

Dysplastic Nevus Atypical Mole... Typical Role?

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What Should I Call You?

- Dysplastic Nevus
- Atypical Mole
- BK Mole syndrome
- Familial atypical mole syndrome
- Nevus with architectural disorder
- Nevus with atypical melanocytic hyperplasia
- Atypical melanocytic proliferation

What Do I Call You?



- Blinded study, expert dermatopathologists, utilizing previously agreed upon criteria, reviewed histologic slides of atypical melanocytic nevi
- Excellent inter-observer concordance and reproducibility

In a controlled setting where criteria are agreed

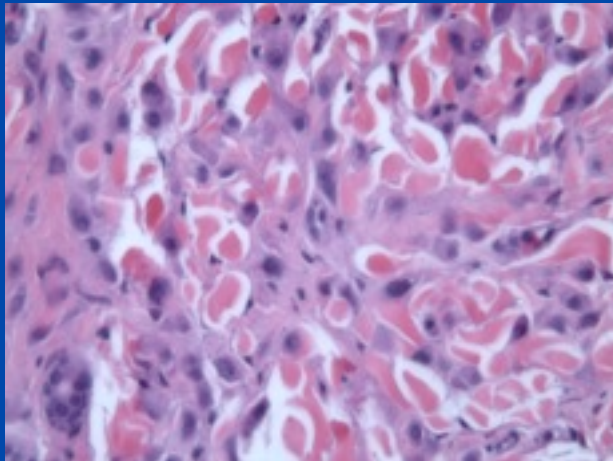
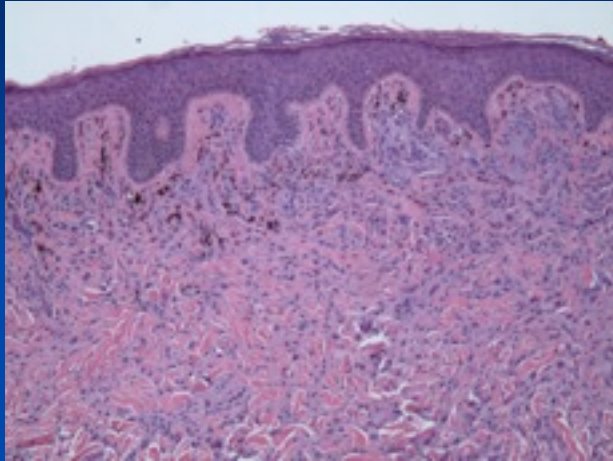
Morphologic Confusion



- Standardized criteria are not adhered to by all pathologists
- About 20% of clinically benign nevi, with no “dysplastic” features, will exhibit histologic changes, indistinguishable from classic dysplastic nevi OR
- Dysplastic nevi are not dysplastic-instead represent the common acquired *Clark's nevus*

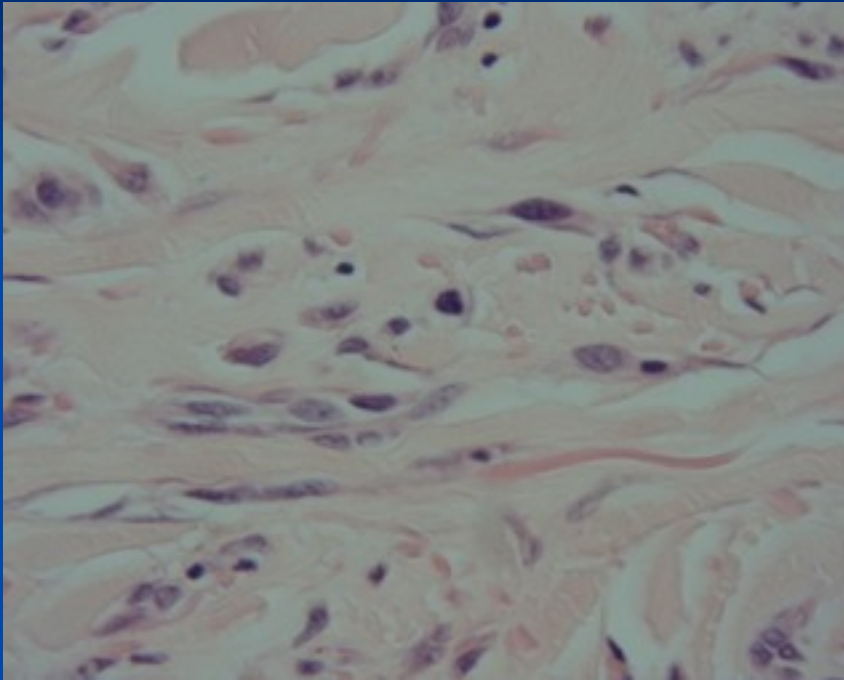


Terminologic Confusion



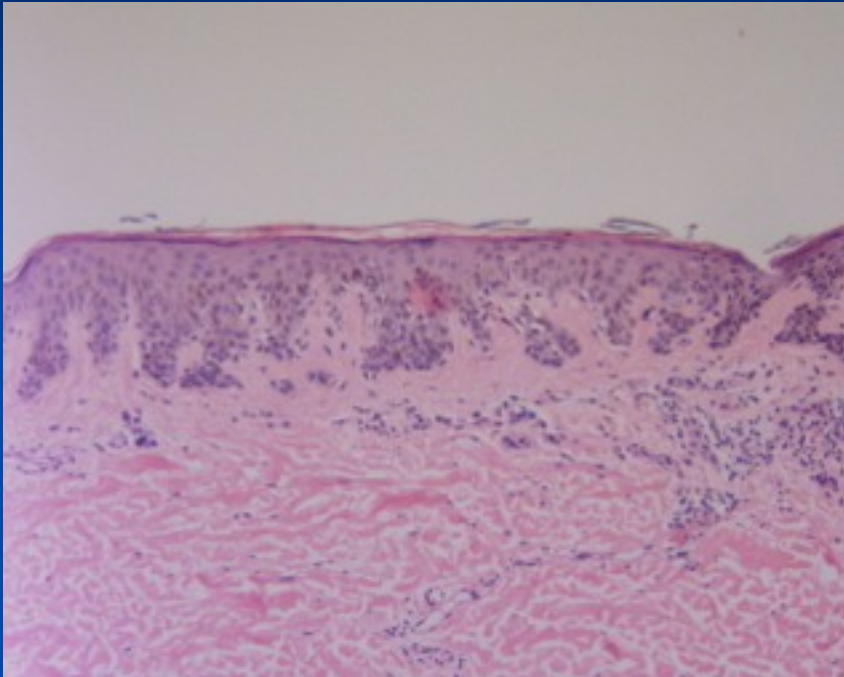
- Benign melanocytic lesions may exhibit considerable and disturbing cytologic and architectural features that taken alone, could be part of a melanoma
- Spitz nevi exhibit an alarming degree of cytologic atypia, complete with atypical mitotic figures
- Deep penetrating nevus, will exhibit atypical melanocytes, situated deep within the reticular dermis

Terminologic Confusion



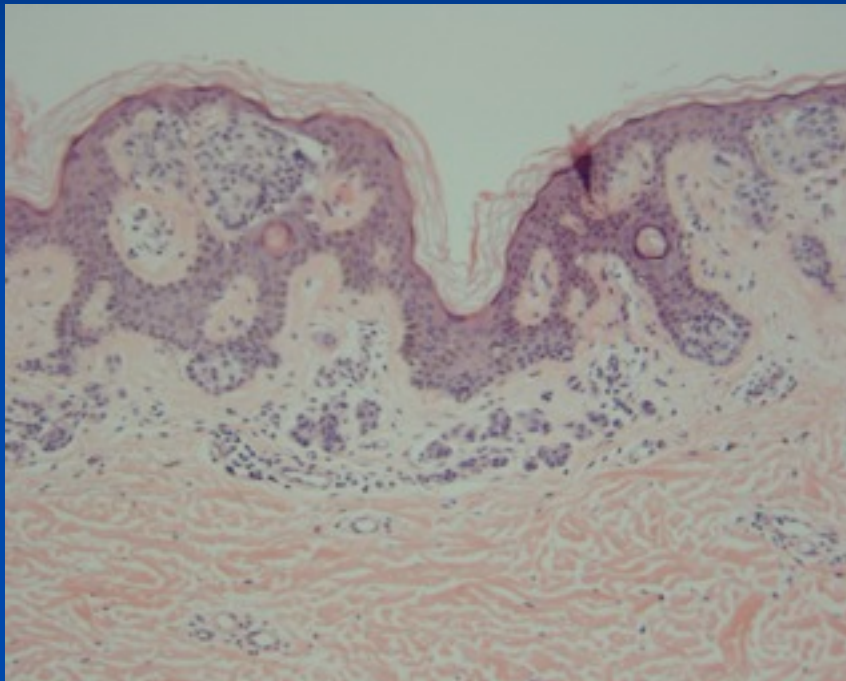
- Desmoplastic melanomas may exhibit only focal or minimal cytologic atypia, easily misdiagnosed as a scar

Histologic Confusion



- Six histologic features analyzed in 253 melanocytic nevi with different clinical appearances
 - Dimension > 5 mm
 - Lentiginous proliferation
 - Disordered nested pattern
 - Melanocytic dyskaryosis
 - Dermal lymphocytic infiltrate
 - Suprabasal melanocytes

Histologic Confusion



- Numeric value of 1 was assigned when each of the studied parameters was present and a value of 0 was assigned when each of these parameters was absent; on the basis of the final scores, nevi were divided in six different classes (classes 0-5)
- Diagnostic categories such as dysplastic nevi and common nevi seem to be inappropriate
- Do not reflect the real histologic complexity of such lesions

Clinical Confusion



- Fifty-eight nevi from 26 volunteer subjects were excised and examined:
 - 5 mm or less in diameter
 - Symmetric
 - Round or slightly oval
 - Uniform pigmentation
 - Distinct and regular margins
 - No erythema



- 87.8% one or more of the histologic features
 - 69% two or more present
 - 29.3% all three histologic features
- Histologic features of dysplastic nevi occur in clinically benign common acquired nevi

J Am Acad Dermatol 1990 Feb;22(2 Pt 1):275-82

Who Are You?



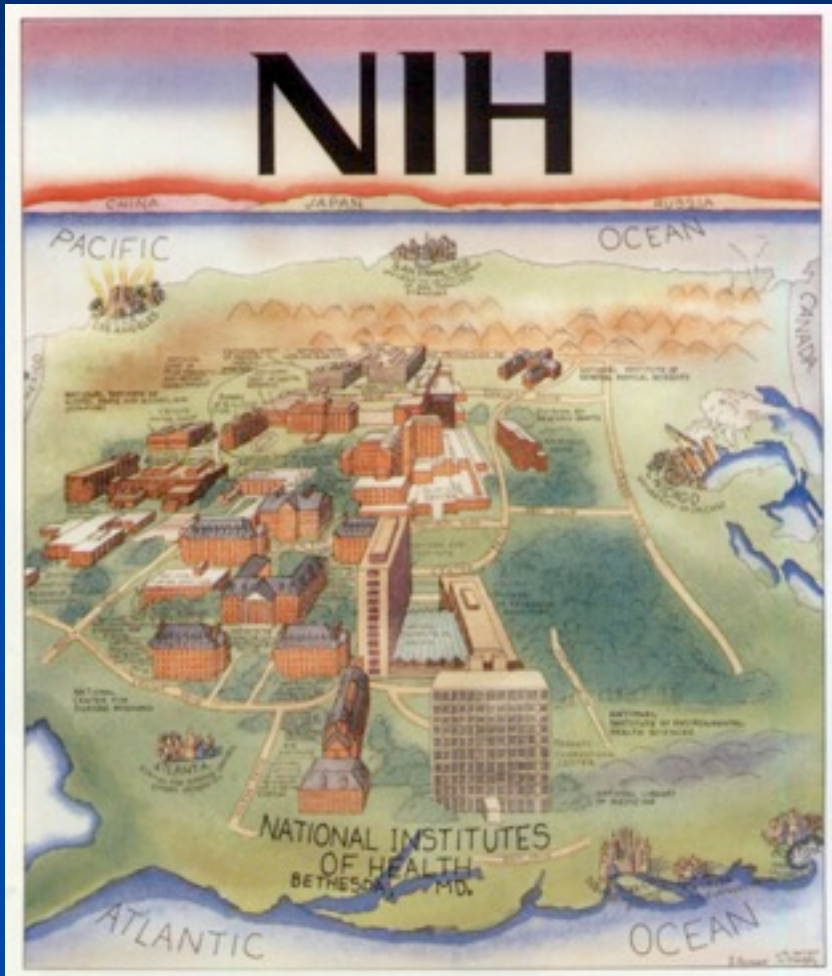
- Phenotype of increased number of atypical nevi in melanoma-prone kindreds.
- Original biopsies of these nevi led to the designation of melanocytic dysplasia
- By 1982, the presence of histologic dysplasia was considered sufficient for a diagnosis of the dysplastic nevus syndrome

What Are You?



- Risk factor for melanoma
- Need careful physical examination, with emphasis on biopsy evaluation of other pigmented lesions
- Patients with multiple pigmented lesions are at definite risk for the development of melanoma
- Problem quantifying the risk
 - Case control studies have found one clinical dysplastic nevus associated with a 2 fold risk
 - 10 or more associated with a 12 fold risk.

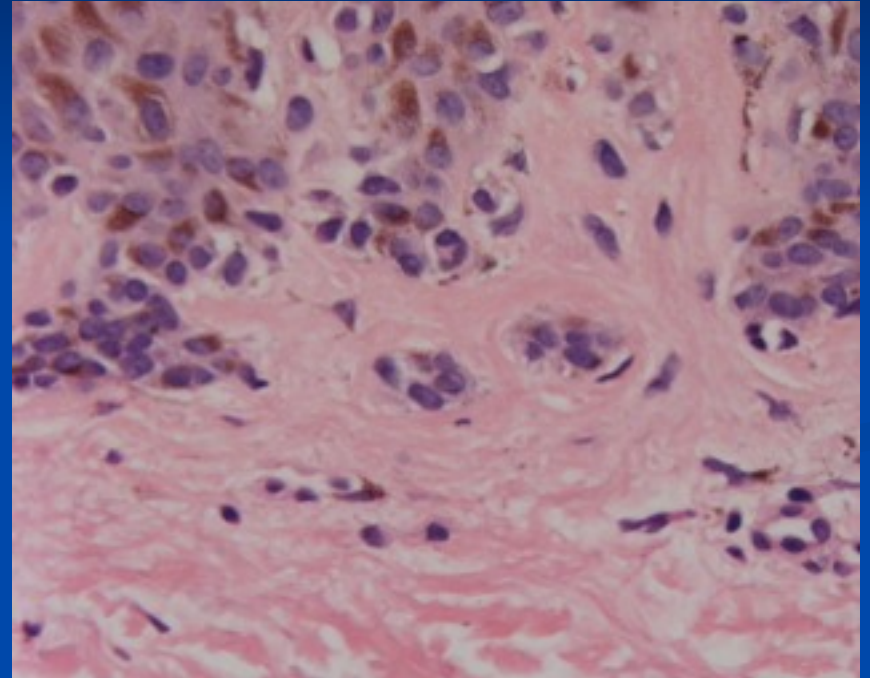
NIH Consensus Conference

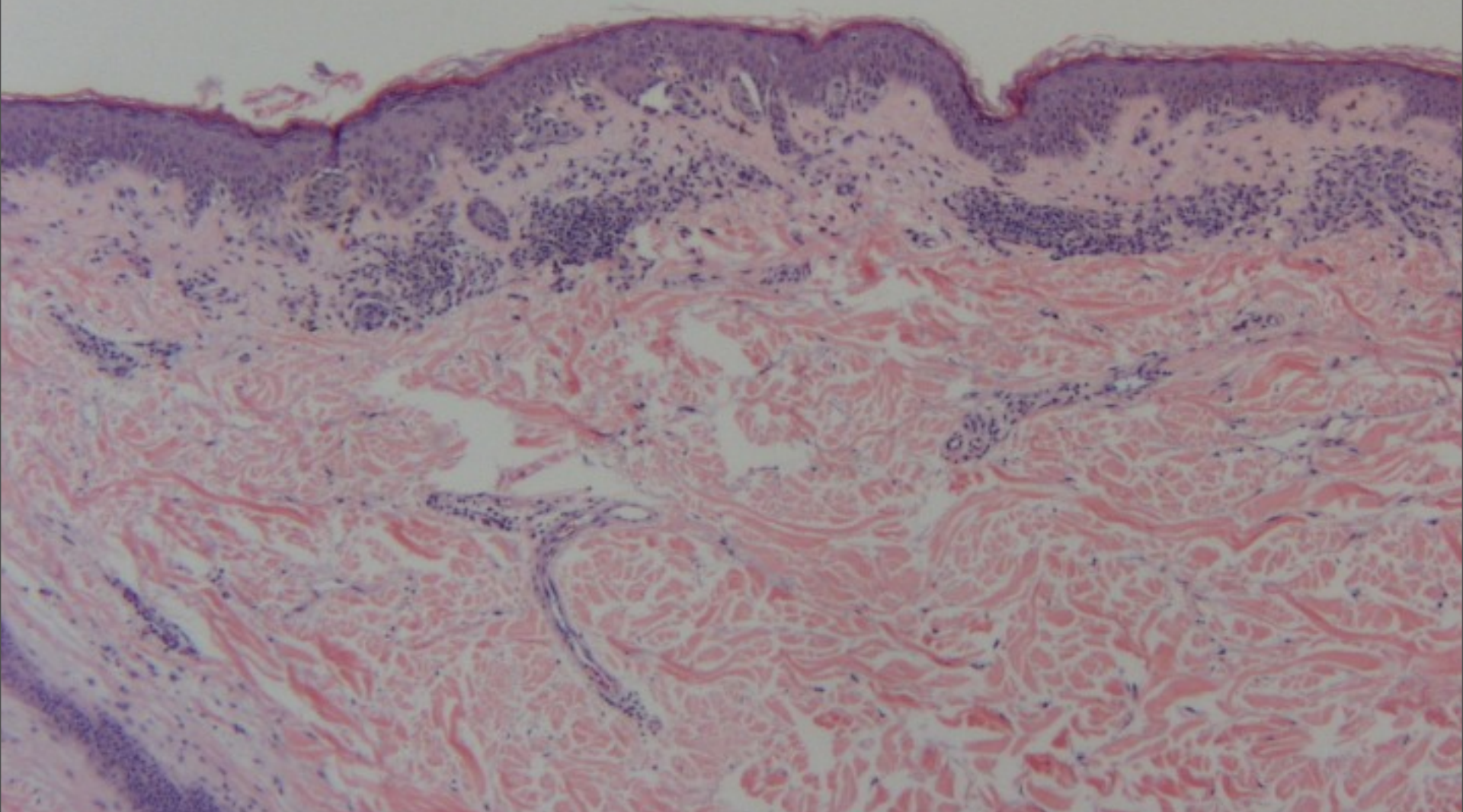


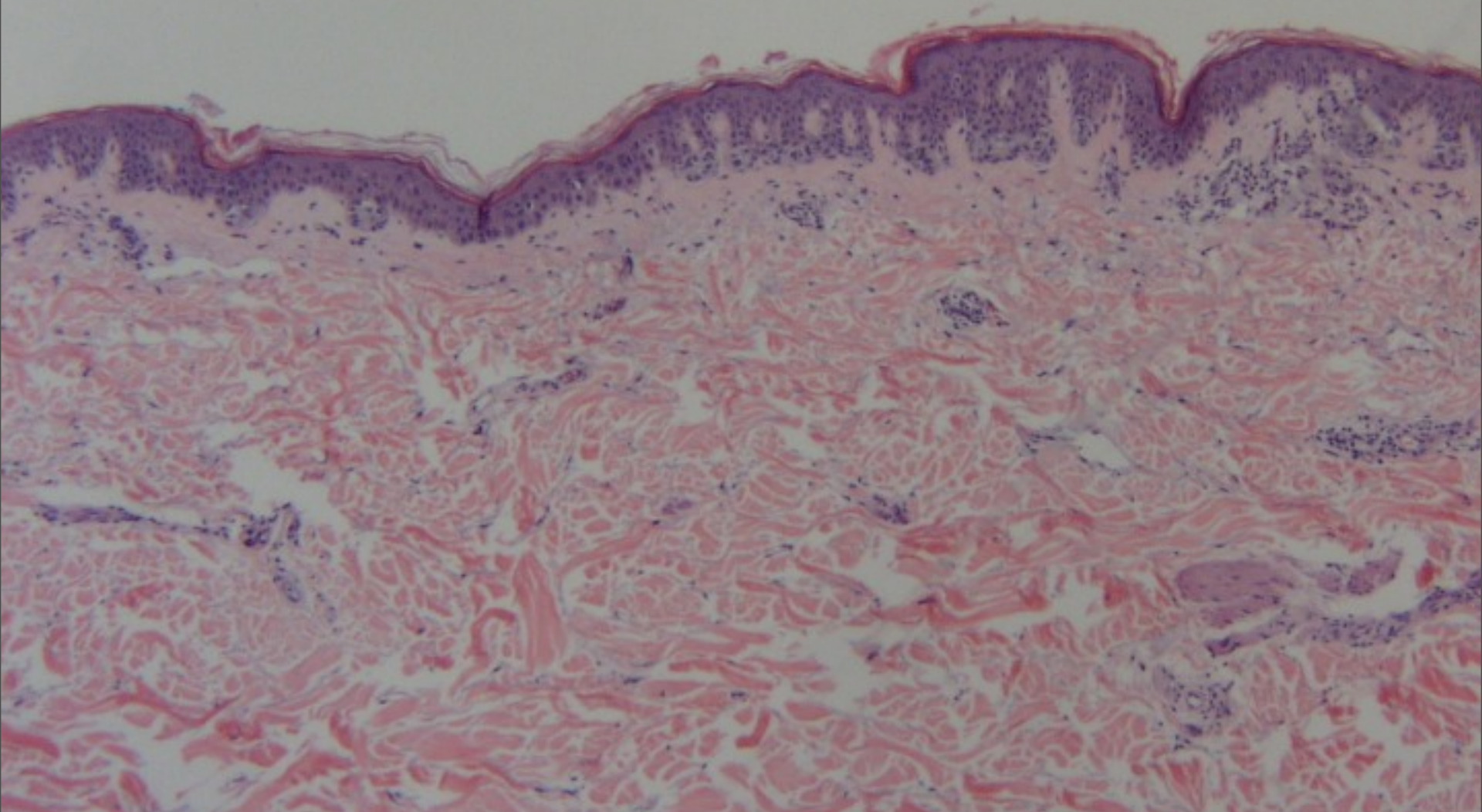
- Architectural disorder with asymmetry
- Shoulder phenomenon (intraepidermal melanocytes extending single or in nests beyond the main dermal component)

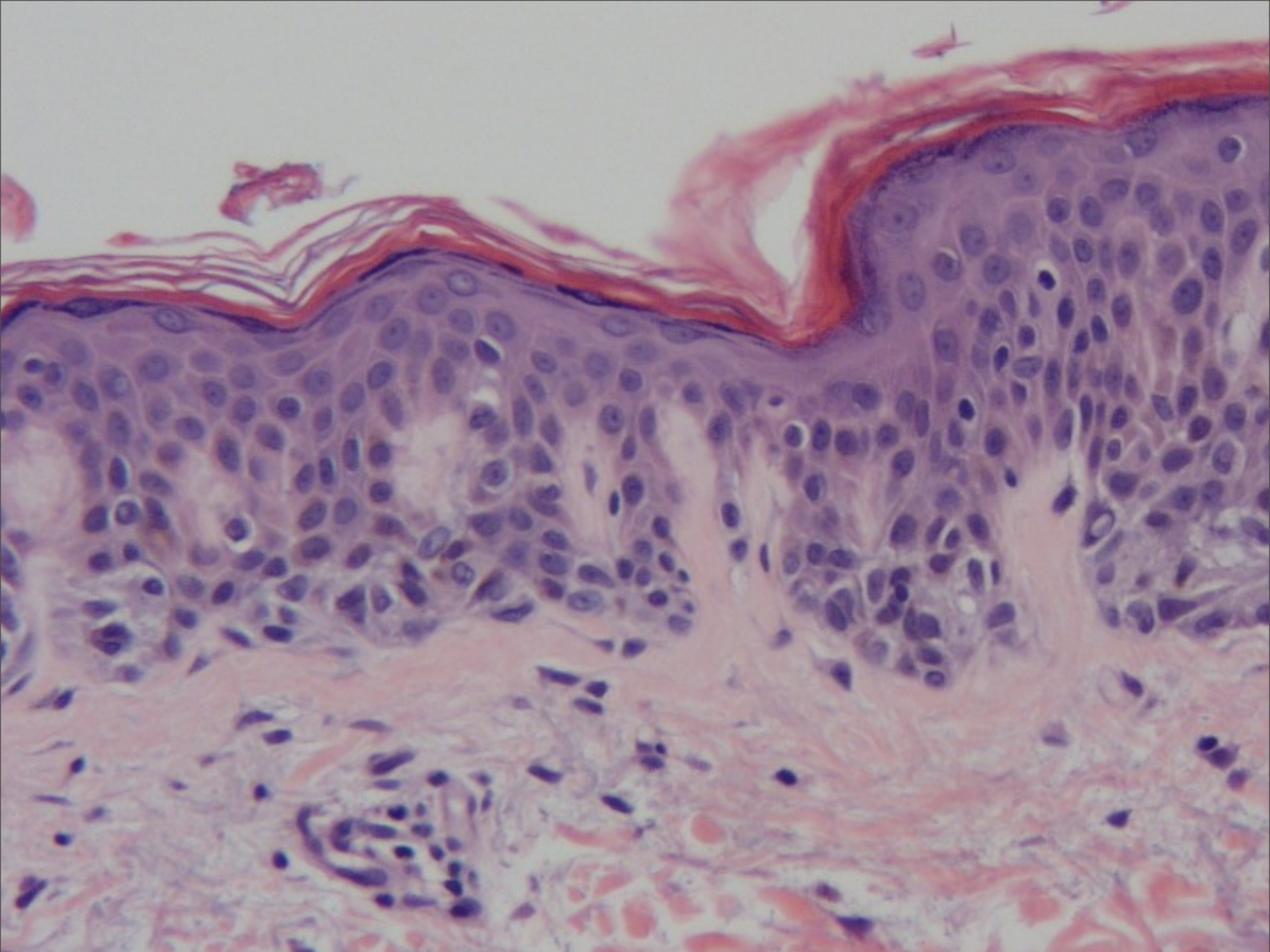
Histopathologic Criteria

- Melanocytes
- Papillae
- Dermis

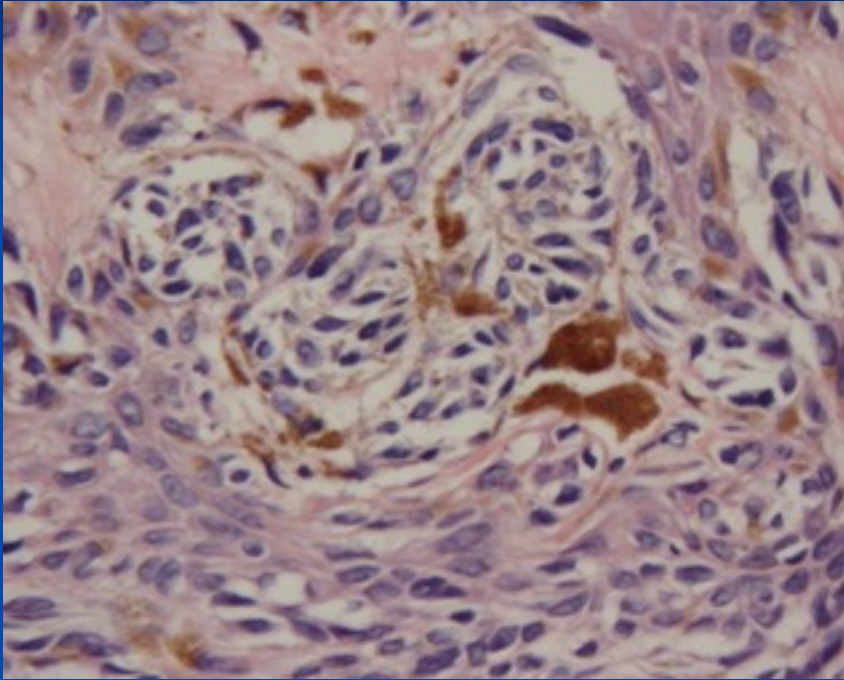




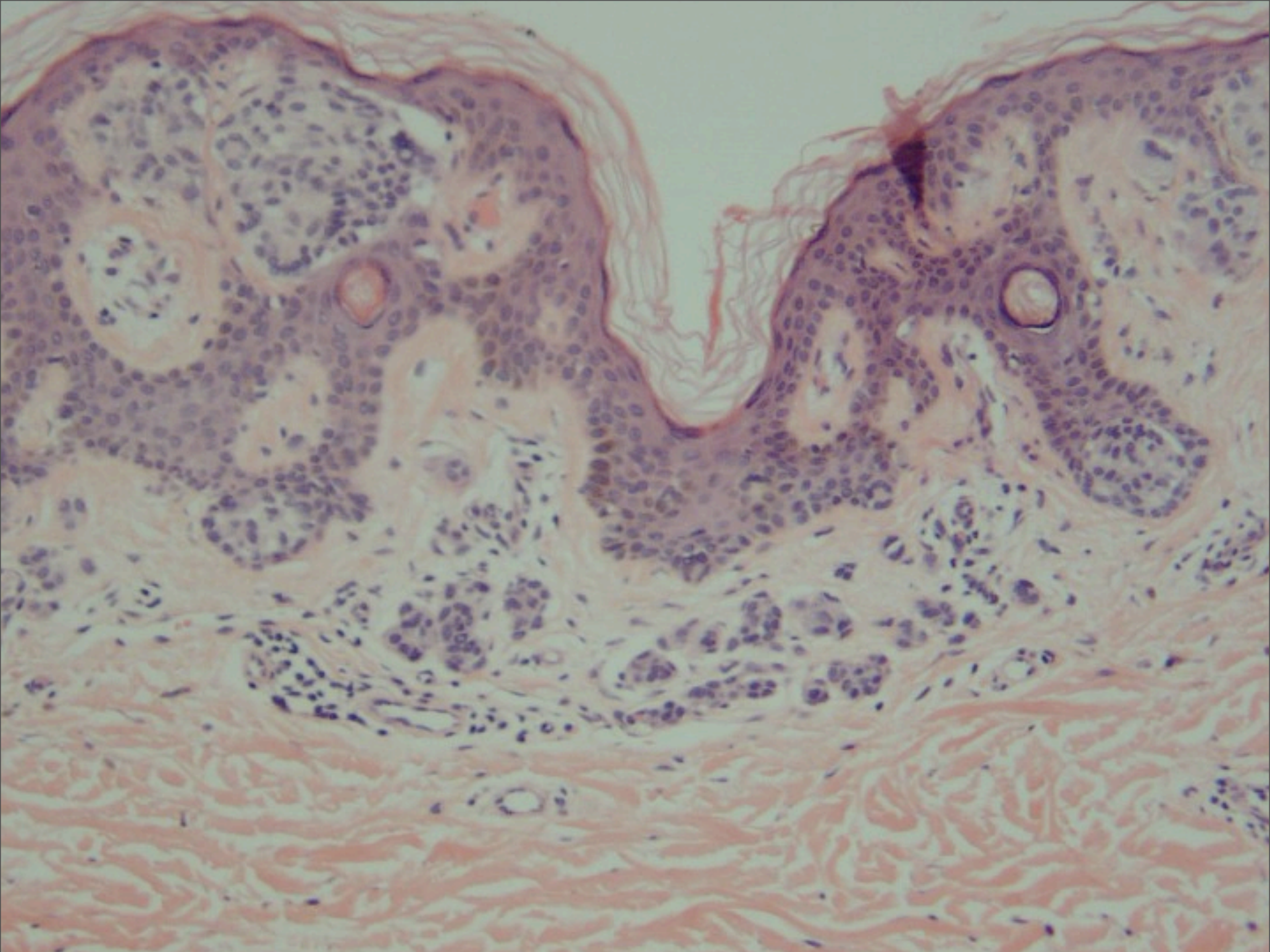


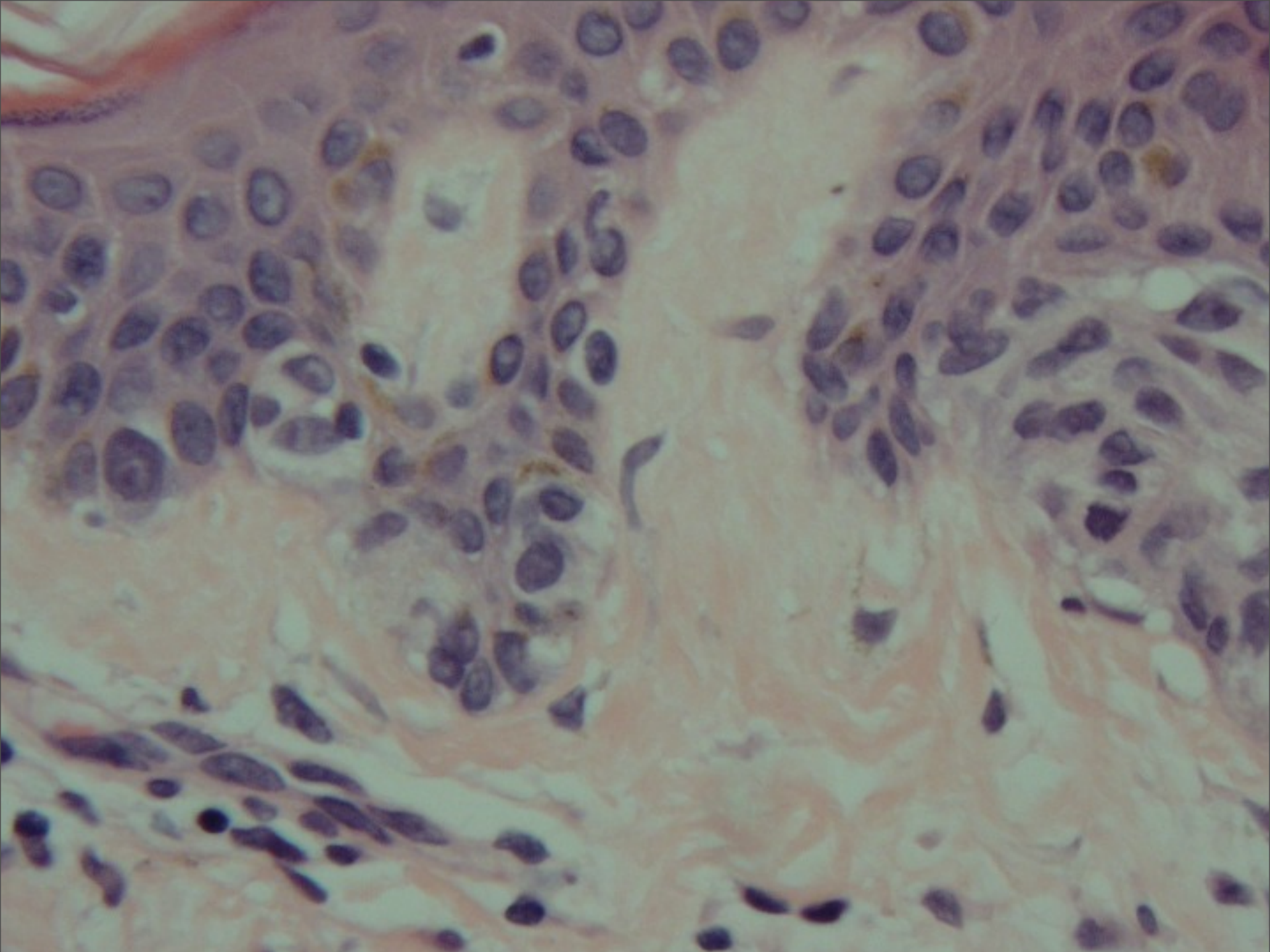


Melanocytes

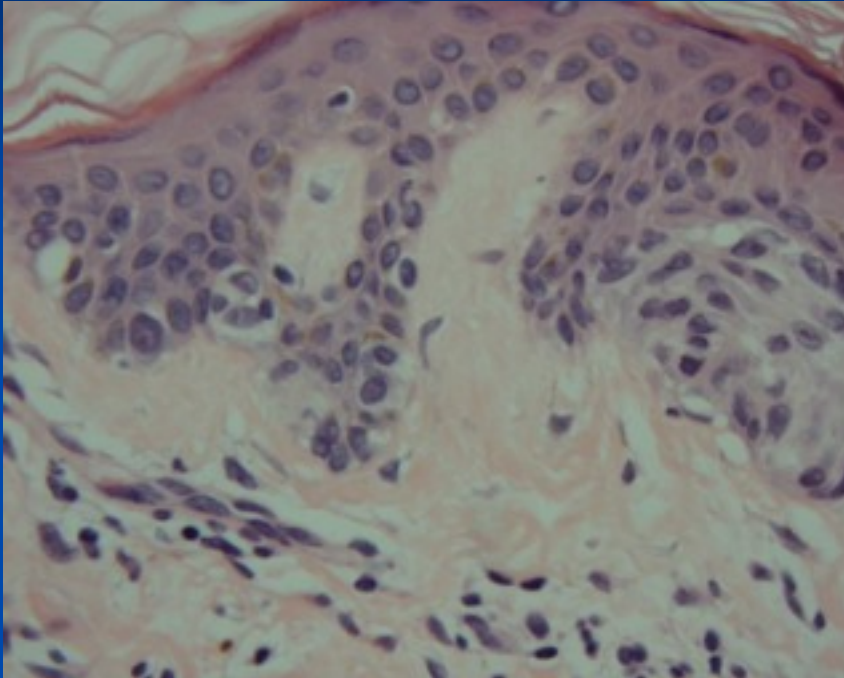


- Lentiginous melanocytic hyperplasia with spindled or epithelioid cell nests aggregating in nests of variable size and forming bridges between adjacent rete ridges
- Melanocytic atypia may be present to a variable degree
- Atypical melanocytes are frequently spindle shaped
- MF infrequent

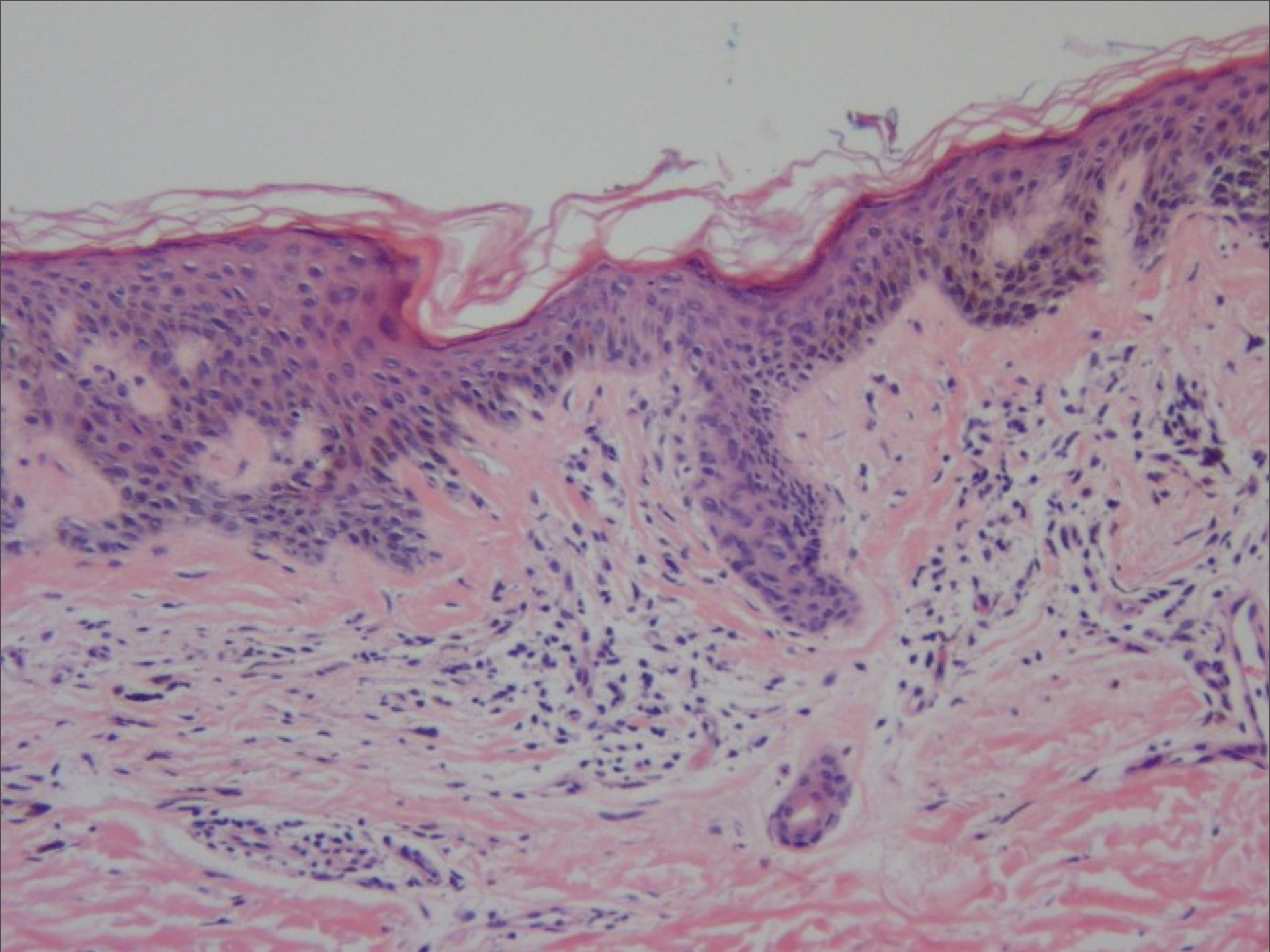


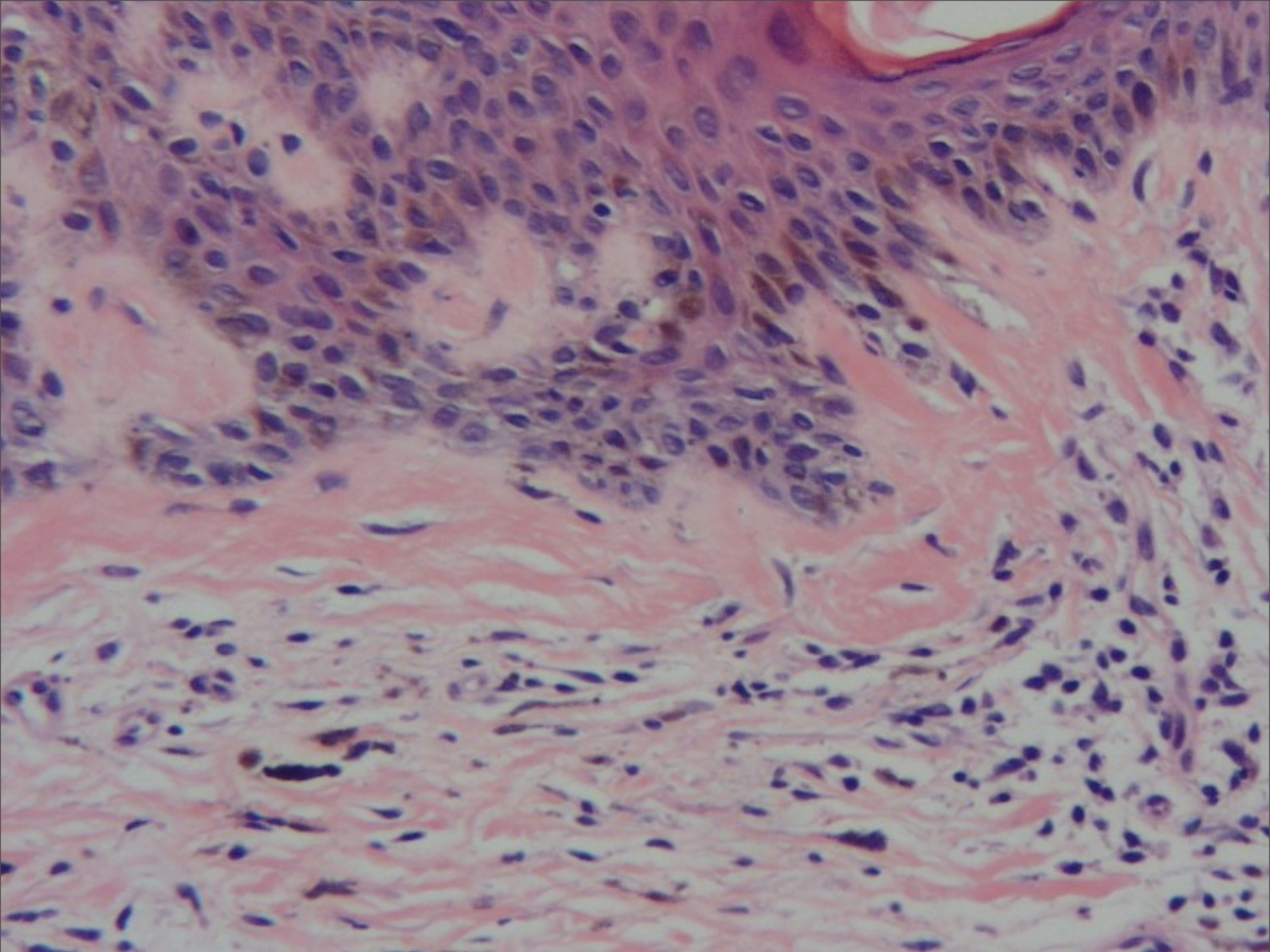


Dermal Papillae

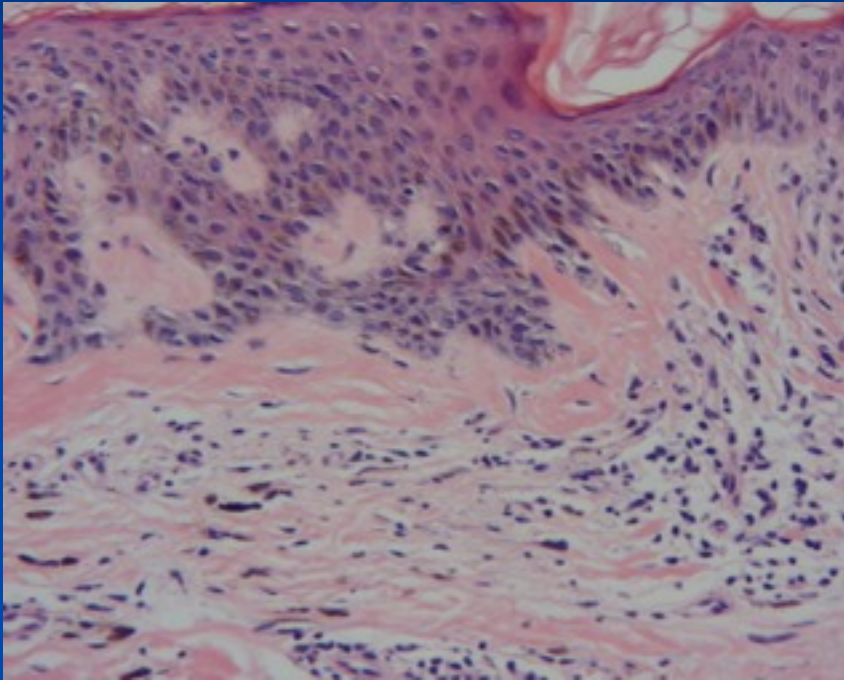


- Subepidermal
(concentric eosinophilia
and/or lamellar)
fibroplasia

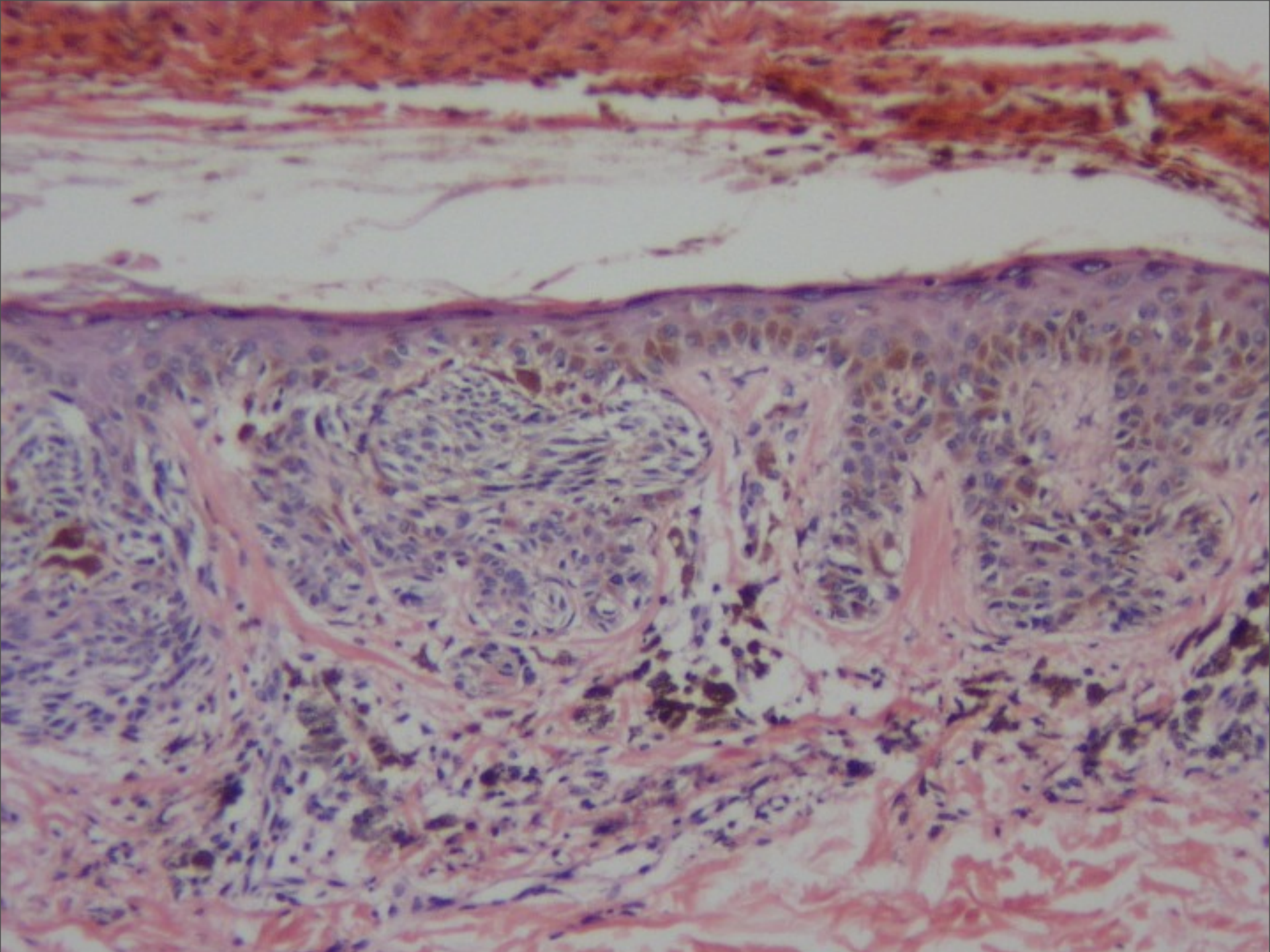


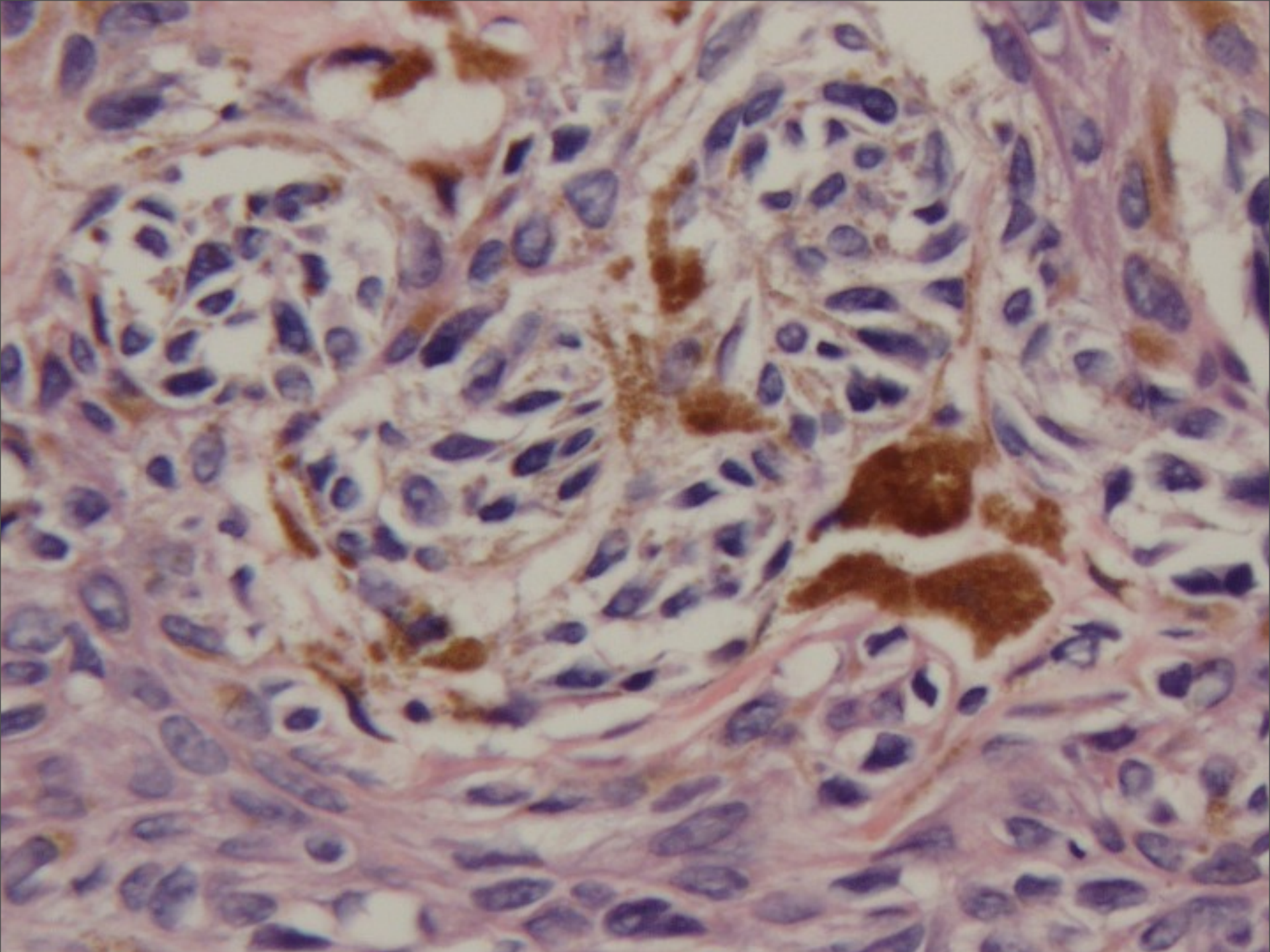


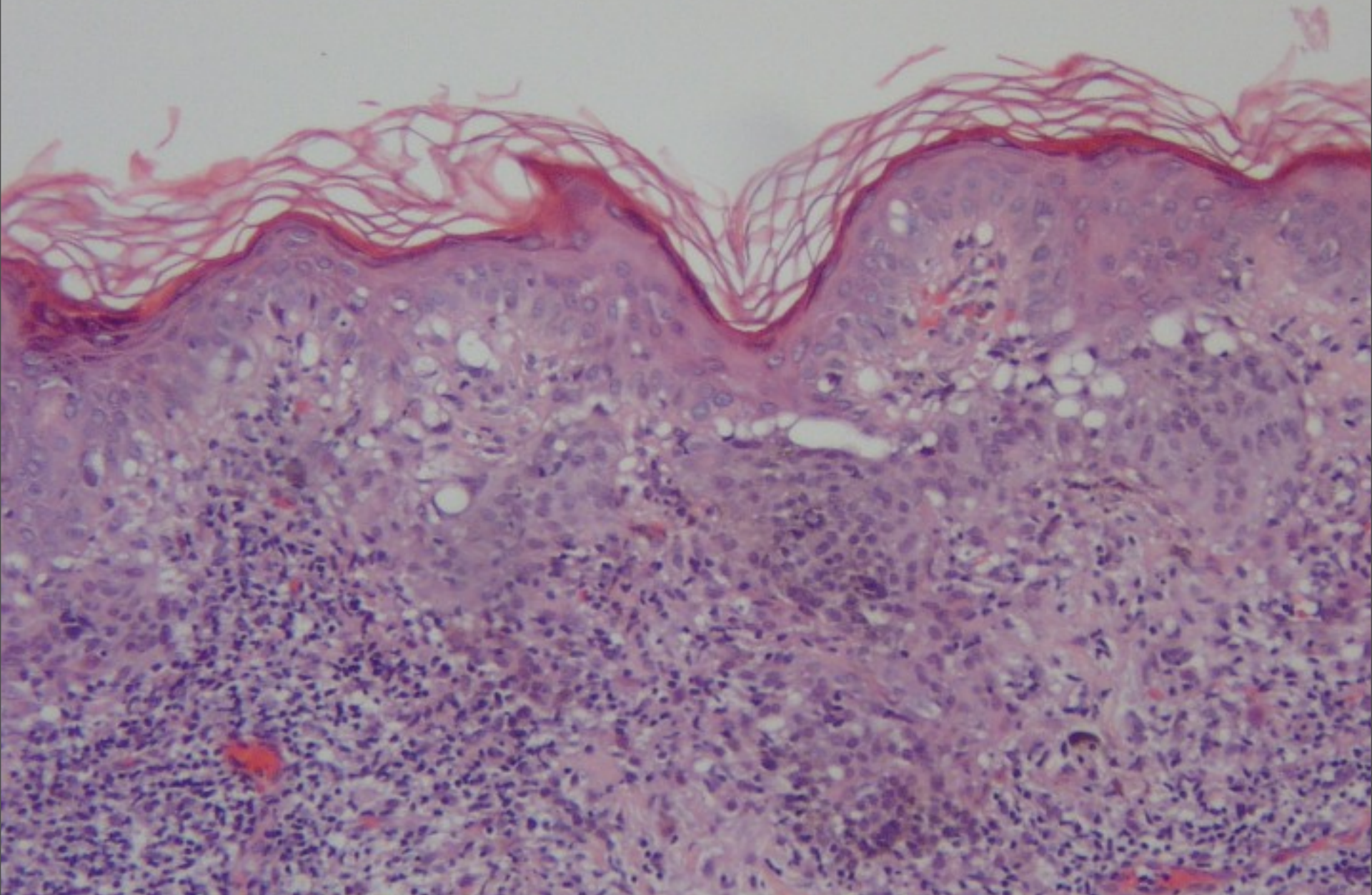
Dermis

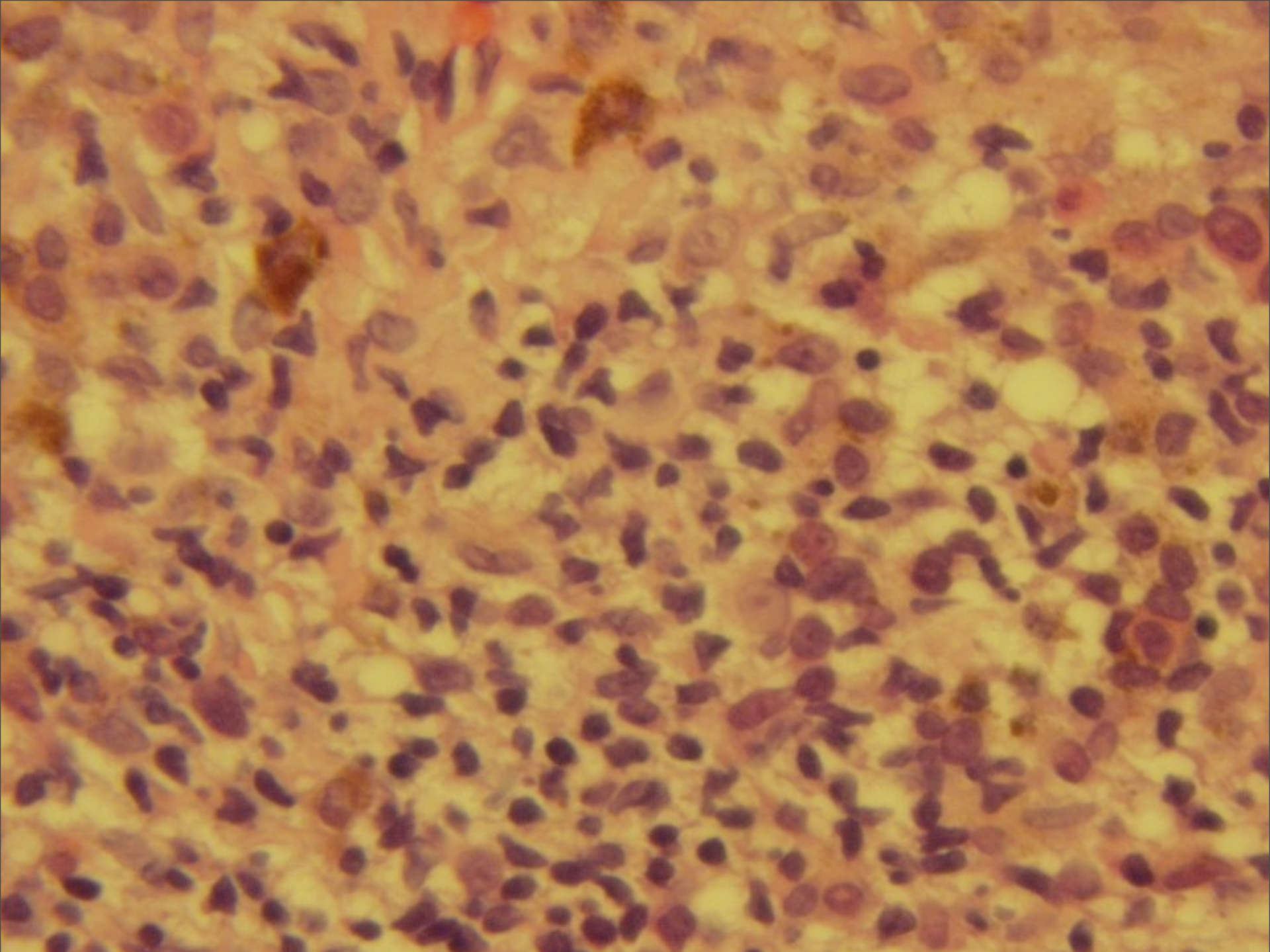


- Nests extend downward into the upper dermis with the long axis of the nests lie parallel to the ED interface
- Dermal lymphocytes may be present
- Inflammatory infiltrate with melanophages is common

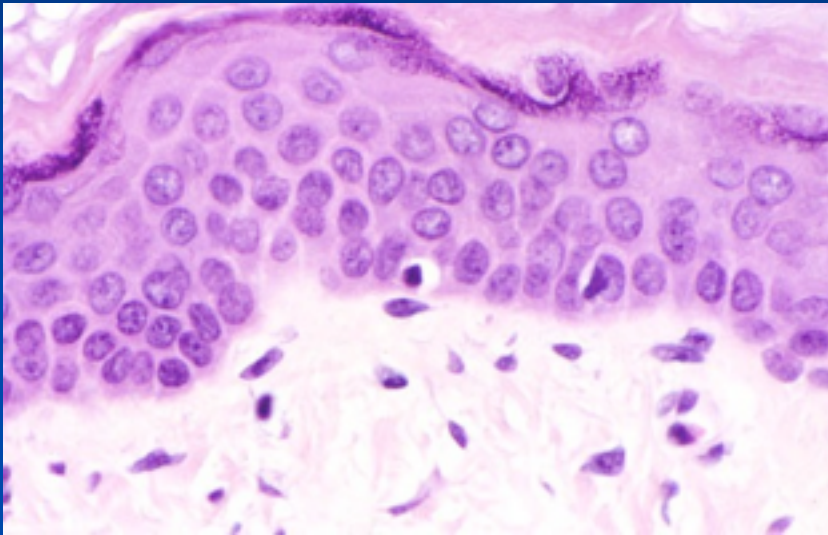








Grading the Atypia



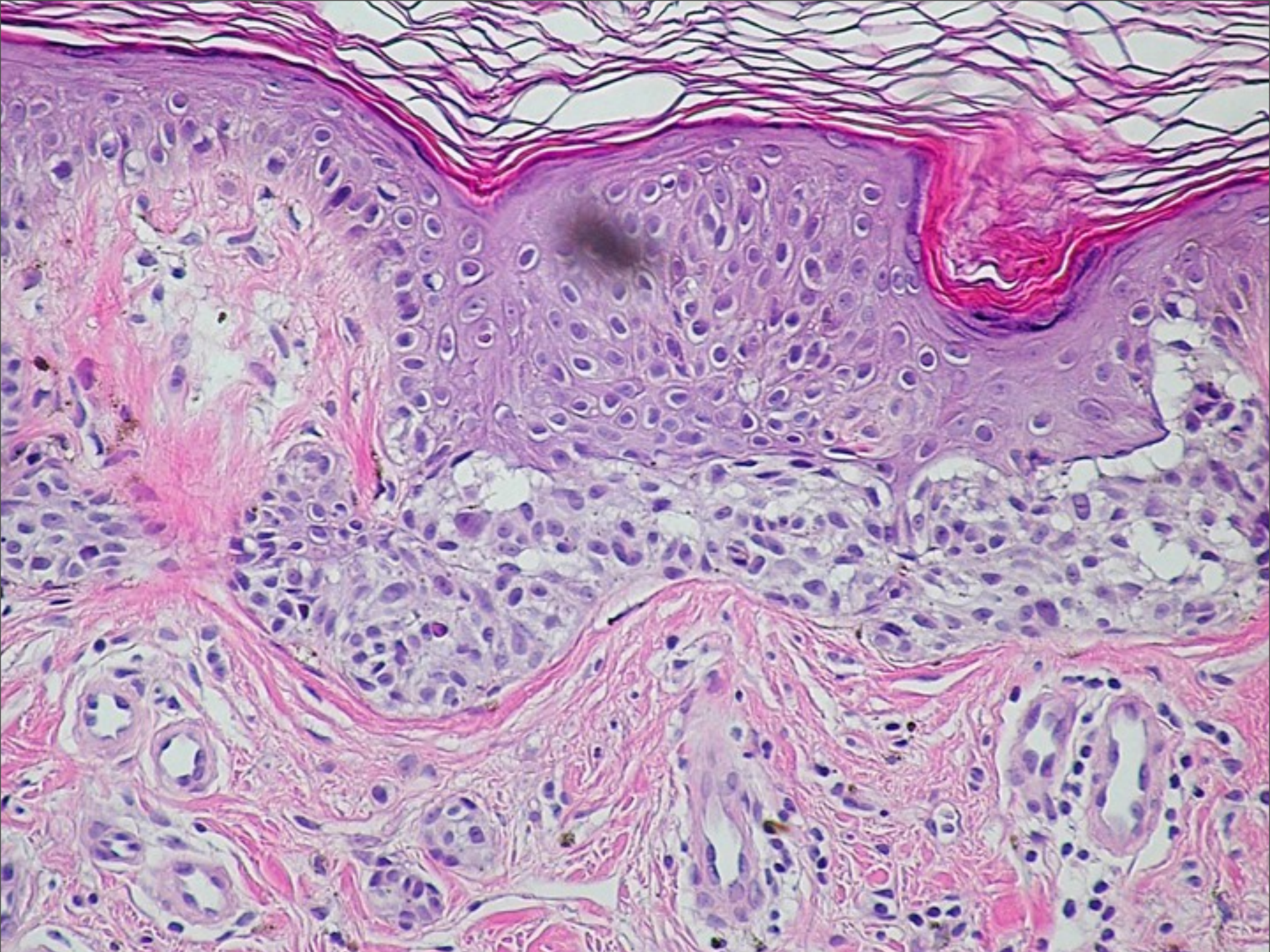
- Nucleus
 - Area
 - Variability
 - Chromatin
 - Nucleolus
- Cytoplasm
 - Quantity
 - Quality

Nuclear Changes

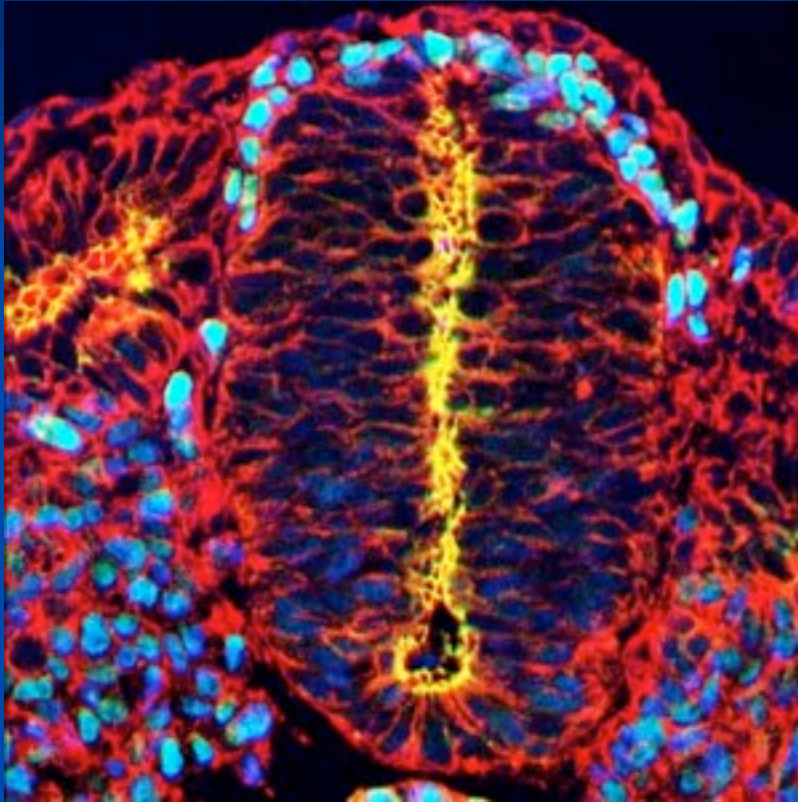
Degree of Atypia	Normal	Mild	Moderate	Severe
Area	Normal (N) 1/2-2/3 area of a basal keratinocyte	1.5-2N	>2N	>2N
Variability	Minimal	Marked	Marked	Marked
Chromatin	Small, regular, aggregates in finely granular homogenous background	Condensed, with loss of all detail	Attenuated, widely spaced aggregates in pale background with condensation on nucleolar membranes	Few, large, irregular aggregates with pale, almost empty background, and condensation on nuclear membranes
Nucleolus	Not visible	Not visible	Large, pale, often multiple	Lavender, often multiple

Cytoplasmic Changes

Degree of Atypia	Normal	Mild	Moderate	Severe
Features				
Quantity	Rarely visible	Small rim, eccentric around nucleus	Increased, eccentric around nucleus	Fully expanded around nucleus
Quality		Densely pink	Pink, pale, finely granular	Pink and finely granular, often bipolar staining



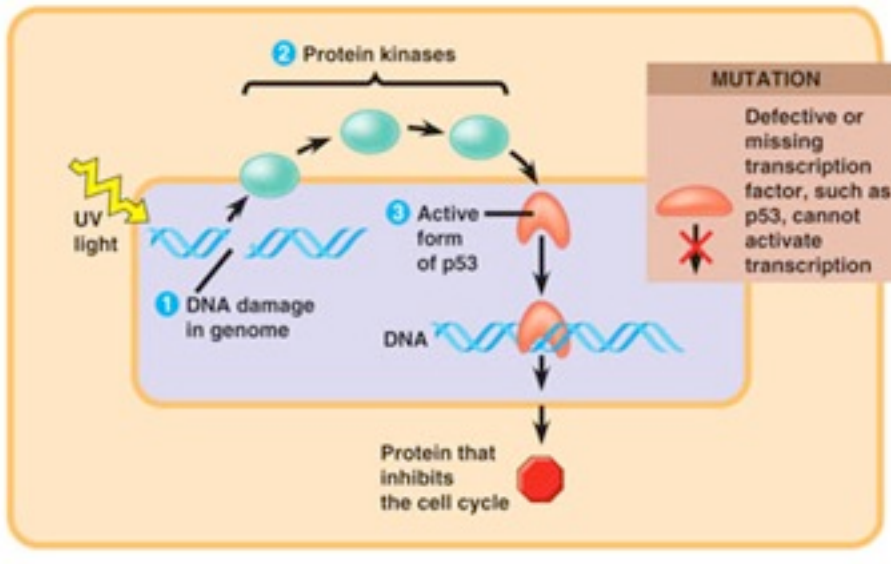
Conceptual Framework



- Melanocytes are neural crest derived cells
- As melanocytes proliferate at the dermo-epidermal junction, progressive changes in architecture and cytologic atypia lead to a fibro-inflammatory host response
- Degree of atypia can be viewed as a spectrum of changes encompassing the architecture, cytology, and host response
- Term atypical melanocytic hyperplasia has been coined and the atypia graded with a three-tiered system
- Overall schema is not significantly different from the other grading systems

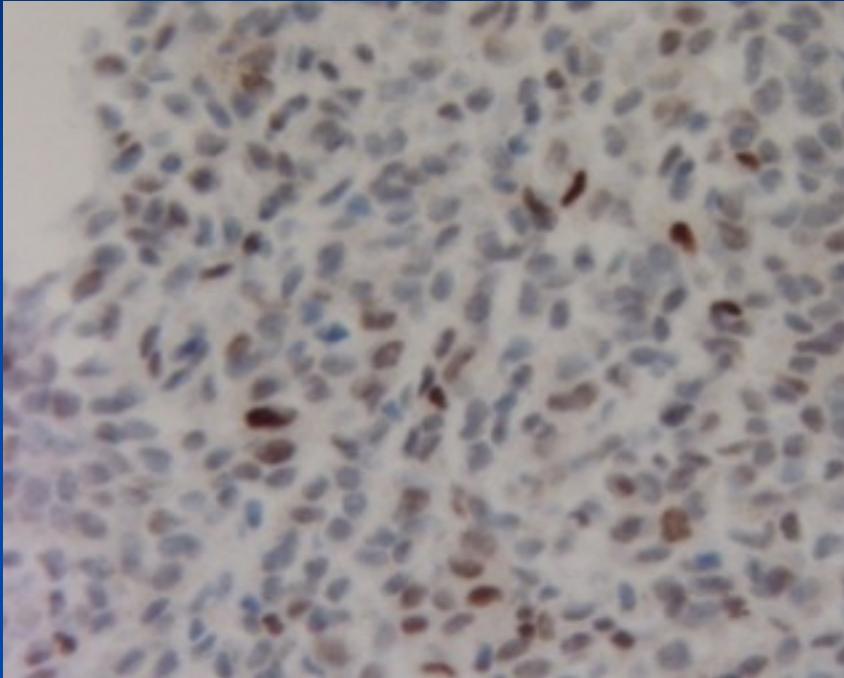
IPOX Help

(b) P53 Cell cycle-inhibiting pathway



- p53
- MIB1 (Ki67)

p53

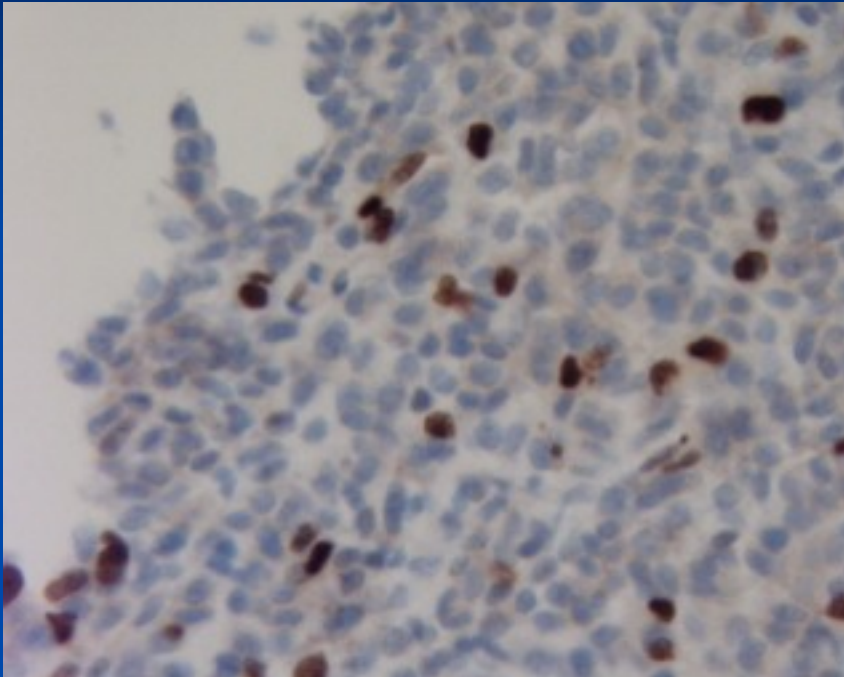


- Positive reactivity
 - Seven (35%) metastatic MMs
 - Eight (31%) primary MMs
 - Two (7%) SNs, only one showed strong nuclear staining
 - None of the CNs

- Immunohistochemical detection of p53 protein with strong nuclear reactivity may prove to be an adjunctive tool in the histopathologic differentiation of MM from SN

Am J Dermatopathol 1995 Dec;17(6):547-50

Ki-67/p53



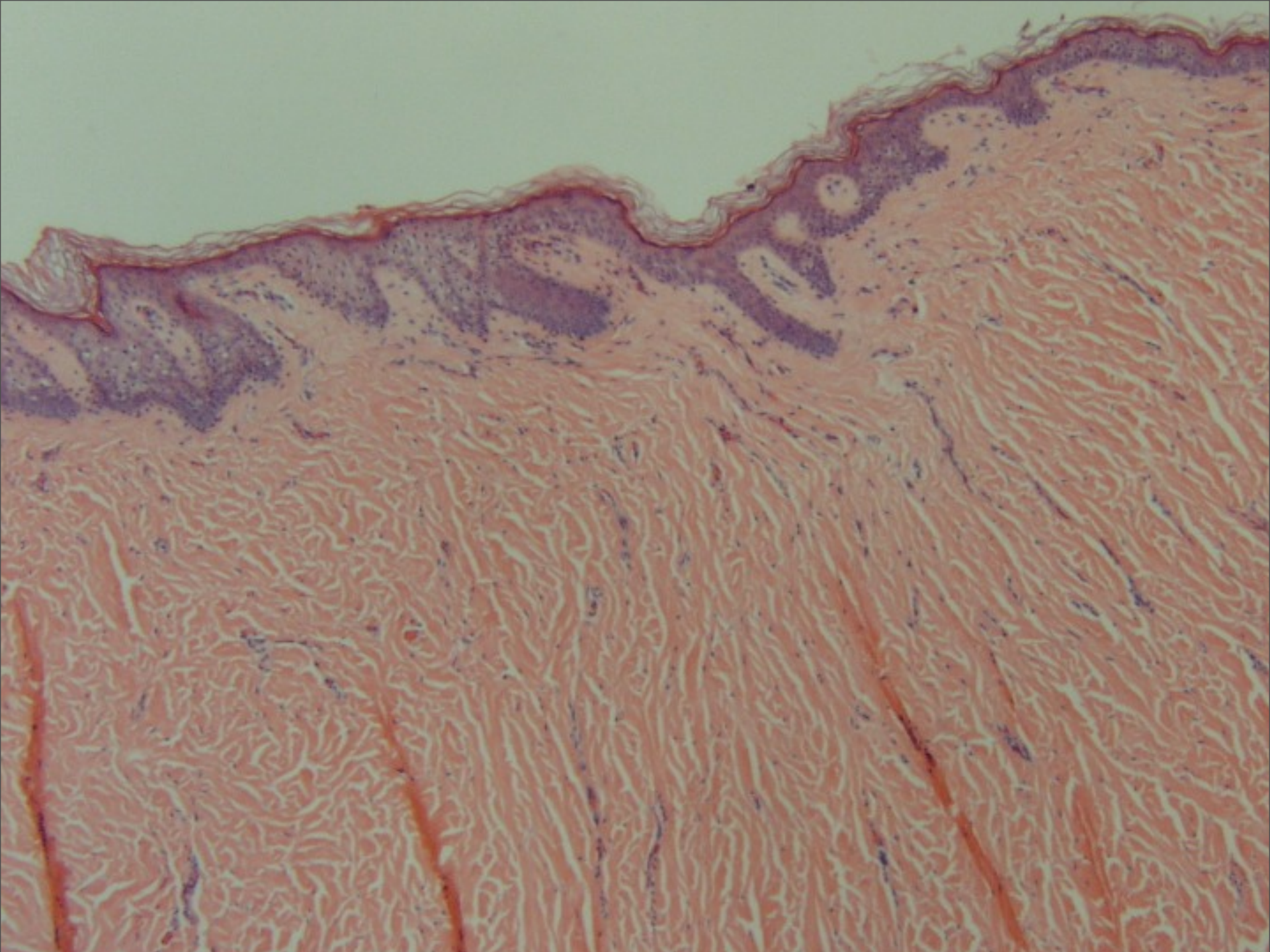
- Negligible Ki-67 and p53 labeling was seen in CN, SN
 - Radial growth-phase SSMMs and LMMs similar to those of melanocytic nevi
- Largest proportion in NMMs, followed by SSMMs
- Ki-67 threshold index of 10% and a p53 index of 5%
 - Correctly indicated the presence of vertical growth in 75% of NMMs
 - Only 8% of radial growth phase melanomas of other types were colabeled at the same levels of reactivity for the two markers

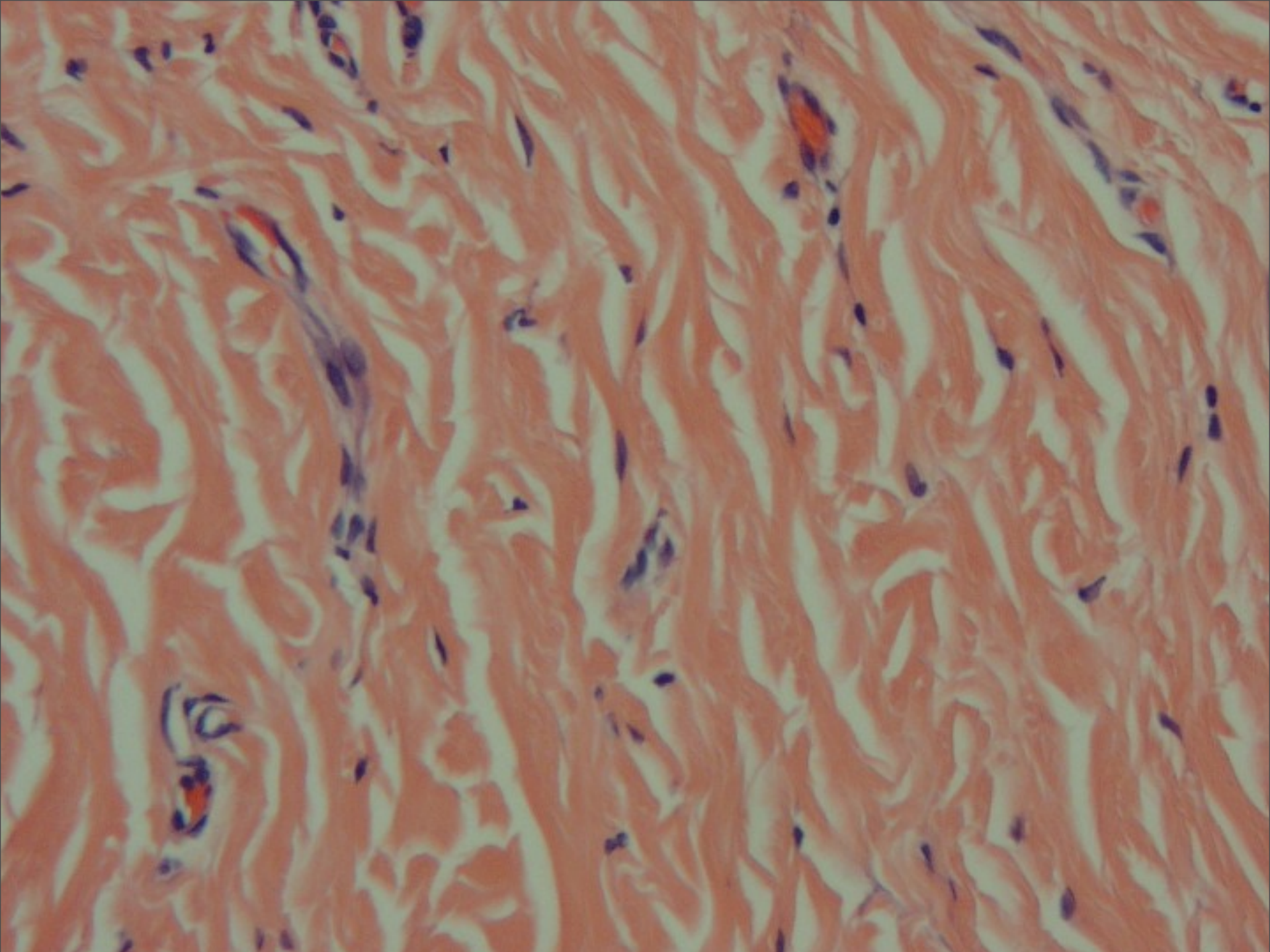
Mod Pathol 2000 Mar;13(3):217-22

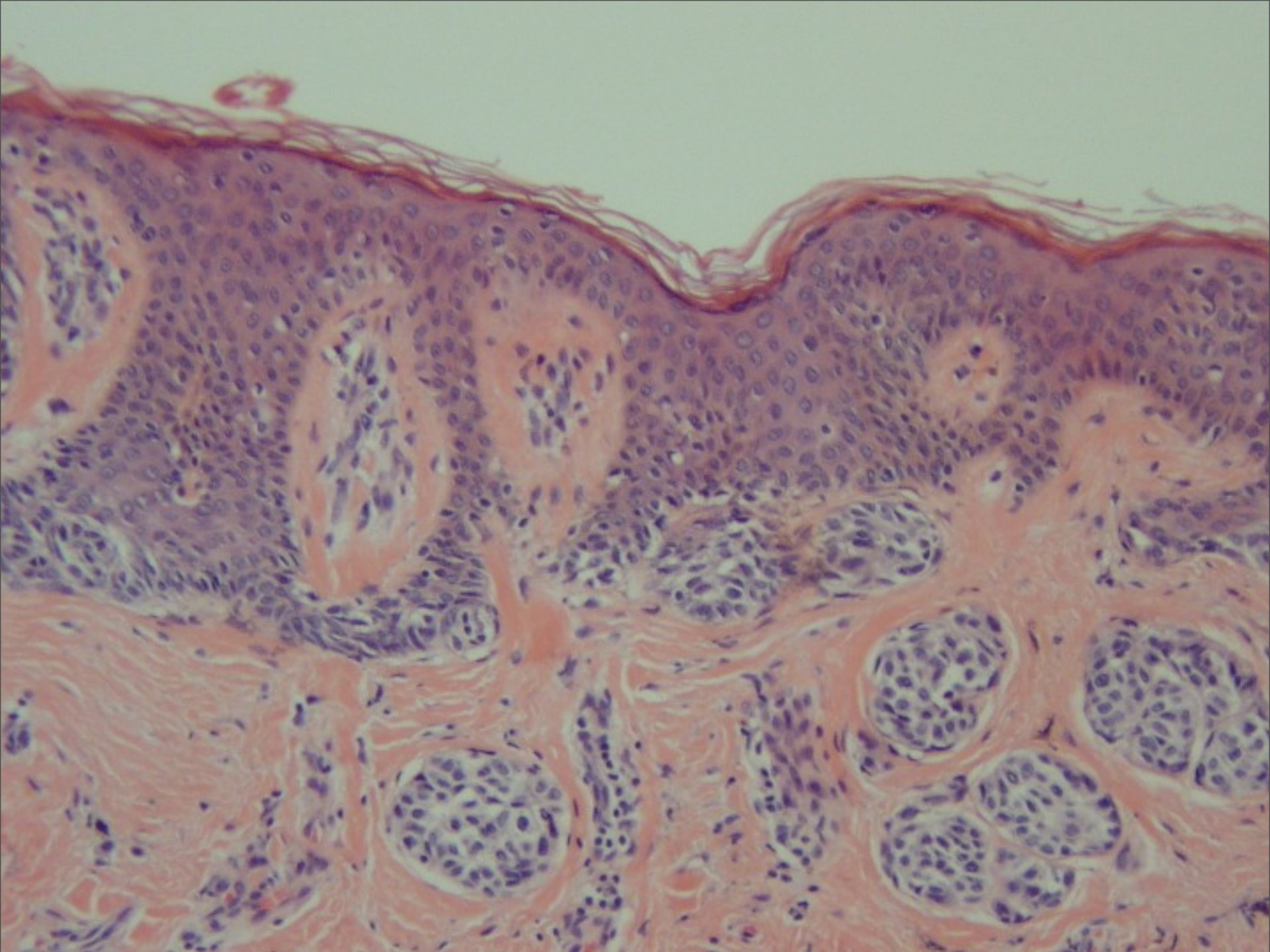
Differential Diagnosis



- Nevi arising in certain body locations
 - Elbow
 - Ear
 - Ankle
 - Genital Skin
 - Umbilicus







Summary



- Sporadic dysplastic nevus is common
- May be associated with increased risk of melanoma, especially in high-risk individuals
- Considerable histologic variability
- Ki-67/p53 may be helpful

Questions



- I know that you believe that you understood what you think I said, but I am not sure you realize that what you heard is not what I meant.

Robert McCloskey, Former State Department spokesman

References

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- Cancer 1980;46:1787-1794
- Am J Dermatopathol 1982;4:455-460
- J Am Med Assoc 1997;277:1439-1444
- Mod Pathol 1989;2:306-319