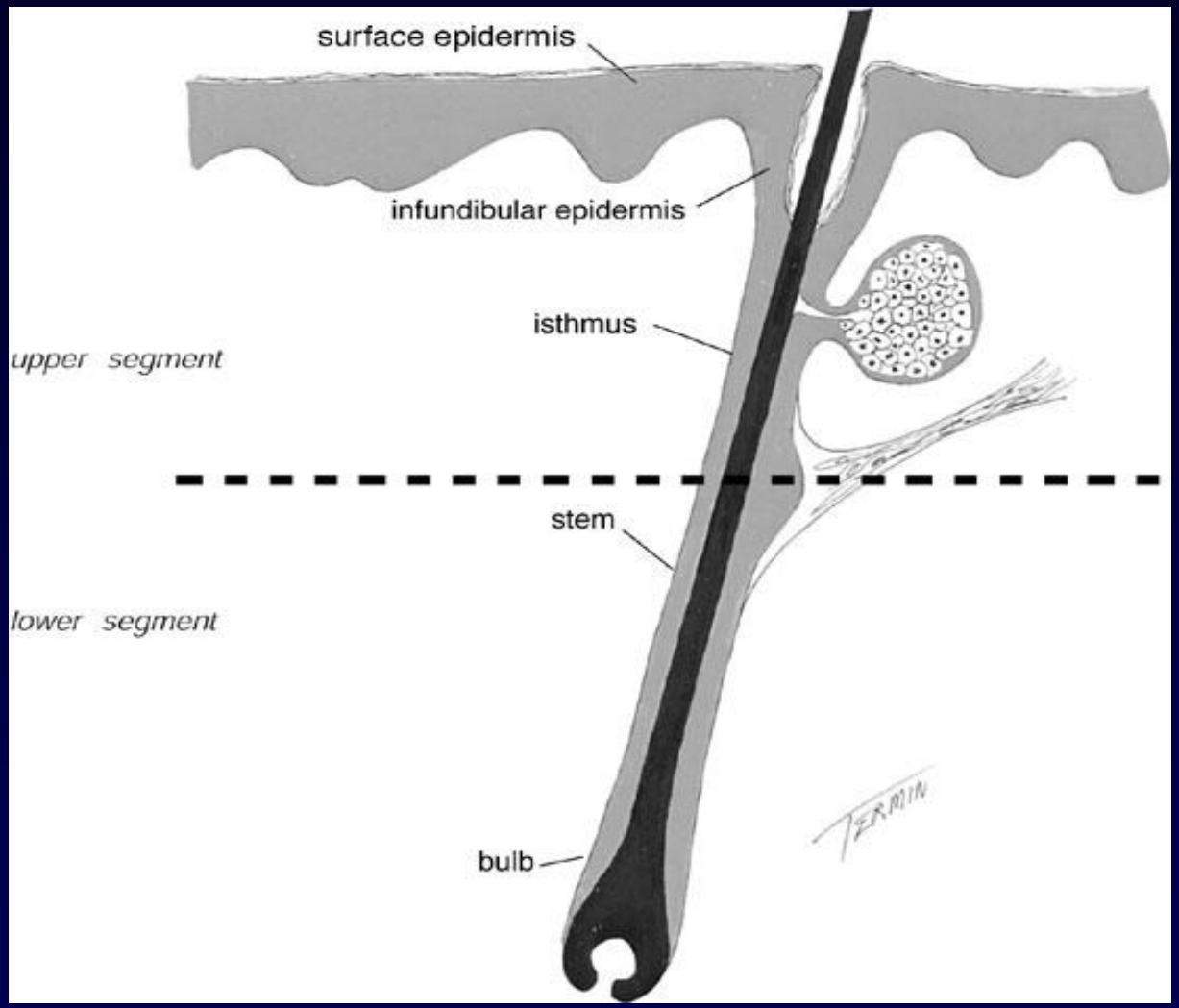

1 2 3 4 5 6 7
1. Medulla
2. Hair shaft cortex
3. Hair shaft and inner root sheath cuticle
4. Huxley's layer
5. Henle's layer
6. Outer root sheath
7. External fibrous layer
1 2 3 4 5 6 7

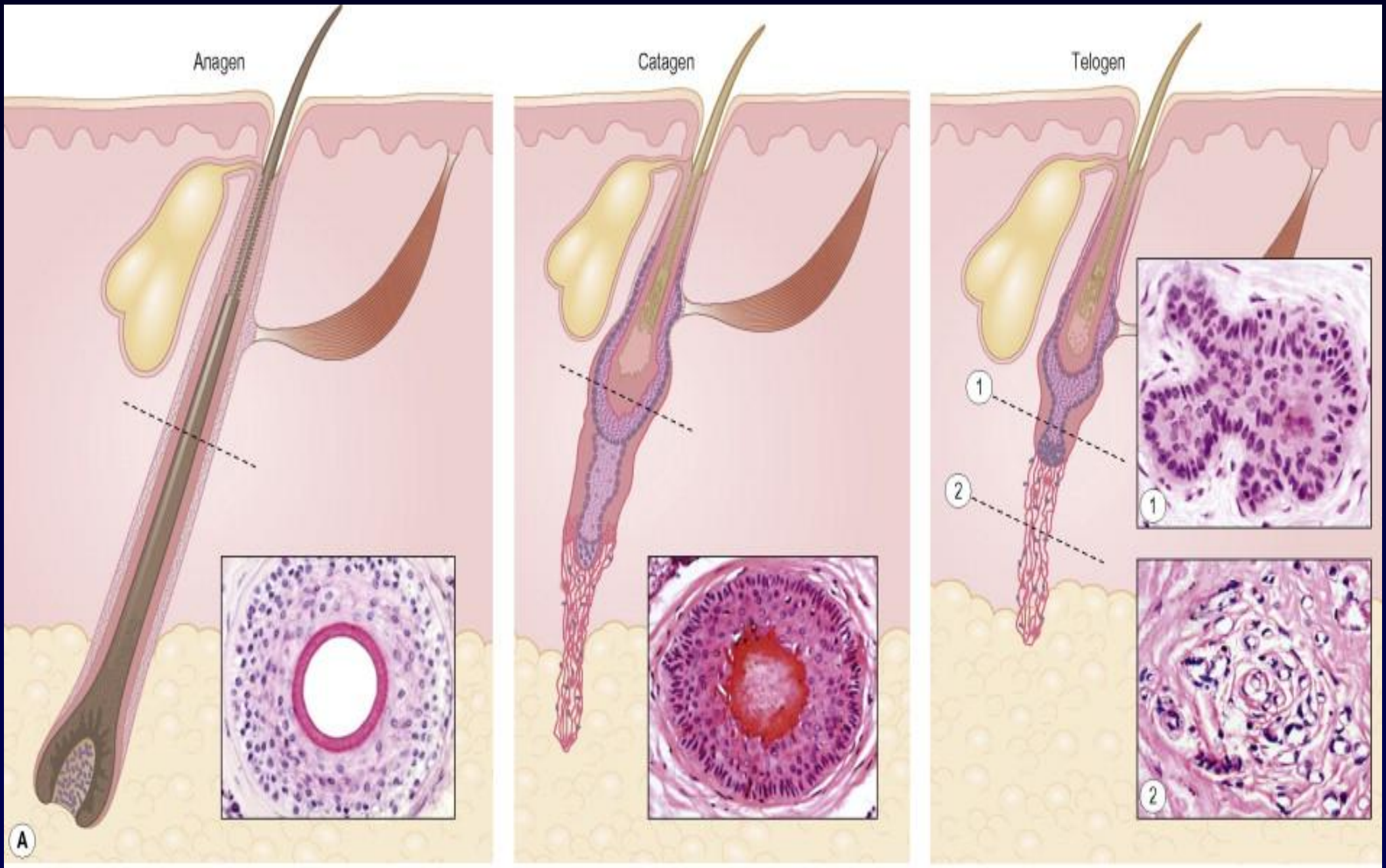
BULGE

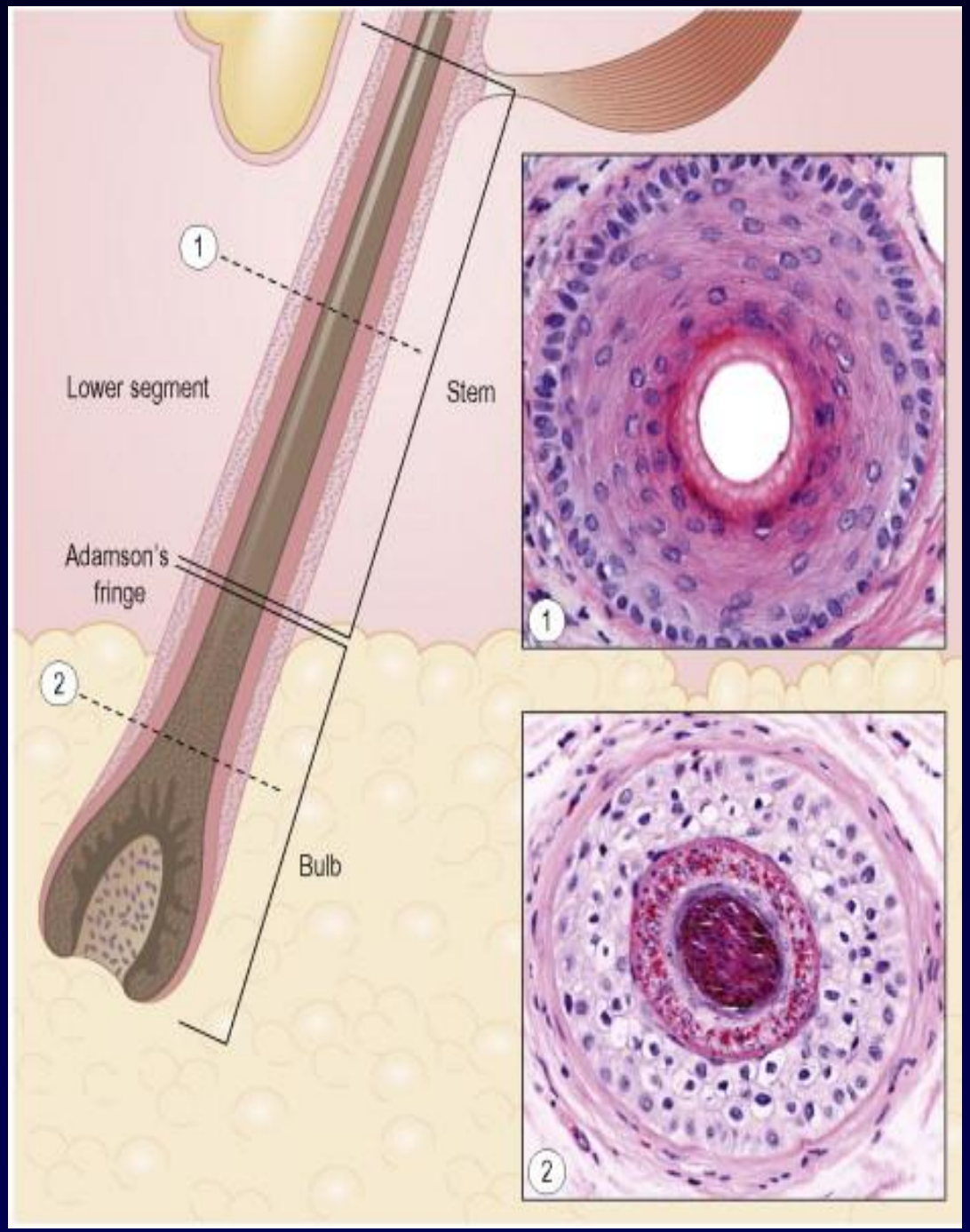


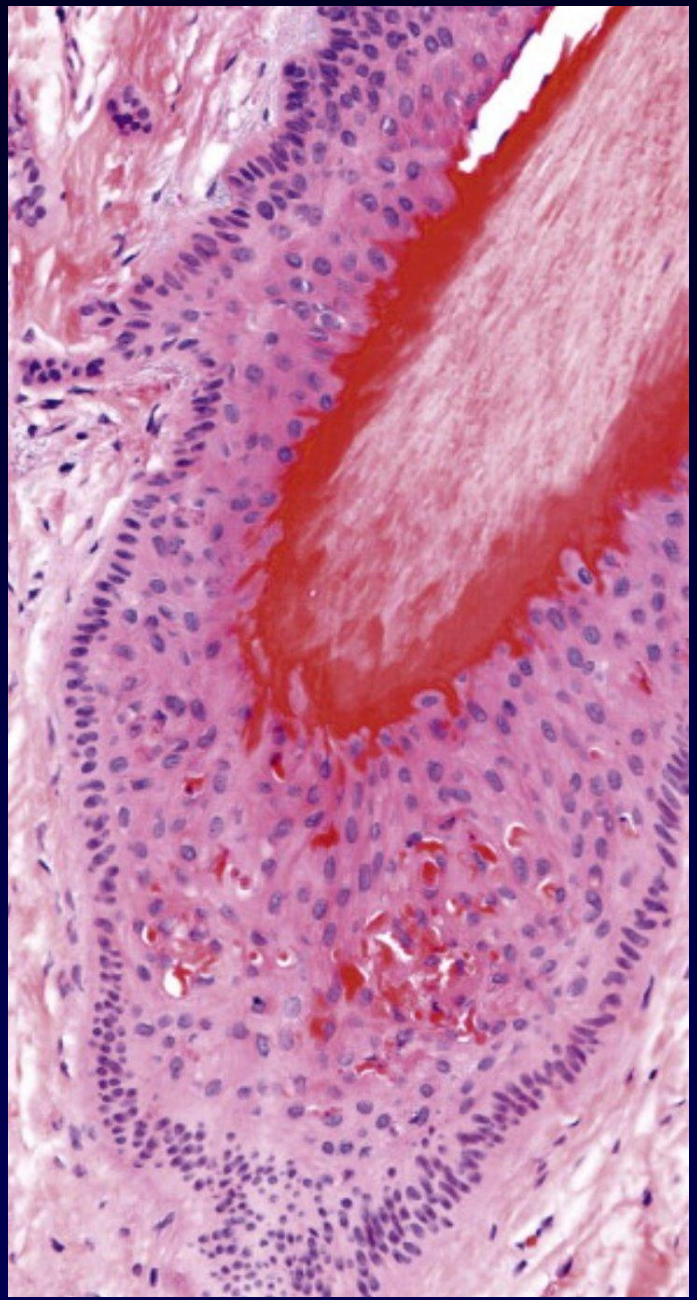


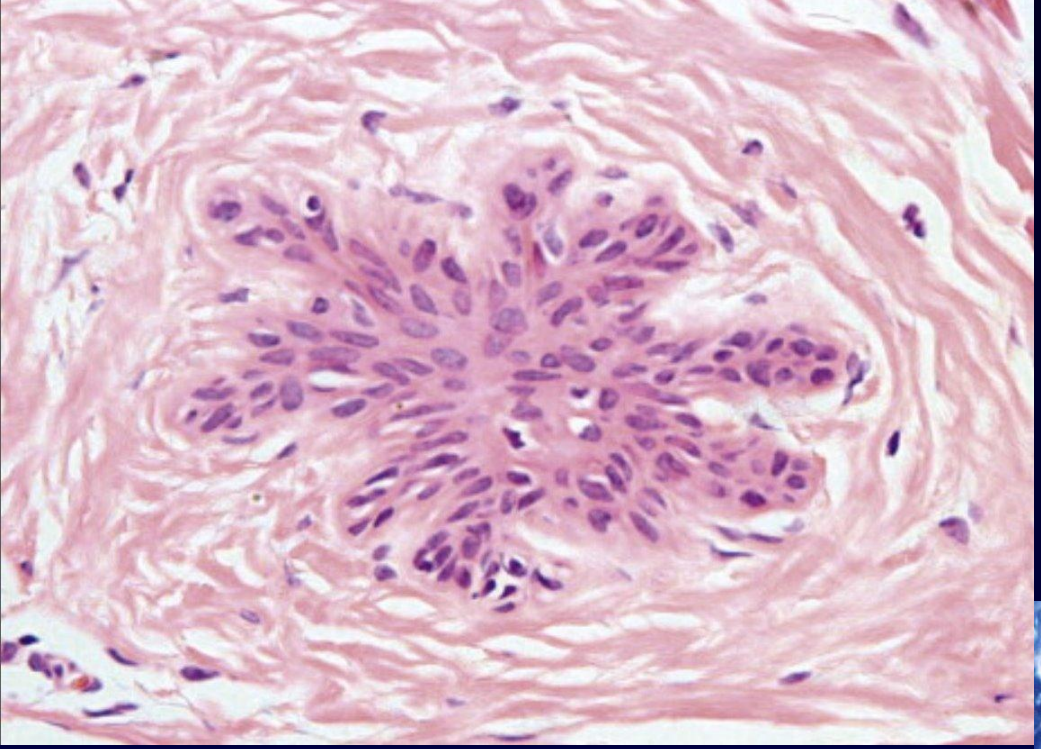
HAIR FOLLICLE

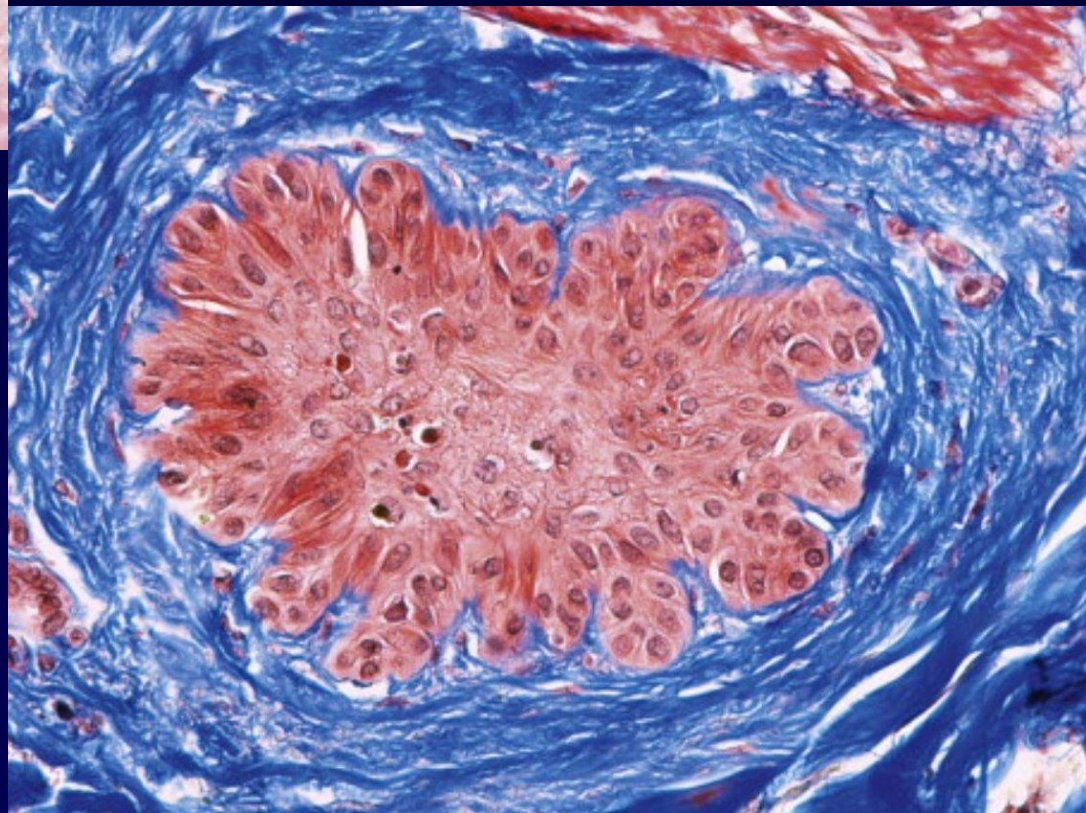



Anagen
Catagen
Telogen
1
2
1
2
A

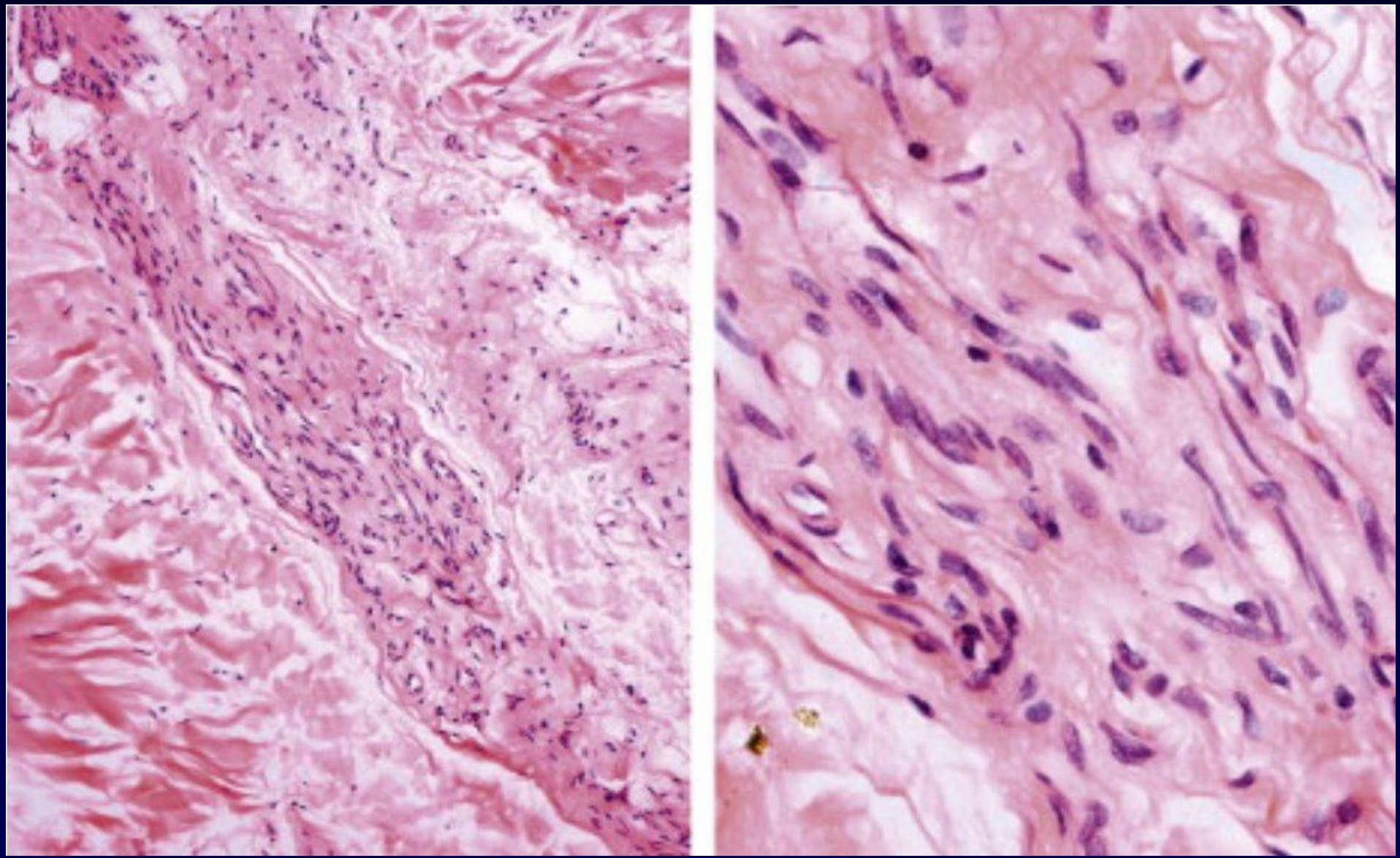

1
Lower segment
Stem
Adamson's fringe
2
Bulb
1
2



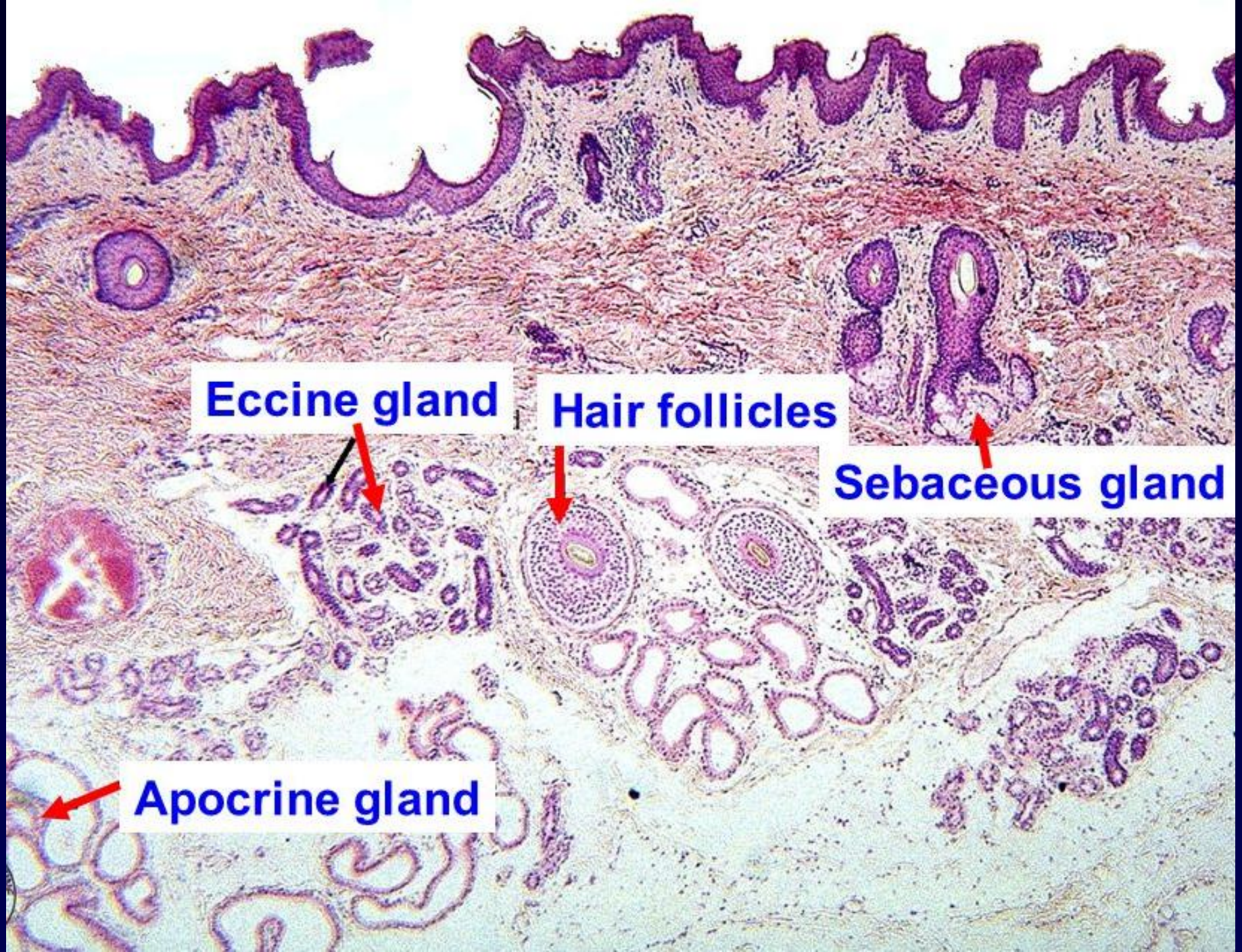




Stelae (streamers)

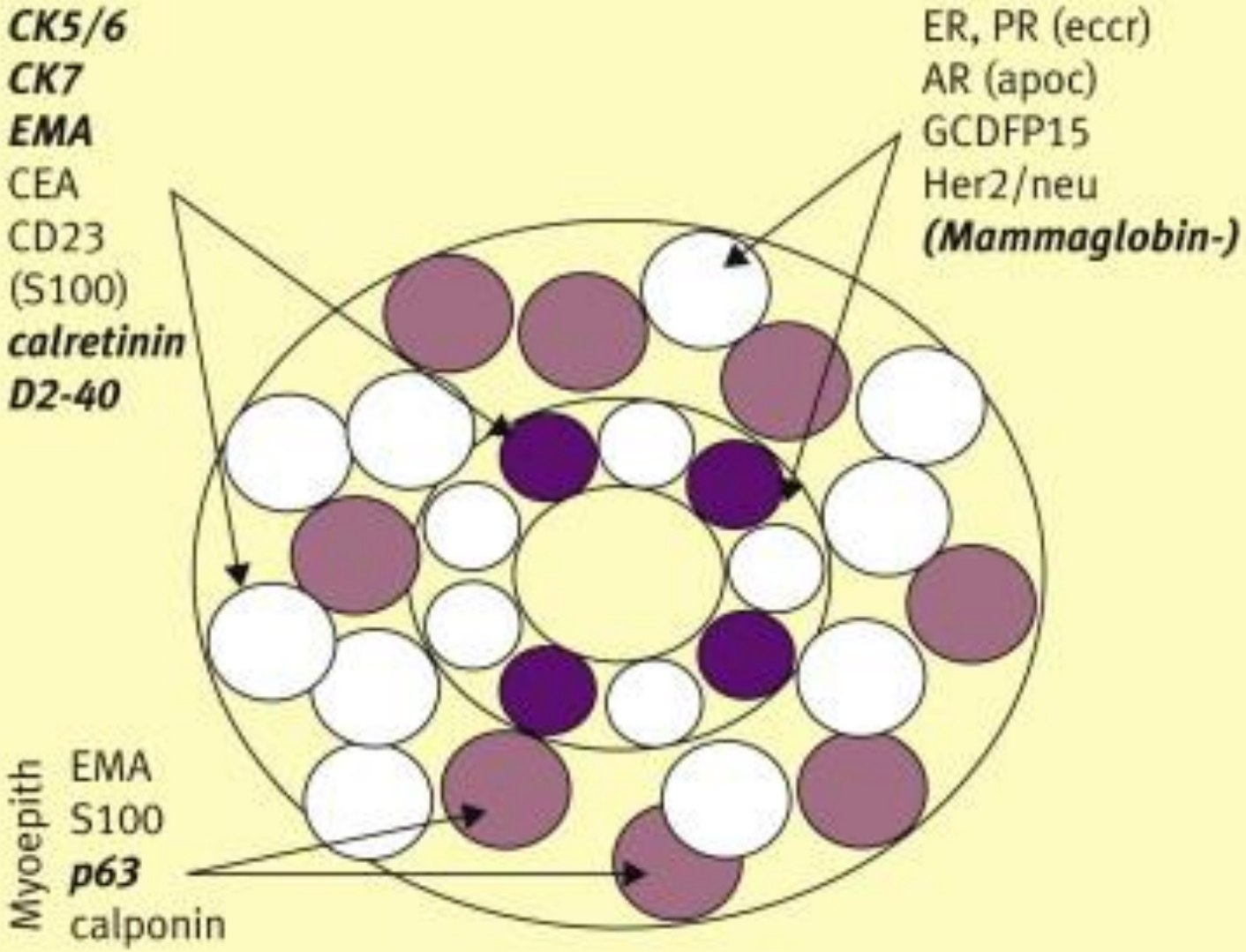


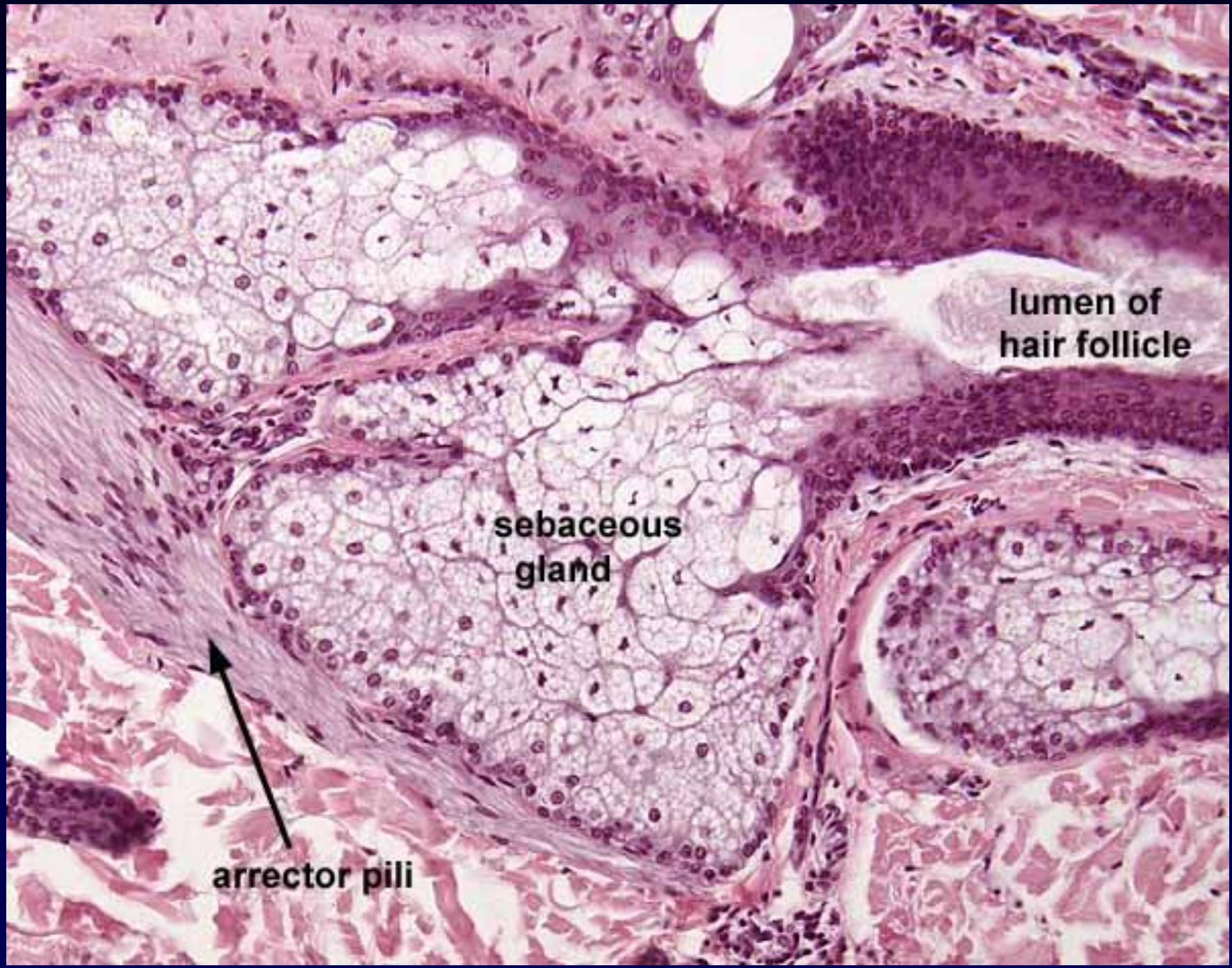
Sweat/sebaceous glands


Eccine gland
Hair follicles
Sebaceous gland
Apocrine gland


excretory duct
secretory tubulus

Immunohistochemical profile of cutaneous glands




lumen of
hair follicle
sebaceous
gland
arrector pili

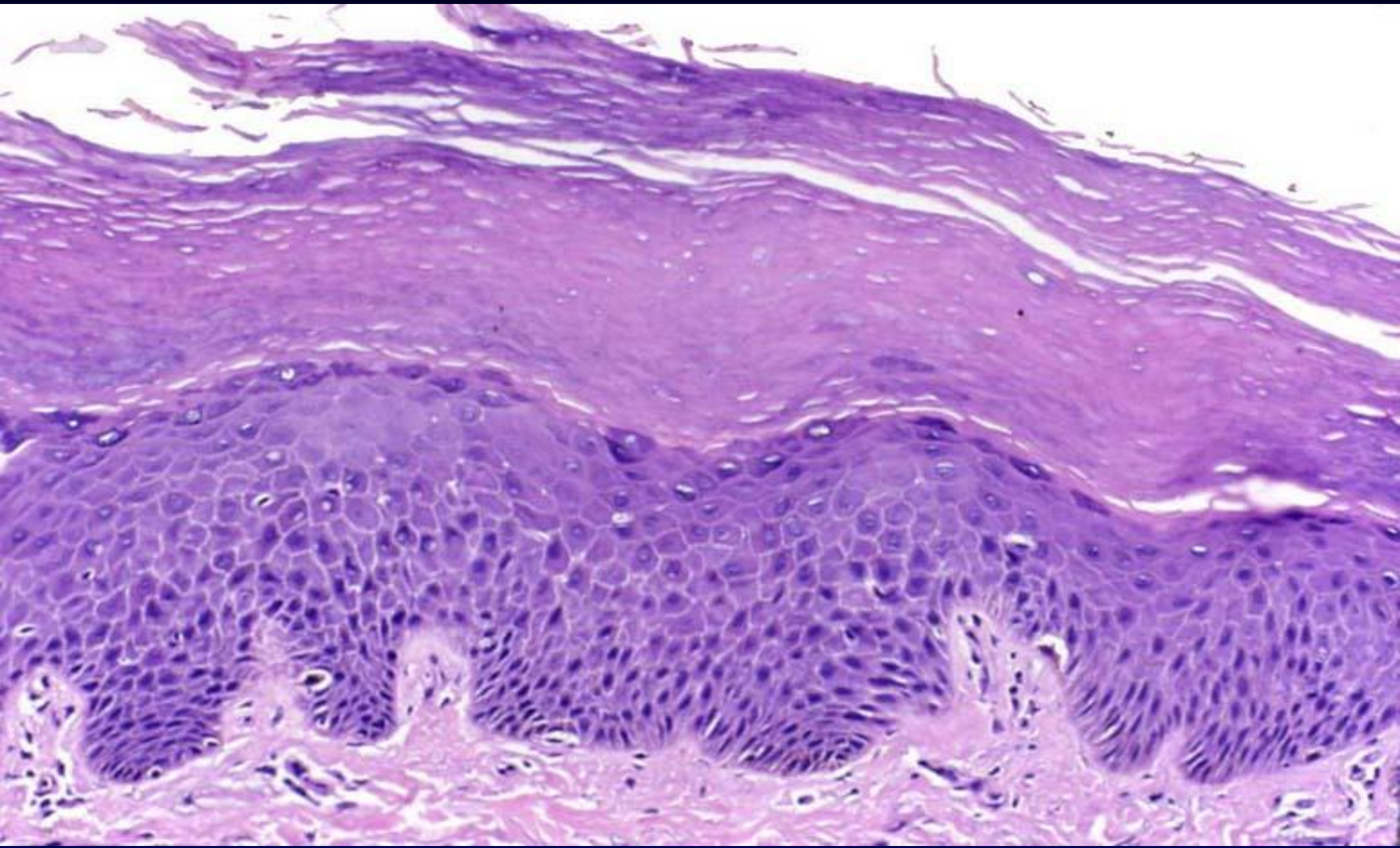

sebum
basal
cells

Anatomical variations of the skin

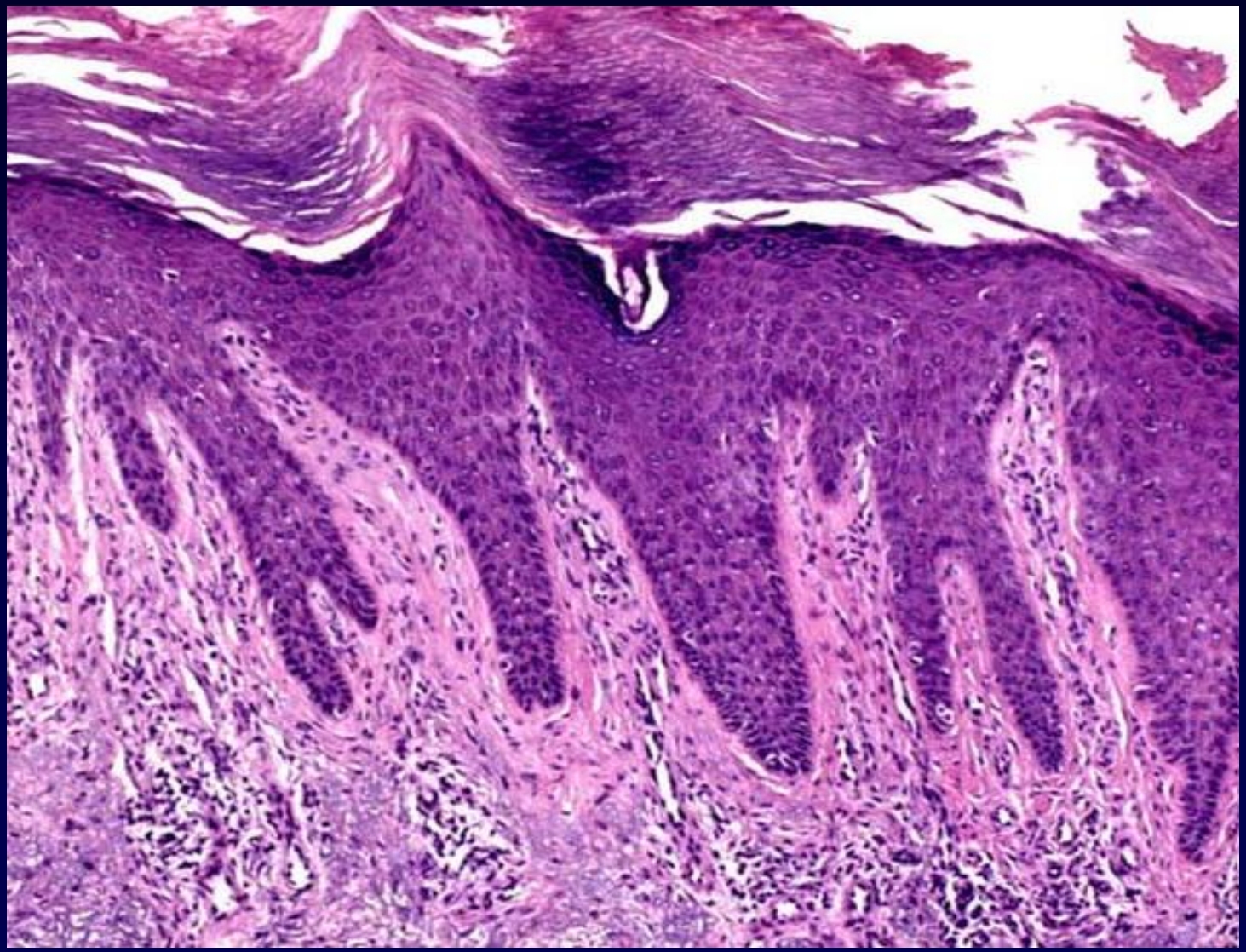
- The skin is remarkably diversified regionally, grossly and microscopically
- These variations correlate with the different functions of the skin

Table 1–2. REGIONAL DIFFERENCES IN HUMAN SKIN AND RELATED DIAGNOSTIC PITFALLS

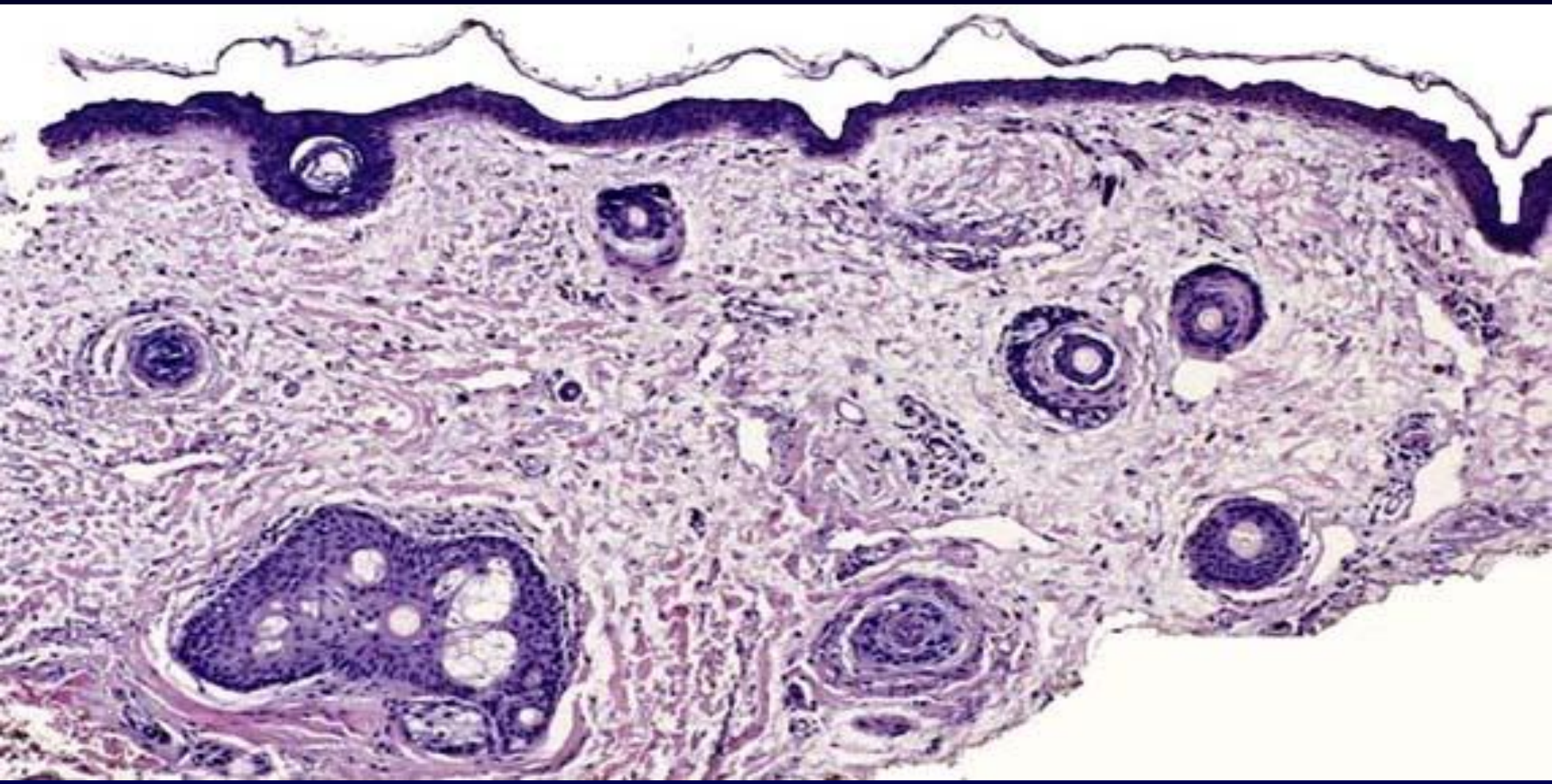
SITE OR TYPE OF SKIN	EPIDERMAL AND ADNEXAL PATTERN	POTENTIAL ERROR
Acral skin	Thick, compacted stratum corneum; thick stratum granulosum; elongated rete	Lichen simplex chronicus
Paramucosa and mucosa	Diminished, compacted, or absent stratum corneum; diminished or absent stratum granulosum; pale, glycogenated cytoplasm	Ichthyosis, psoriasis, pale cell acanthoma
Eyelid	Thin epidermis; basaloid buds and small, rudimentary hairs	Atrophy, basal cell carcinoma
Nose	Numerous, well-developed sebaceous glands	Sebaceous hyperplasia
Axilla	Admixed pilosebaceous units and apocrine glands	Nevus sebaceus



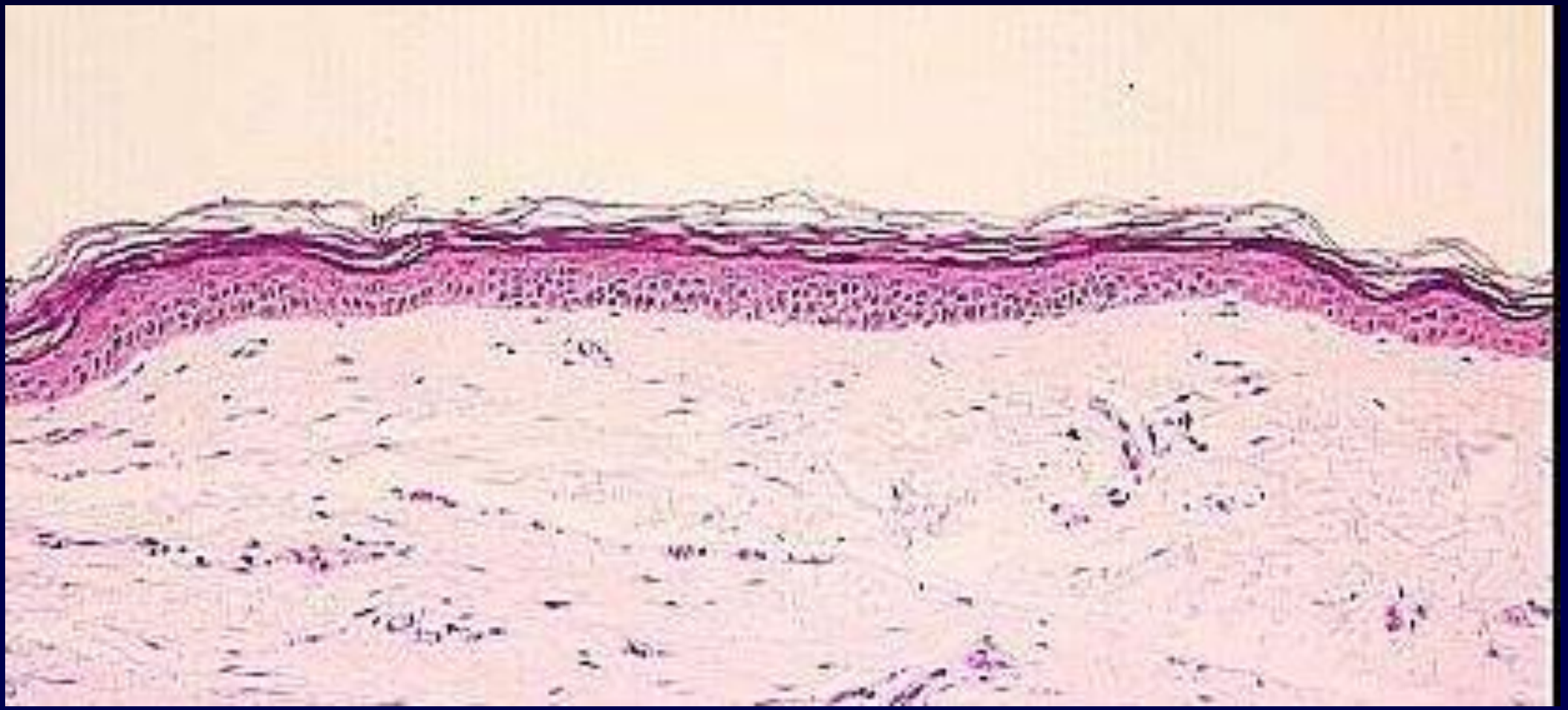
Lichen simplex chronicus



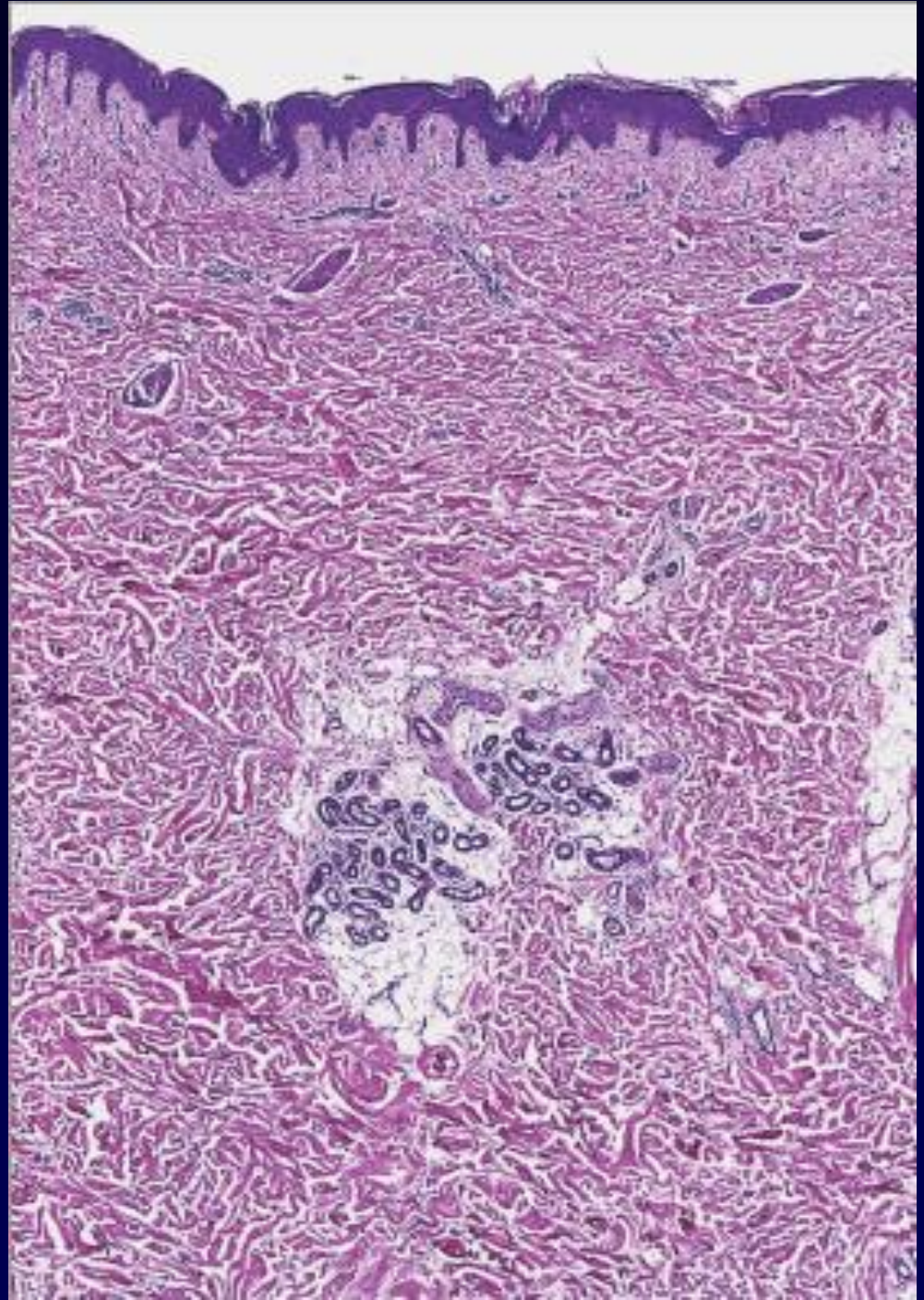
The eyelid



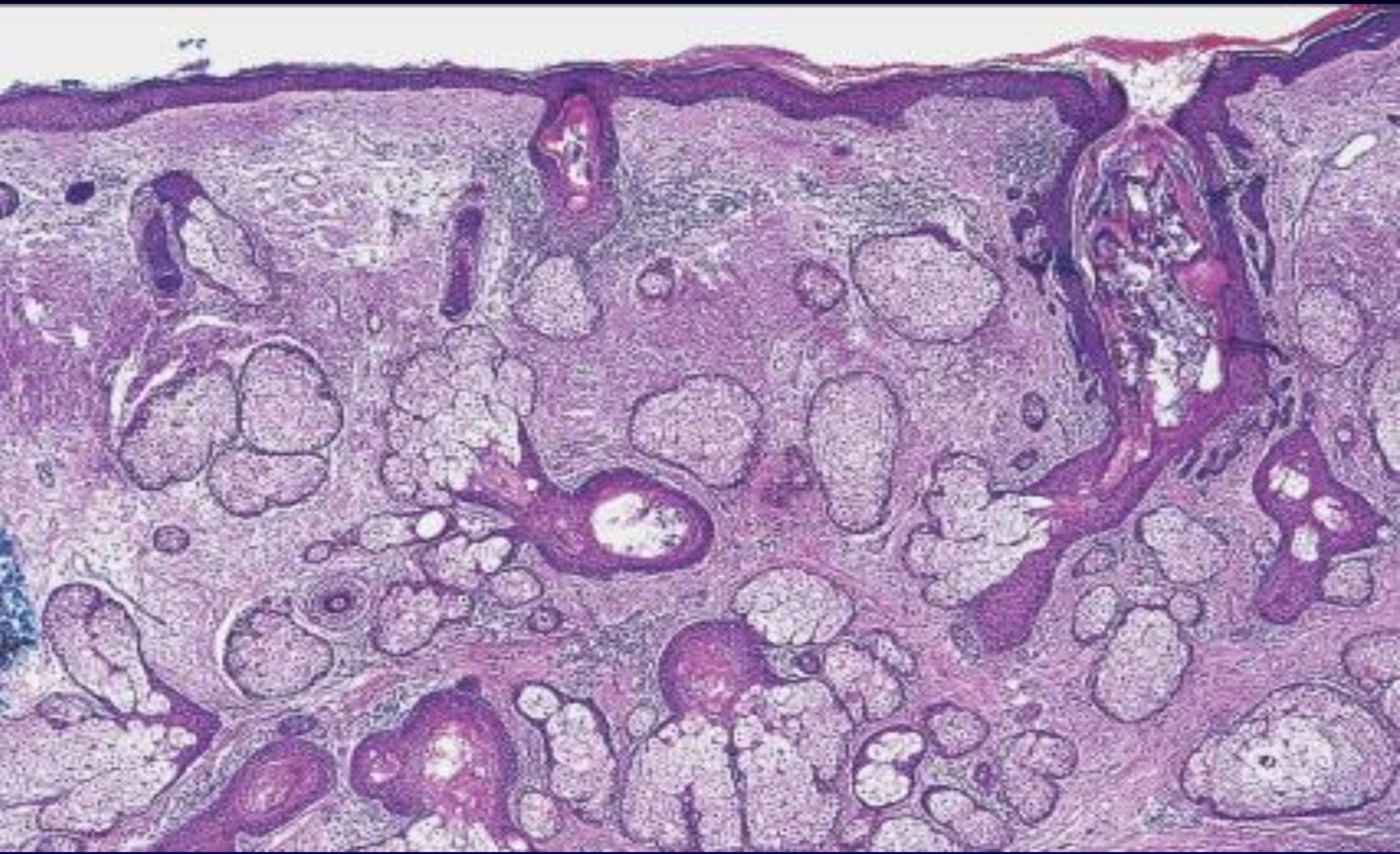
Skin atrophy



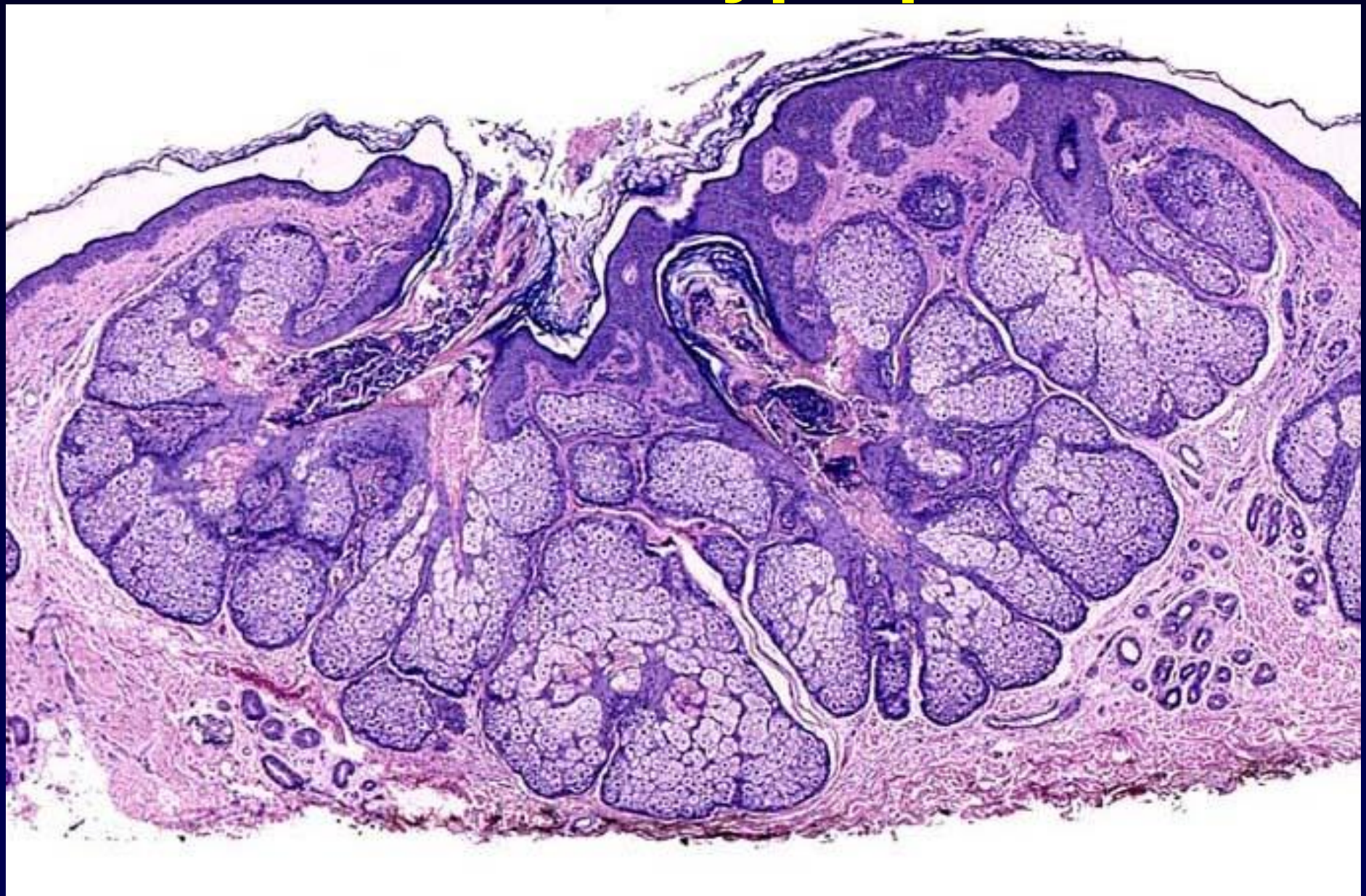
The back



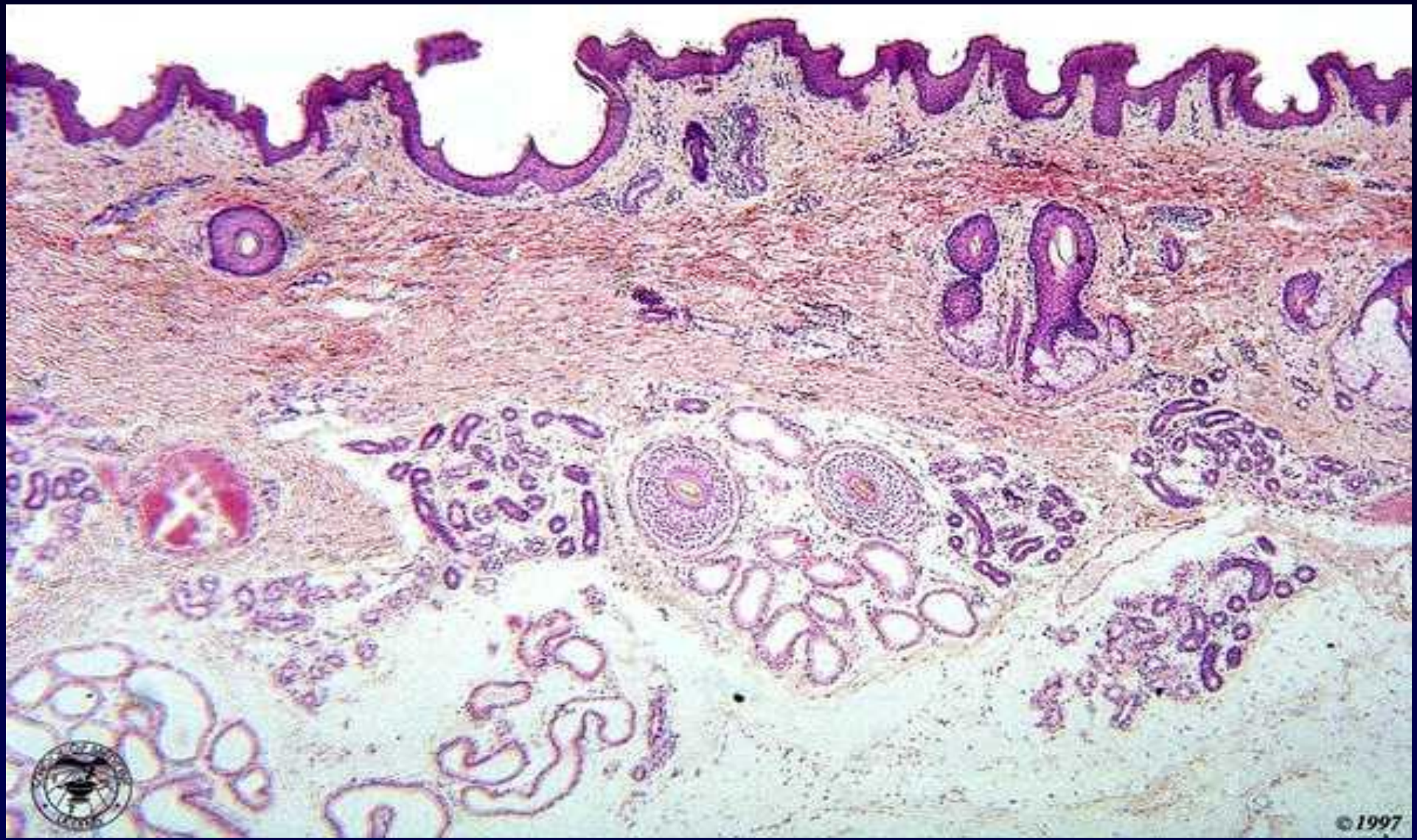
The nose



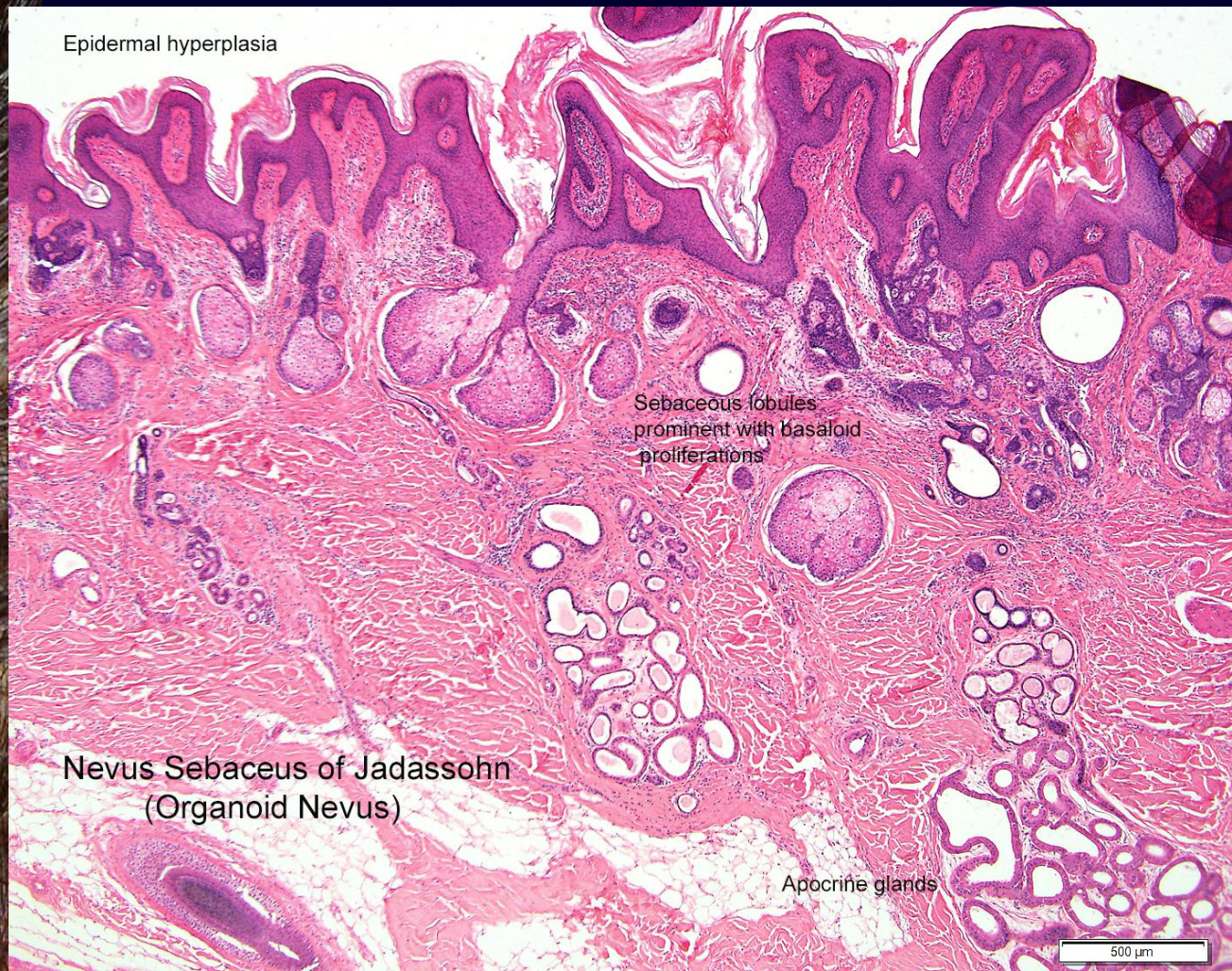
Sebaceous hyperplasia



The axilla


© 1997

Nevus sebaceous



Part 2

The travel begins

ORIGINAL ARTICLE

Volume 23 October - December 2007 (Part-I) Number 5

Abstract
PDF of this Article

Clinician's Responsibility in Pre-Analytical Quality Assurance of Histopathology

Muhammad Ashraf Sharif[1], Sajid Mushtaq[2], Nadira Mamoon[3], Shahid Jamal[4], Muhammad Luqman[5]

ABSTRACT

Objective: To ascertain the adequacy of information provided by clinicians when requesting a histopathology investigation and to study the quality control parameters of the specimen containers.

Methodology: This is an observational descriptive study which was carried out at Armed Forces Institute of Pathology in December 2006 on 500 specimen requests for histopathology.

Results: Out of 500 specimens, age was not mentioned in 29 (5.8%) cases. No clinical history or differential diagnosis was given in 170 (34%) cases. Site of biopsy was absent in 65 (13%) cases and the name of requesting clinician or any contact information was present in only 115 (23%) of request forms. One hundred forty three (28.7%) containers were inadequate relative to the size of the specimen. Adequate volume of fixative was absent in 176 (38.2%) samples. There were 22 (4.3%) samples which did not have any sort of label mentioning either patient's name or type of specimen. Injection bottles constituted the highest number of containers (n=204; 40.8%) used to submit the histopathology specimen.

Conclusion: Clinicians of all grades and specialties must be educated and made aware of their primary responsibility to request the service appropriately for the benefit of the patient and patient care.

KEY WORDS: Quality control, Histopathology, Specimen.

Pak J Med Sci October - December 2007 (Part-I) Vol. 23 No. 5 720-723

Optimal sample-fixative volume ratio: 1:10

WHAT DOES THE PATHOLOGIST NEED TO KNOW?

- Patient age, sex, and site of lesion
- pertinent medical history
  - Pregnant?
  - Autoimmune disorder?
  - Diabetic?
  - Pertinent family history?
  - HIV infection?
  - Transplant patient?
  - Other?

WHAT DOES THE PATHOLOGIST NEED TO KNOW? (CONT.)

- Distribution of lesion/lesions
  - solitary or multiple
  - regional distribution, symmetric?
- Description of lesion/lesions
- Your opinion ("lesion" is not an opinion)
  - Neoplastic?
  - Inflammatory?
  - Pigmented lesion?
  - Other more specific opinions


LyP
PLEVA

Differential diagnosis PL-LyP

Pityriasis lichenoides	Lymphomatoid papulosis
• Young pts.	• Young/middle-aged pts.
• Duration: months (prolonged smallpox) to years (chronic)	• Duration: years (smallpox not in ddx) with a fluctuating behaviour
• Large number, small size; no evolution into nodules	• Small number, large size, also nodular
• Parakeratosis/lichenoid/ erythrocytes/V shape/apoptosis	• PLEVA criteria possible but not definitional
• Rare CD30+ cells (?)	• CD30+ definitional

Your clinical opinion should guide the type of biopsy

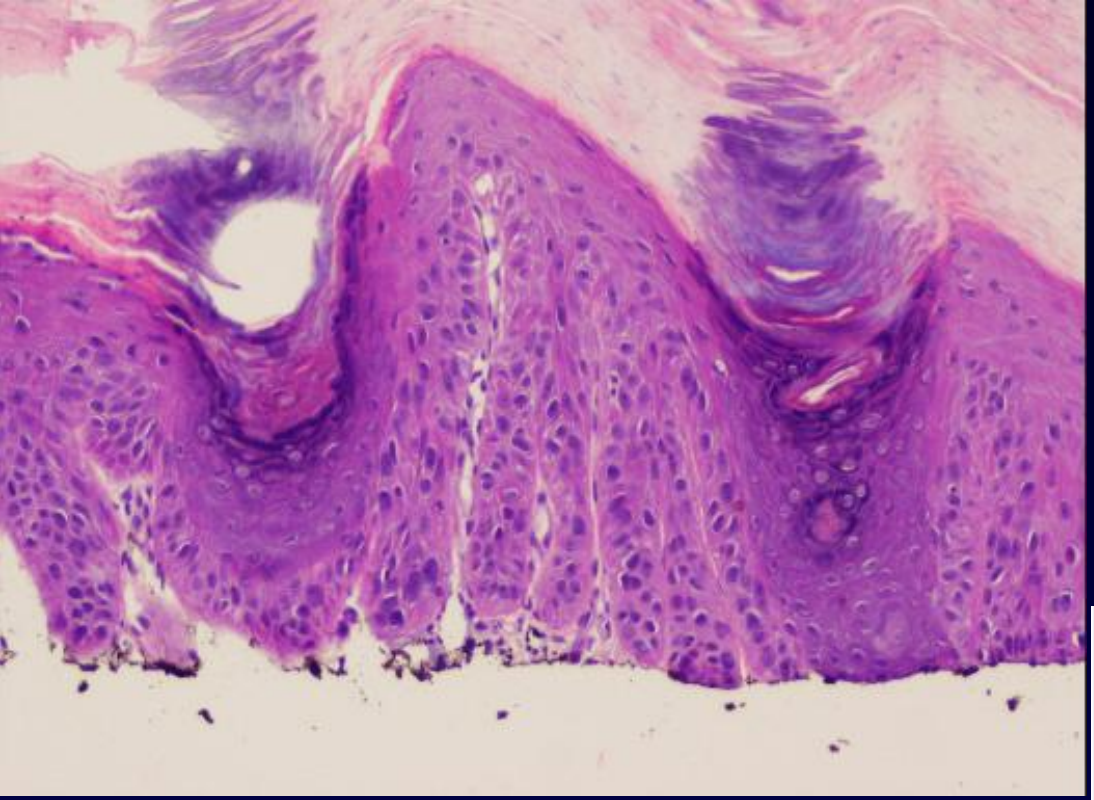
- Biopsy types:
  - excision
  - shave biopsy/curetting
  - incisional biopsy
  - Punch biopsy
- Don’t do the biopsy if you have no working diagnosis
  - Follow-up

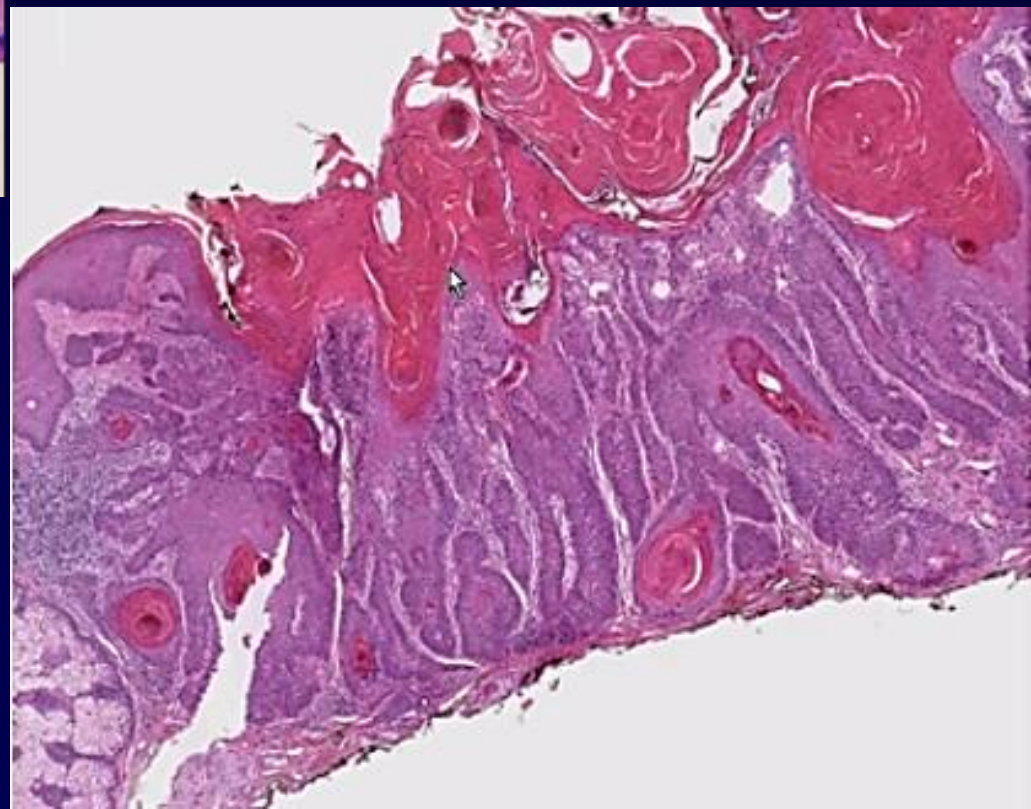
EXCISIONAL BIOPSY:

- Used to completely remove a lesion so that margins can be evaluated
- Recommended for: ALL TUMORS

SHAVE BIOPSY/CURETTING:

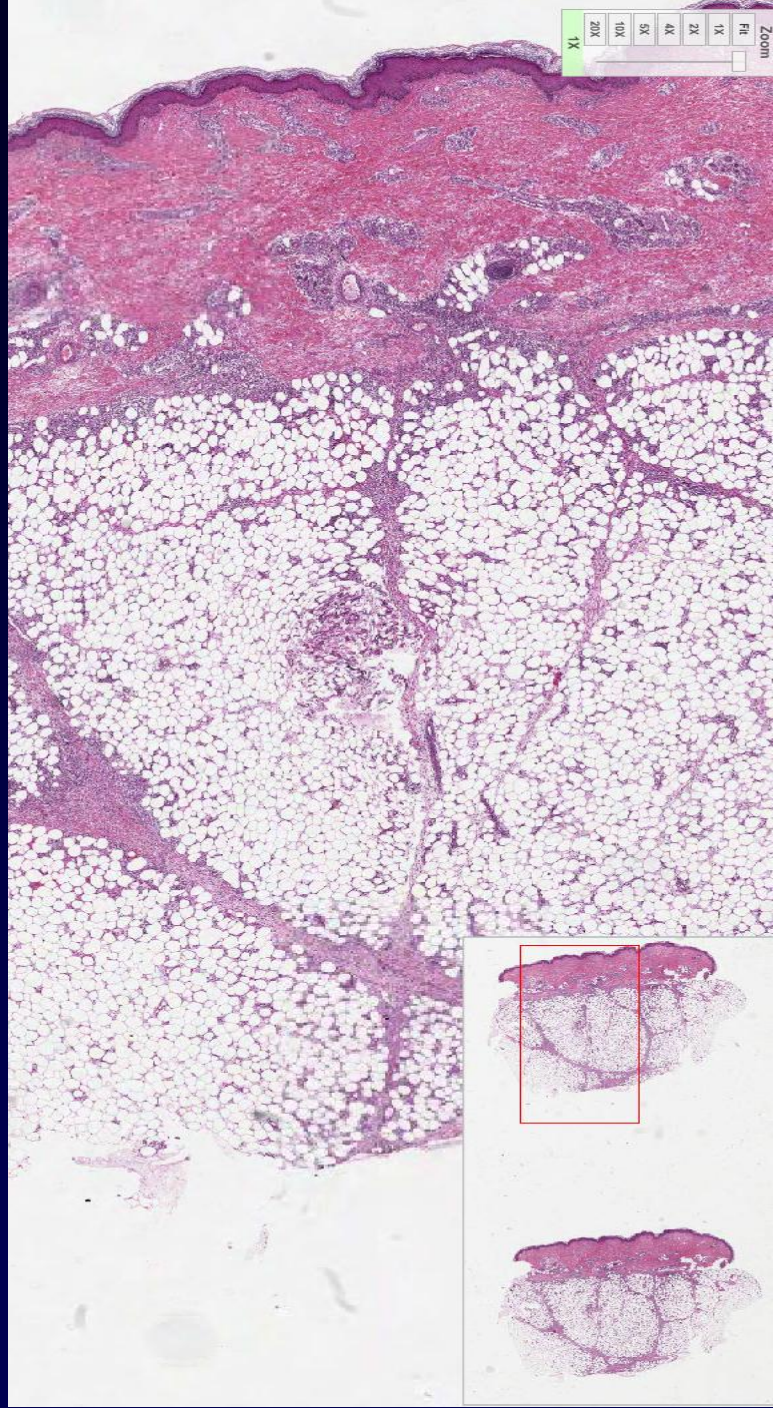
- Useful for lesions resting upon the epidermis : seborrheic keratosis, benign nevi, verruca
- Used also for actinic keratosis and squamous cell carcinoma, but sometimes the biopsy may be too superficial to adequately assess invasion
- Not recommended for: melanoma





INCISIONAL BIOPSY

- Larger scalpel biopsy to include substantial subcutaneous tissue
- Useful for evaluation of panniculitis


Zoom
Fit
1X
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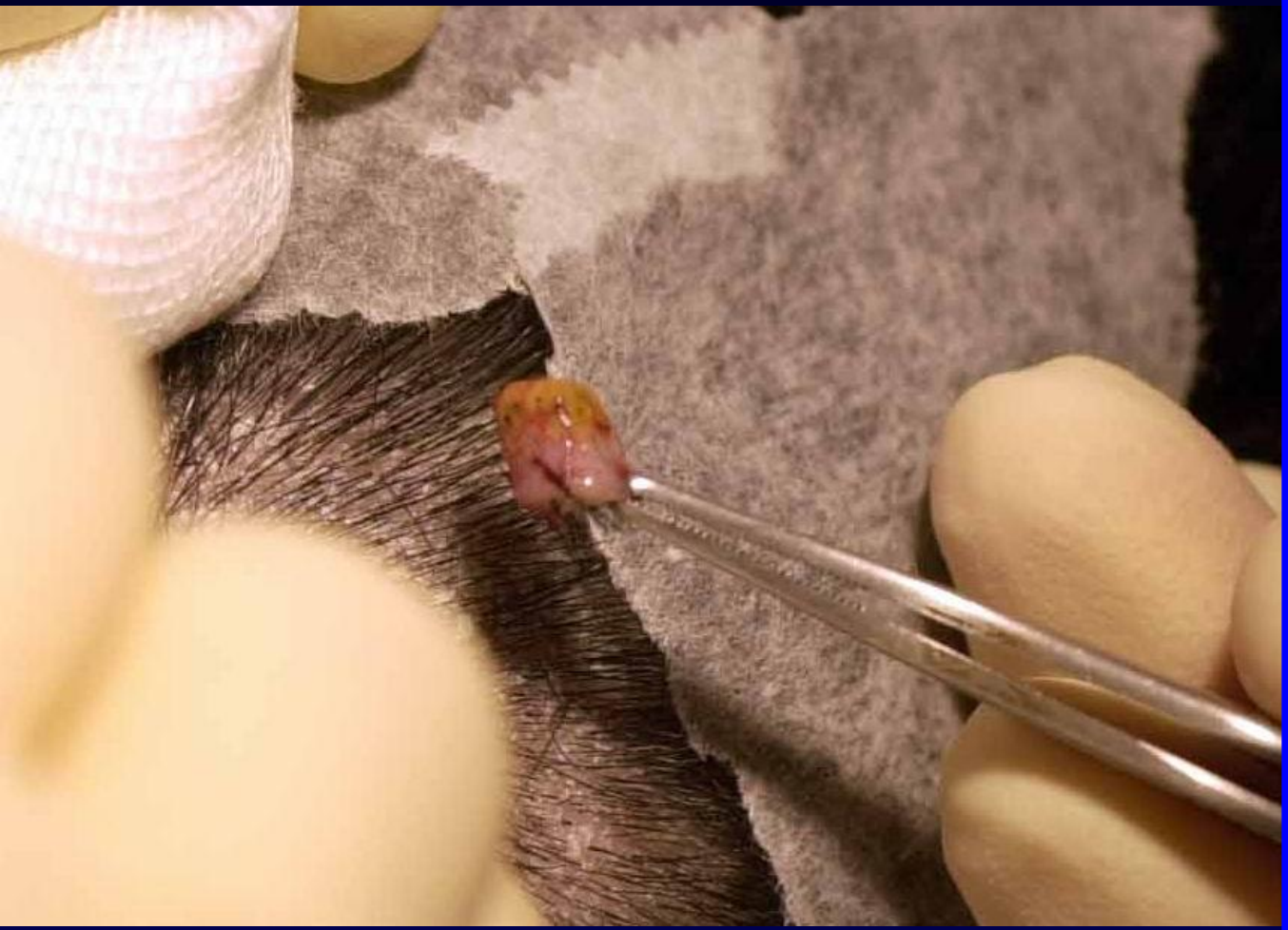
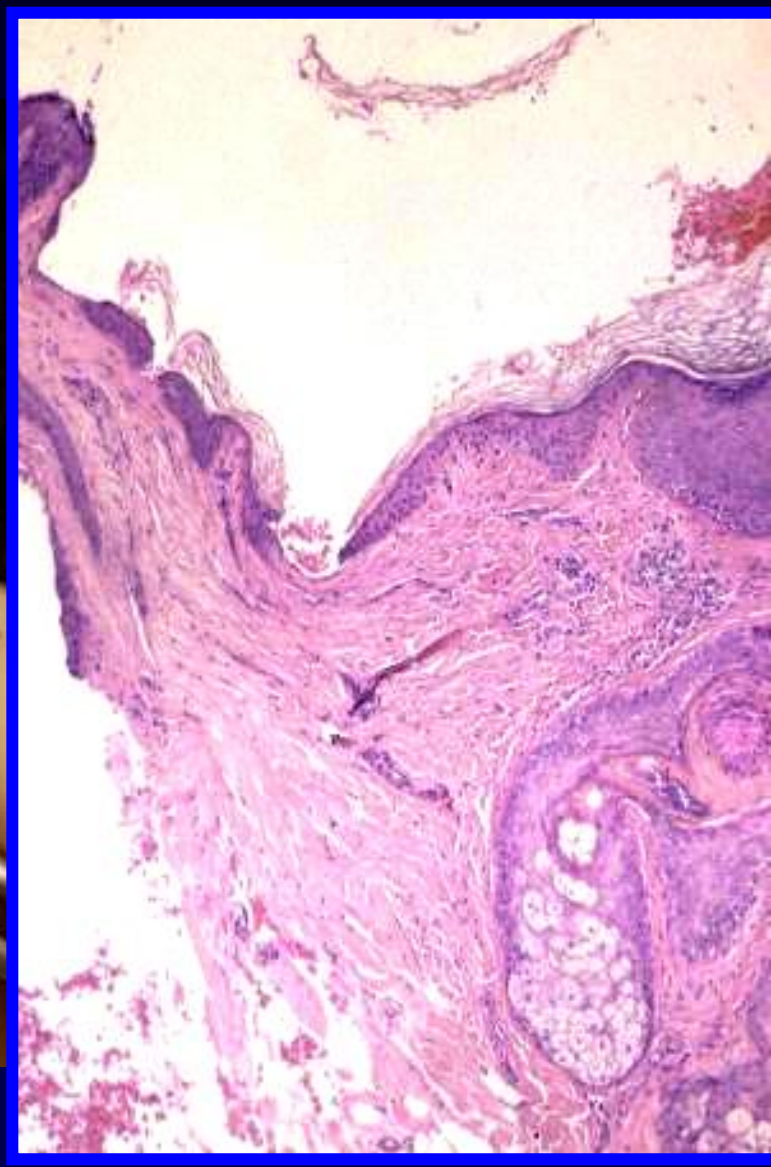
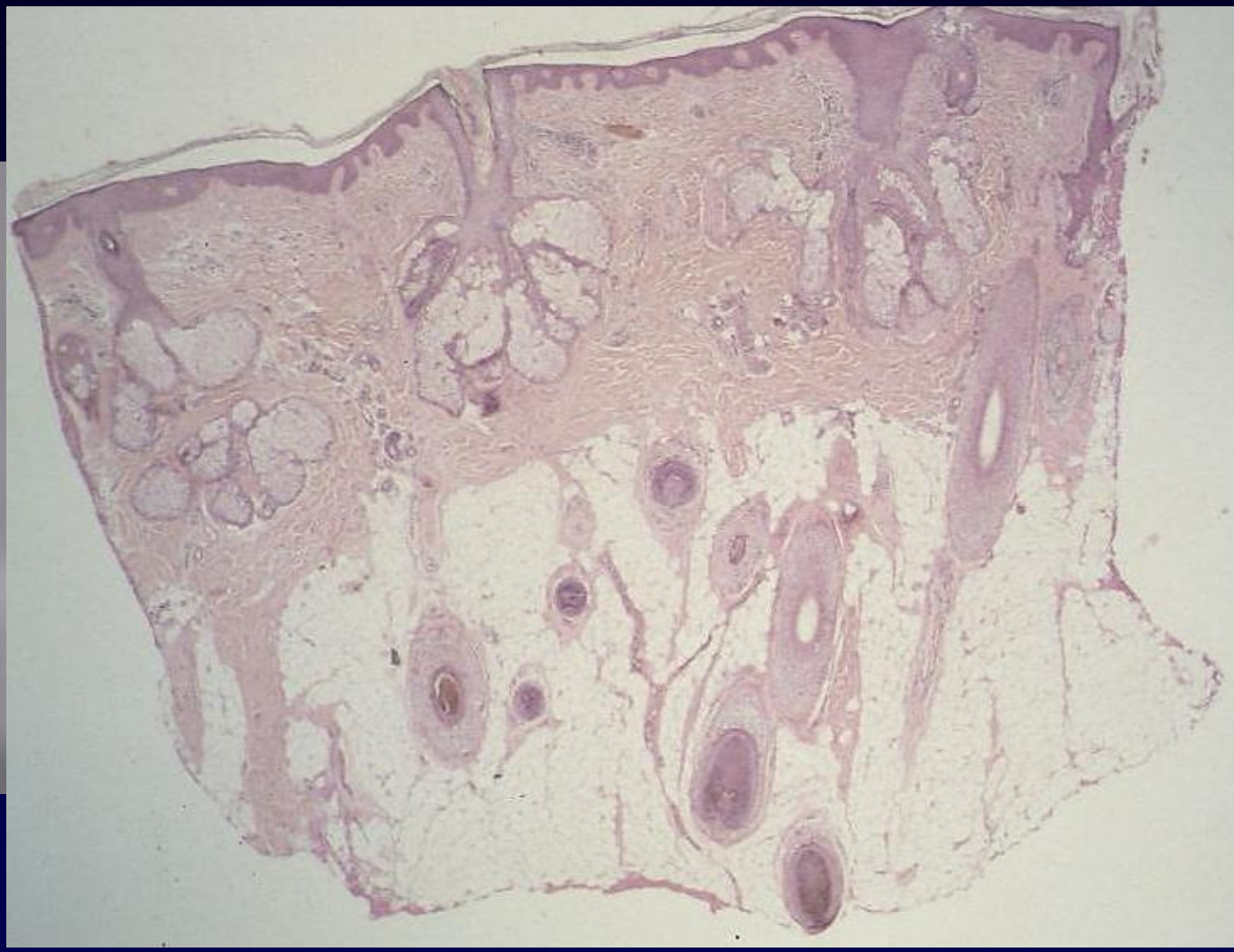
10X
20X

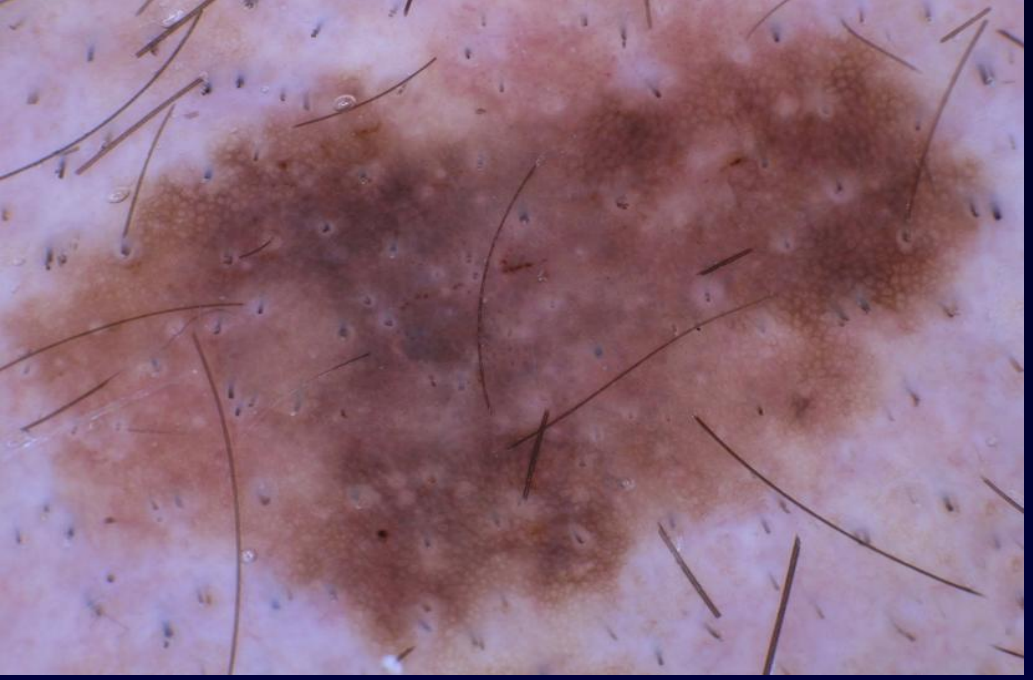
PUNCH BIOPSY:

- Useful for MOST inflammatory dermatoses (includes the superficial and deep plexuses and superficial subcutaneous tissue)
- Useful for deeper benign dermal lesions or tumors not adequately evaluated with a shave biopsy
- Useful for recurrent tumors and metastatic lesions
- Often insufficient for subcutaneous lesions

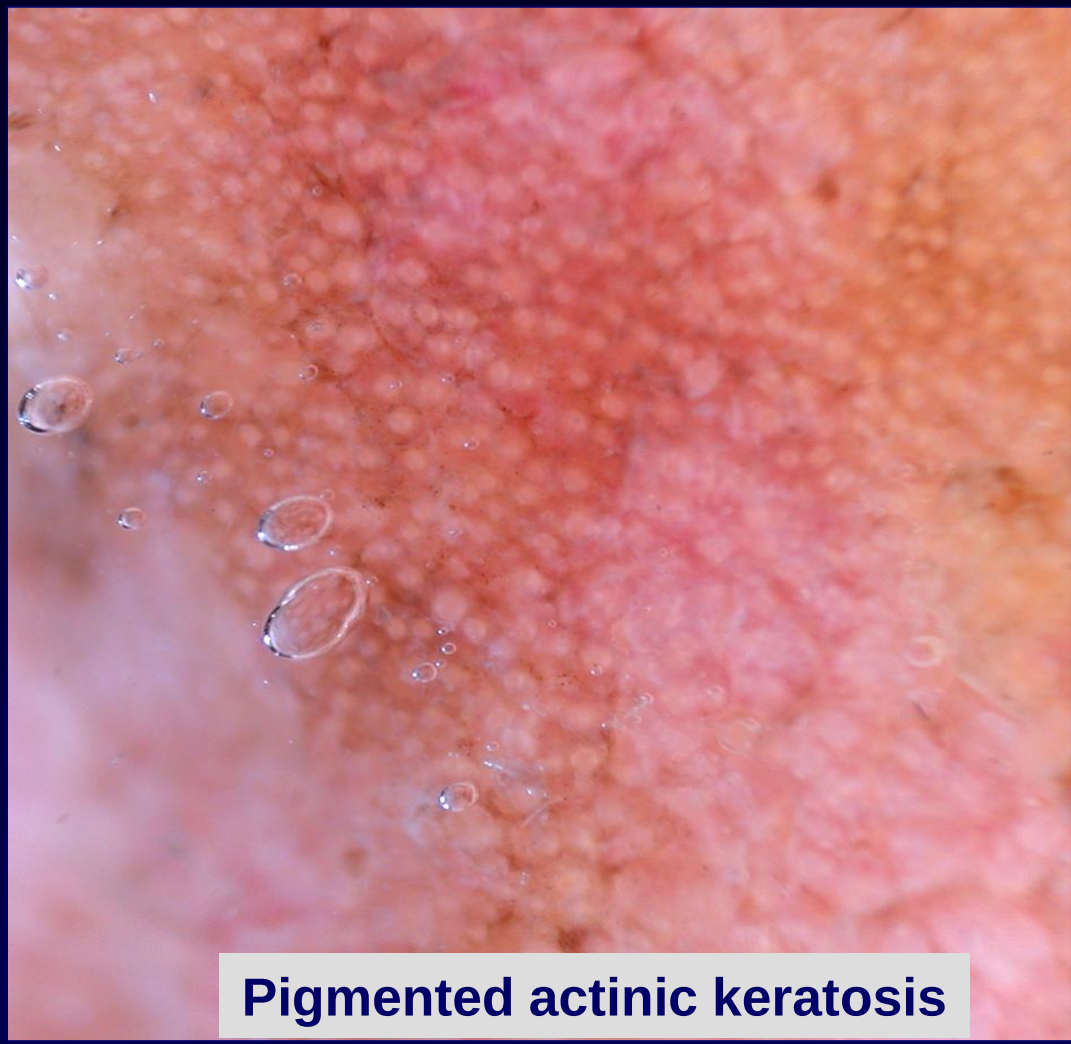









Seborrheic keratosis

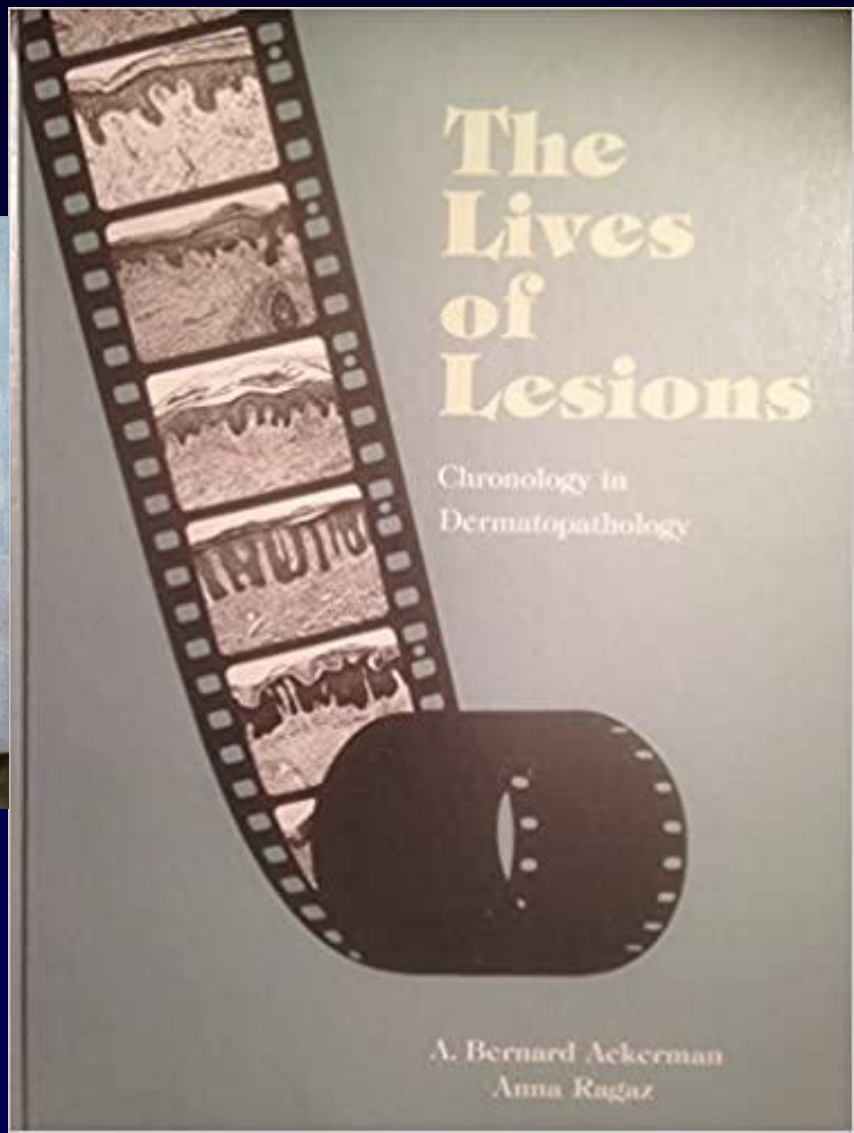

Pigmented actinic keratosis

Histopathological diagnoses on a punch biopsy sample

- Non melanocytic lesion/neoplasm (subcorneal hemorrhage, seborrheic keratosis, BCC…)
- Melanoma
- Melanocytic nevus
  - CAVE: The final differential diagnosis between ‘nevus’ and ‘melanoma’ MUST be deferred to the examination of the excision biopsy specimen

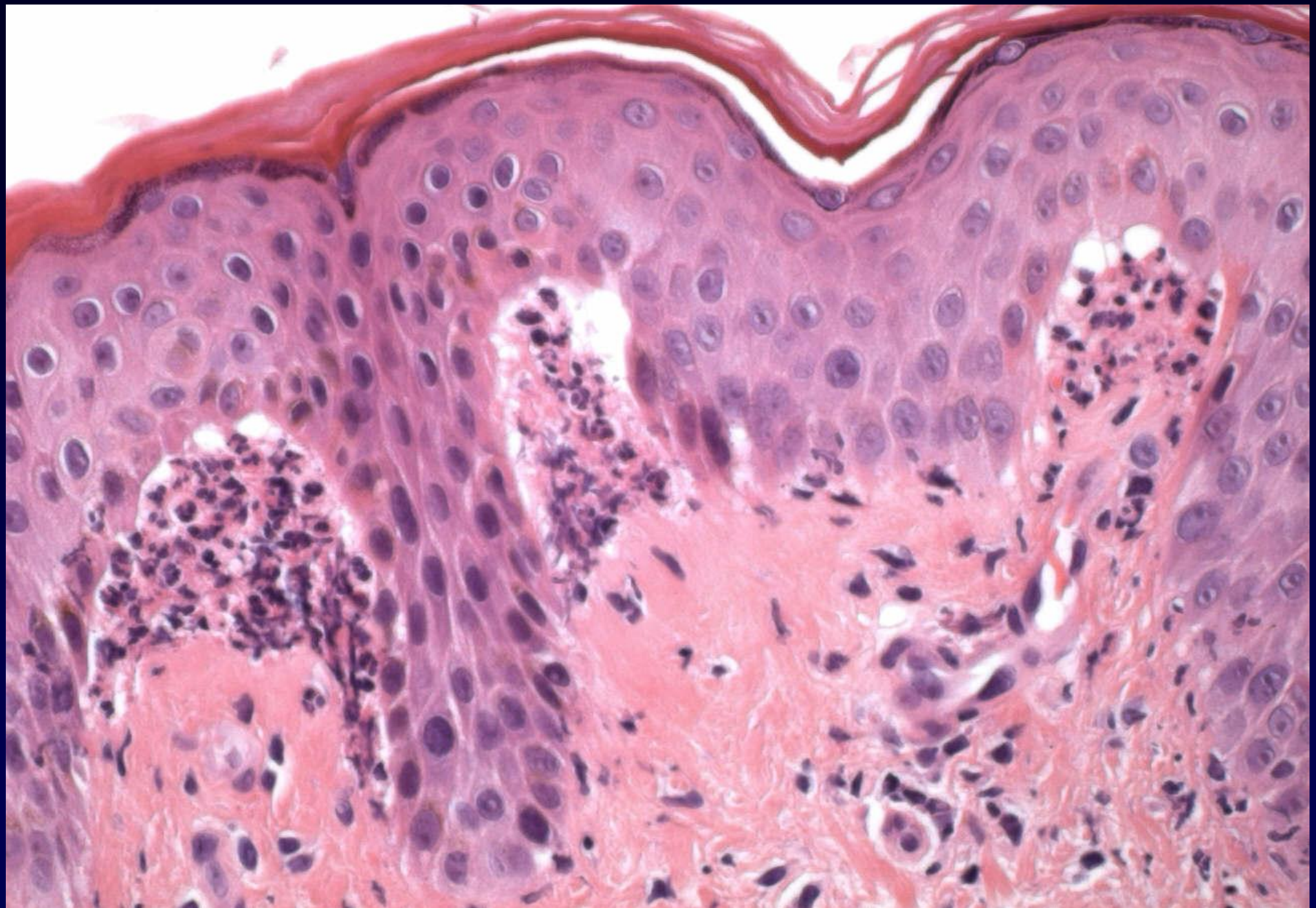
Epidermis and papillary dermis	Melanocytic nevus, age spots, seborrheic keratosis, fibroepithelial polyps, common wart Superficial basal cell carcinoma, melanoma in situ, mycosis fungoides, actinic keratosis, Paget disease (mammary and extramammary) Contact dermatitis (allergic and irritant), atopic dermatitis, seborrheic dermatitis, plaque psoriasis, scabies, lichen ruber planus, Gibert pityriasis rosacea, vesiculobullous dermatoses
Papillary and reticular dermis	Melanocytic nevus, neurofibroma, hemangioma, glomangioma/glomus tumor, sebaceous nevi (hamartomas of the sebaceous follicle), follicular cysts Basal cell carcinoma (solid, sclerodermiform), melanoma, squamous cell carcinoma Photoallergic dermatitis, phototoxic dermatitis: polymorphic light eruption, scleroderma, morphea, scabietic nodules, leukocytoclastic vasculitis, cutaneous lupus erythematosus, urticaria, granuloma annulare
Reticular dermis and subcutaneous tissue	Blue nevus, lipoma, dermatofibroma, epidermoid or trichilemmal cysts Melanoma, cutaneous lymphoma, dermatofibrosarcoma protuberans, metastasis (melanoma, breast cancer, etc.) Panniculitis, sarcoidosis, rheumatoid nodules, nodular vasculitis, polyarteritis nodosa, thrombophlebitis, granuloma annulare

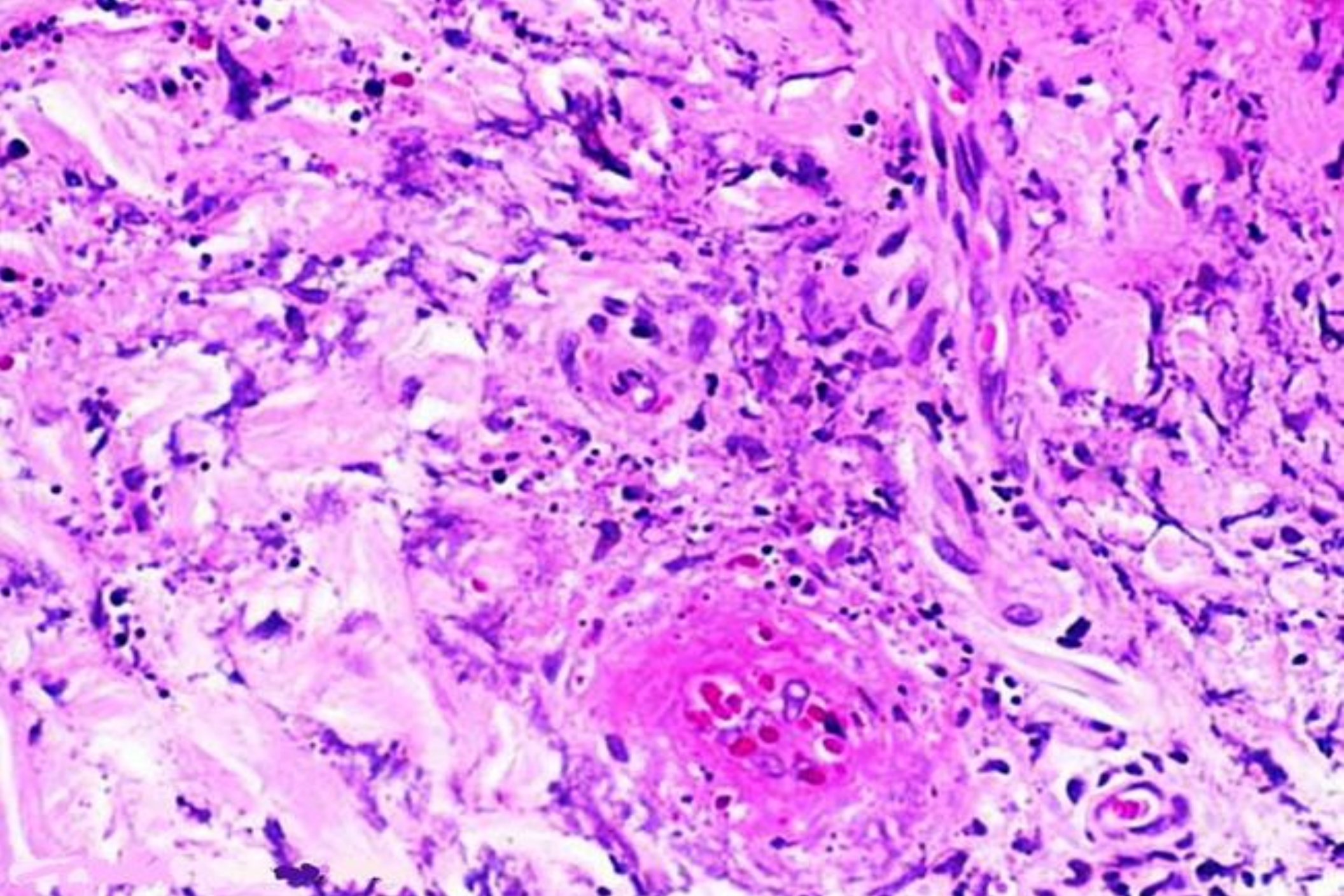
Punch Biopsy: Where and when?



Where

- Classical, well-formed, non-modified (by scratching or any topical application) lesion
- When the patient has polymorphic lesions, never hesitate to take more than one biopsy
- Biopsy of an early lesion is preferred in:
  - Henoch Schönlein purpura
  - Dermatitis herpetiformis
  - Panniculitis





Special situations

- Scalp biopsy

- Biopsy for bullous disease

Scalp biopsy

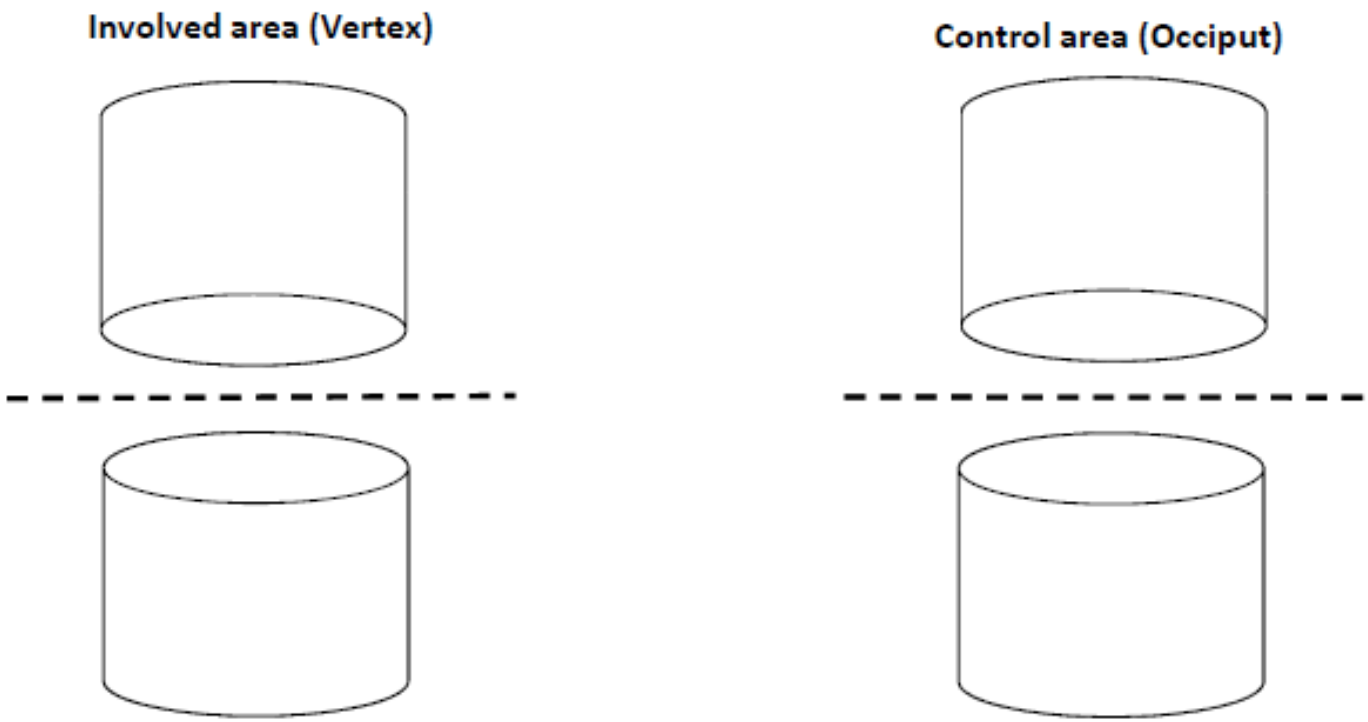
- Consider the vasculature of the scalp. The sould be performed about 20 min after the xylocaine-adrenaline anesthetic injection

- Consider the depth of hair papillae. The biopsy must go deep into the subcutis

- Consider the trichoglyphics. A skin ellipse should be performed in a direction parallel to the direction of emergence of hairs from the scalp

Non-scarring Alopecia

Two 4-mm punch biopsies:
1 from the center of the involved area, and 1 from a non-involved area (as control)



Both biopsies to be sent intact to the DP lab for horizontal sectioning

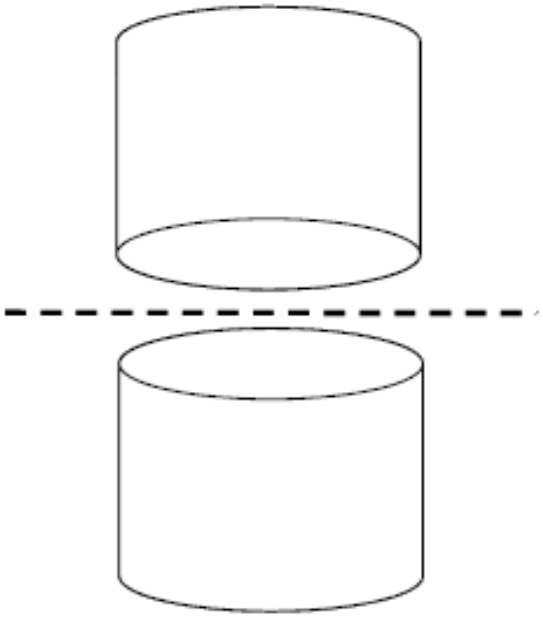

Axlab Innovation
BiopSafe


Bio-Optica

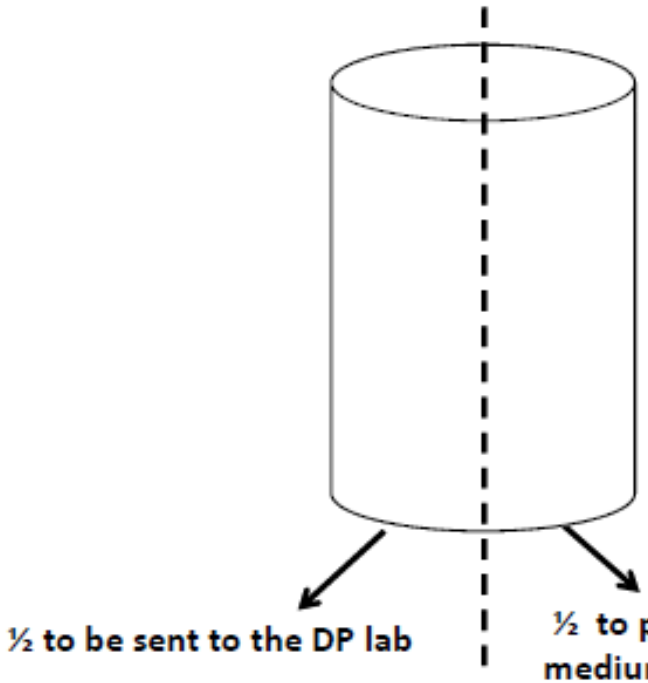
Scarring Alopecia

Two 4-mm punch biopsies taken at the "active border" of the scarring process

4mm punch biopsy: to be sent intact to the DP lab: this will be bisected horizontally



4mm punch biopsy to bisect vertically in the clinic



½ to be sent to the DP lab

½ to place in Michel's medium and to be sent to IMF lab

Steps in Direct Immunofluorescence

HistoLine

Tissue preparation

- After biopsy, place tissue in Michel's transport medium (3.12 M ammonium sulfate, 5 mM N-ethylmaleimide (NEM), and 5 mM magnesium sulfate heptahydrate)
- When ready to cut, wash ammonium sulfate from specimen with PBS for 30 minutes.
- Freeze specimen in isopentane and store at -70 C until ready to cut.
- Cut sections at 5-6 microns, save first and last cuts for H&E staining.
- Dry slides at 56° C for 30 minutes.

JOURNAL OF INVESTIGATIVE DERMATOLOGY

See related article:
http://www.nature.com/jid/journal/v133/n1/full/jid2012455a.html

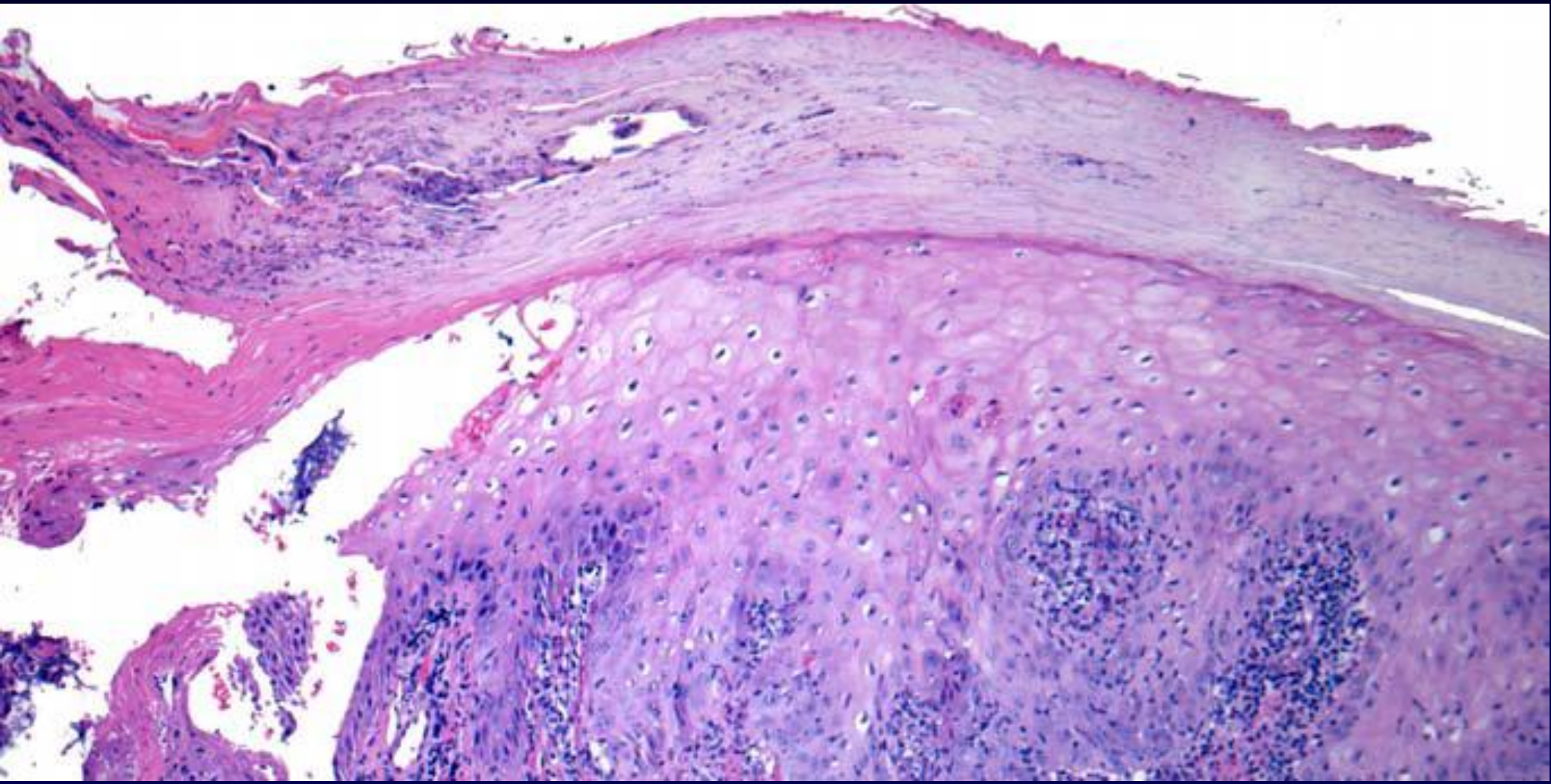
Biopsy for bullous disease

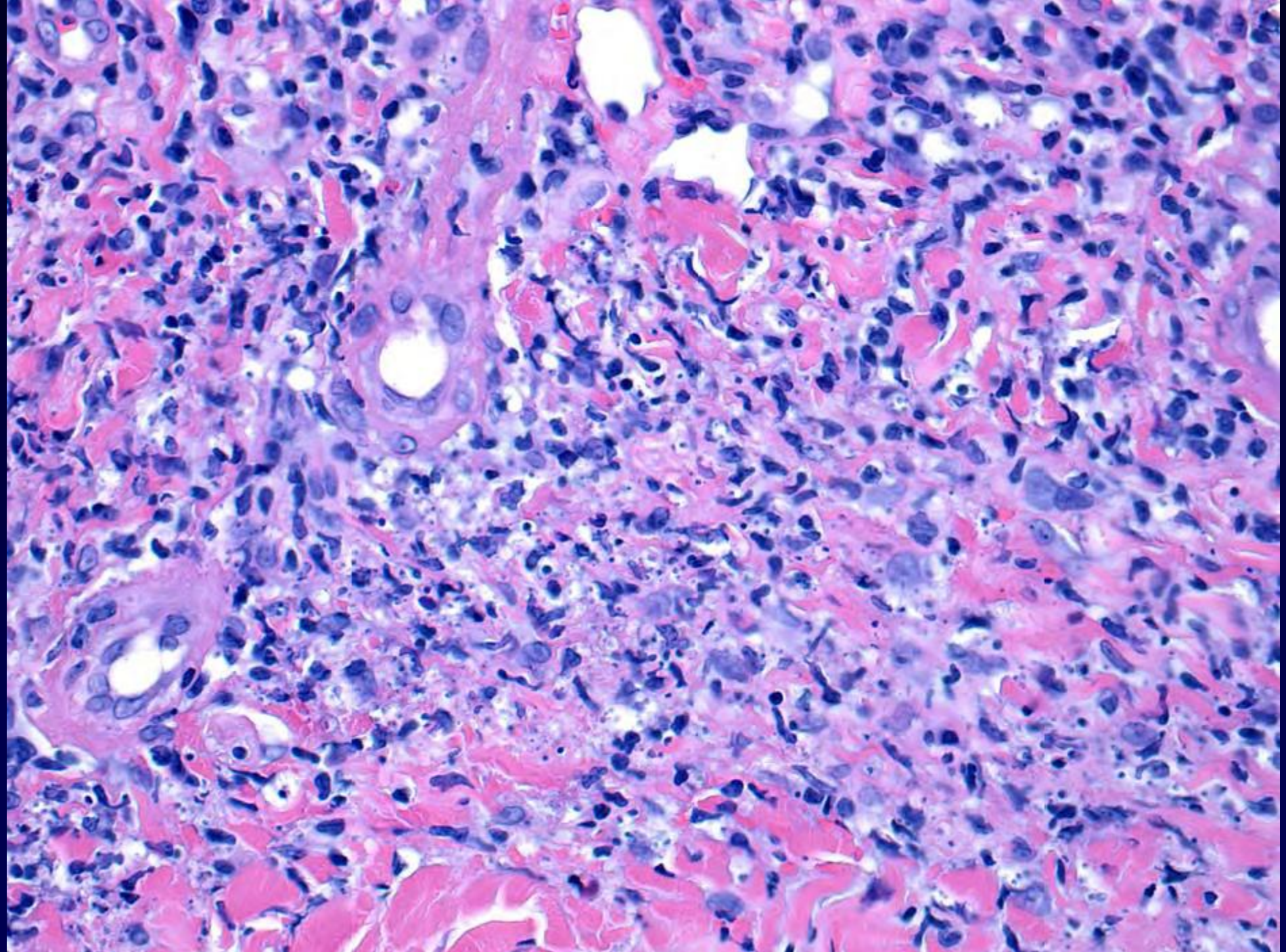
- Remove a fresh intact bulla
- Avoid friction areas (elbows, knees)
- Avoid lower extremities
- Handle with a forceps or with a needle along the deep aspect of the sample
- Place in 10% neutral buffered formalin

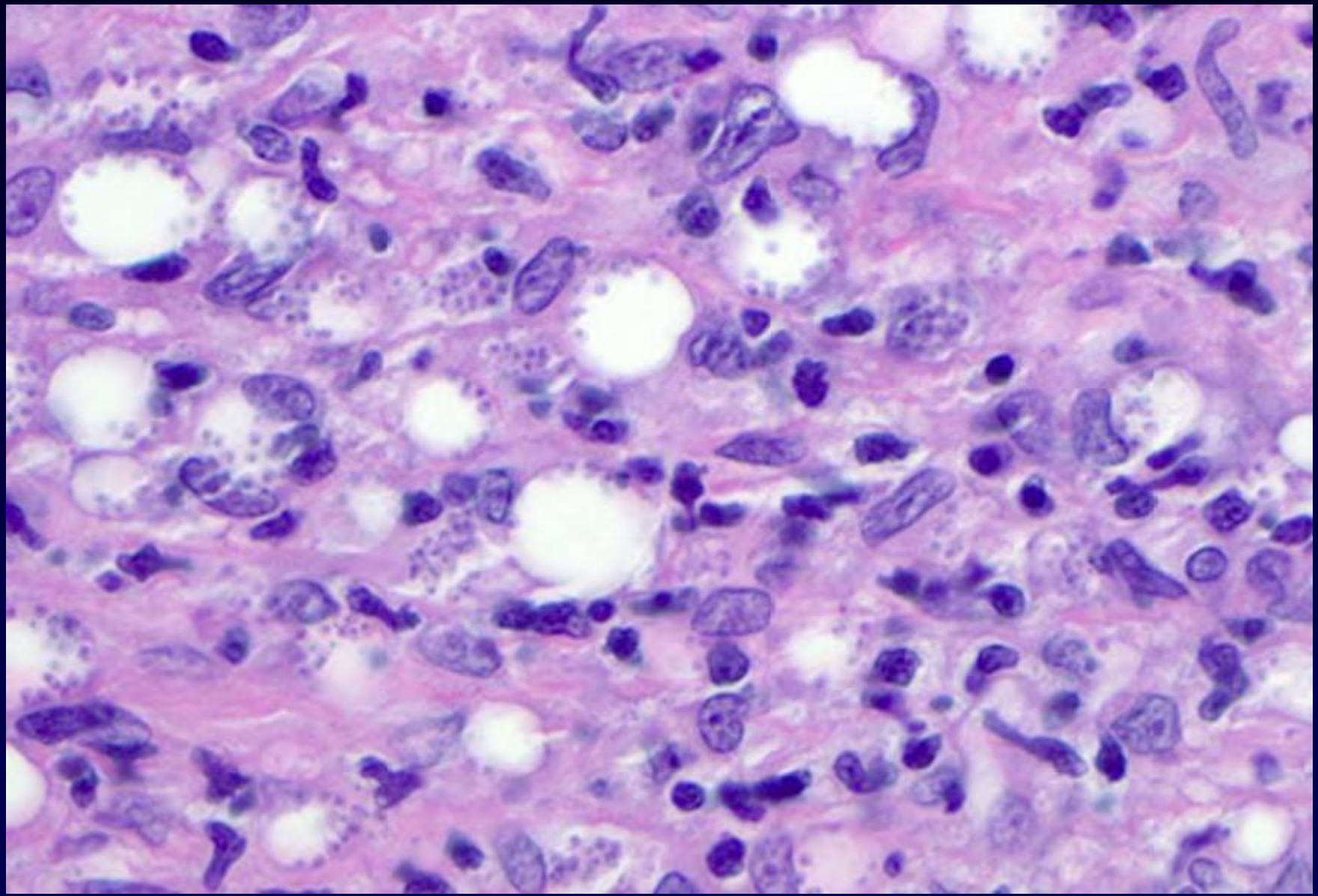
- Take a ≥4 mm biopsy sample of perilesional skin ≤1 mm from the bulla for DIF (Michel's medium)

Part 3

The travel is now back

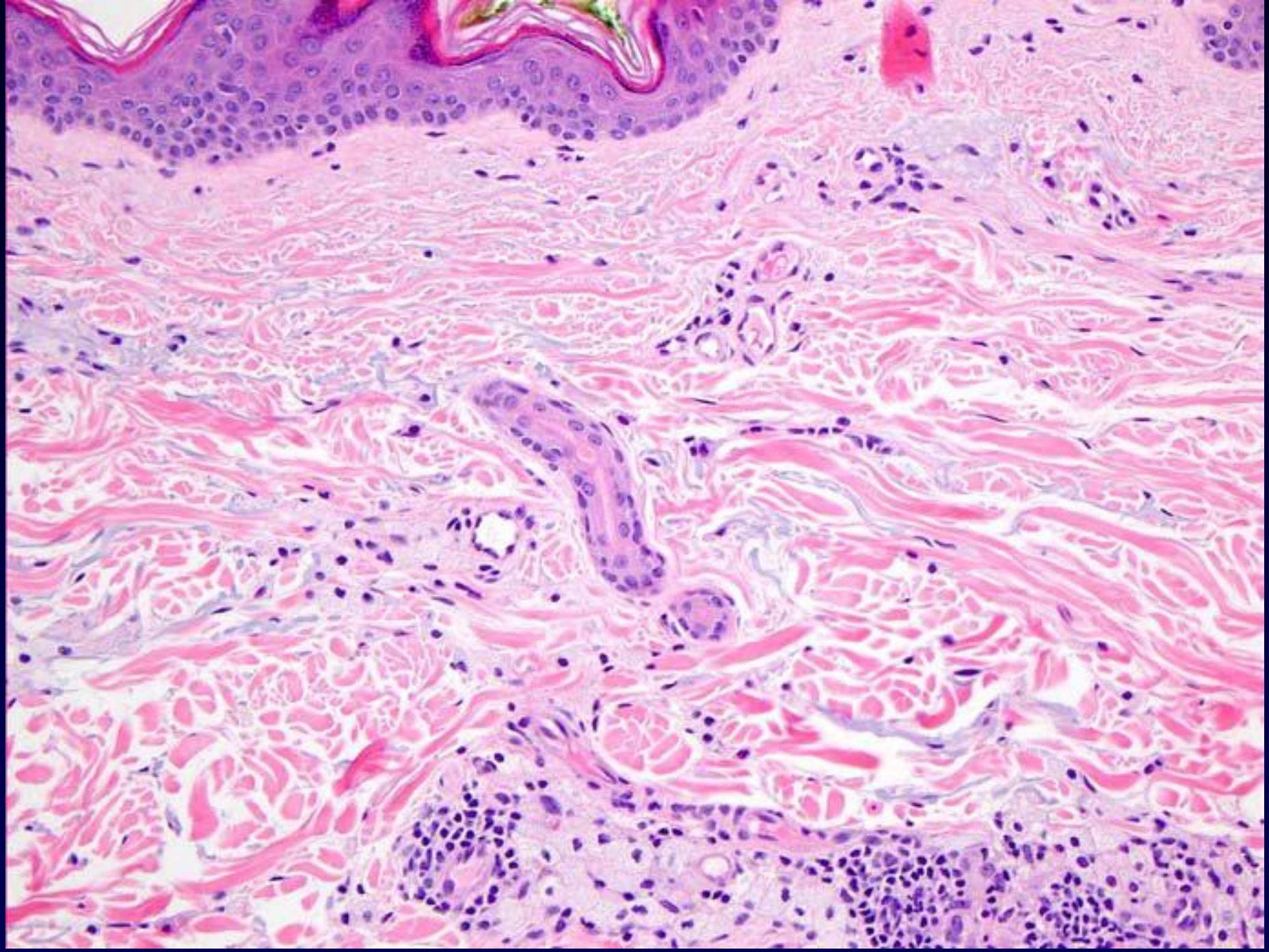


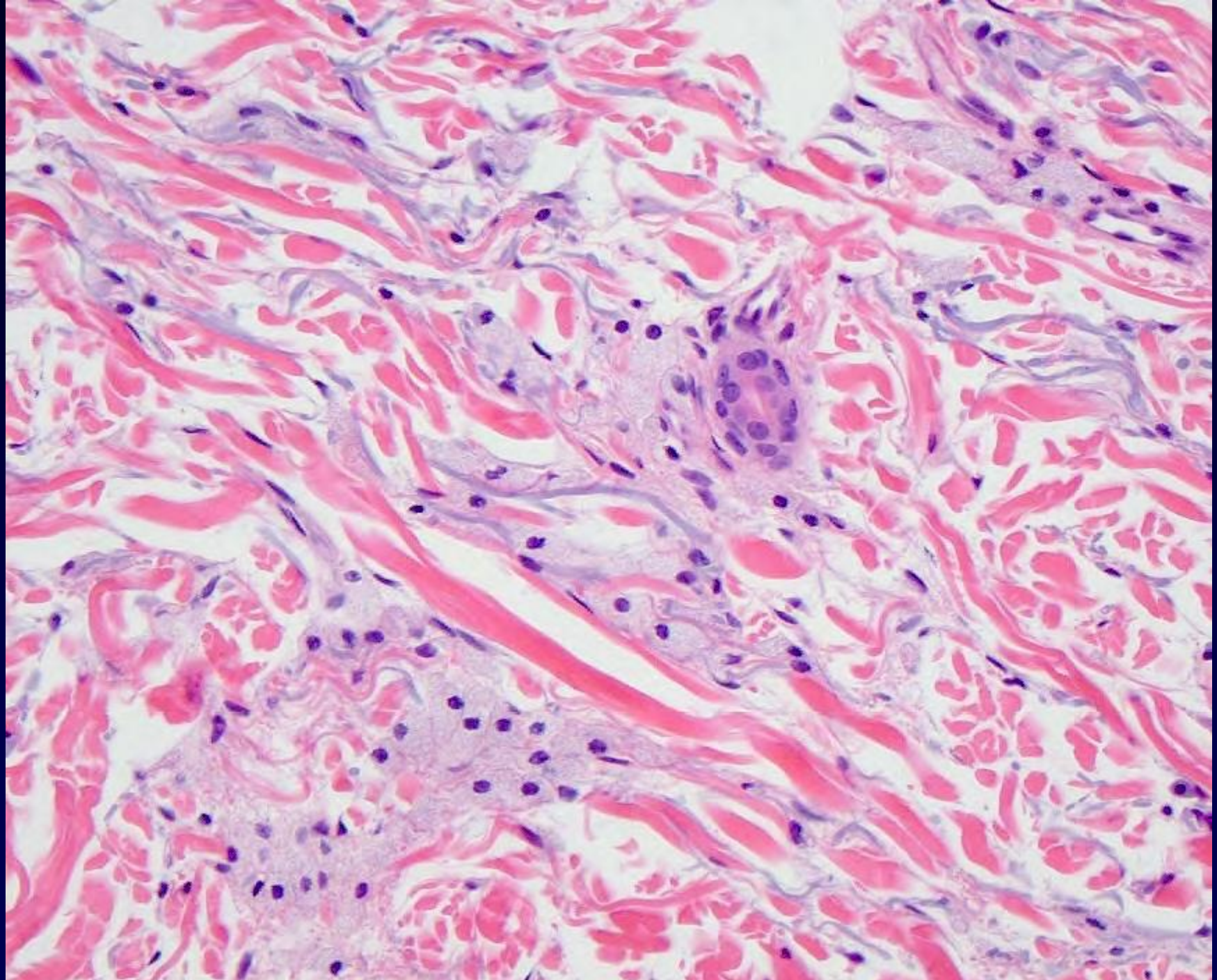




Leismaniasis


Dott. Carlo Cota





(Normolipemic) planar xanthoma

Diffuse Normolipemic Plane Xanthoma (DNPX) of the Neck without Xanthelasma Palpebrum

Uwe Wollina[1*], Jacqueline Schönlebe[2], Georgi Tchernev[3,4], Torello Lotti[5]

[1]Städtisches Klinikum Dresden - Department of Dermatology and Allergology, Dresden, Sachsen, Germany; [2]Städtisches Klinikum Dresden - Institute of Pathology "Georg Schmorl", Dresden, Germany; [3]Department of Dermatology, Venereology and Dermatologic Surgery, Medical Institute of Ministry of Interior, Sofia, Bulgaria; [4]Onkoderma, Policlinic for Dermatology and Dermatologic Surgery, Sofia, Bulgaria; [5]University G. Marconi of Rome - Dermatology and Venereology, Rome, Italy

Citation: Wollina U, Schönlebe J, Tchernev G, Lotti T. Diffuse Normolipemic Plane Xanthoma (DNPX) of the Neck without Xanthelasma Palpebrum. Open Access Maced J Med Sci. 2018 Jan 25; 6(1):123-125. https://doi.org/10.3889/oamjms.2018.037

Keywords: Diffuse normolipemic plane xanthoma; Non-Langerhans histiocytosis; Histology; Treatment; Xanthelasma palpebrarum

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Abstract

Diffuse normolipemic plane xanthoma (DNPX) is an uncommon subtype of non-Langerhans histiocytosis. DNPX is characterised by xanthelasma palpebrarum, diffuse plane xanthoma of the head, neck, trunk, or extremities, and normal plasma lipid levels. The neck is the most common site. We report about a 62-year-old female Caucasian patient, who developed an asymptomatic fine wrinkling and loose skin on the neck and décolleté about three years ago. The skin colour became yellowish. Xanthelasma was absent. Histopathology of a skin biopsy confirmed the diagnosis of DNPX. The patient had a medical history of chronic myeloblastic leukaemia. No other laboratory abnormalities were found. Laser treatment was offered but opposed by the patient.

Introduction

Diffuse normolipemic plane xanthoma (DNPX) was first described by Altman and Winkelmann in 1962 [1]. It is now considered as an uncommon subtype of non - Langerhans histiocytosis [2].

DNPX is characterized by xanthelasma palpebrarum, diffuse plane xanthoma of the head, neck, trunk, or extremities, and normal plasma lipid levels. The neck is the most common site [1][3]. Xanthelasma palpebrarum usually appears first [1].

The clinical presentation is characterised by the presence of symmetric, asymptomatic, yellowish-orange plaques [1][2]. Oral lesions are extremely rare [3].

variable numbers of Touton giant cells, lymphocytes, and foamy histiocytes are present; sometimes only foam cells can be seen [4][5].

DNPX has been associated with systemic diseases, particularly multiple myeloma and monoclonal gammopathy [4][5][6]. In other cases, malignant haematological or lymphoproliferative disorders have been observed [7][8].

Case report

A 62-year-old female Caucasian patient developed an asymptomatic fine wrinkling and loose

Conclusion

- A safe journey starts from the clinical and ends to the clinical
- EVERY cutaneous lesion excised/biopsied must be phtographed; the pics must be then e+re-evaluated after receivig the histopathological report
- CLINICAL and HISTOLOGY must be reciprocally consistent

Definition of **consistent**

From: the Online Oxford Dictionary

adjective

1 acting or done in the same way over time, especially so as to be fair or accurate:

the parents are being consistent and firm in their reactions

a consistent worldwide application of its policies

- unchanging in nature, standard, or effect over time:

he is Rangers' most consistent player this season

the mixtures are of consistent quality

2 (of an argument or set of ideas) not containing any logical contradictions:

a consistent explanation

3 [*predic.*] compatible or in agreement with something:

the injuries are ***consistent with*** *falling from a great height*