This 2009 lecture is far superior to the lecture delivered in 2011. However, streaming videos and VAP's may not match. Dr. H

SKIN NEOPLASMS

-the goal of the first skin lecture was to learn the vocabulary
-now we should focus on learning "clues for detection"

APPROVED

Maria Angelica Selim, MD
Director Dermatopathology Unit
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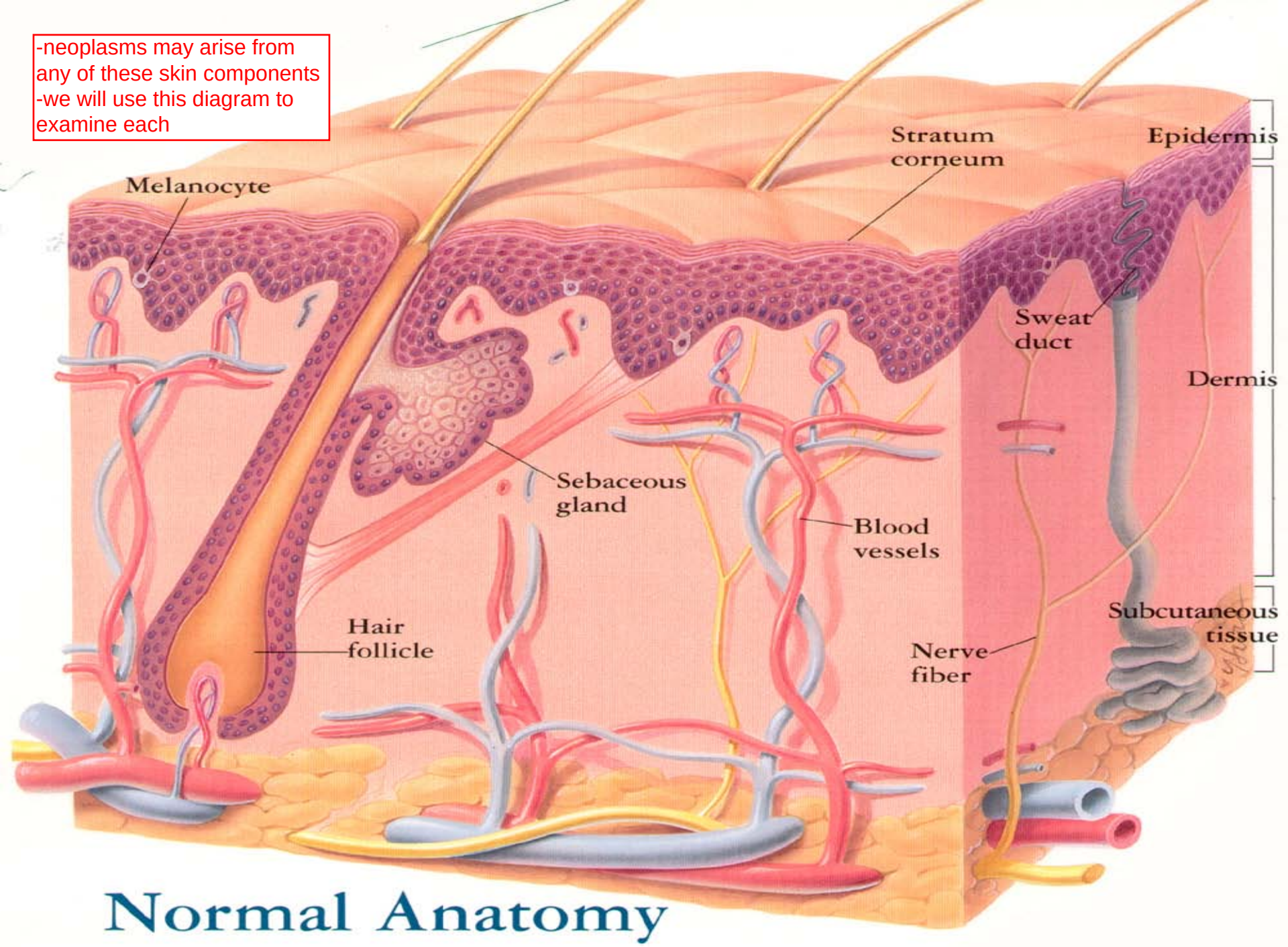
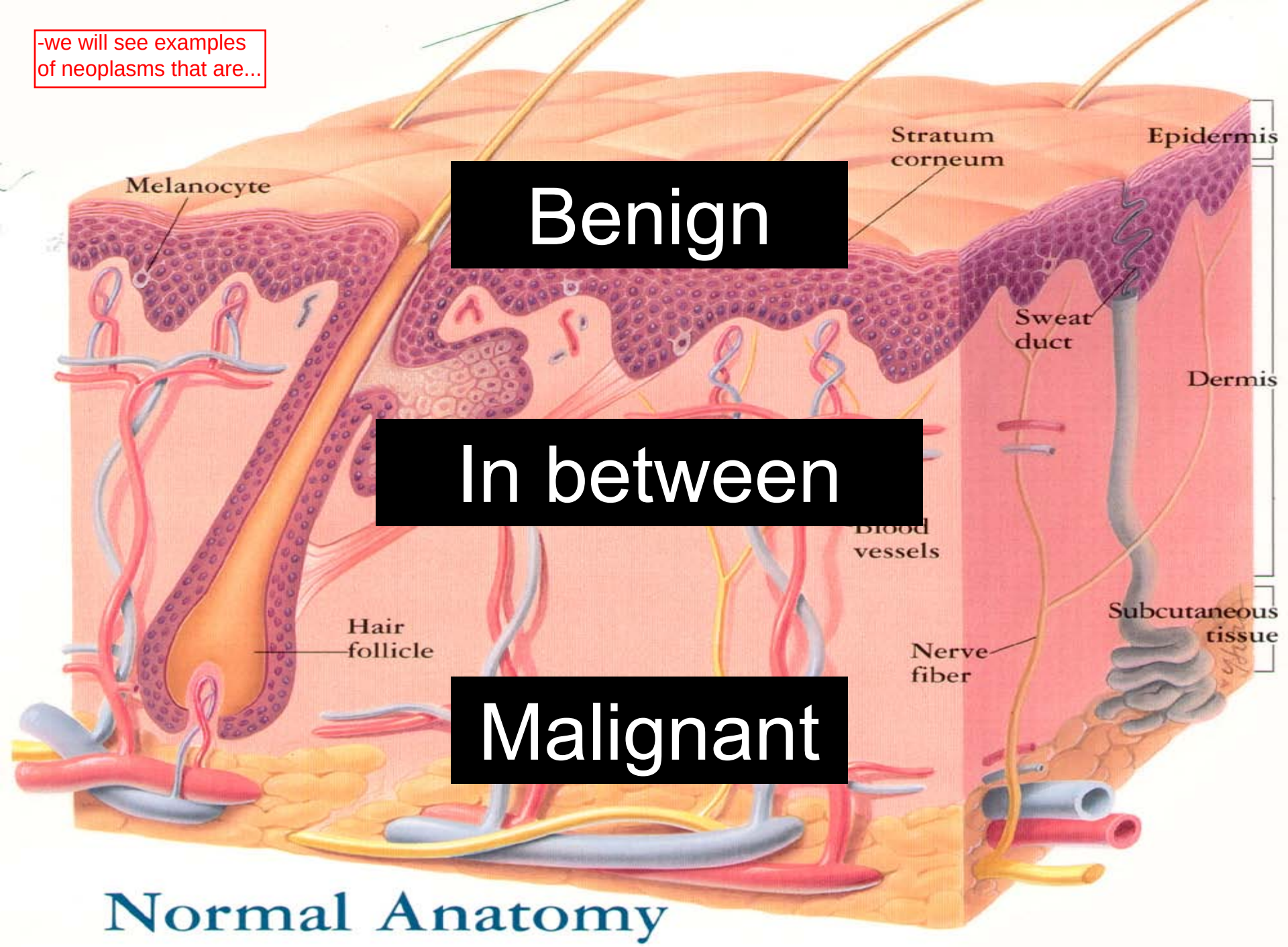
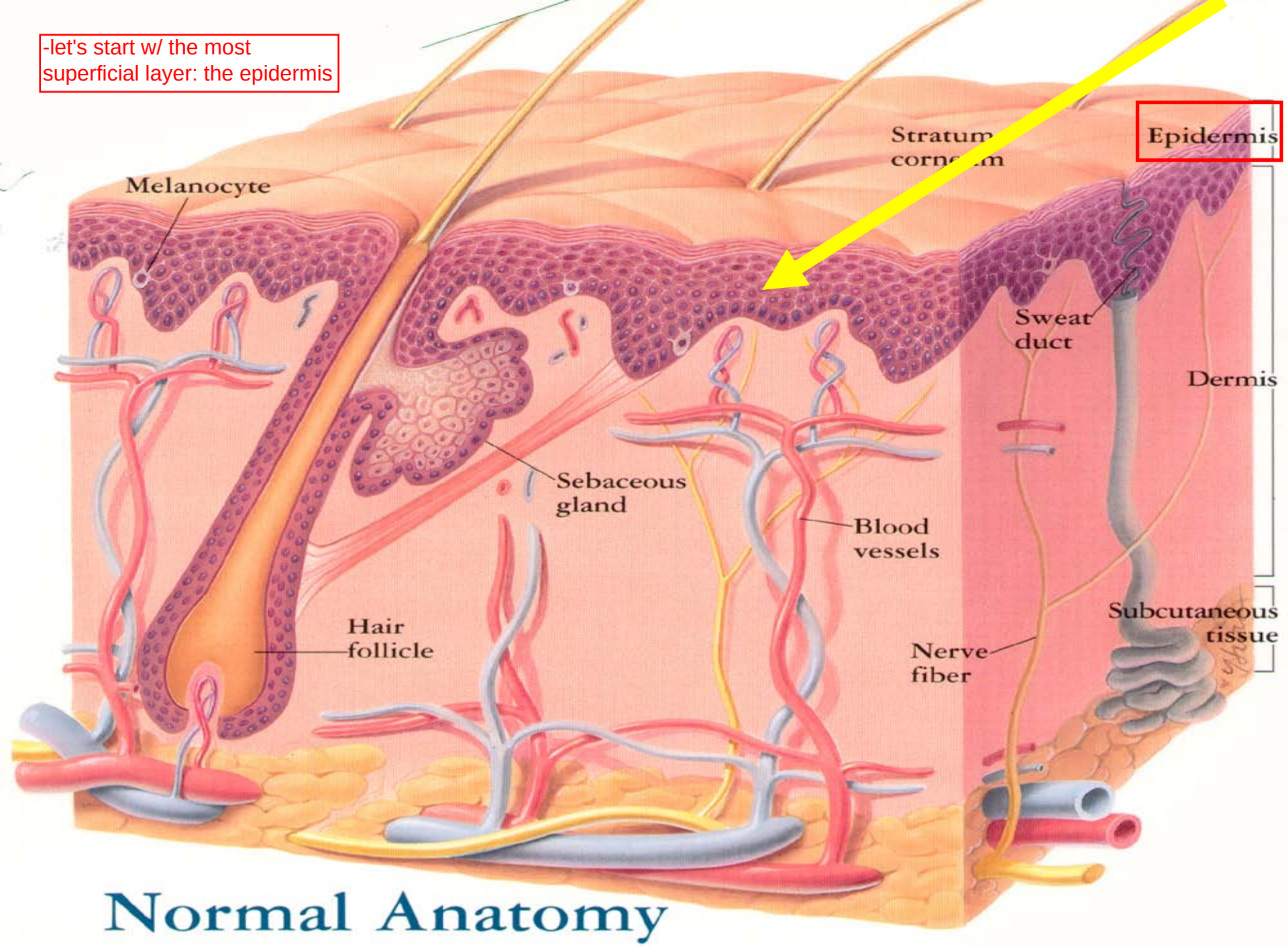
-neoplasms may arise from any of these skin components
-we will use this diagram to examine each



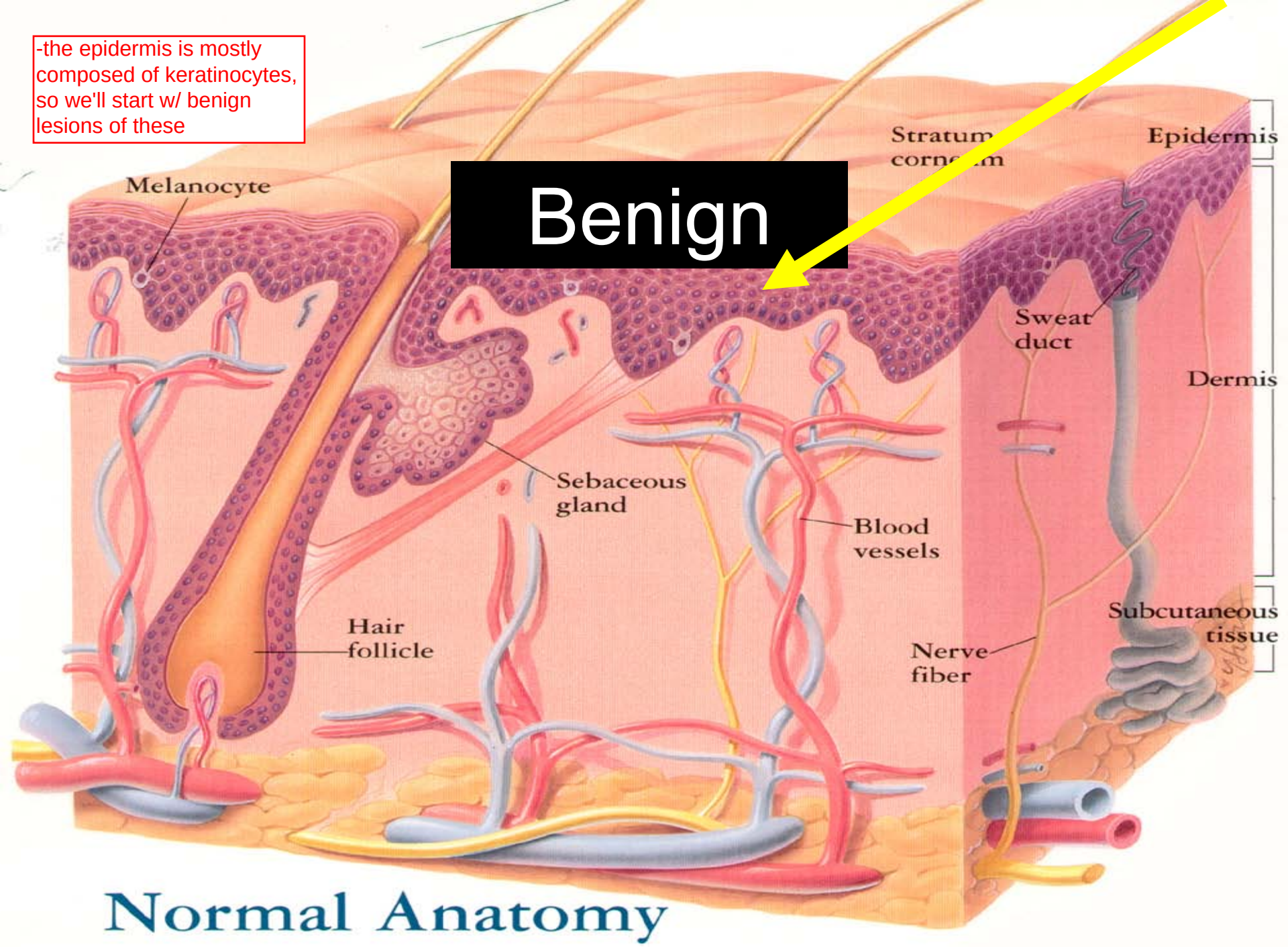
-we will see examples of neoplasms that are...



-let's start w/ the most superficial layer: the epidermis



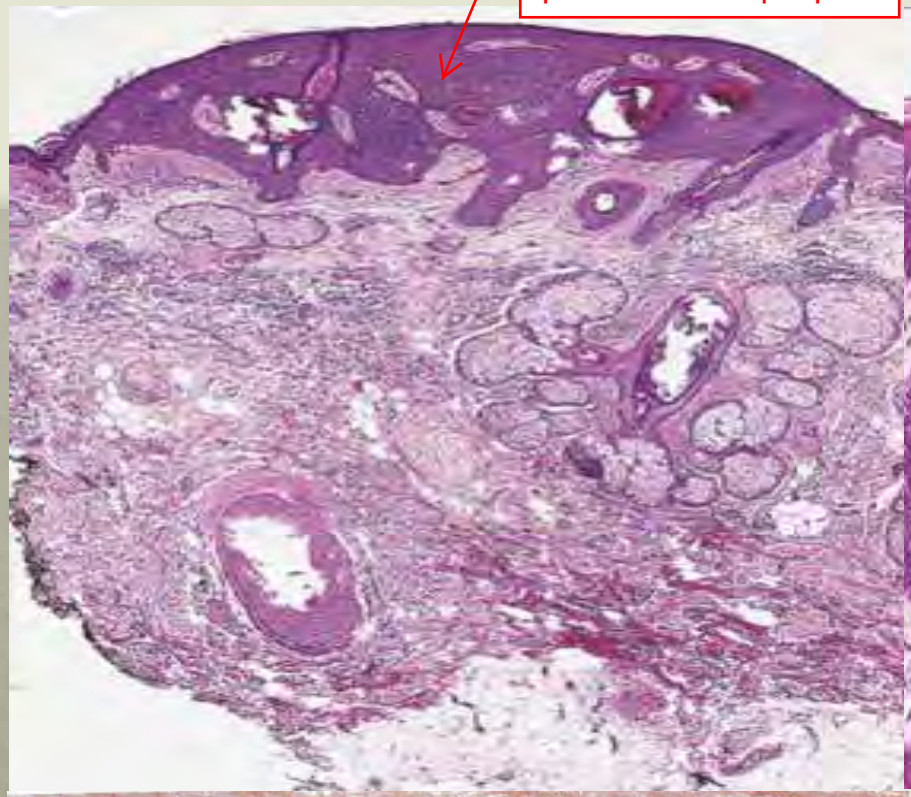
-the epidermis is mostly composed of keratinocytes, so we'll start w/ benign lesions of these



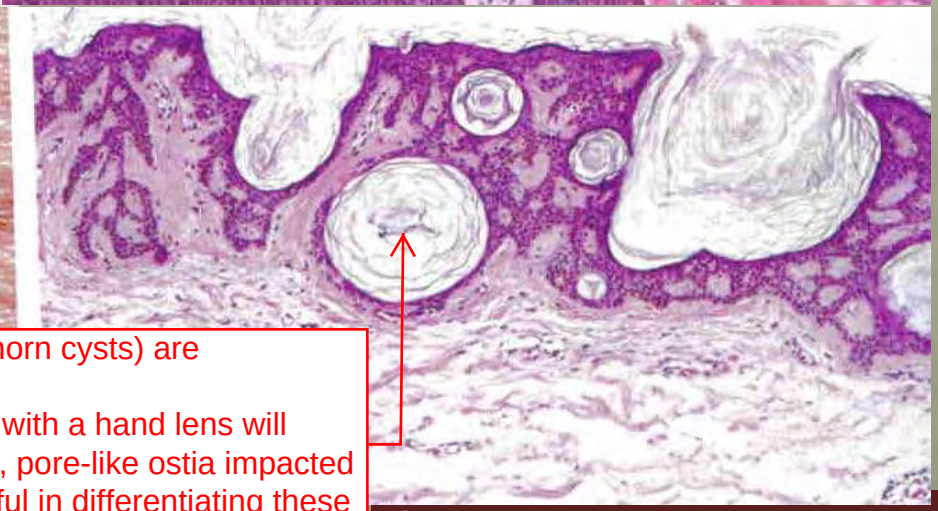
Seborrheic Keratosis

Seborrheic Keratosis

-note the thickening of the epidermis at the plaque



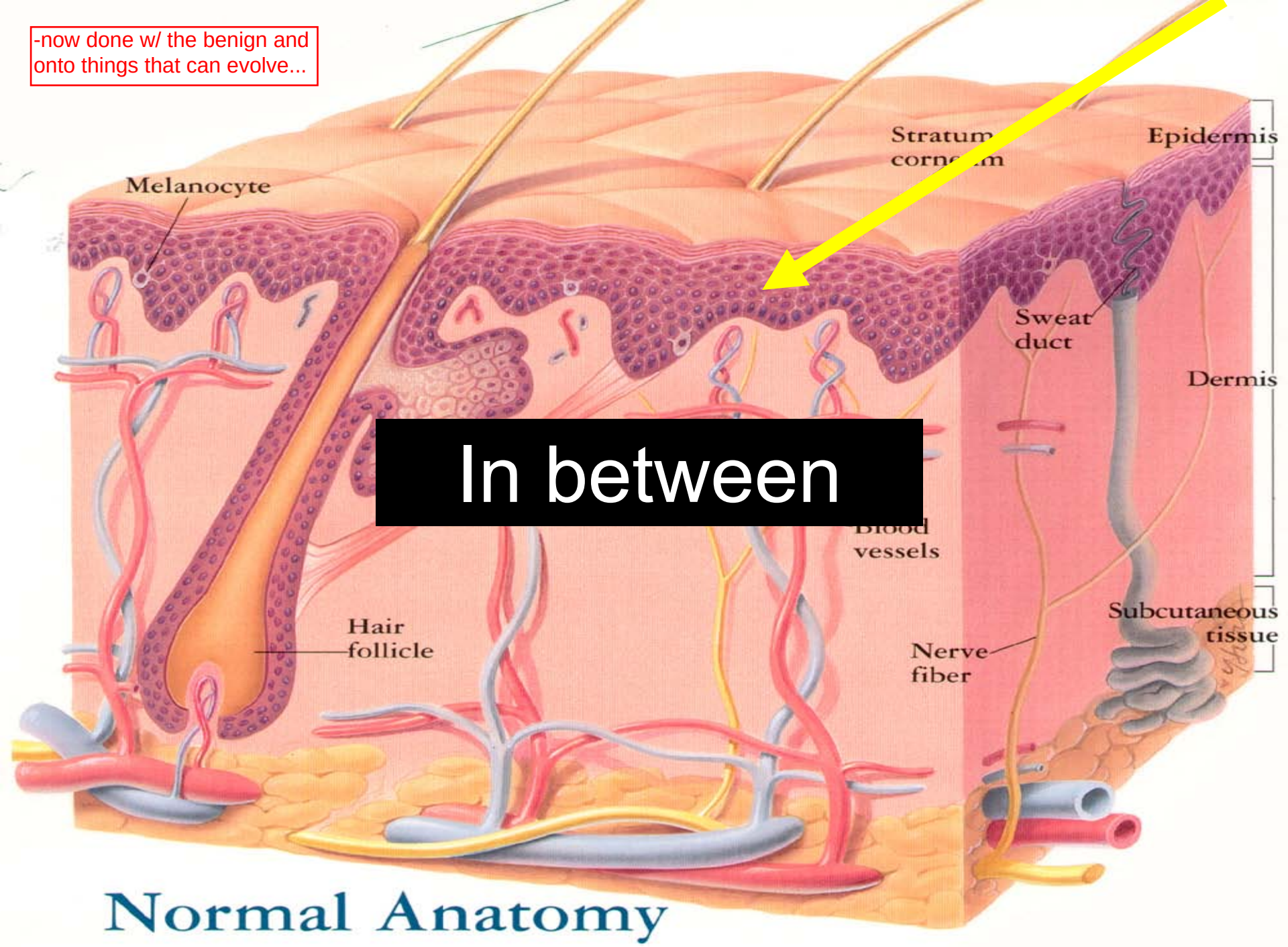
-at higher power, the cells appear small and equal in size and shape, indicating a benign lesion



-small keratin-filled cysts (horn cysts) are characteristic features
-inspection by the clinician with a hand lens will usually reveal small, round, pore-like ostia impacted with keratin, a feature helpful in differentiating these pigmented lesions from melanomas

Seborrheic Keratosis

-now done w/ the benign and onto things that can evolve...



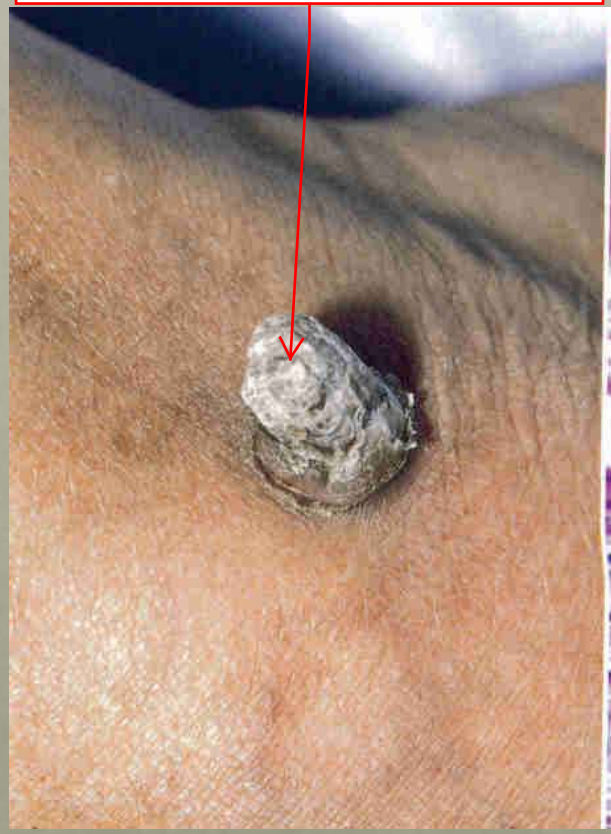
Actinic Keratosis

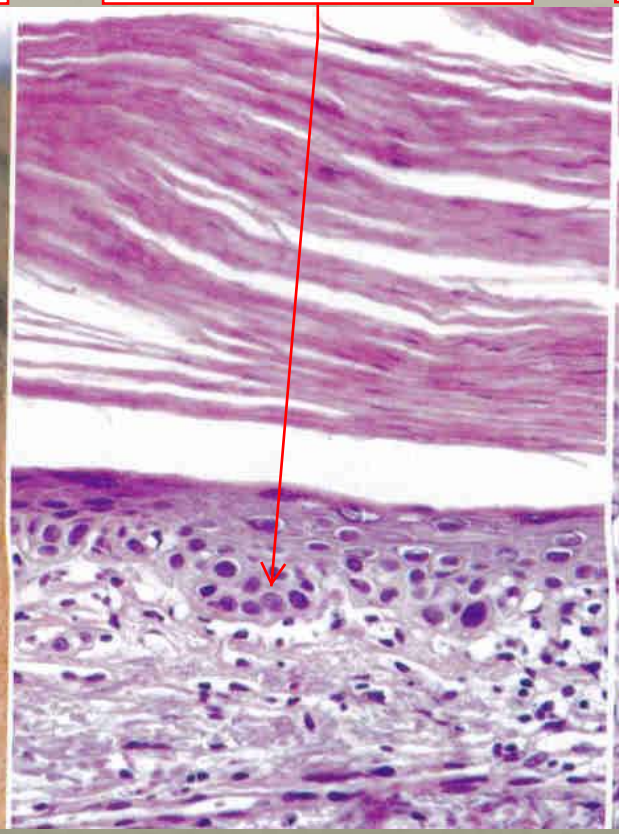
Actinic Keratosis

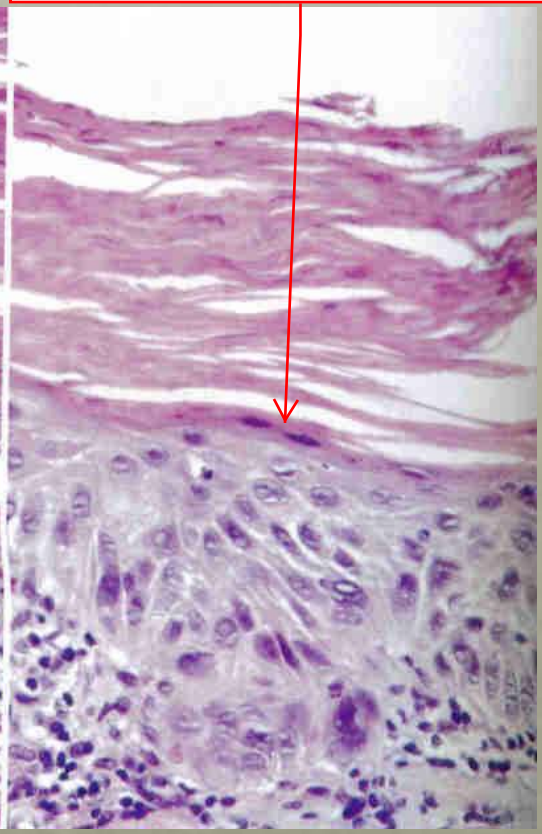
-some lesions may produce so much keratin that a "cutaneous horn" develops
-such horns may become so prominent that they actually resemble the horns of animals!

-looking at h&e, keratinocytes show signs of dysplasia (enlarged, hyperchromatic nuclei w/ prominent nucleoli)

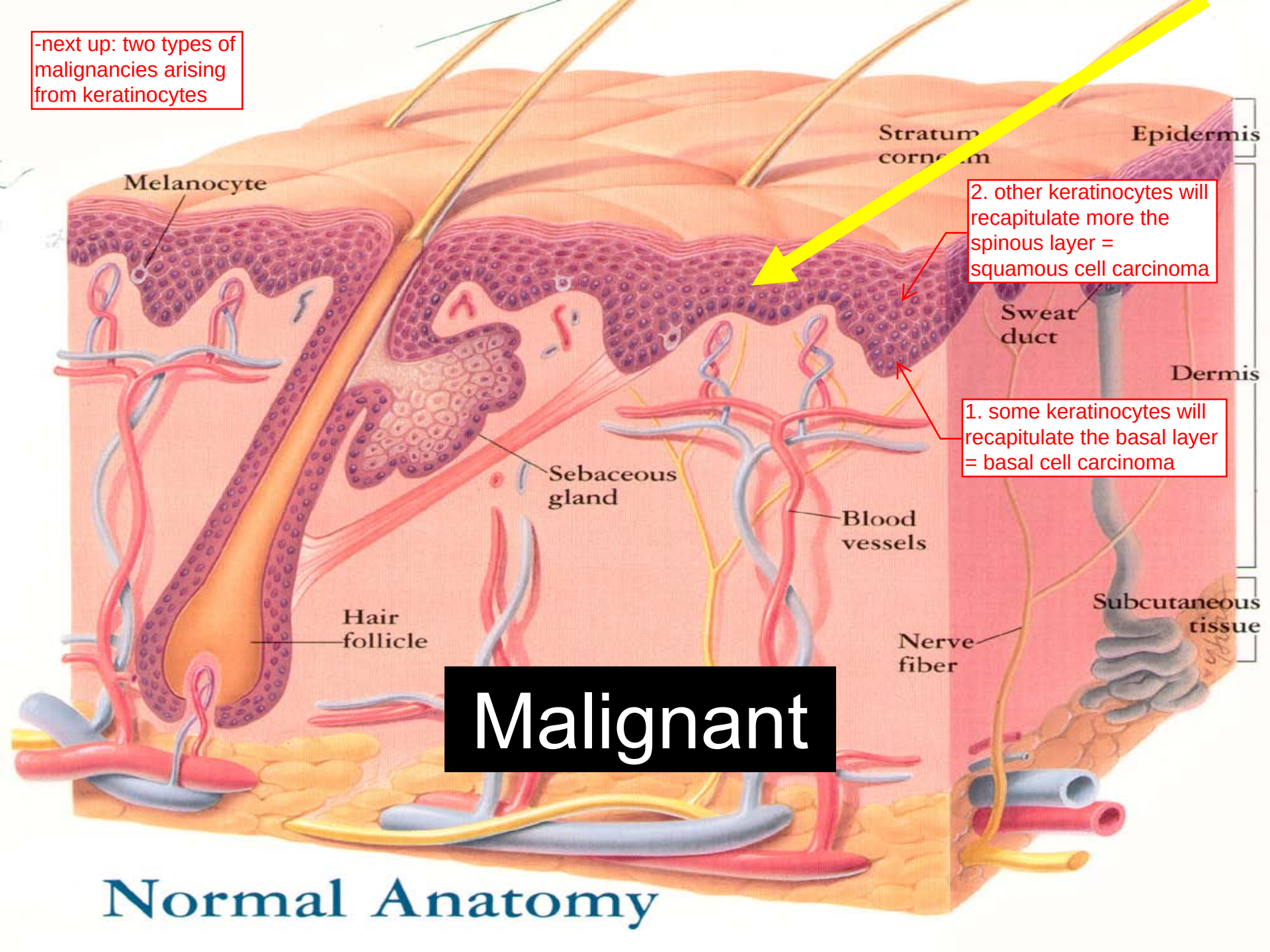
-there is a progressive loss of normal epidermal polarization
-nuclei in the stratum corneum are often retained, a pattern termed parakeratosis
-most of the atypia is seen in the lowermost layers of the epidermis, which distinguishes from a full-thickness malignancy







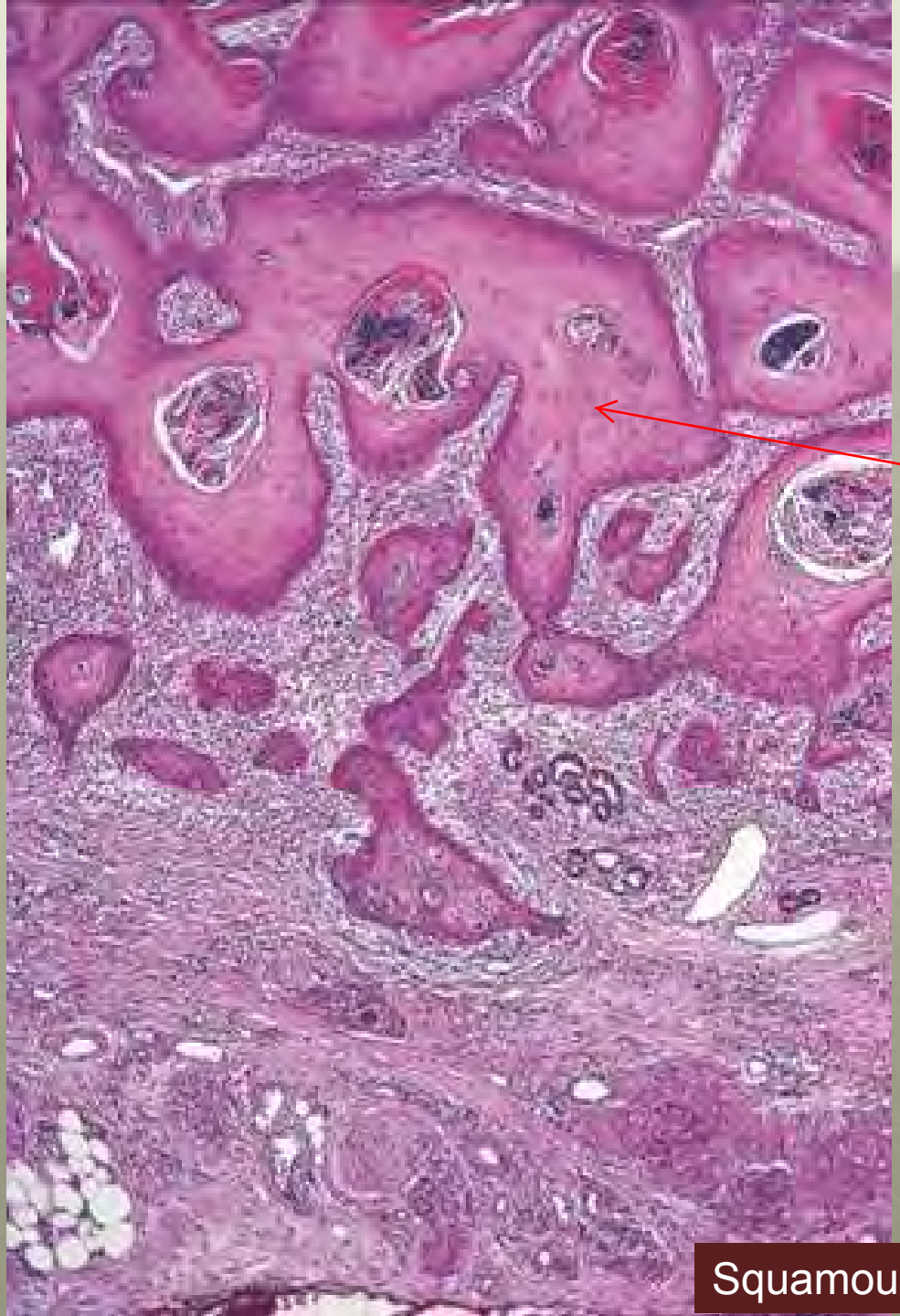
Actinic Keratosis


-next up: two types of malignancies arising from keratinocytes
Melanocyte
Stratum corneum
Epidermis
2. other keratinocytes will recapitulate more the spinous layer = squamous cell carcinoma
Sweat duct
Dermis
1. some keratinocytes will recapitulate the basal layer = basal cell carcinoma
Sebaceous gland
Blood vessels
Hair follicle
Nerve fiber
Subcutaneous tissue
Malignant
Normal Anatomy

Squamous Cell Carcinoma

-more advanced lesions are nodular, show variable keratin production appreciated clinically as hyperkeratosis, and ulcerate as seen here

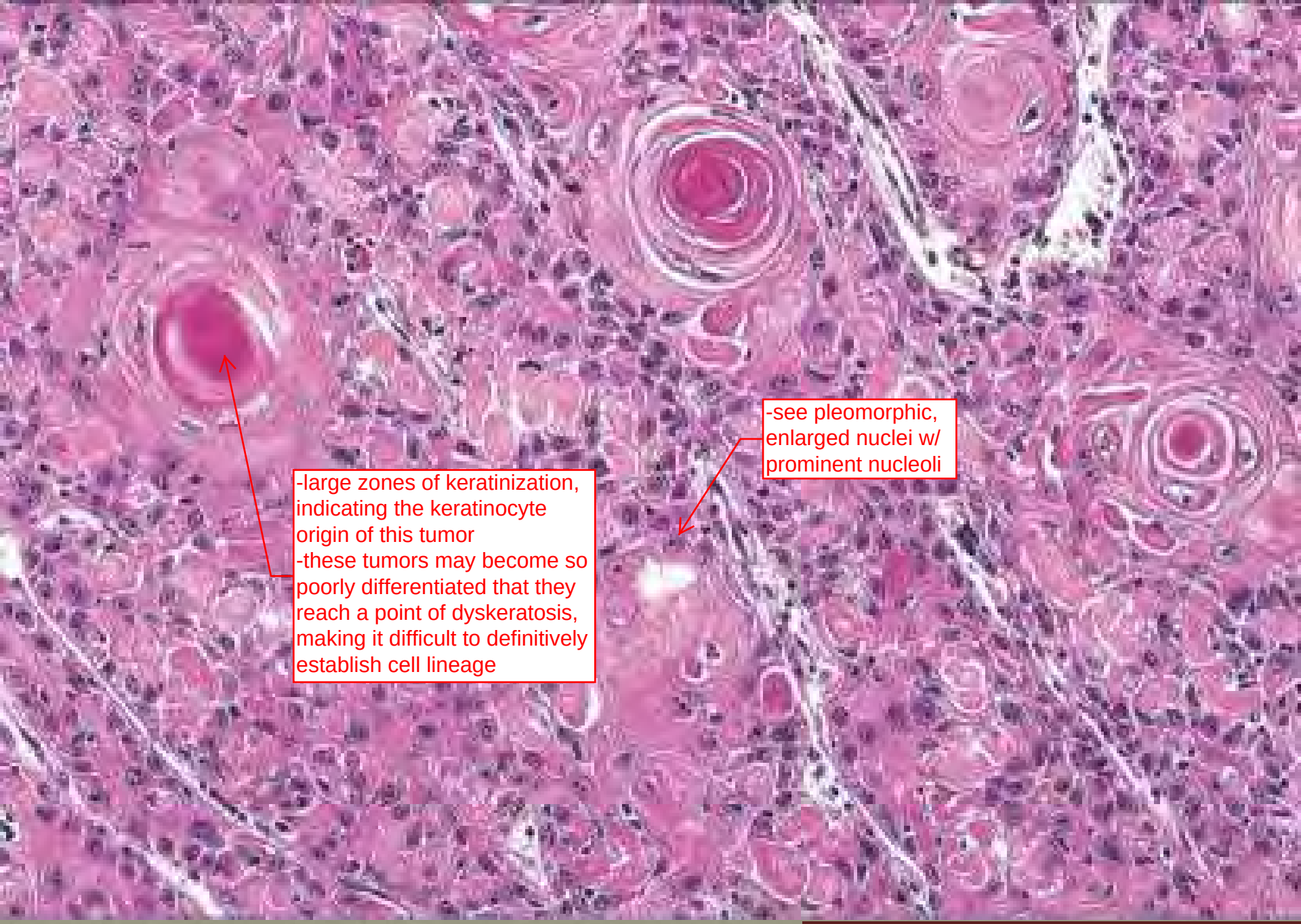
Squamous Cell Carcinoma



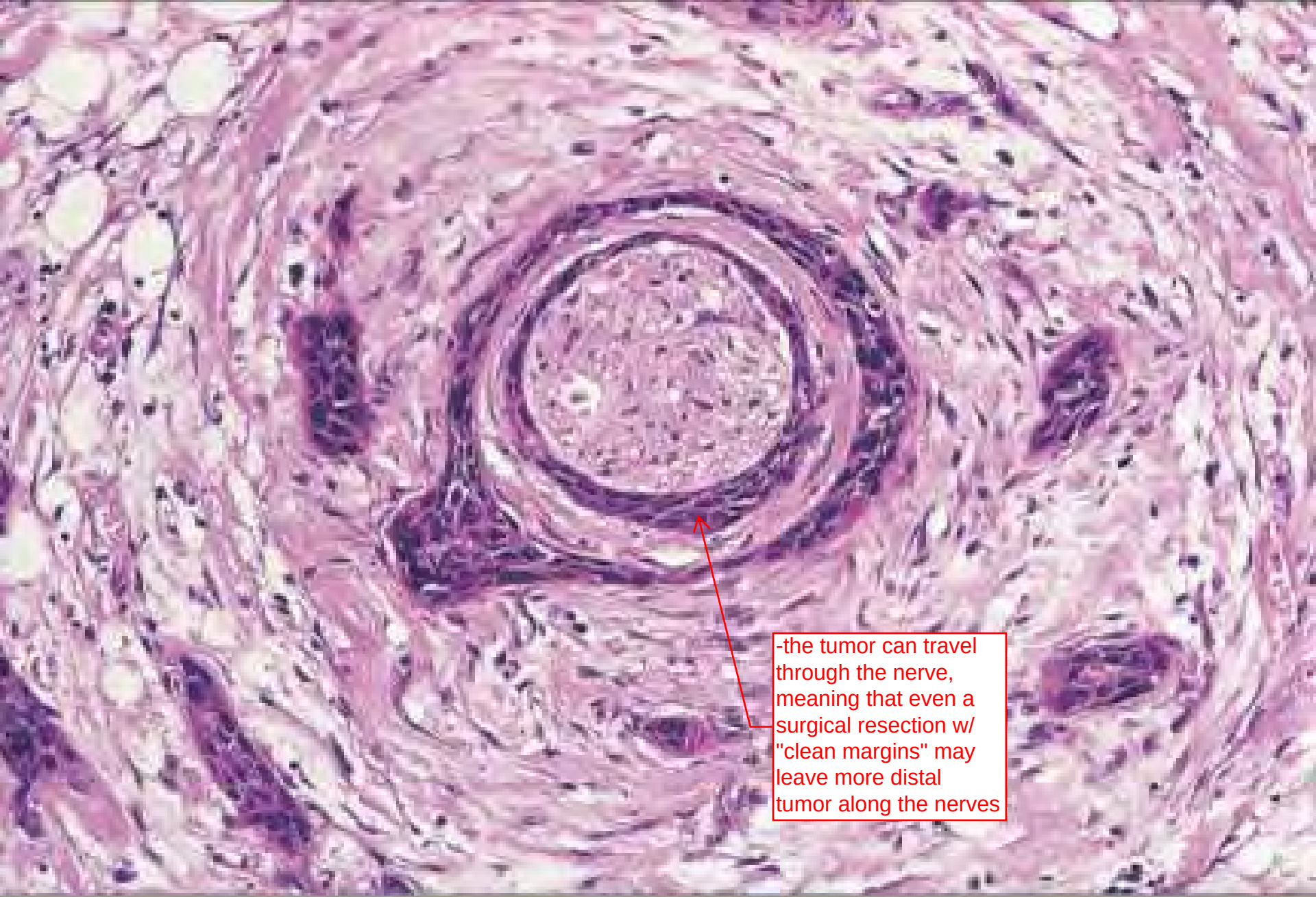
-looking at h&e, you can see the keratinocytes taking on the appearance of the mid-epidermis
-they are pink due to keratin production
-here the cells are infiltrating into the dermis, making this an invasive squamous cell carcinoma (see vocab lesson below)

-VOCABULARY
+actinic keratosis: cytologic atypia limited to the lowermost layers of the epidermis
+SCC in situ: progression to full-thickness nuclear atypia, but bound by the basement membrane of the dermoepidermal junction
+invasive SCC: crossing the basement membrane into the dermis
-these distinctions are important for prognosis; once the dermis is invaded, there is metastatic potential due to vascular access

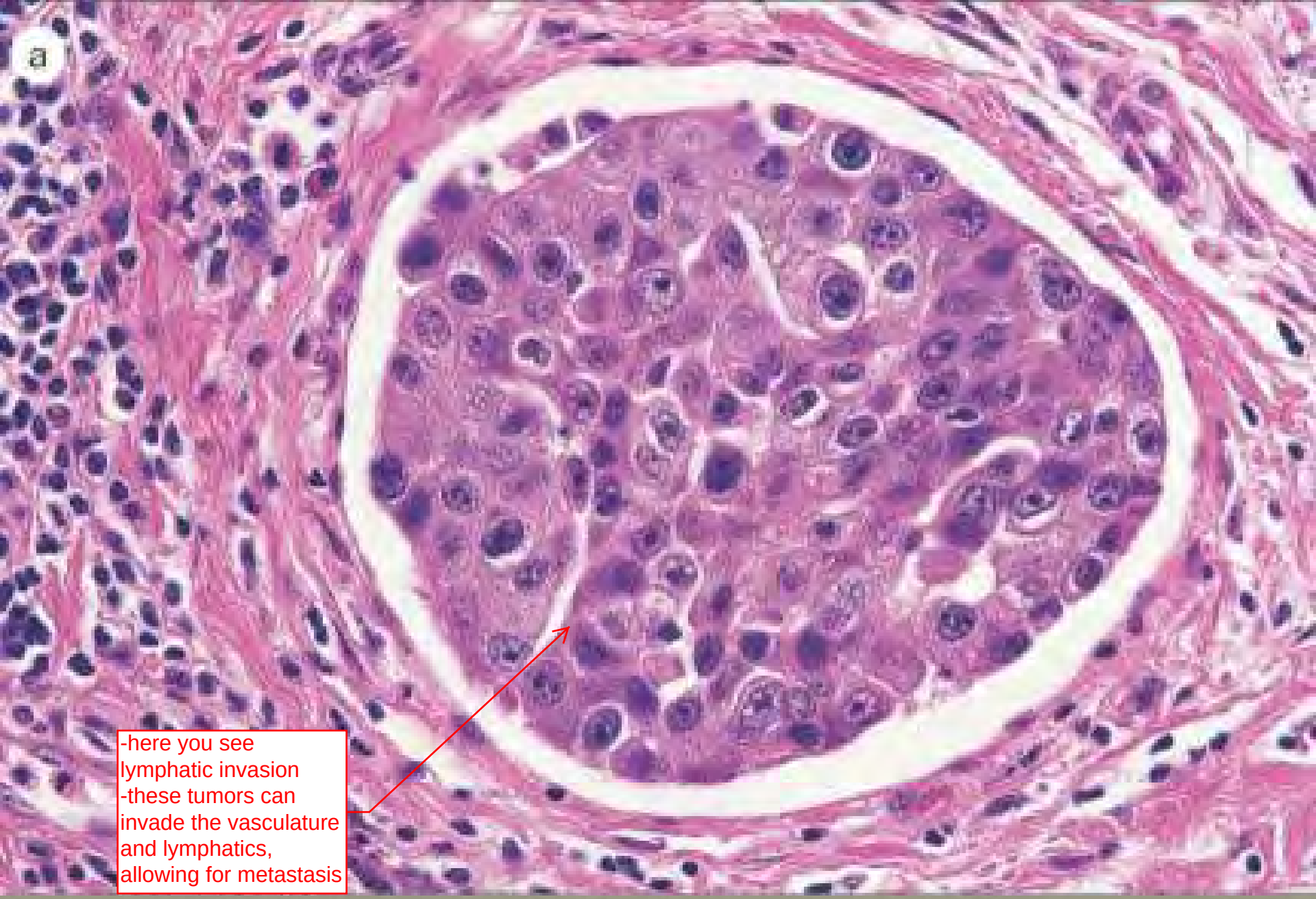
Squamous Cell Carcinoma



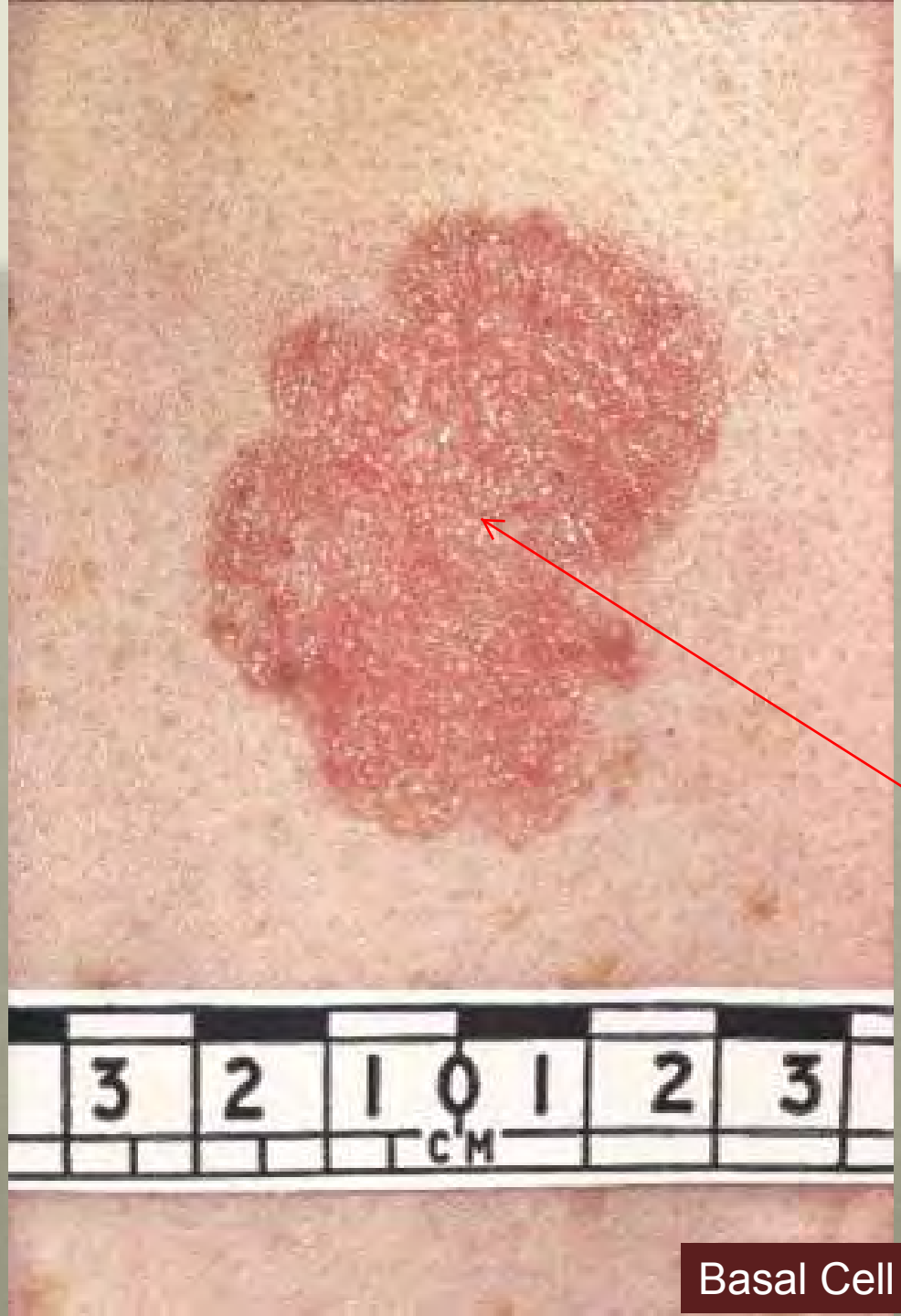
Squamous Cell Carcinoma



Squamous Cell Carcinoma

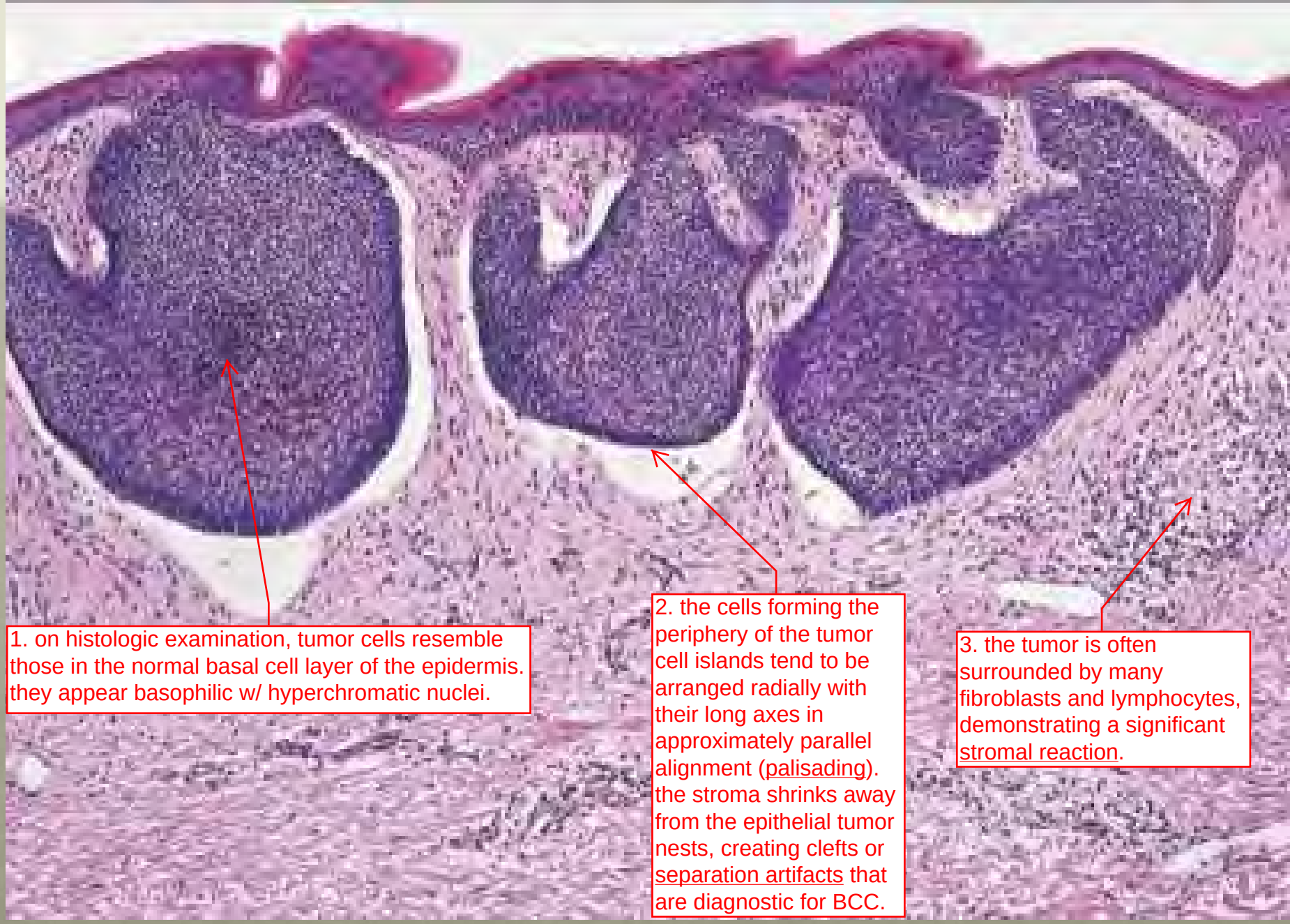


Squamous Cell Carcinoma



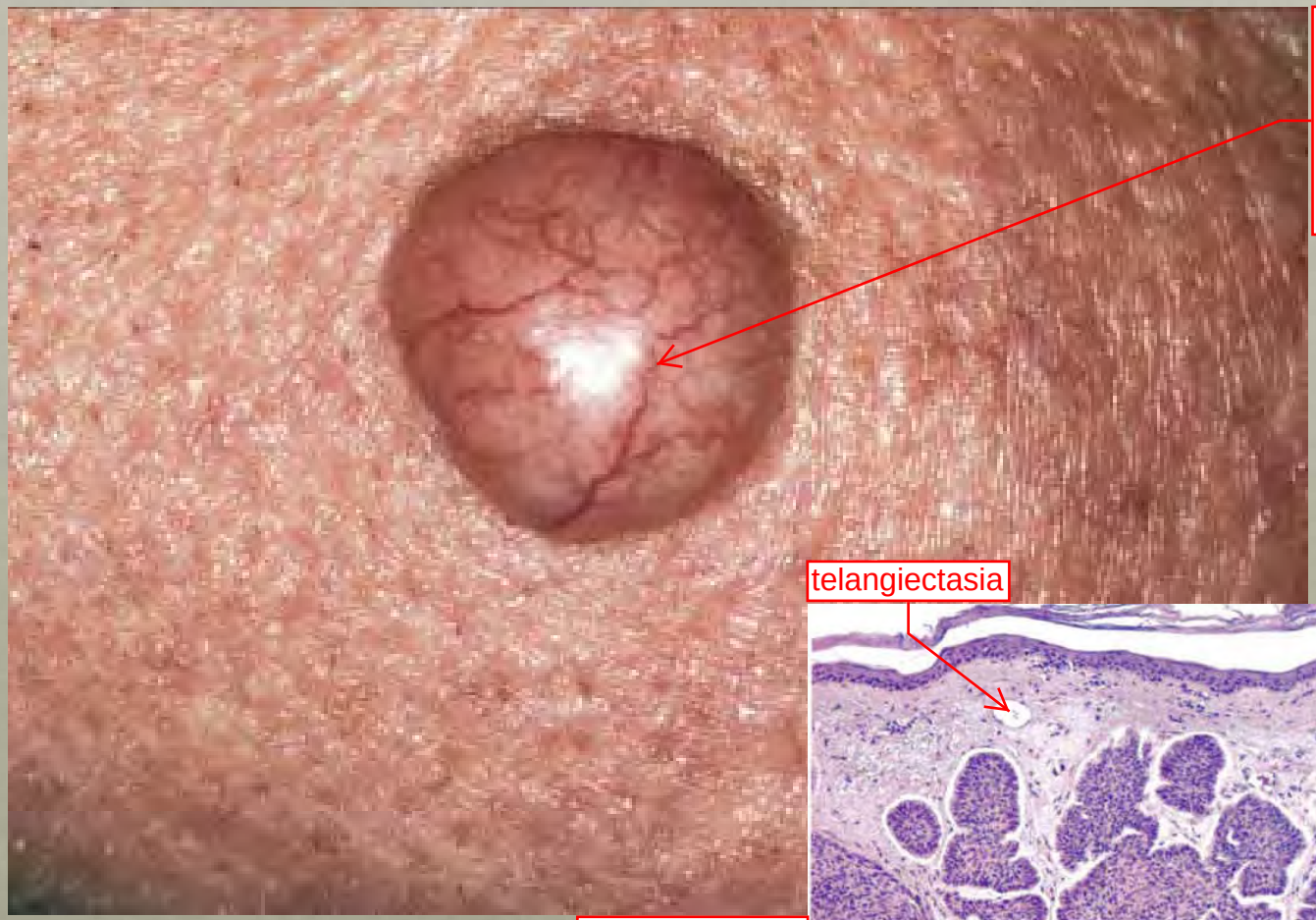
-the second (and the most common) epidermal malignancy is basal cell carcinoma
-BCC recapitulates the basal layer of the epidermis
-it can present clinically as more superficial or deep
-here you see the flat and erythematous appearance of superficial BCC

Basal Cell Carcinoma

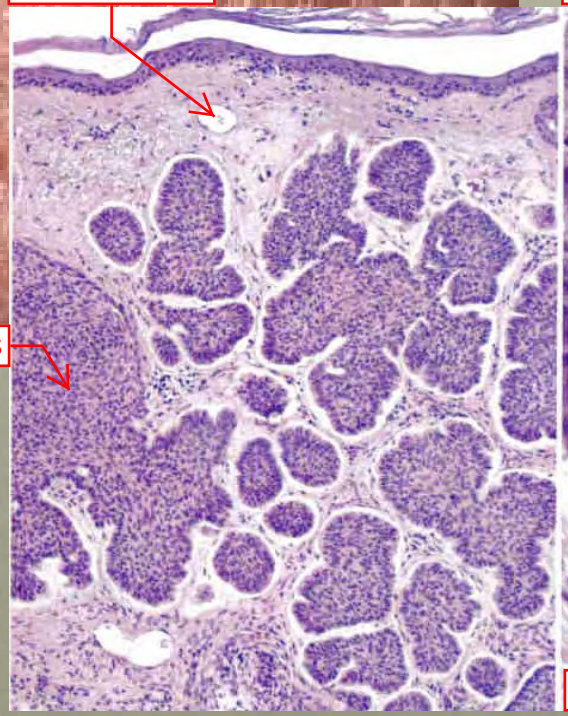


Basal Cell Carcinoma

Basal Cell Carcinoma

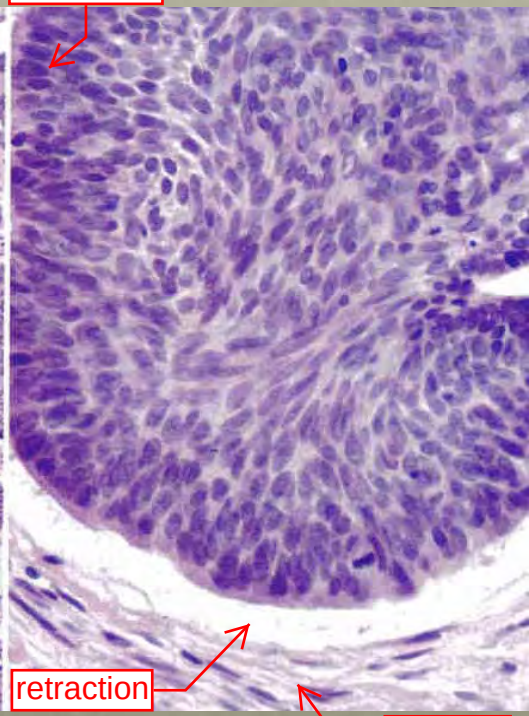


-this is the classic presentation of BCC
-a pearly papule containing prominent, dilated blood vessels (telangiectasias)



telangiectasia

tumor cell nests



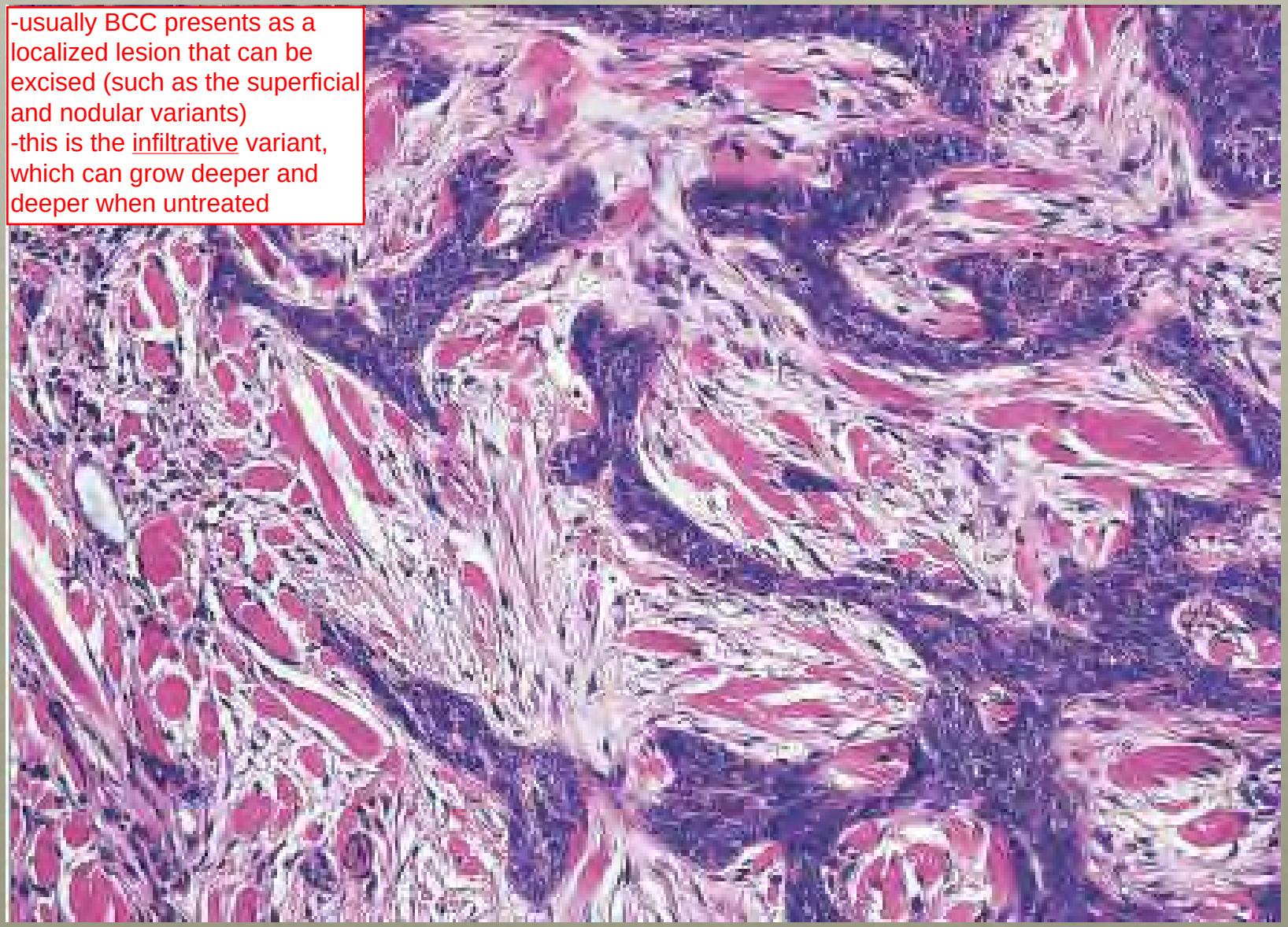
palisading

retraction

stromal reaction

Basal Cell Carcinoma

-usually BCC presents as a localized lesion that can be excised (such as the superficial and nodular variants)
-this is the infiltrative variant, which can grow deeper and deeper when untreated



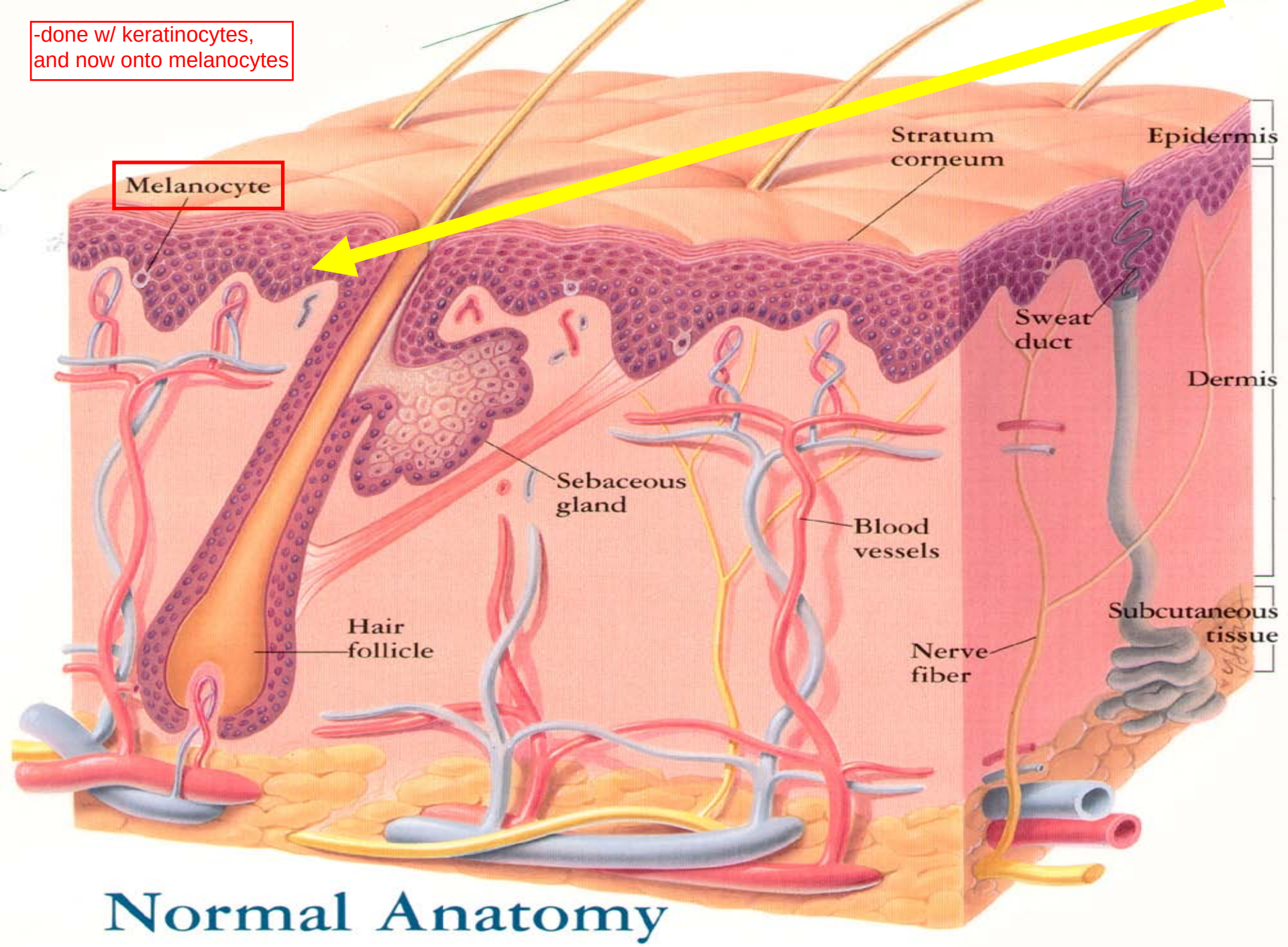
-most of the time BCC presents as a small, pearly papule
-if you let it grow, you can get these kinds of problems

Basal Cell Carcinoma

Basal Cell Carcinoma

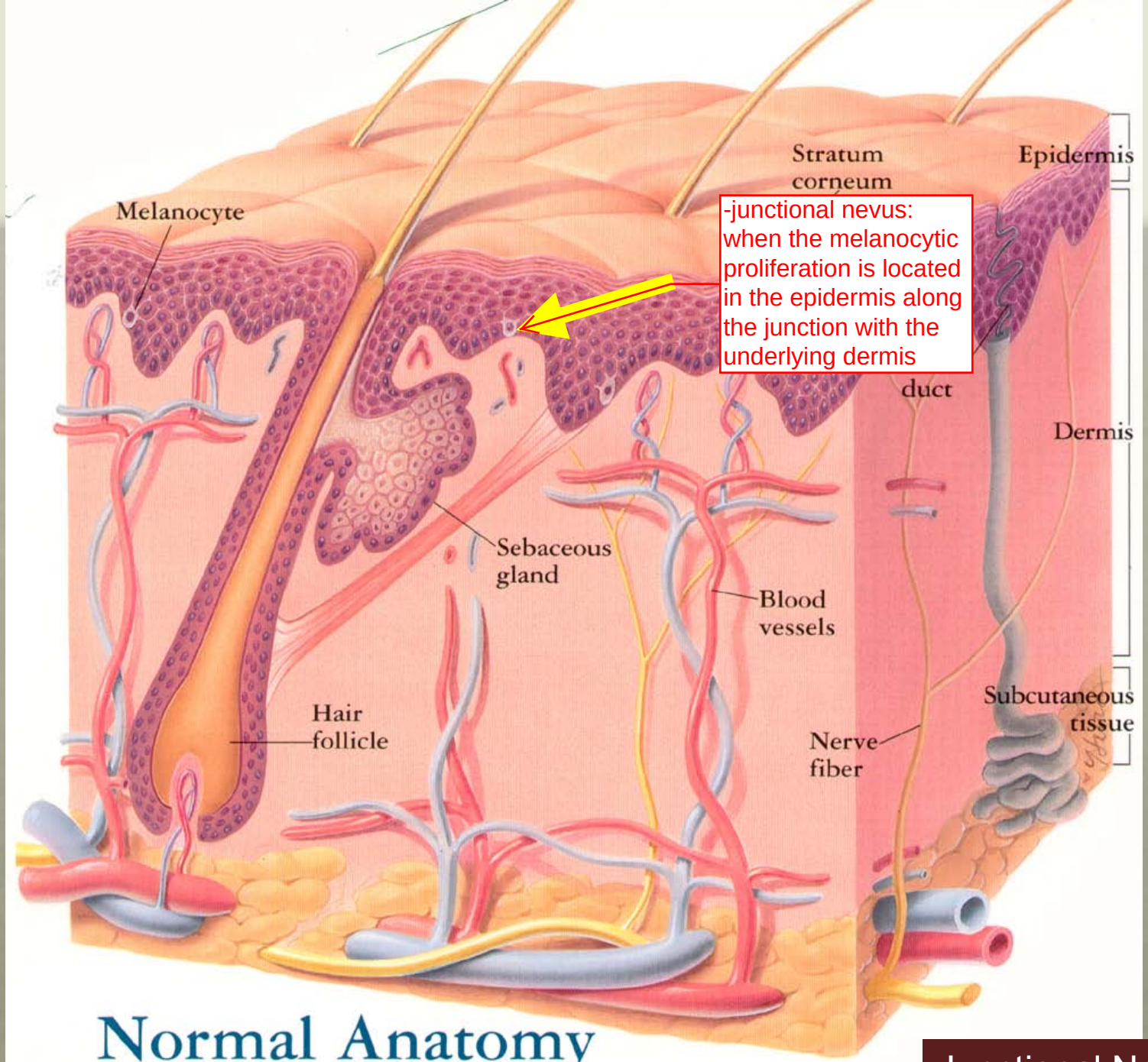
Basal Cell Carcinoma

-done w/ keratinocytes,
and now onto melanocytes

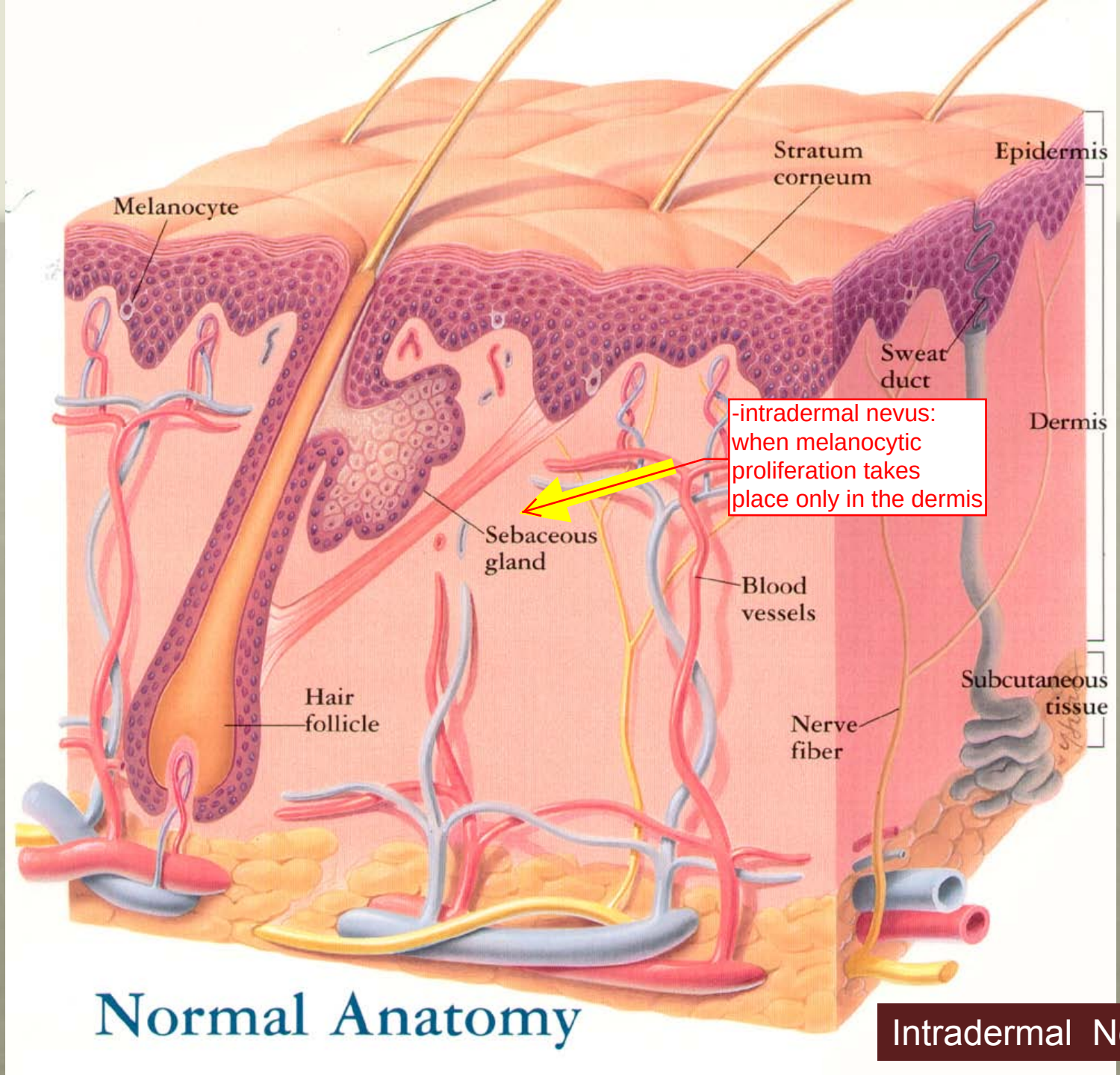


-a nevus is a type of hamartoma (a benign mass of tissue of disproportionate size and distribution but composed of the normal tissue of the region)
-here the benign proliferation is of melanocytes, so a mole is properly called a "melanocytic nevus"

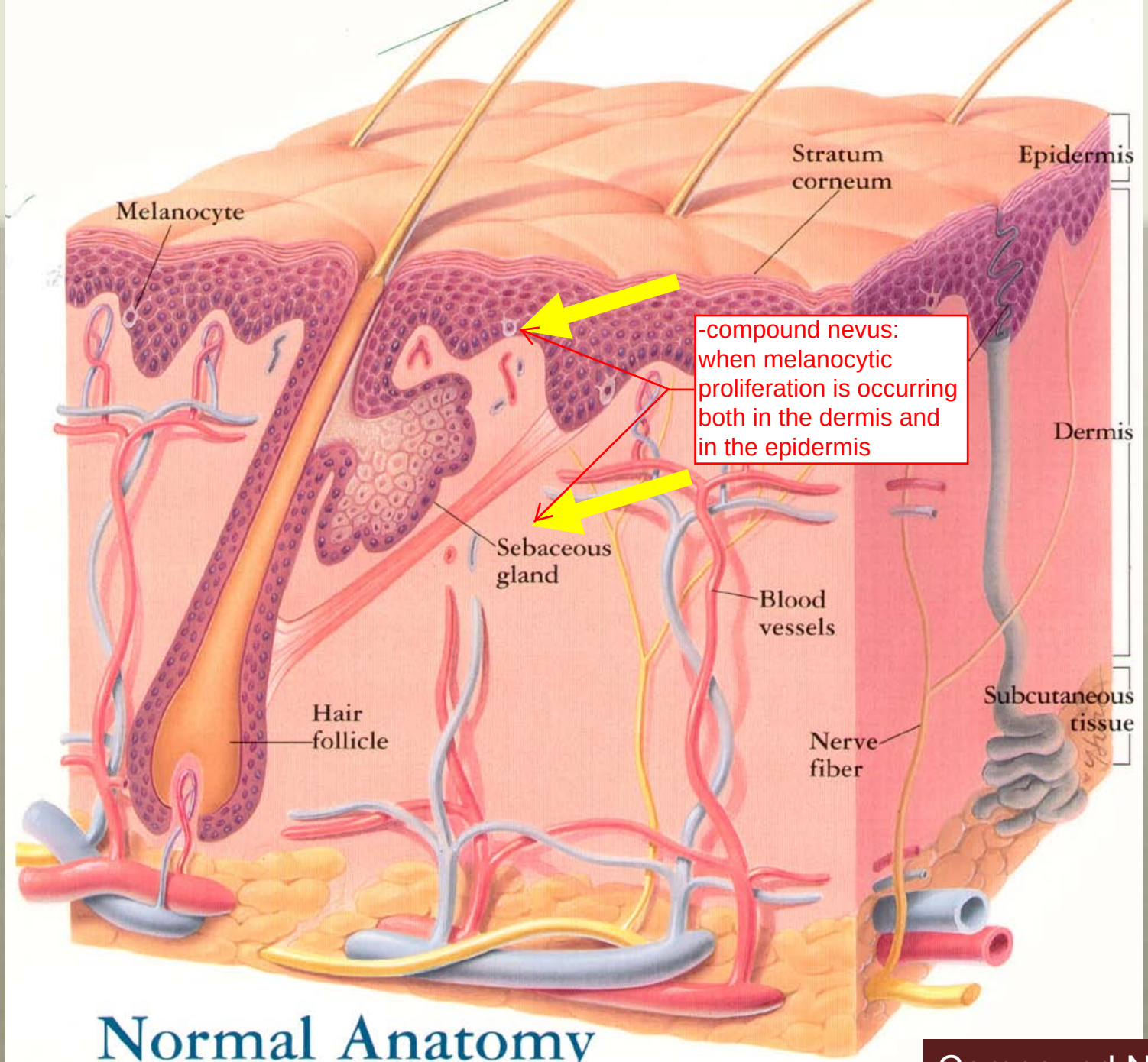
Nevus (mole)



Junctional Nevus



Intradermal Nevus



Compound Nevus

Junctional Nevus

-junctional nevi are characterized by rounded nests of melanocytes originating at the tips of rete ridges (inward projections of the epidermis into the dermis)

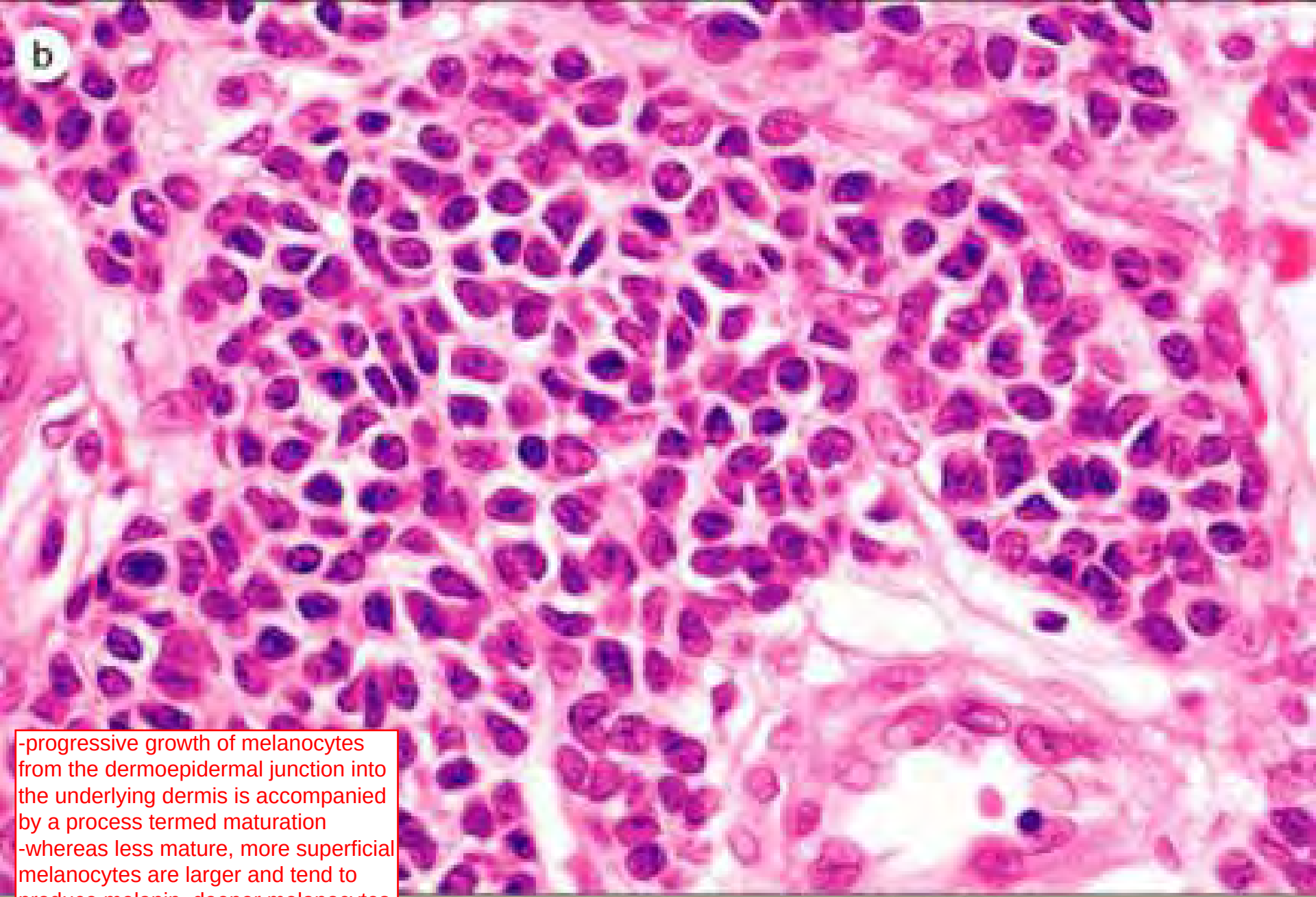
Junctional Nevus

-intradermal nevi are raised due to proliferation in the underlying dermis

Intradermal Nevus

-upon biopsy, see benign proliferation of melanocytes in the dermis

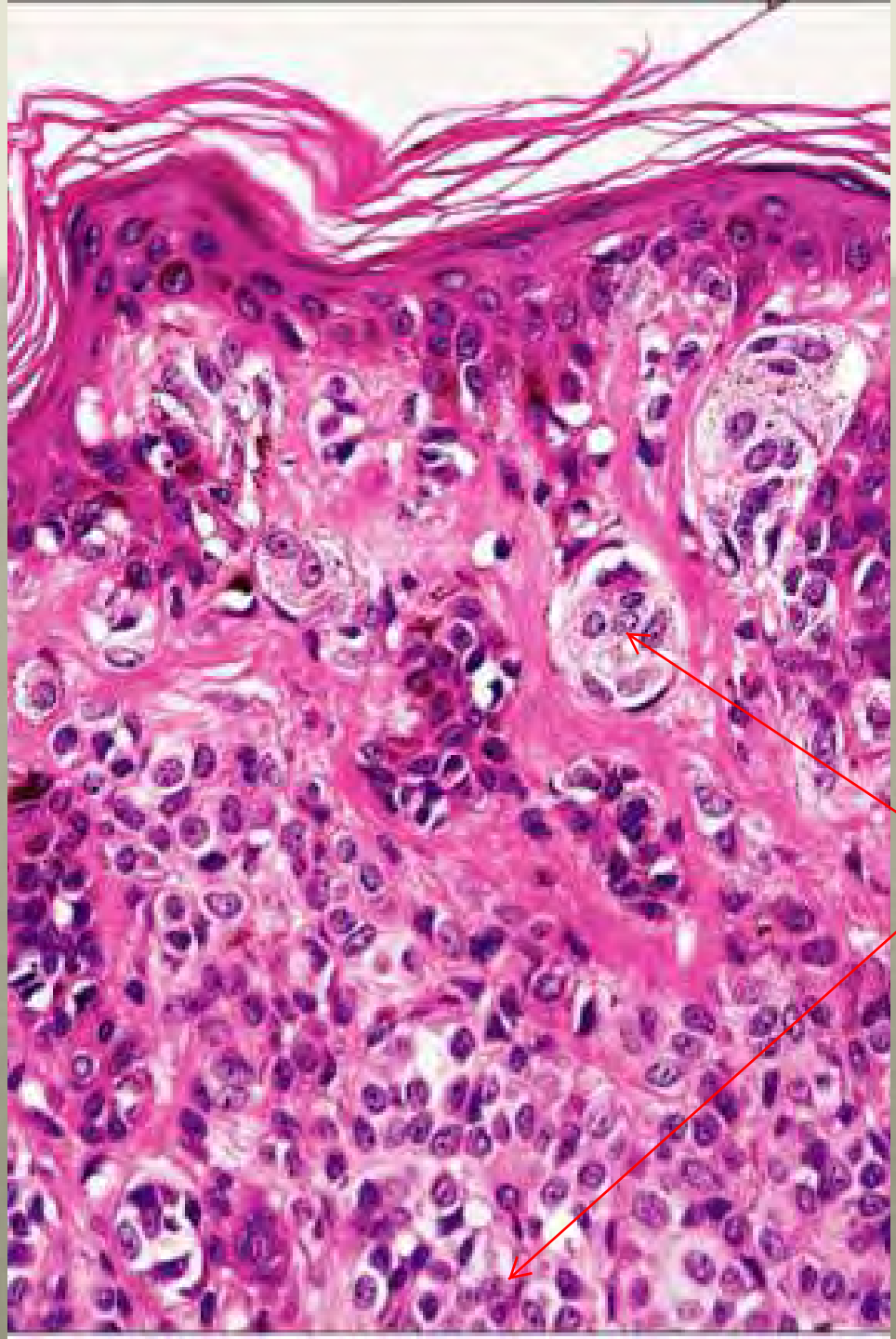
Intradermal Nevus



-progressive growth of melanocytes from the dermoepidermal junction into the underlying dermis is accompanied by a process termed maturation
-whereas less mature, more superficial melanocytes are larger and tend to produce melanin, deeper melanocytes seen here are smaller and produce little or no pigment

Intradermal Nevus

Compound Nevus

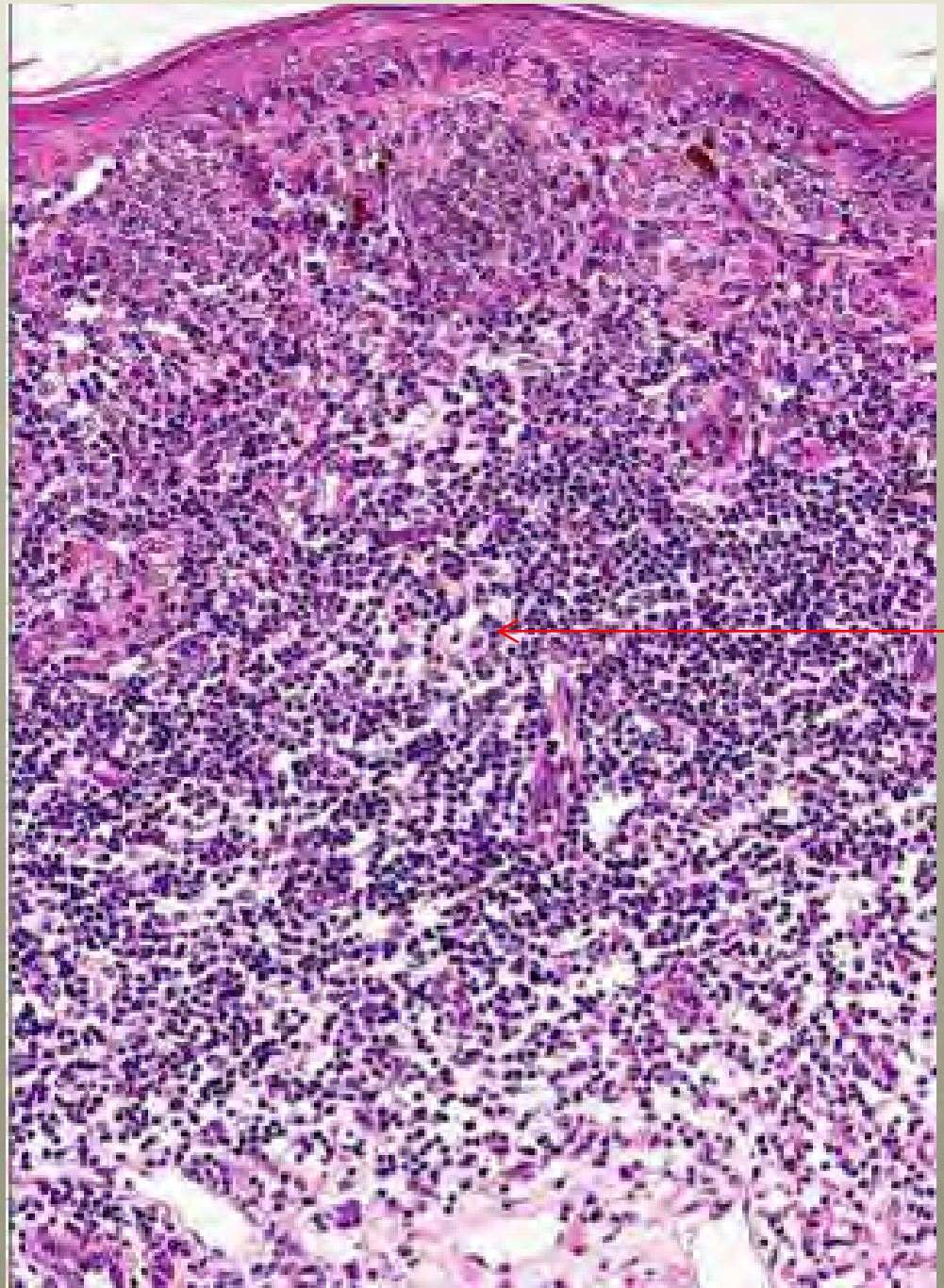


-see both nests in the epidermis and mature melanocytes in the dermis

Compound Nevus


-in a halo nevus, there is a host immune response against the nevus
-when the lymphocytes kill off the melanocytes, this white ring remains

Halo Nevus



-lymphocytic infiltrate
-this may represent a response to either benign or malignant lesions

Halo Nevus

-we're now moving into the malignant proliferation of melanocytes = melanoma
-features include: irregular border, nodular, pigmented w/ multiple colors, asymmetrical, growing

Melanoma

-here are the ABCDE's of melanoma

ASYMMETRY in shape—one half unlike the other

BORDER is irregular—edges irregularly scalloped

COLOR is mottled—haphazard display of colors: shades of brown, black, gray, red, and white

DIAMETER is usually large—greater than the tip of a pencil eraser (6.0 mm)

nevi usually 4-5mm

ENLARGEMENT—a history of an increase in the size of lesion is perhaps one of the most important signs of malignant melanoma

A

B

C

D

E

-dr. selim here applied the ABCDE's to these two lesions
-"if you take anything from this lecture, take the recognition of melanoma."
-stream @ 28:48

Melanoma

-if you don't try to stop it, it can grow like this

Melanoma

-the distinction between the nevi and melanoma is "easy" at this stage
-you need to catch melanoma early, when the nevi first start to change

Melanoma vs Nevi

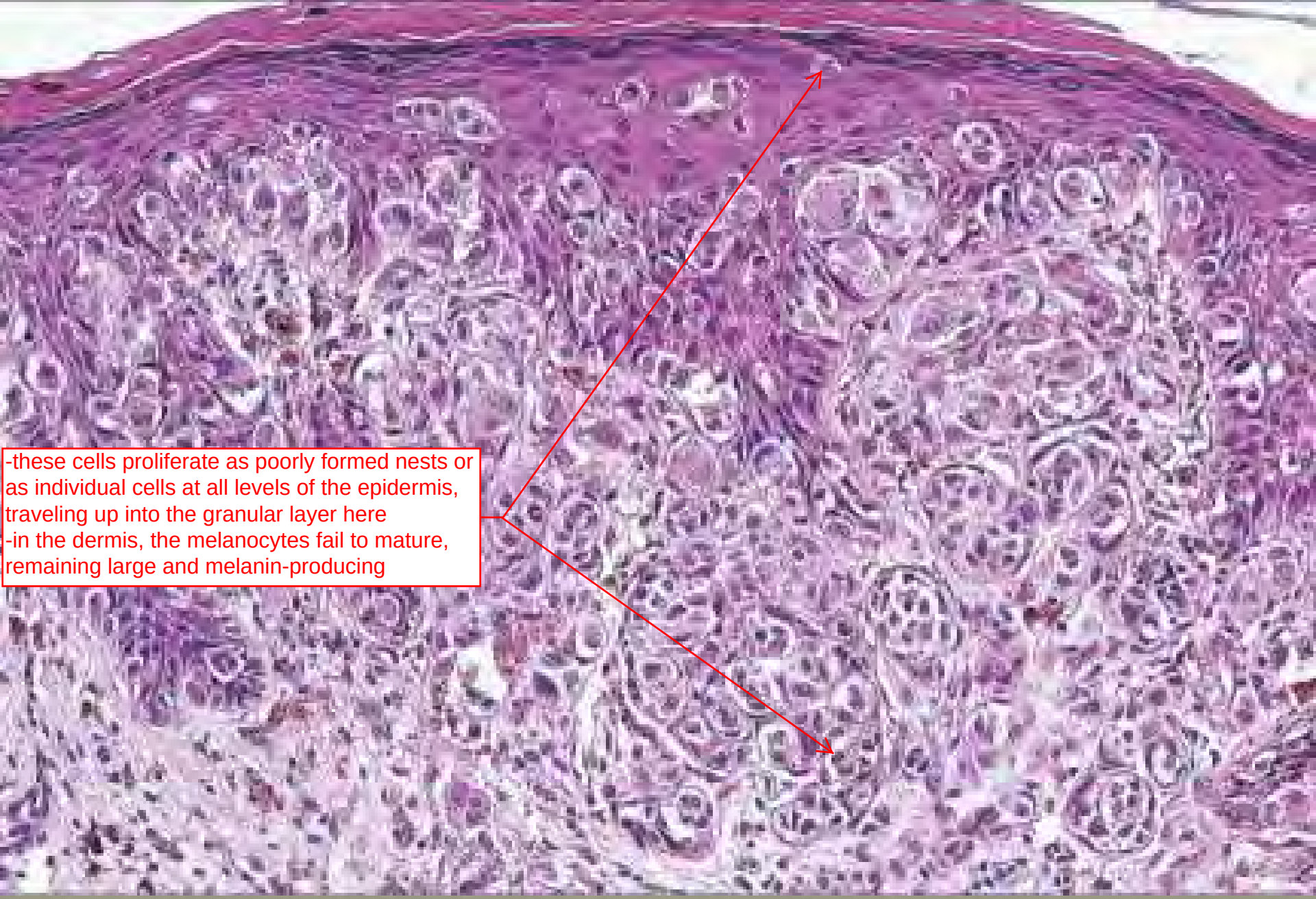
-superficial spreading is most common

-pagetoid = upward spread through the epidermis

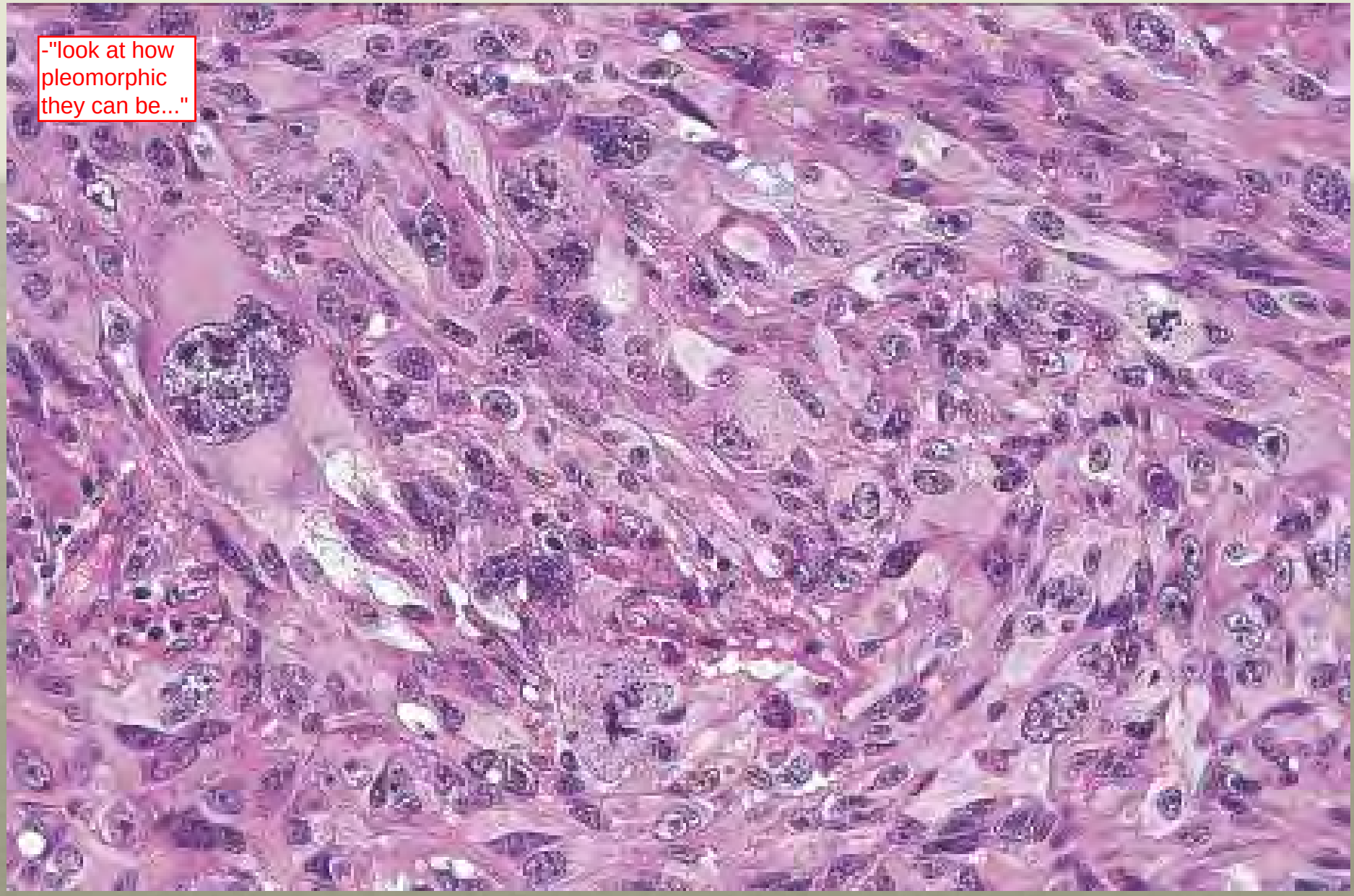
DIFFERENT TYPES OF MALIGNANT MELANOMA				
Type of melanoma	**Frequency (%)**	**Site**	**Radial growth**	**Special features**
Superficial spreading melanoma	60–70	Any site, preference for lower extremities (female), trunk (male)	Yes	More pagetoid, less solar elastosis
Nodular melanoma	15–30	Any site, preference for trunk, head, neck	No	Nodule with vertical growth
Lentigo maligna melanoma	5–15	Face, especially nose and cheeks	Yes	Slower growth over years on sun-damaged skin
Acral lentiginous melanoma	5–10	Palms, soles, subungual	Yes	Most common melanoma in patients with darker skin types

-acral lentiginous shows up on the foot and is more common in pts w/ darker skin

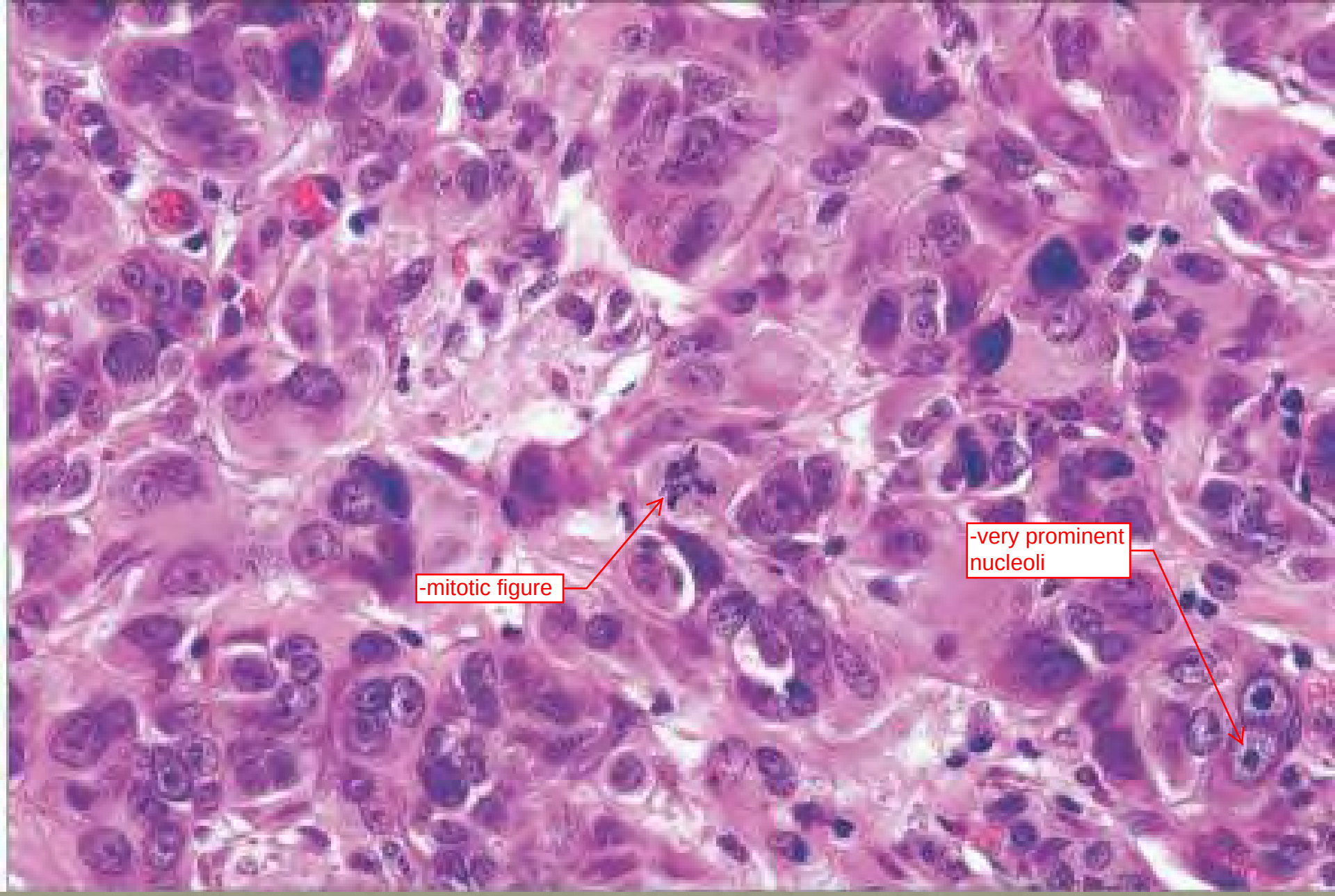
-typical presentation of lentigo maligna is an older pt w/ a flat, brown lesion in a sun-exposed area that suddenly starts to change after yrs


-these cells proliferate as poorly formed nests or as individual cells at all levels of the epidermis, traveling up into the granular layer here
-in the dermis, the melanocytes fail to mature, remaining large and melanin-producing

Melanoma



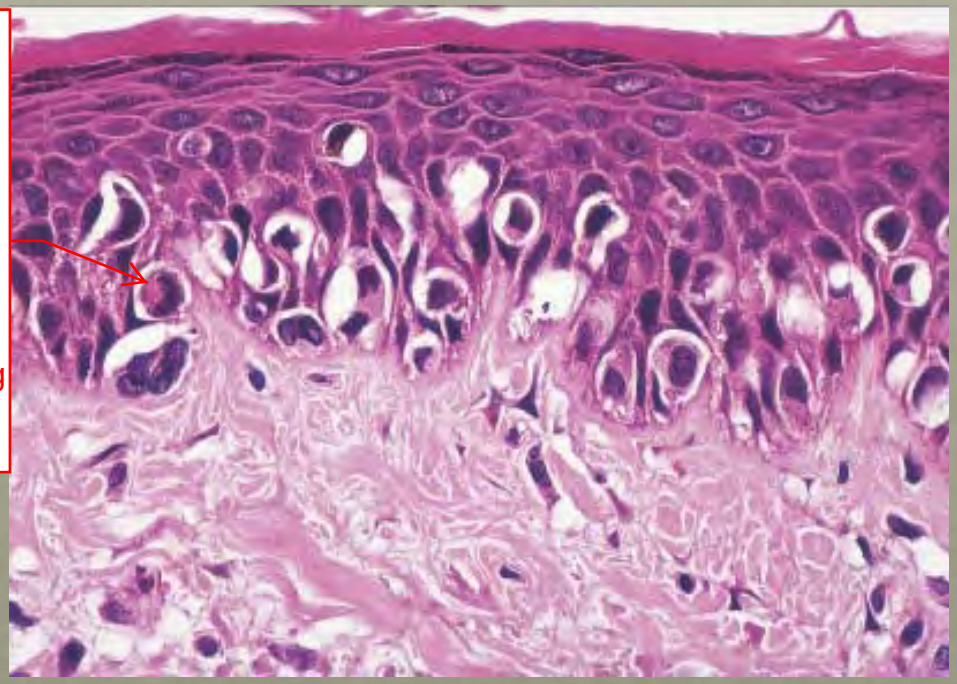
Melanoma



Melanoma

-this is lentigo maligna
-typical presentation of an older pt w/ darkening in a sun-exposed area that has developed over time

-lentigo maligna (seen here) is composed of individual malignant melanocytes limited to the epidermis; it is a melanoma *in situ*
-lentigo maligna melanoma occurs when melanocytes of lentigo maligna-type turn invasive
-this terminology is confusing but important for proper communication



HISTOPATHOLOGICAL REPORTING OF CUTANEOUS MELANOMA

-in addition to reporting a diagnosis, the pathologist is able to predict behavior based on these features

Diagnosis

Thickness (Breslow depth)

-the measure of thickness estimates tumor volume
-more tumor = worse behavior

Mitoses/mm^2

Level of invasion (Clark)

Regression, tumor infiltrating lymphocytes, presence of plasma cells

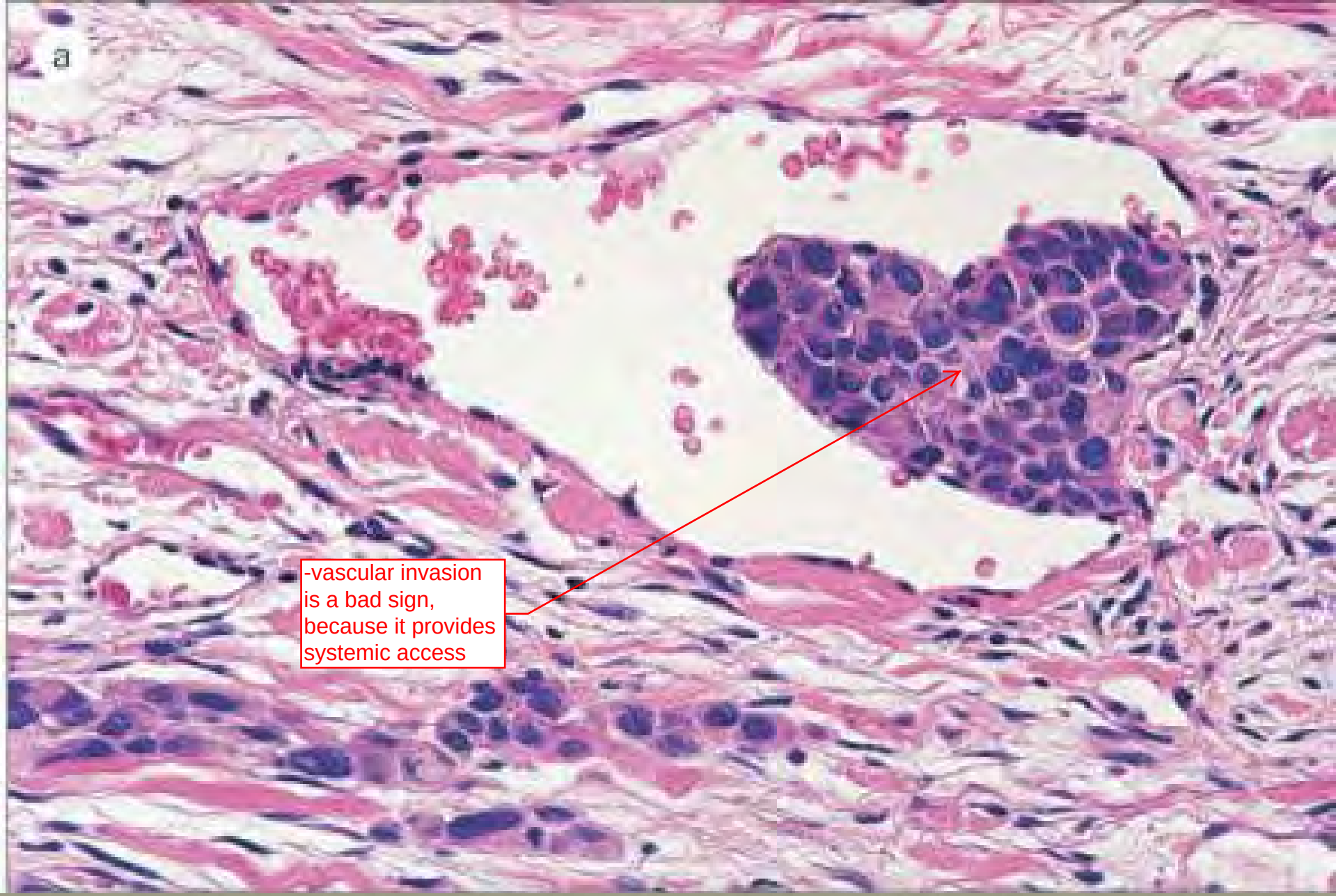
Ulceration

Vascular invasion

Microscopic satellites

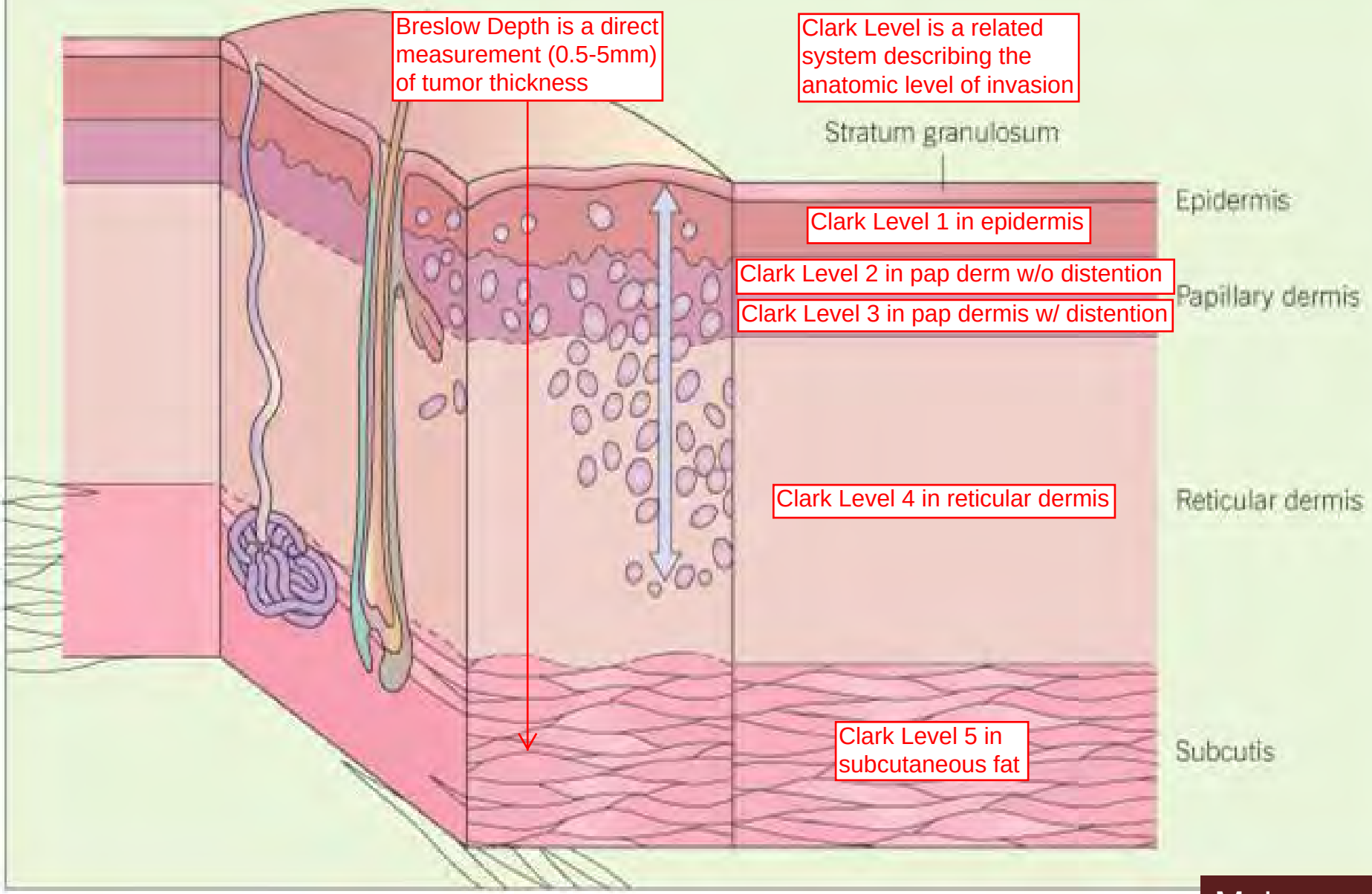
Associated nevus

Margins


a
-vascular invasion is a bad sign, because it provides systemic access

Melanoma

MICROSTAGING OF CUTANEOUS MELANOMA – BRESLOW'S METHOD



-all of these features translate into the familiar TNM staging system

MELANOMA TNM CLASSIFICATION		
T classification	**Thickness**	**Ulceration status**
T1	1.0 mm	a: Without ulceration and level II/III b: With ulceration or level IV/V
T2	1.01–2.0 mm	a: Without ulceration b: With ulceration
T3	2.01–4.0 mm	a: Without ulceration b: With ulceration
T4	> 4.0 mm	a: Without ulceration b: With ulceration
N classification	**Number of metastatic nodes**	**Nodal metastatic mass**
N1	1 node	a: Micrometastasis* b: Macrometastasis
N2	2–3 nodes	a: Micrometastasis* b: Macrometastasis† c: In transit met(s)/satellite(s) without metastatic node(s)
N3	4 or more metastatic nodes, or matted nodes, or in transit met(s)/satellite(s) with metastatic node(s)	
M classification	**Site**	**Serum lactate dehydrogenase**
M1a	Distant skin, subcutaneous, or nodal mets	Normal
M1b	Lung metastases	Normal
M1c	All other visceral metastases Any distant metastasis	Normal Elevated

-"don't look at all this; it's too much information."
-the point is that stage is predictive of survival, so try to catch early while localized (IA)

PROPOSED STAGE GROUPINGS FOR CUTANEOUS MELANOMA

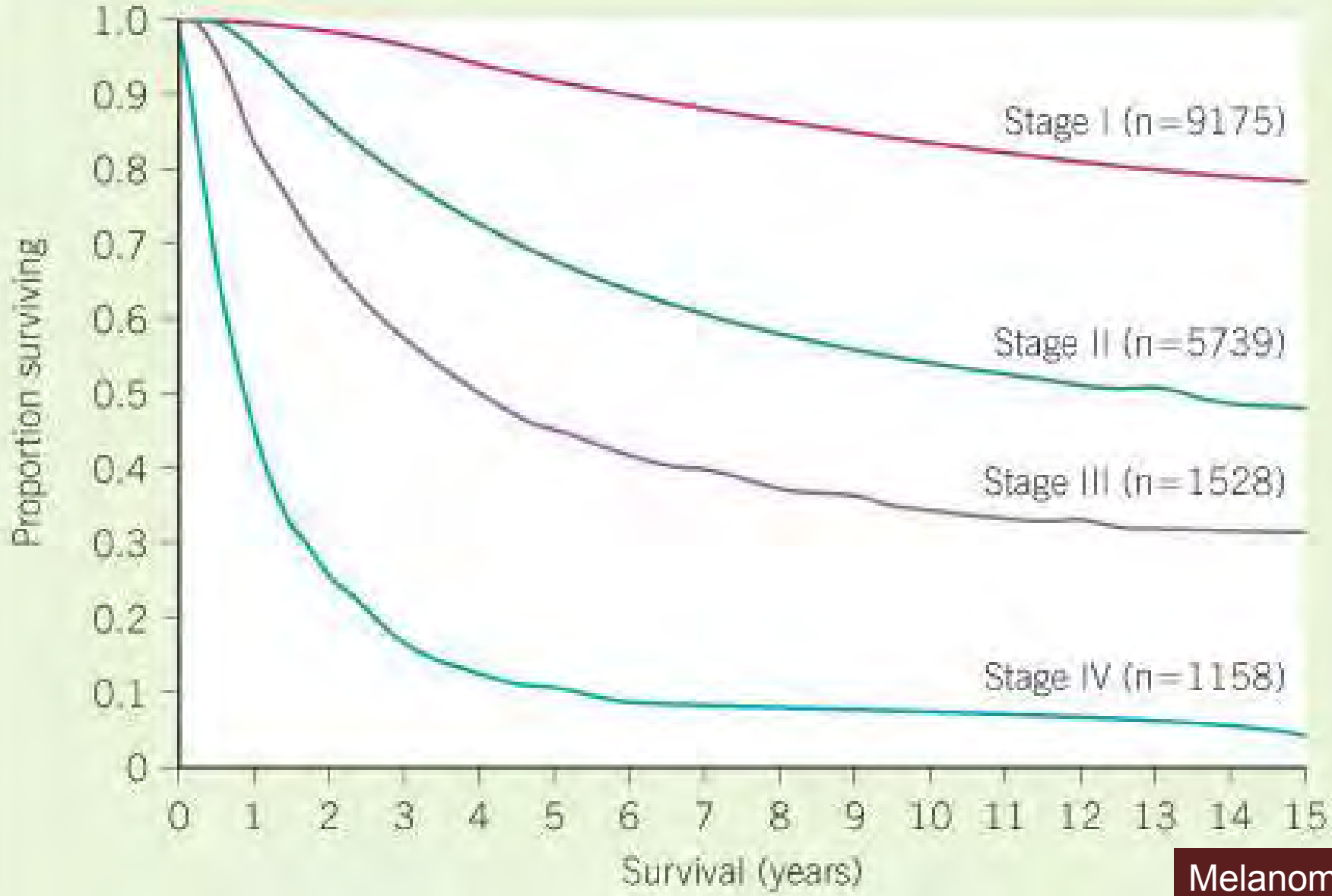
	Survival (%)*	Clinical staging†			Pathologic staging‡		
		T	N	M	T	N	M
0		Tis	N0	M0	Tis	N0	M0
IA	95	T1a	N0	M0	T1a	N0	M0
IB	90	T1b T2a	N0	M0	T1b T2a	N0	M0
IIA	78	T2b T3a	N0	M0	T2b T3a	N0	M0
IIB	65	T3b T4a	N0	M0	T3b T4a	N0	M0
IIC	45	T4b	N0	M0	T4b	N0	M0
III#		Any T	N1 N2 N3	M0			M0
IIIA	66				T1-4a T1-4a	N1a N2a	M0
IIIB	52				T1-4b T1-4b T1-4a T1-4a T1-4a/b	N1a N2a N1b N2b N2c	M0
IIIC	26				T1-4b T1-4b Any T	N1b N2b N3	M0
IV	7.5–11	Any T	Any N	Any M1	Any T	Any N	Any M1

-terrible survival at Stage IV

Melanoma

-same point as last

COMPARISON OF SURVIVAL CURVES IN FOUR STAGES OF MELANOMA



Melanoma

-Breslow Depth also determines excision margins in surgery

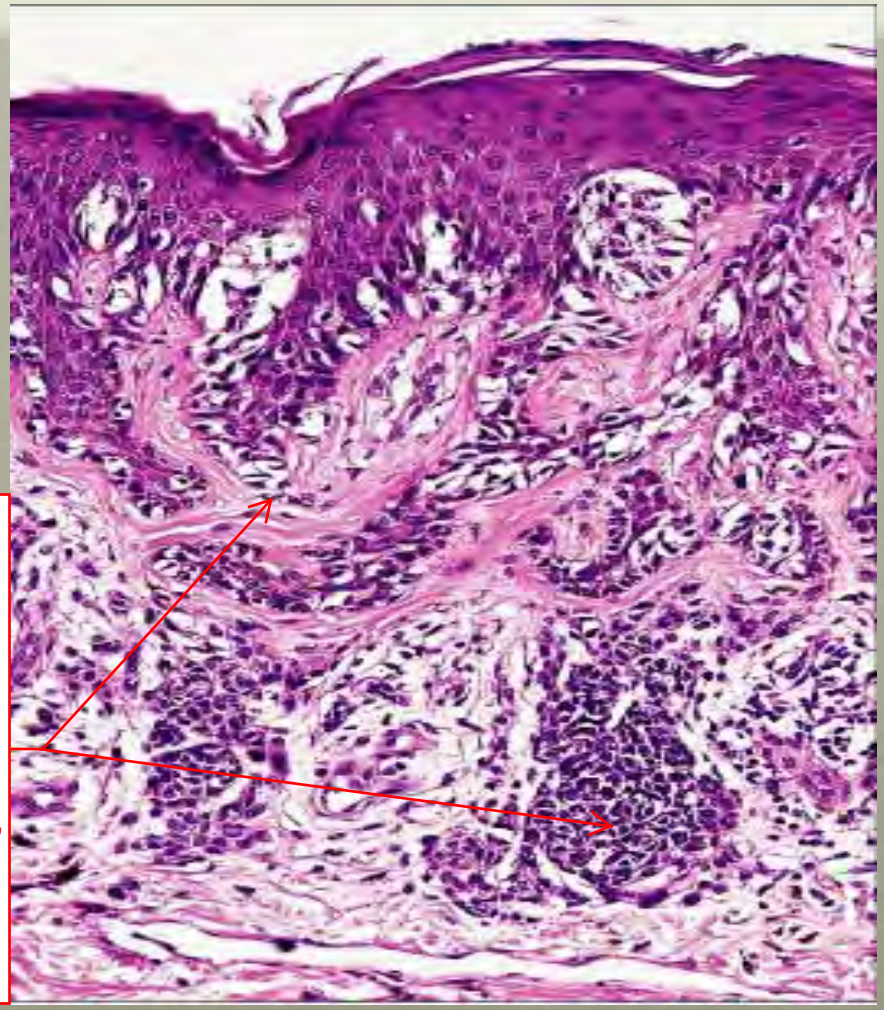
SURGICAL TREATMENT OF PRIMARY MELANOMA

Thickness	Excision margins (cm)	Comments
In situ	0.5	No randomized studies, lentigo maligna of the face might be treated with radiotherapy in specialized centers[93]
<1 mm	1.0	AAD task force suggests 1 cm margin for melanoma <2 mm[67]
1–4 mm	2.0	AAD task force suggests 2 cm margin for melanoma ≥2 mm[67]
>4 mm	2.0–3.0	No randomized studies

-pts w/ dysplastic nevus syndrome have hundreds of irregular lesions on the body surface
-dysplastic nevi are associated w/ an increased risk of developing melanoma
-these fall somewhere between benign melanocytic nevi and malignant melanoma

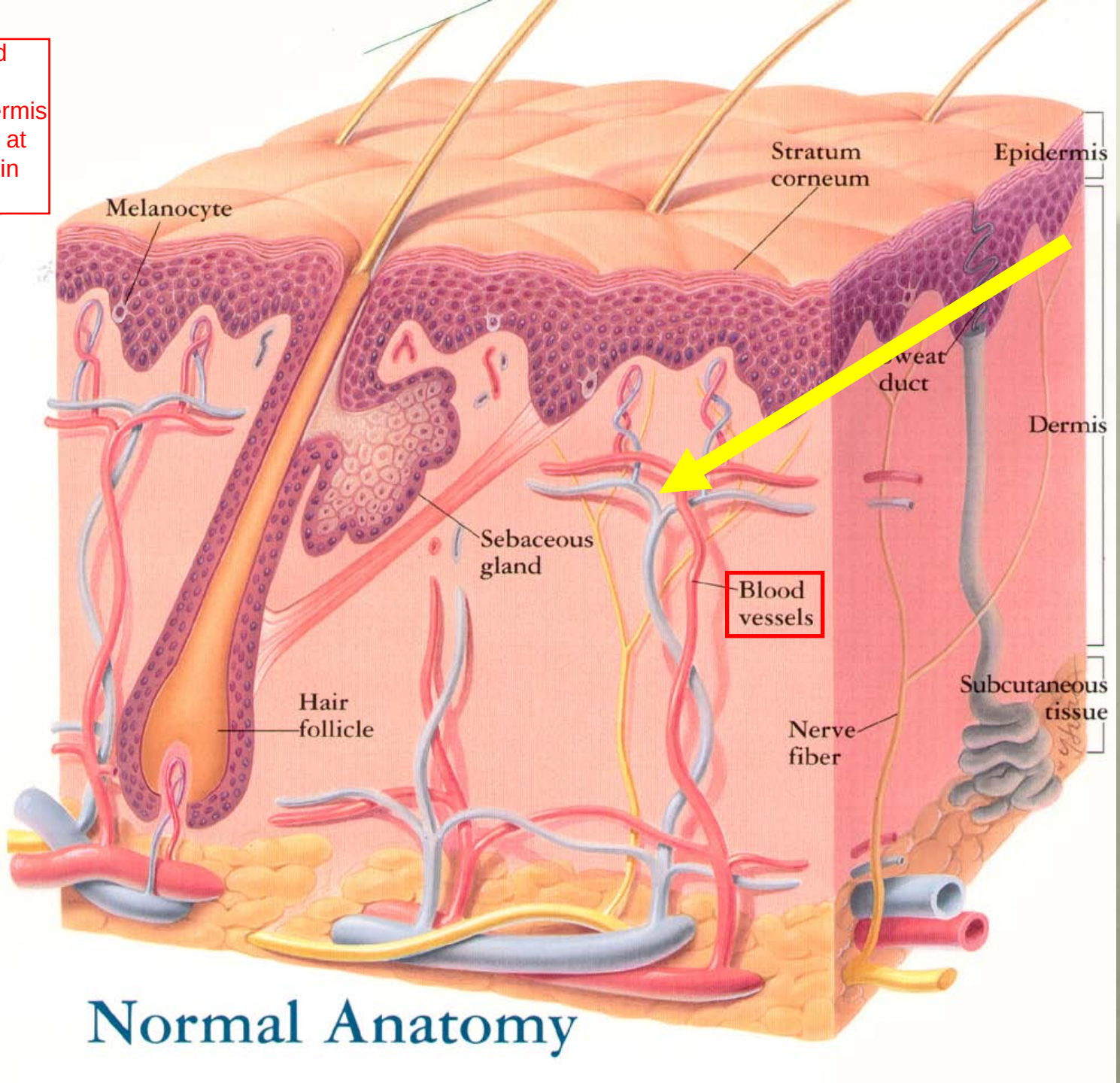
Dysplastic Nevus

-dysplastic nevi show both architectural and cytologic evidence of abnormal growth
-nests within the epidermis may be enlarged and exhibit abnormal fusion or coalescence with adjacent nests
-melanocytes are still maturing as they descend into the dermis, meaning that they are not becoming malignant
-this process is between benign and malignant



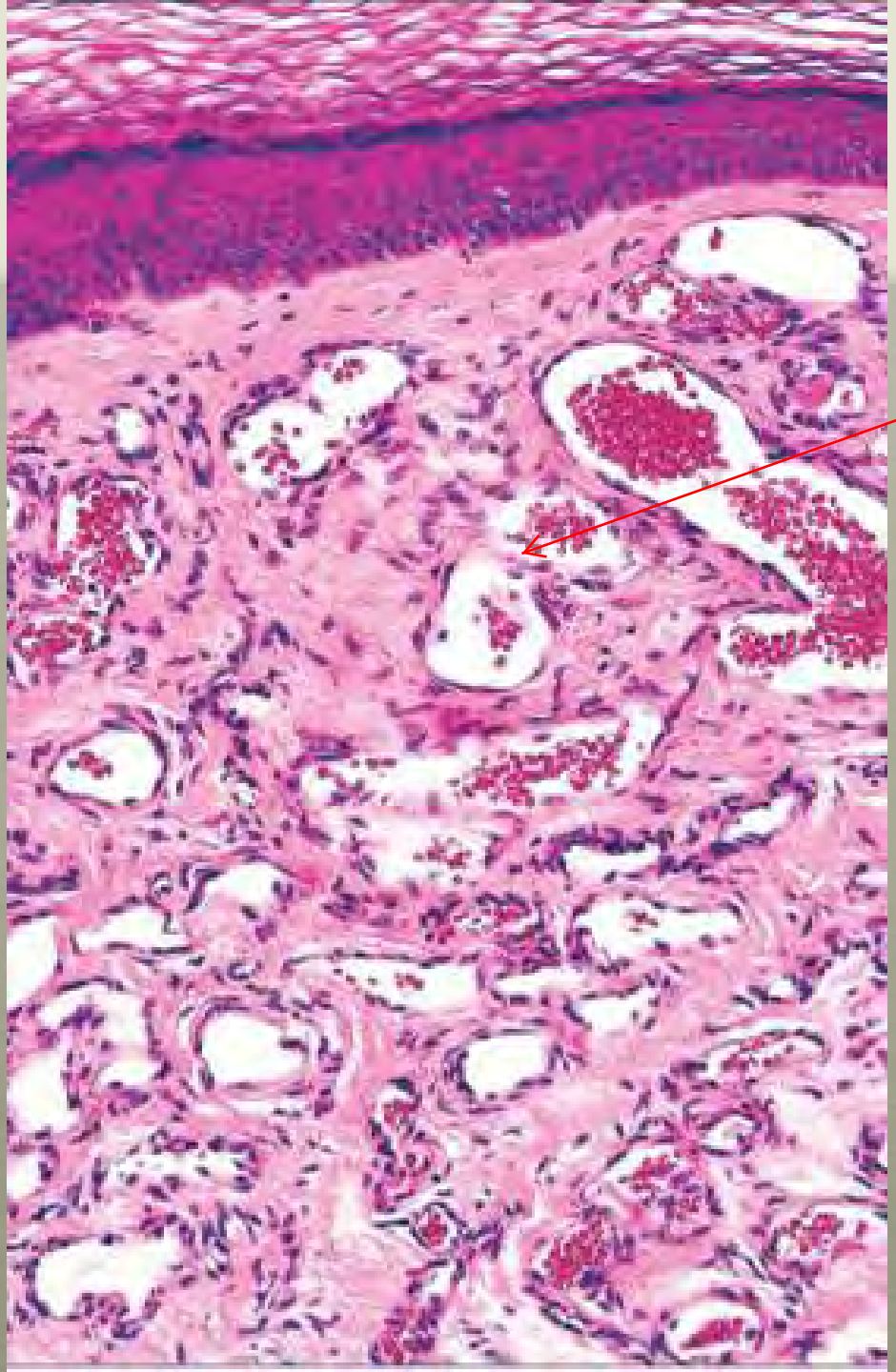
Dysplastic Nevus

-finally finished lesions arising from the epidermis
-now let's look at blood vessels in the dermis...



-hemangioma = a benign vascular neoplasm
-can tell it's vascular by its red color
-when a child presents w/ a cutaneous lesion of vascular origin, most of the time it is benign

Hemangioma



-see back-to-back proliferation of vessels in the dermis
-the endothelial lining appears benign

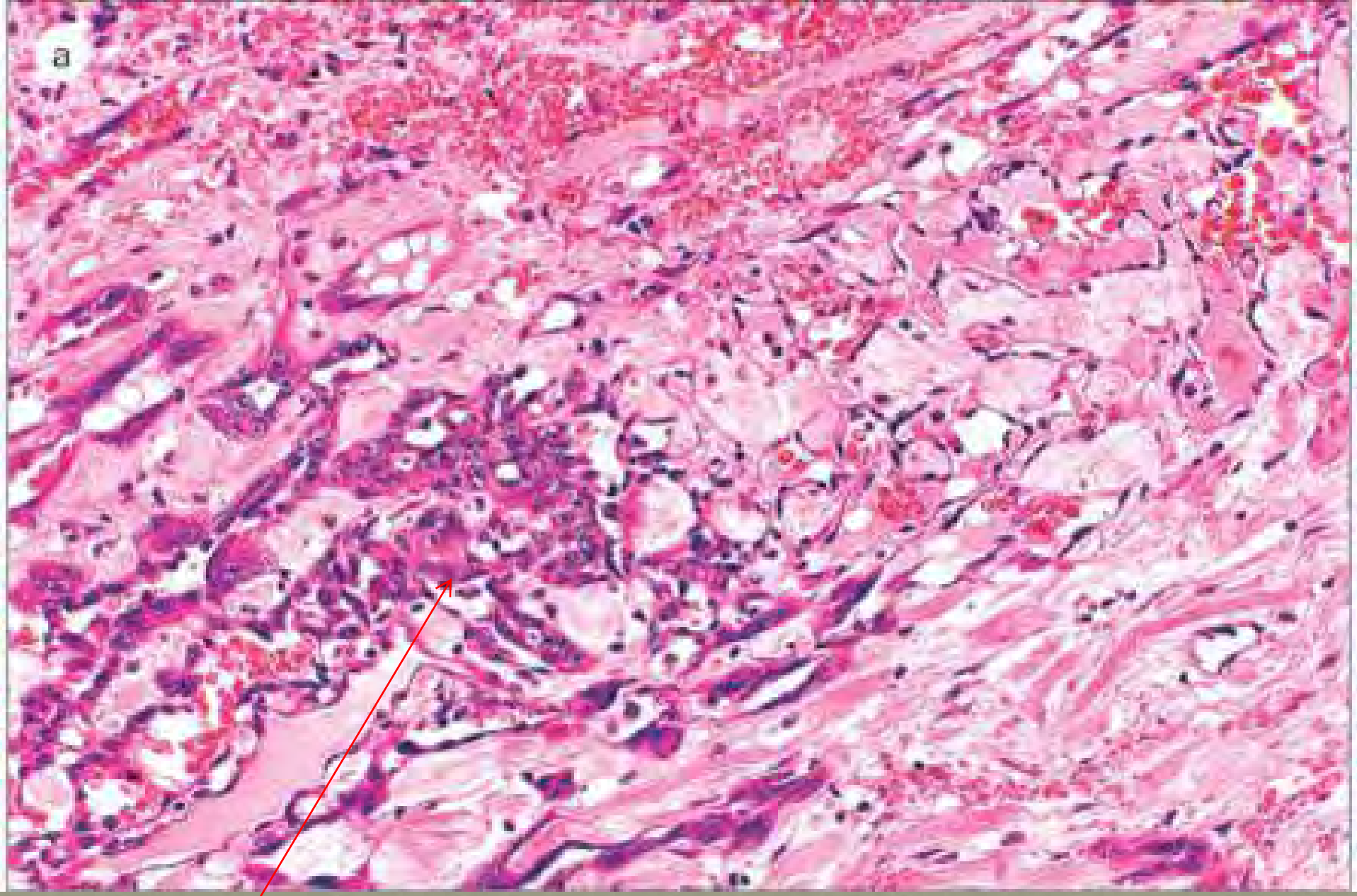
Hemangioma

-with laser, you can burn out the vessels and treat superficial lesions if they appear in cosmetically significant areas

Hemangioma

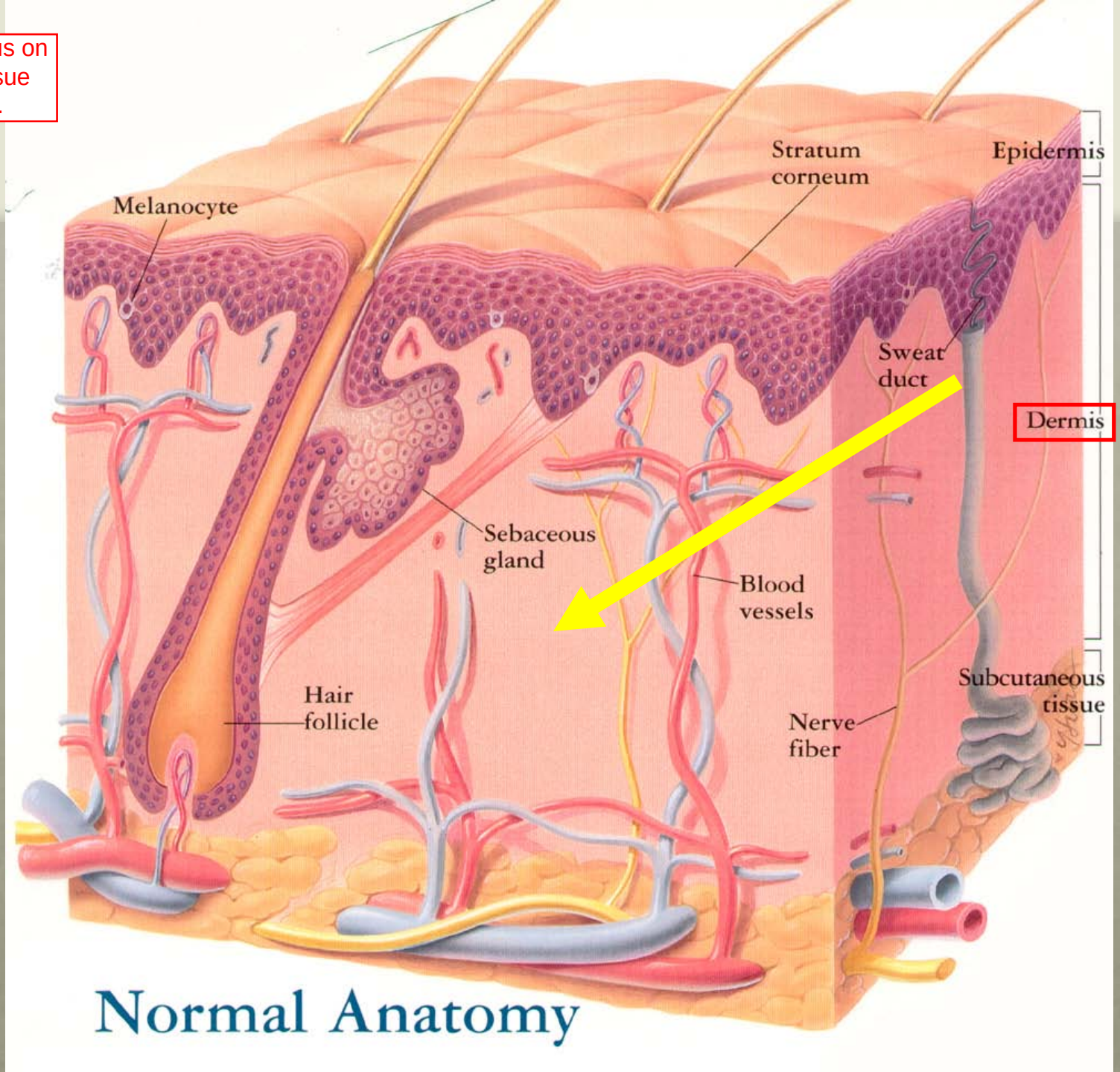
-angiosarcoma = a malignant endothelial neoplasm
-see irregularity, ulceration, bleeding, masses being formed

Angiosarcoma



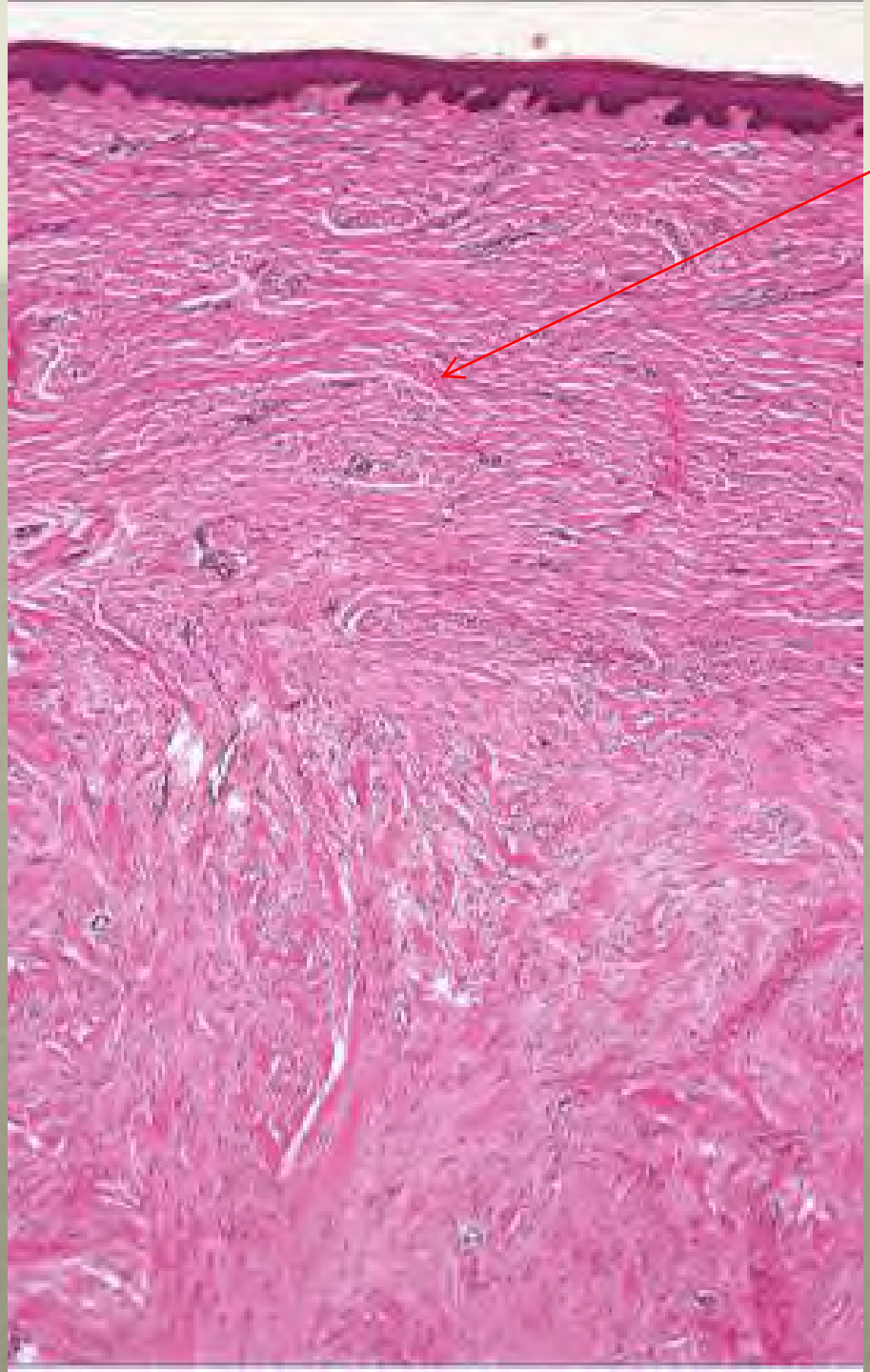
Angiosarcoma

-now we'll focus on connective tissue in the dermis...



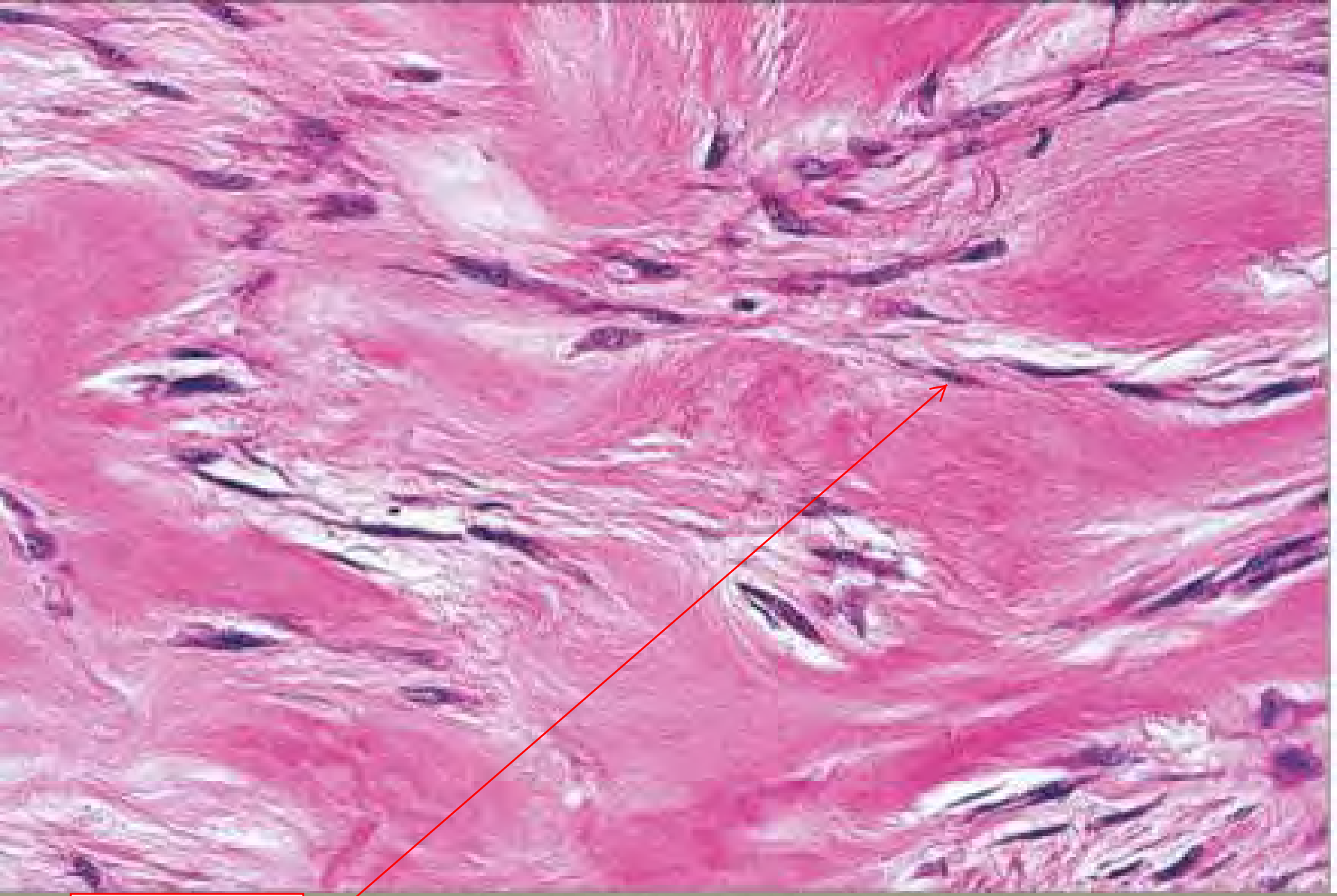

-keloid = a benign overgrowth of collagen that forms a hypertrophic scar in response to trauma

Keloid



-Note the very thick bundles of collagen deposition in the dermis
-totally benign; only a cosmetic issue

Keloid

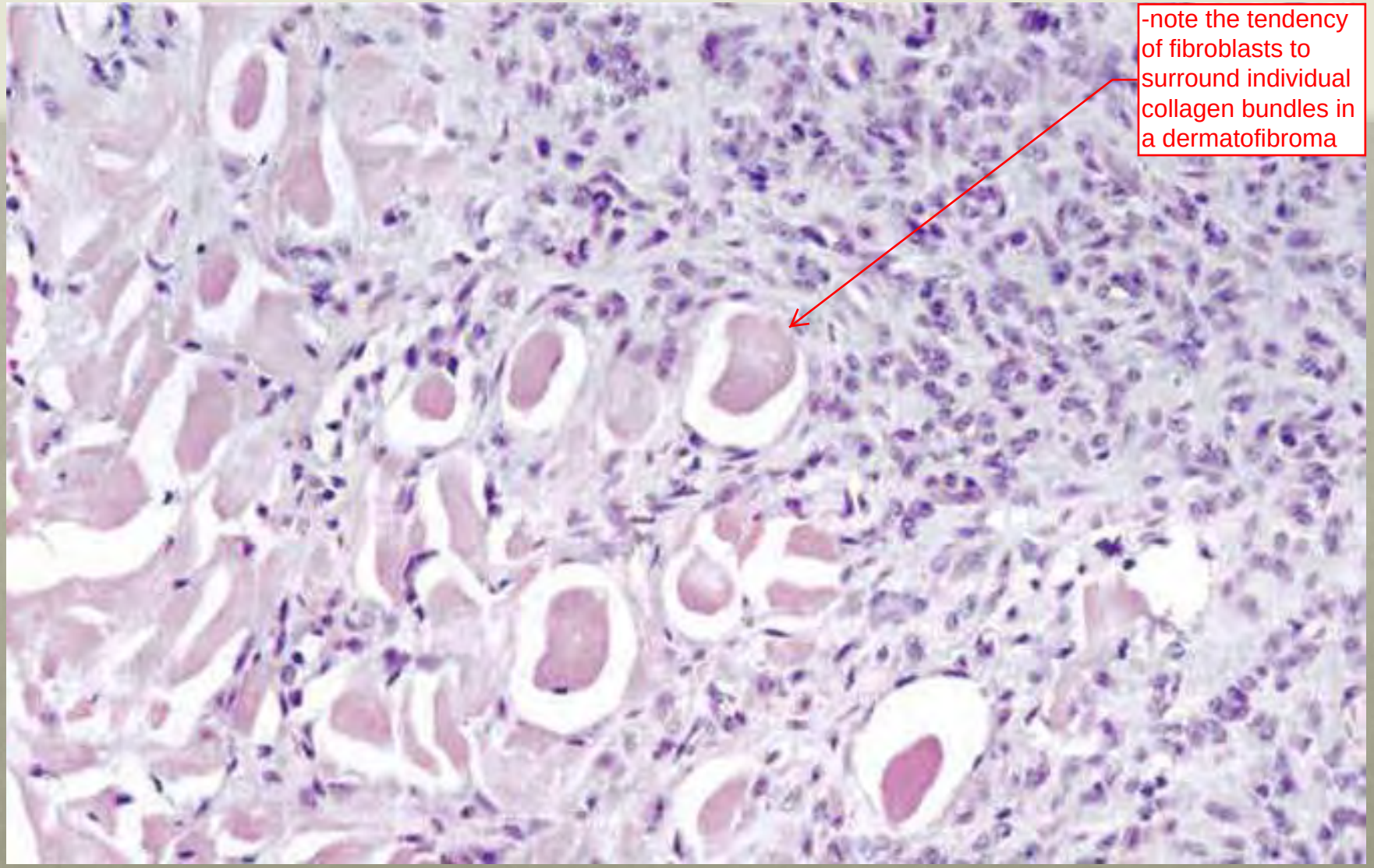


Keloid

-dermatofibroma = a benign dermal neoplasm of fibroblasts
-usually seen in adults, and often occur on the legs of young to middle-aged women
-many cases have a history of antecedent trauma, suggesting an abnormal response to injury and inflammation
-these neoplasms are firm, tan to brown papules
-dimple inward on lateral compression, which is helpful for distinguishing w/o biopsy

Dermatofibroma

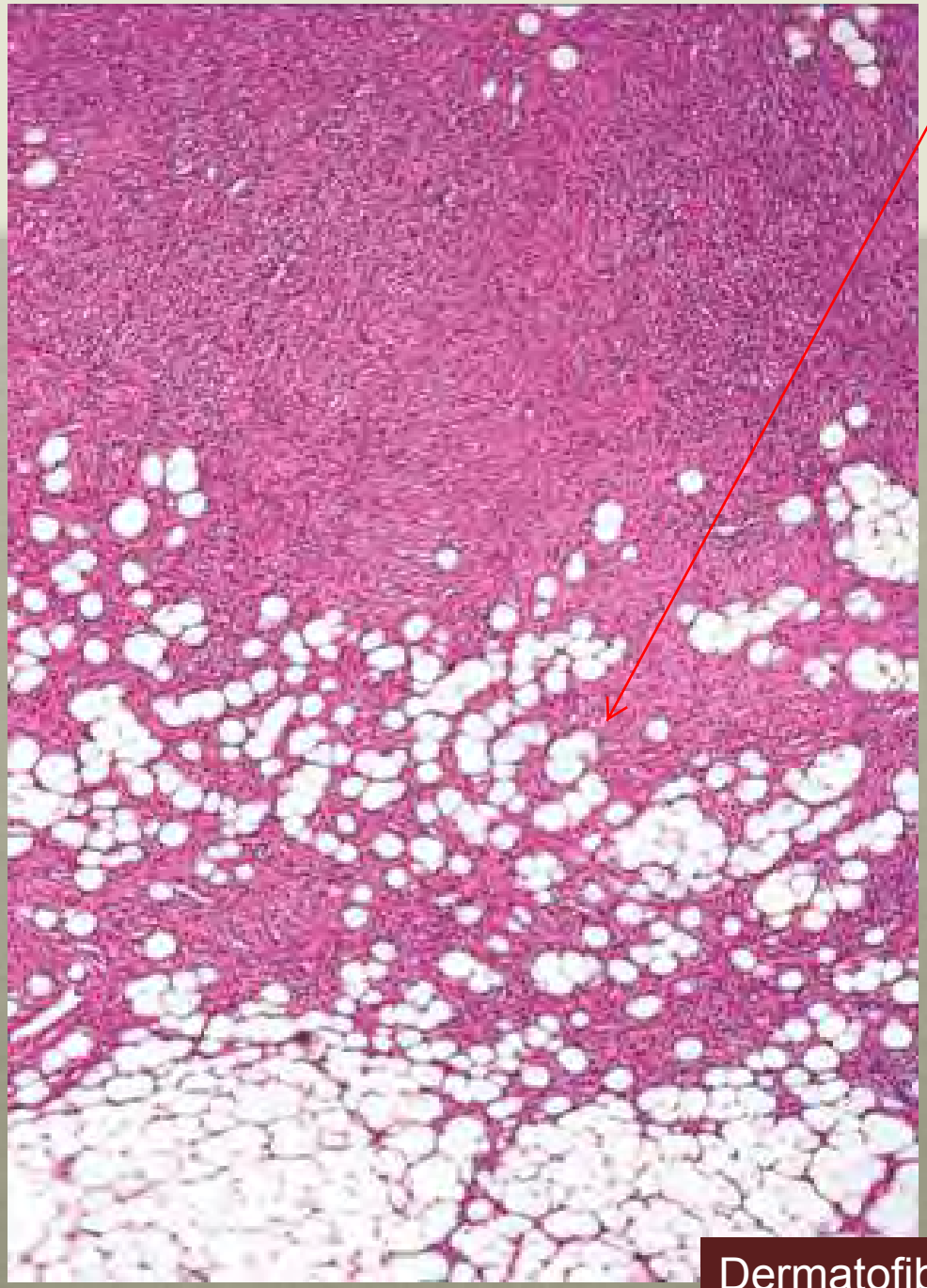
Dermatofibroma



Dermatofibroma

-dermatofibrosarcoma protuberans is best regarded as a well-differentiated, primary fibrosarcoma of the skin
-these tumors are slow growing, and although they are locally aggressive, they rarely metastasize; thus, this is an "in between" lesion
-called "protuberans", because it develops as aggregated protuberant nodules

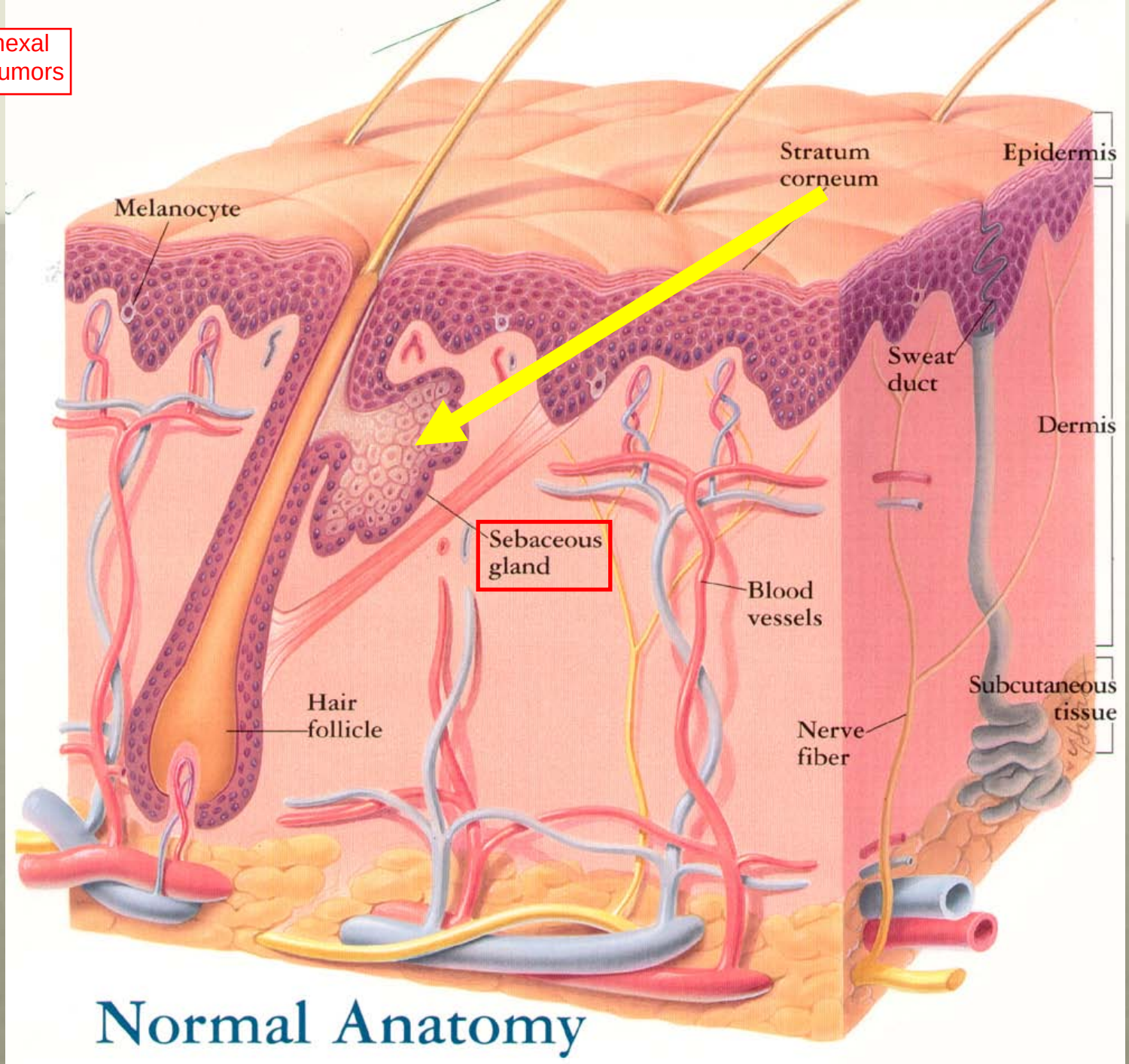
Dermatofibrosarcoma protuberans



-very cellular
-deep extension from the dermis into subcutaneous fat, producing a characteristic "honeycomb" pattern

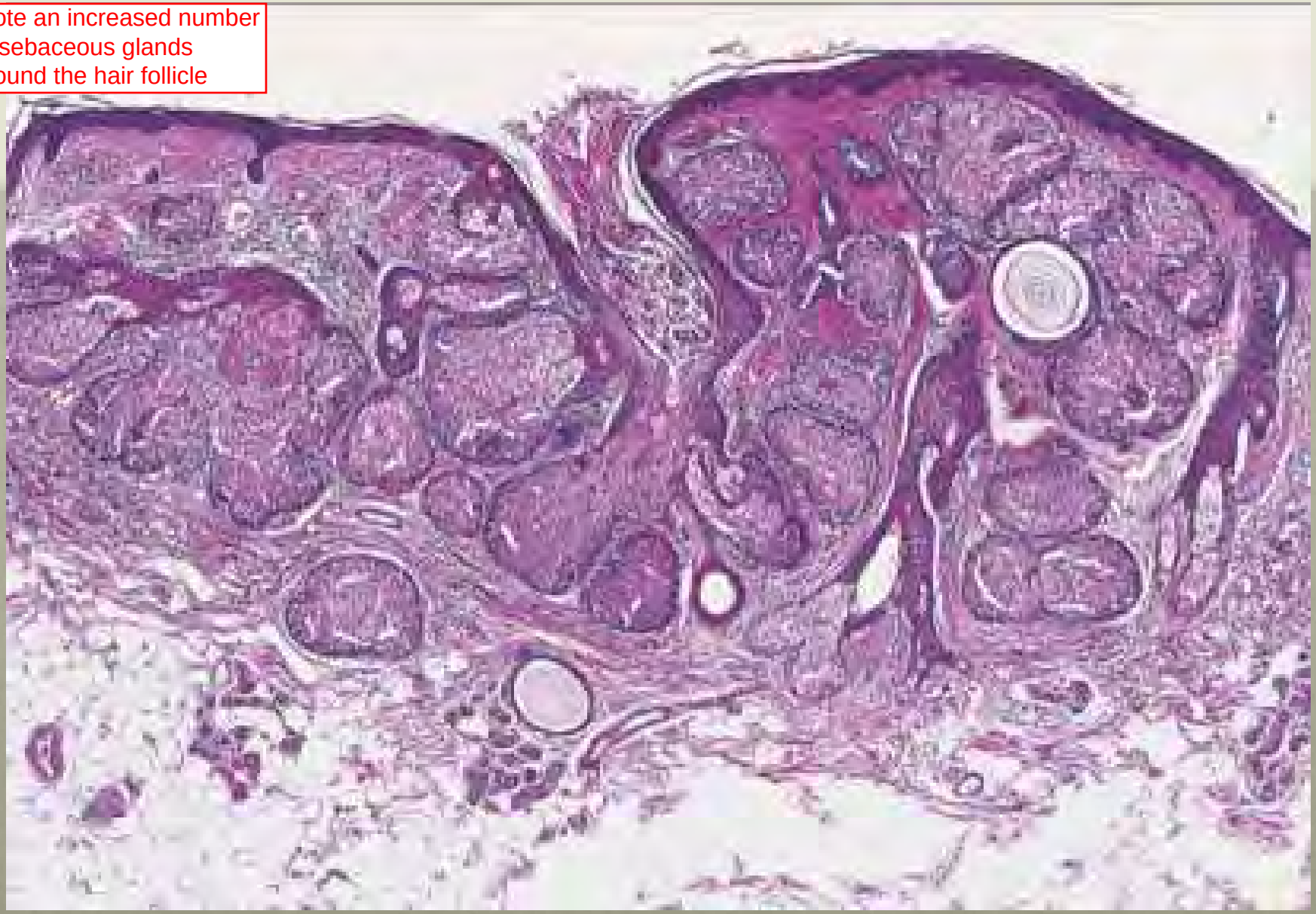
Dermatofibrosarcoma protuberans

-also have adnexal (appendage) tumors



Sebaceous Hyperplasia

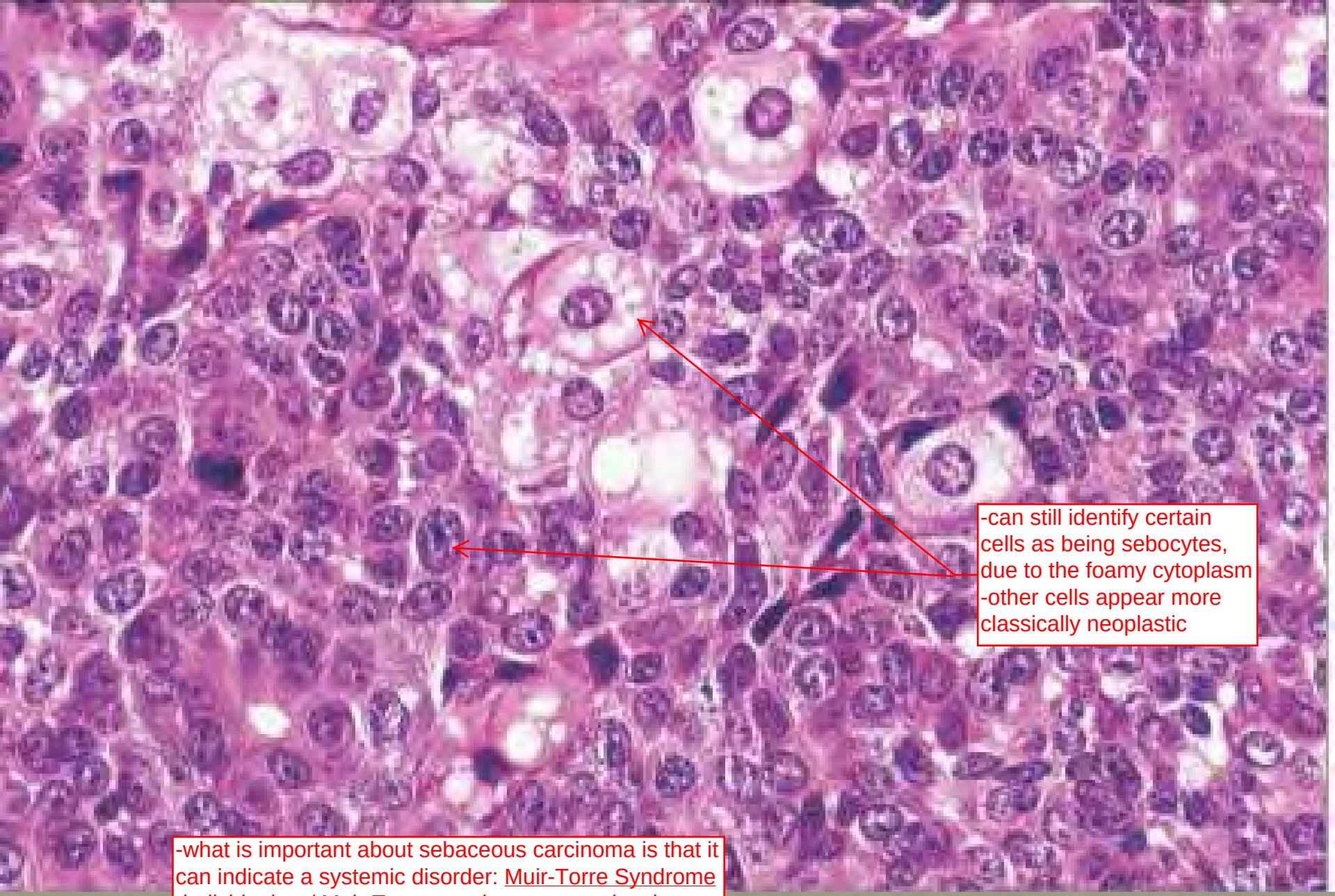
-note an increased number of sebaceous glands around the hair follicle



Sebaceous Hyperplasia

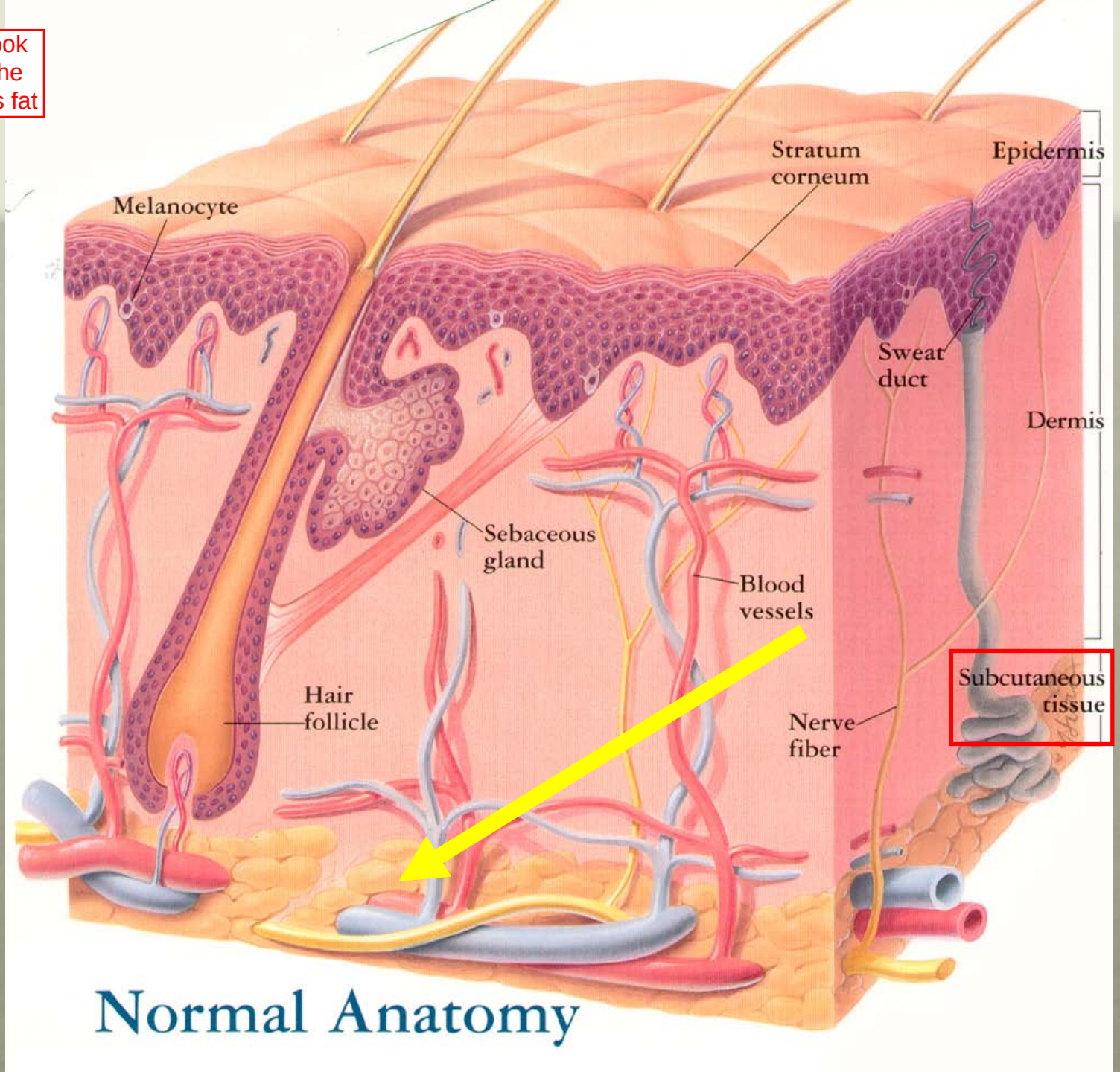
-sebaceous carcinoma is an aggressive, uncommon, cutaneous tumor, thought to arise from sebaceous glands

Sebaceous Carcinoma



Sebaceous Carcinoma

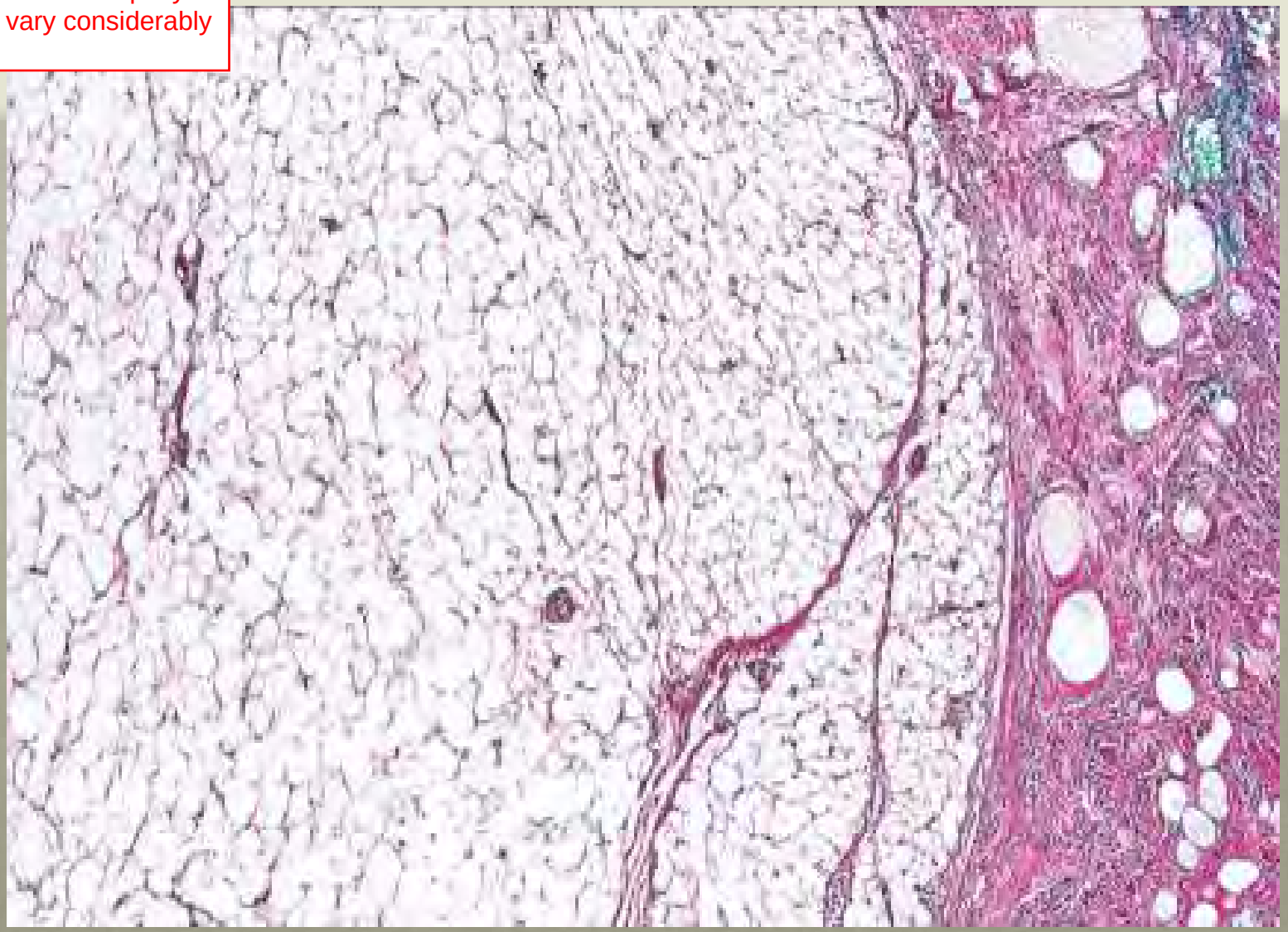
-lastly, we'll look at lesions of the subcutaneous fat




-lipomas = benign tumors of fat
-they are soft, mobile, and generally painless nodules that can be multiple

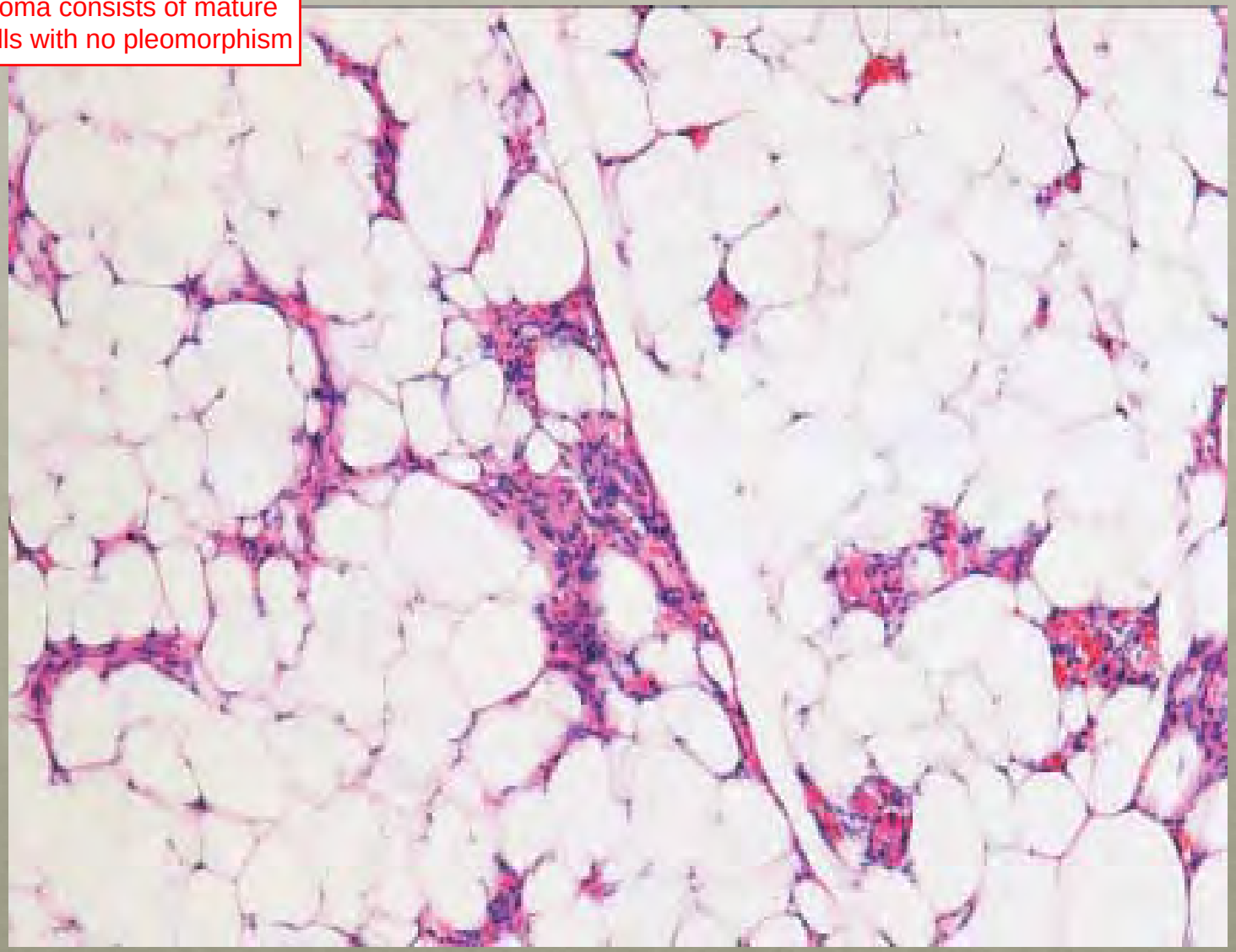
Lipoma

-see a well-encapsulated mass of mature adipocytes that can vary considerably in size



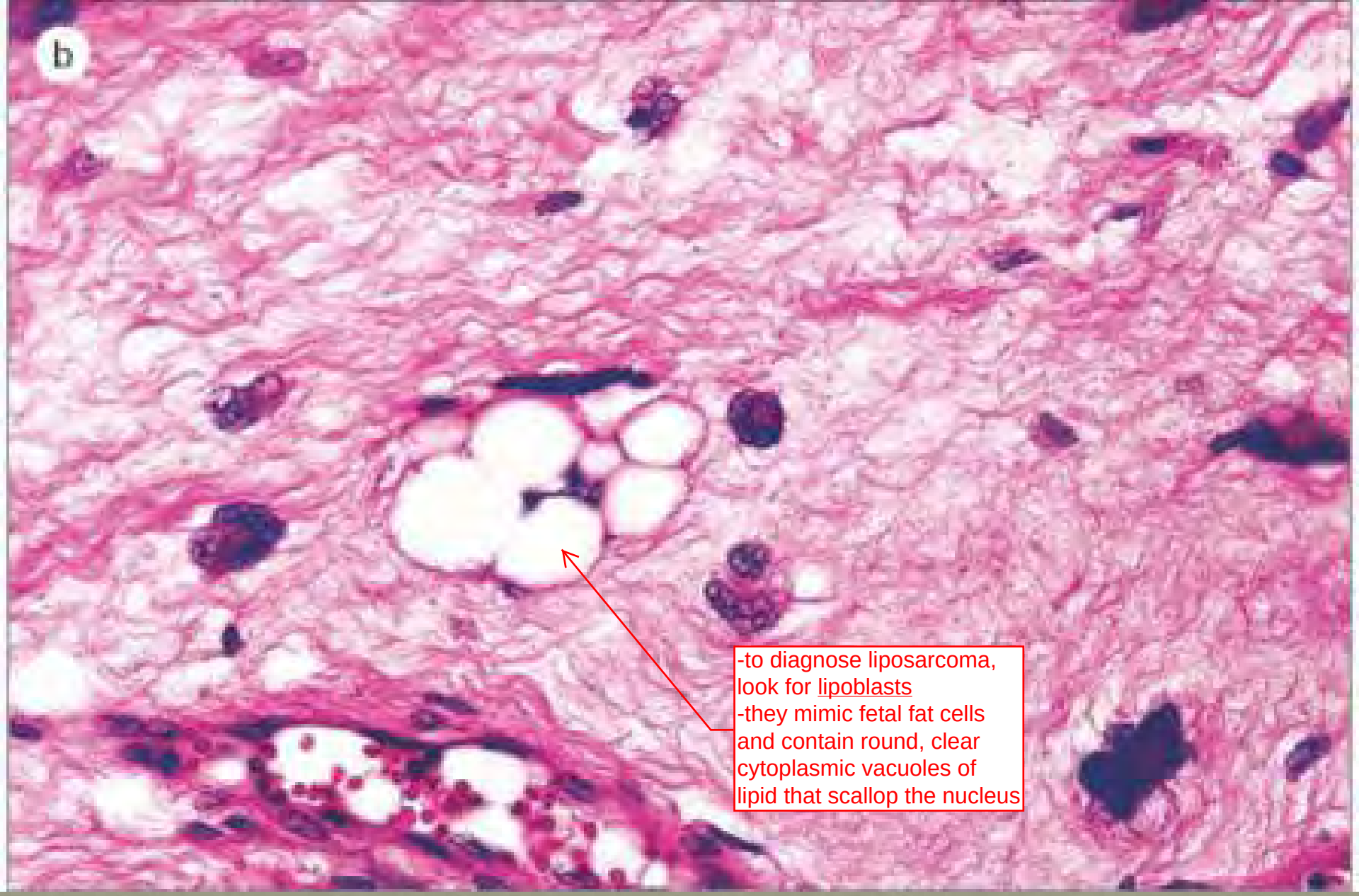
Lipoma

-at higher power, you can verify that a benign lipoma consists of mature white fat cells with no pleomorphism



-can also have bad malignancies arising from fat cells
-they usually occur in the deep soft tissues of the proximal extremities (such as the thigh) and in the retroperitoneum
-requires surgical excision, not biopsy

Liposarcoma



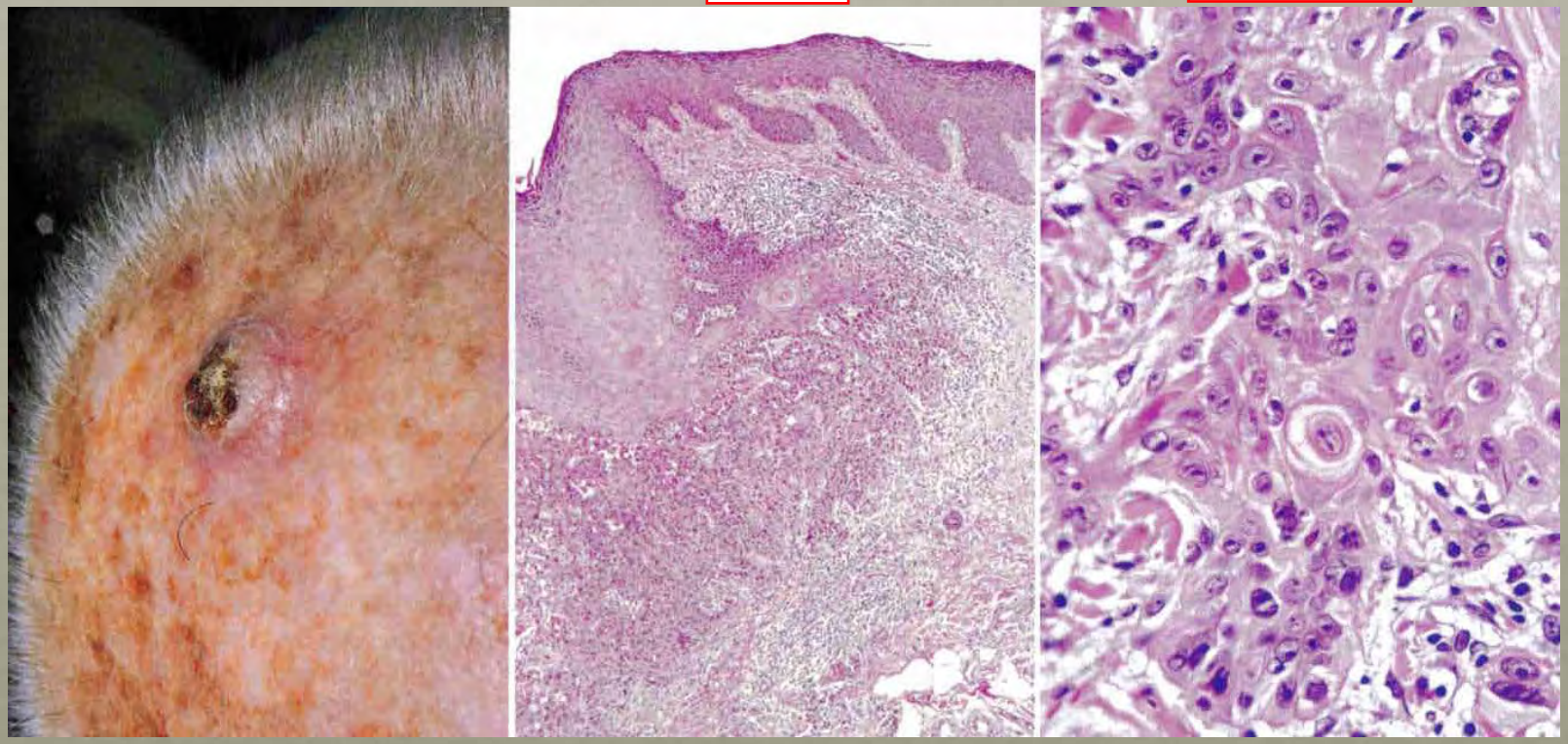
Liposarcoma

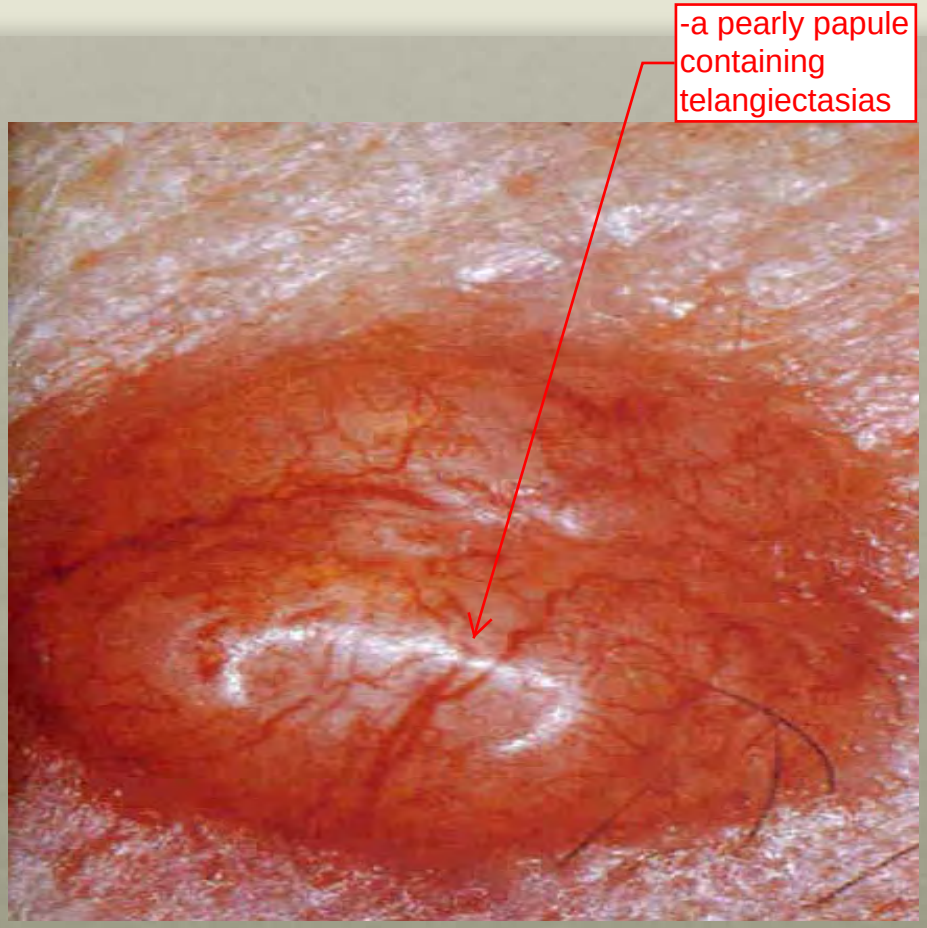
THANK YOU

-the remaining slides contain 3 cases which served as an end-of-lecture "quiz"

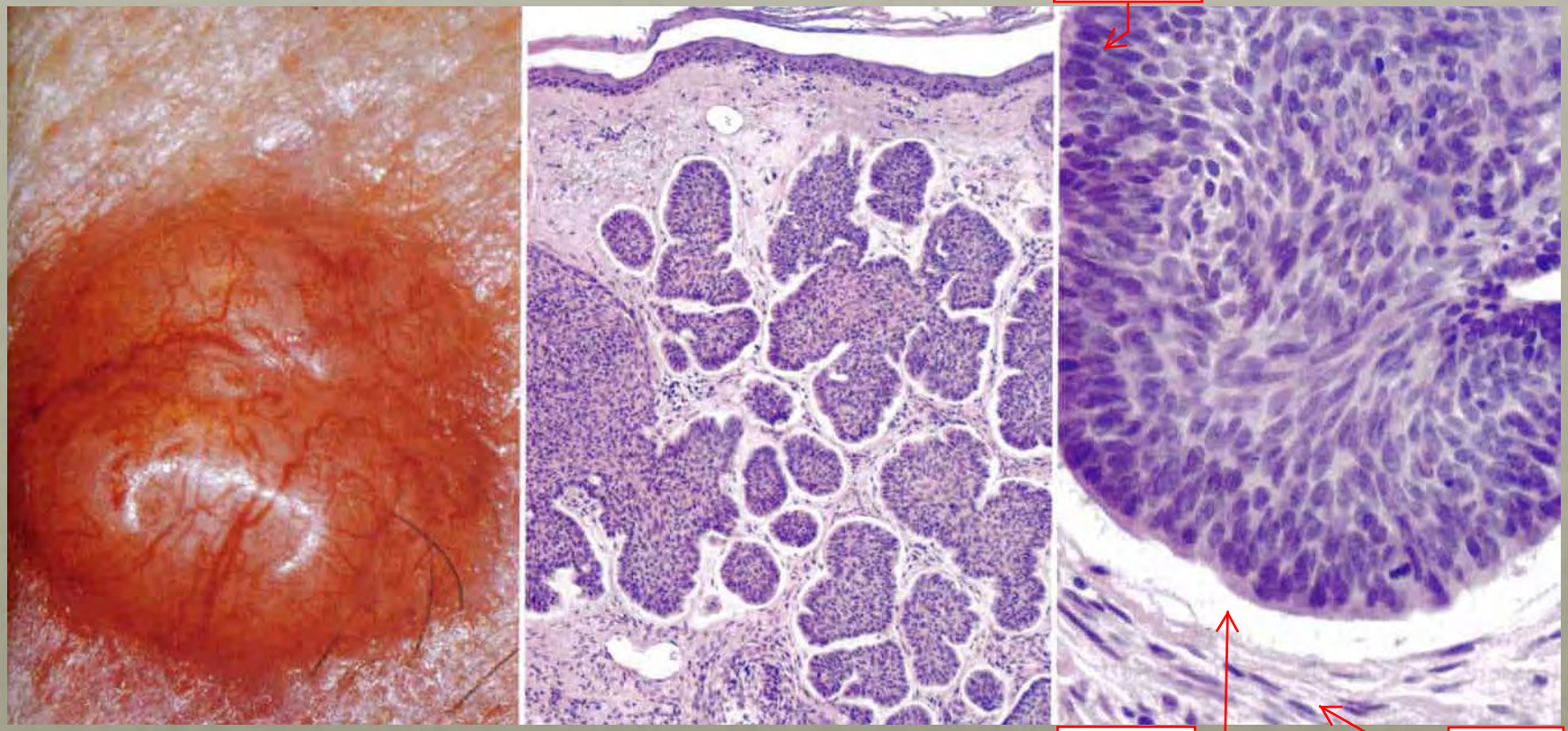

-a nodular,
ulcerative lesion
w/ hyperkeratosis

-dx: invasive squamous cell carcinoma



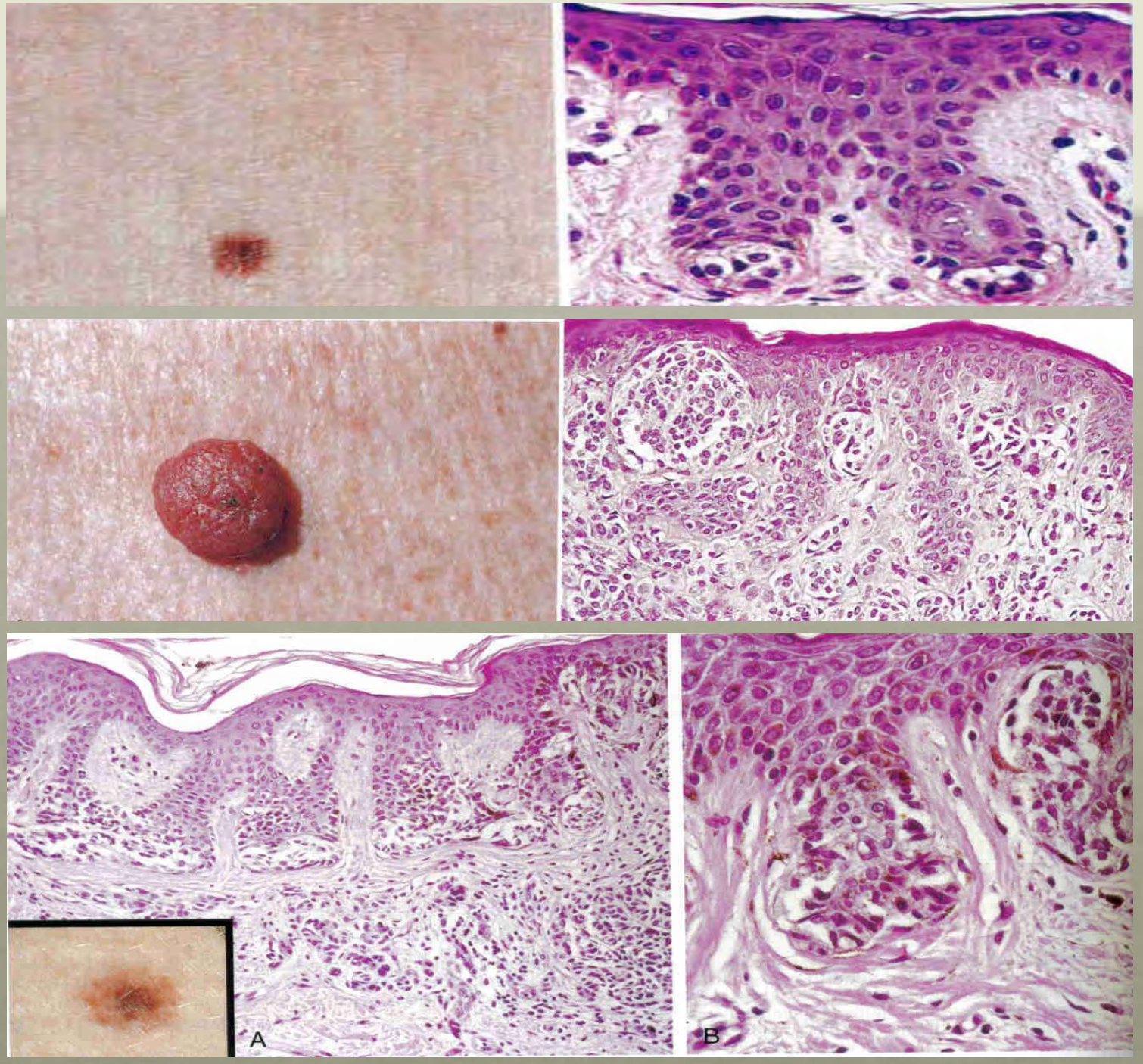

-a pearly papule containing telangiectasias

-dx: nodular basal cell carcinoma




-a benign junctional nevus (flat and brown)


-a benign dermal nevus (raised)
-does NOT meet the ABCDE's
-this lesion is symmetric, has regular borders, uniform color, normal diameter (4-5mm or less), and should not be enlarging


A
B


A

-dx: melanoma

-again, note the ABCDE's
-you need to catch this and confirm w/ biopsy to prevent metastasis