



University of Pennsylvania, Founded by Ben Franklin in 1740

08.15 Introduction. [Raymond Barnhill](#)  
08.20 Criteria for melanocytic lesions : an introduction.  
[Raymond Barnhill](#)  
08.50 Immunohistochemistry for pathologists. [Klaus Busam](#)  
09.20 Molecular diagnostics for pathologists. [Boris Bastian](#)  
10.00 Coffee Break  
10.30 MPath classification. [Raymond Barnhill](#)  
10.50 AJCC 8<sup>th</sup> edition guidelines. [David Elder](#)  
11.10 Sentinel lymph nodes and prognostic factors in  
melanoma, [Lyn Duncan](#)  
11.30 Treatment recommendations for melanocytic lesions.  
[David Elder](#)  
12.00 Lunch  
01.00 <sup>PM</sup> Classification of melanoma for pathologists. [Boris  
Bastian](#)  
01.30 <sup>PM</sup> Lentigo maligna melanoma. [Klaus Busam](#)  
01.50 <sup>PM</sup> Ocular conjunctival and uveal melanocytic lesions:  
Clinical aspects. [Denis Malaise](#)  
02.10 <sup>PM</sup> Conjunctival melanocytic lesions: Pathological  
aspects. [Ian Cree](#)  
02.25 <sup>PM</sup> Uveal melanoma: Pathological aspects. [Raymond  
Barnhill](#)  
02.40 <sup>PM</sup> Angiotropic extravascular migratory metastasis.  
[Claire Lugassy](#)  
03.00 <sup>PM</sup> Coffee Break  
03.30 <sup>PM</sup> Case presentations  
(10 cases, 10 min/case with discussion)  
05.45 <sup>PM</sup> Welcome cocktail

08.10 Acquired melanocytic nevi. [David Elder](#)  
08.40 Spitz nevus, atypical Spitz tumor, Spitz melanoma.  
[Raymond Barnhill](#)  
09.10 Blue nevus and melanoma arising in blue nevus.  
[Arnaud de la Fouchardière](#)  
09.40 Site-specific nevi (including scalp, breast and milk-line,  
flexural, perianal). [David Elder](#)  
10.00 Coffee Break  
10.30 Combined melanocytic nevi: BAP1, deep penetrating,  
Pigmented epithelioid melanocytoma, etc [Arnaud de la  
Fouchardière](#)  
10.50 Pediatric melanocytic lesions. [Raymond Barnhill](#)  
11.10 Acral melanocytic nevi and melanoma. [Richard Scolyer](#)  
11.40 Melanoma of unknown primary: differential diagnosis,  
[Lyn Duncan](#)  
12.10 Lunch  
01.10 <sup>PM</sup> Nevoid melanoma. [Klaus Busam](#)  
01.30 <sup>PM</sup> Desmoplastic nevi and desmoplastic melanoma.  
[Klaus Busam](#)  
01.50 <sup>PM</sup> Oral and genital melanocytic lesions. [Ian Cree](#)  
02.10 <sup>PM</sup> Sinonasal melanoma, [Lyn Duncan](#)  
02.30 <sup>PM</sup> Gene expression profiling in melanocytic lesions: an  
update, [Matthew Goldberg](#)  
03.00 <sup>PM</sup> Coffee Break  
03.30 <sup>PM</sup> Case presentations continued

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# **Nevi of Special Sites**

Paris 2024

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# **Nevi of Special Sites**

Dealing with Uncertainty

# Significance of Nevi

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- Nevi are important almost exclusively in relation to melanoma
- Significance as
  - Simulants of melanoma
  - Markers of individuals at increased risk for melanoma
  - Potential precursors of melanoma

# Special Site Nevi

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- Simulants, but not thought (at present) to be risk markers or potential precursors of melanoma

# Nevi of Special Sites:

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- Simulants of melanomas and of dysplastic nevi.
- Not precursors, not risk markers
- The “special sites” include flexures such as axillae and umbilicus, the skin of the breast, genital skin especially in young women, scalp, ear and acral skin.



# General Considerations

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- Existence of “special site” nevi does not preclude presence of authentic dysplastic nevi and melanomas on these same sites.
- Under- and over- diagnosis are both problematical
- In case of uncertainty, patients deserve to understand that the differential diagnosis may include dysplastic nevus or melanoma



# Uncertainty in Pigmented Lesion Diagnosis

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- Uncertainty should be expressed directly with a descriptive diagnosis and a differential diagnosis
- Superficial atypical melanocytic proliferation of uncertain significance – SAMPUS
  - Lesions with atypical nontumorigenic components
  - Risk of local persistence/recurrence, not metastasis
- Melanocytic tumor of uncertain potential – MELTUMP
  - Lesions with atypical tumorigenic components
  - Risk of metastasis with or without local recurrence

# Uncertainty in Pigmented Lesion Diagnosis

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- Differential diagnosis should be provided to clinician, including microstaging (thickness etc)
- Management should be discussed with informed patient
  - complete excision (at least) for SAMPUS lesions
  - consider SLN sampling for MELTUMP lesion

# Epidemiology of SSN

(Pathology Outlines 2023)

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- Breast is the most common special site (56%), followed by axilla (16%) and then scalp (12%) ([J Cutan Pathol 2020;47:664](#))
- SSN of the ear have a wide age distribution (5 - 86 years, mean: 42.4) and occur equally in both sexes (F:M = 1.1:1) ([J Cutan Pathol 2005;32:40](#))
- Scalp SSN are more common in adolescents with a slight predominance of males; adults and children are less commonly affected ([Br J Dermatol 2011;165:137](#))
- Breast SSN are more common in younger females ages 30 - 40 but may occur in both men and women ([J Am Acad Dermatol 2016;75:364](#), [J Cutan Pathol 2004;31:137](#))
- Genital SSN most commonly present in premenopausal, reproductive age woman with a median age of 26 years but may occur in children and commonly involve mucosal sites ([Am J Surg Pathol 2008;32:51](#))
- Acral SSN have a frequency of 10 - 30% in the population and are more common in patients of color ([Arch Dermatol 2010;146:1085](#))

# Histopathology of SSN

## (Pathology Outlines 2023)

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Nevi site	Atypical nevi features	Differentiating features from melanoma
Scalp	Lentiginous growth, pagetoid spread, loss of symmetry	Lack of severe atypia (uniform atypia), dermal maturation, lack of deep or atypical mitoses
Ear	Pagetoid spread, irregular nesting pattern, cytologic atypia, may induce host inflammatory response	Dermal maturation, lack of severe atypia (uniform atypia), symmetry, lack of deep or atypical mitoses
Breast	Dyshesive nests, cytologic atypia, rete effacement	Dermal maturation, symmetry, effacement of rete limited to center, lack of deep or atypical mitoses
Genital	Large dyshesive nests, lentiginous growth, asymmetry is common, pagetoid spread	Dermal maturation, lack of deep or atypical mitoses, limited pagetoid spread
Acral	Lentiginous growth, pagetoid spread	Lentiginous growth does not involve crista profunda intermedia, lack of deep or atypical mitoses, dermal maturation

# Nevi of Flexural Sites

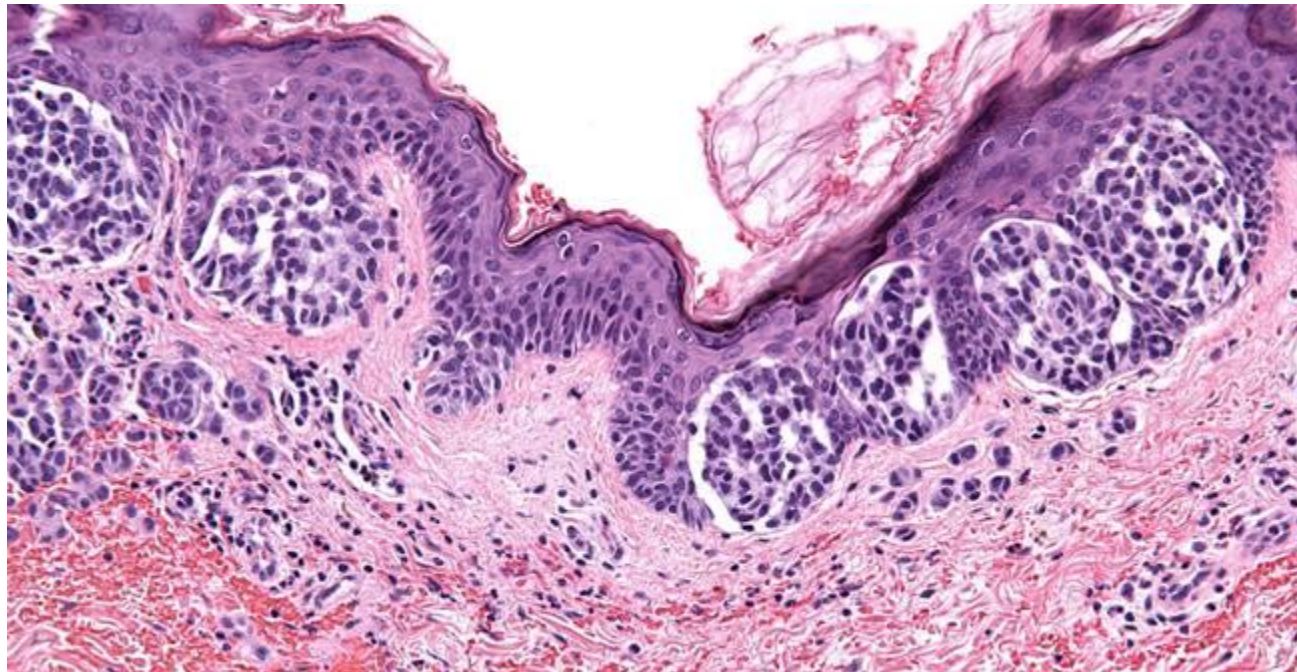
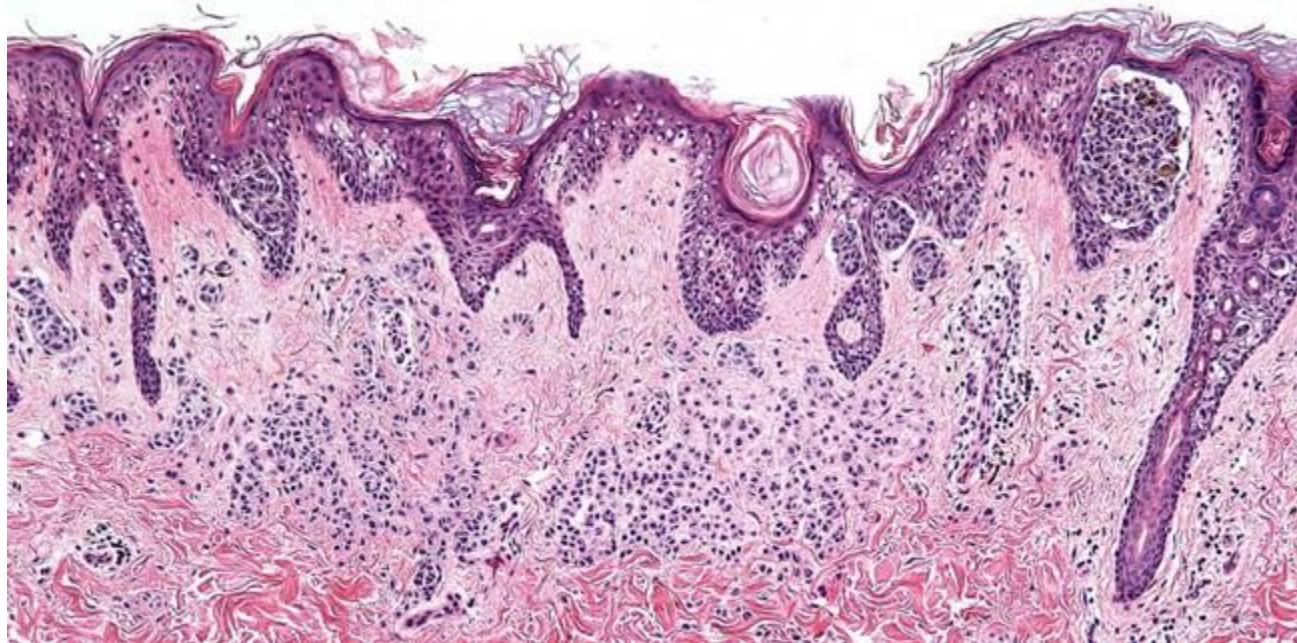
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- Nevi of flexural skin may show unusual features:
  - greater variability in the size of junctional nests as well as origin of nests at the edges of rete and in inter-rete regions,
  - these features may also occur in dysplastic nevi.
    - however, cytologic atypia and associated stromal alterations typical of dysplastic nevi are lacking in nevi of the flexural type
  - lesional location may be of some significance in interpreting significance of nevi.
- Rongioletti F, Ball RA, Marcus R, and Barnhill RL: Histopathological features of flexural melanocytic nevi: a study of 40 cases. J Cutan Pathol 2000, 27: 215-217



# Axillary Nevus

- variably sized nests
- origin of nests at the edges of rete
- nests in inter-rete regions



# Nevi of the Breast

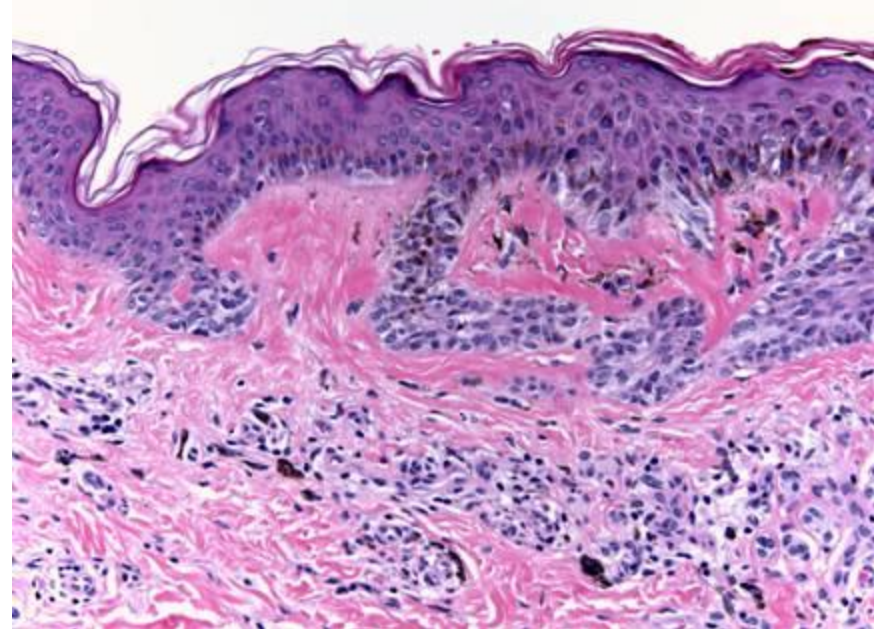
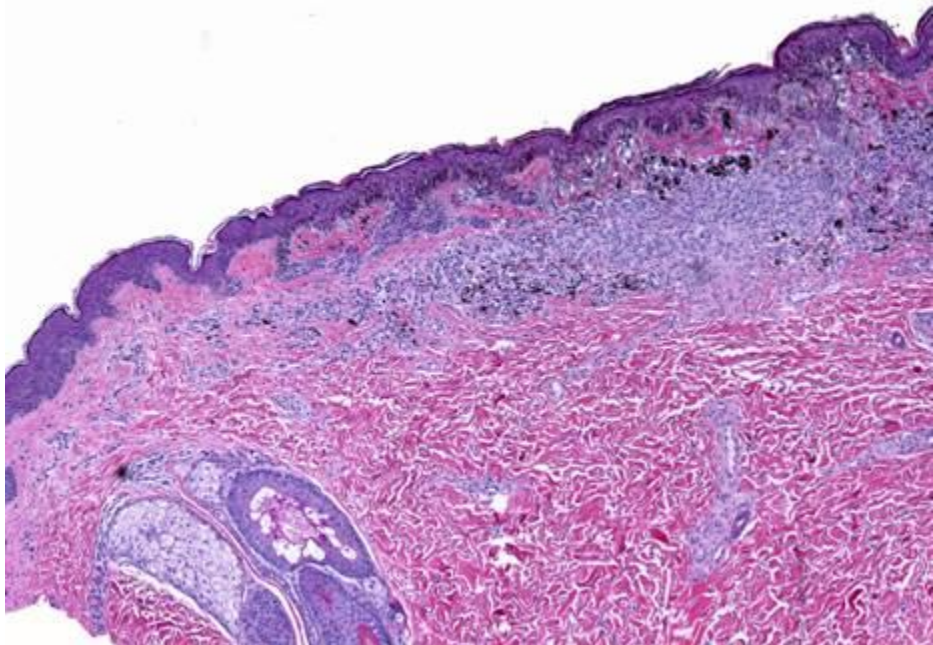
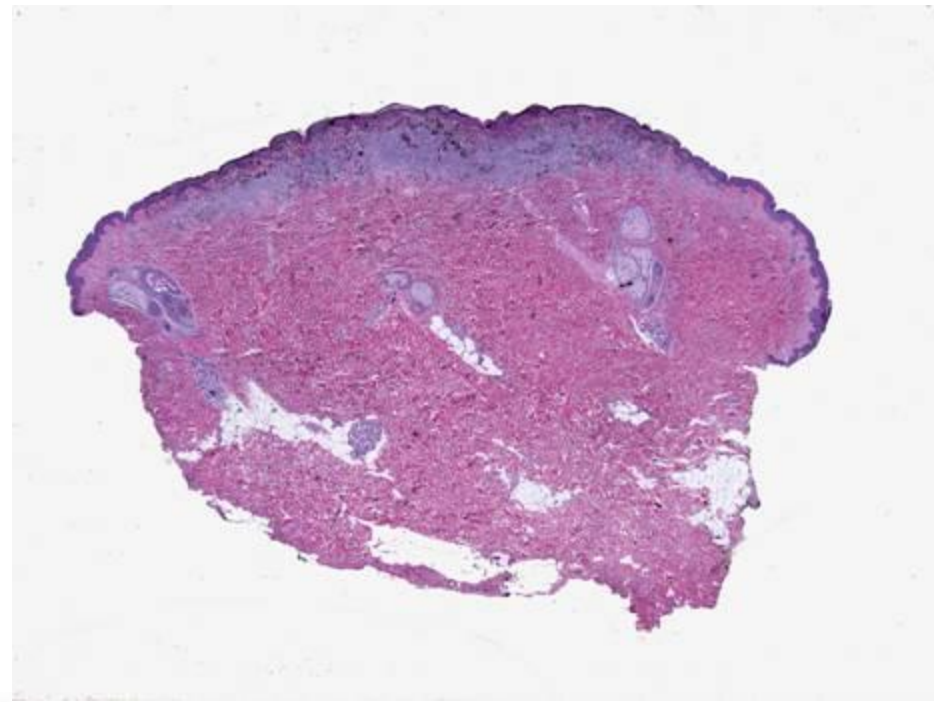
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- 101 nevi from the breast area were compared with 97 from elsewhere.  
Rongioletti et al, J Cutan Pathol 2004
  - Breast nevi had more atypical features than nevi from other sites
  - Prominent intraepidermal melanocytes, melanocytic atypia, and dermal fibroplasia.
  - Interestingly, there was no gender difference.
- Overlap with dysplastic nevi – is the atypia due to neoplastic progression (dysplasia) or is it reactive?
  - We report the atypia.
  - May recommend consideration of conservative complete excision.
  - May recommend consideration of surveillance, especially if patient has other clinically atypical nevi, or a family or personal history of melanoma.



# Breast Skin Nevus, F11

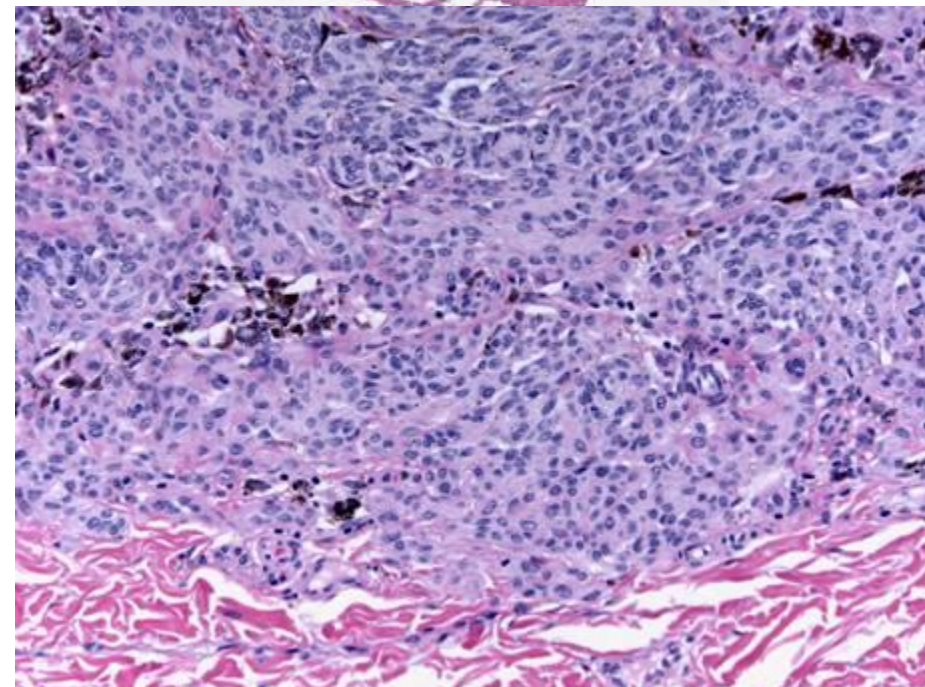
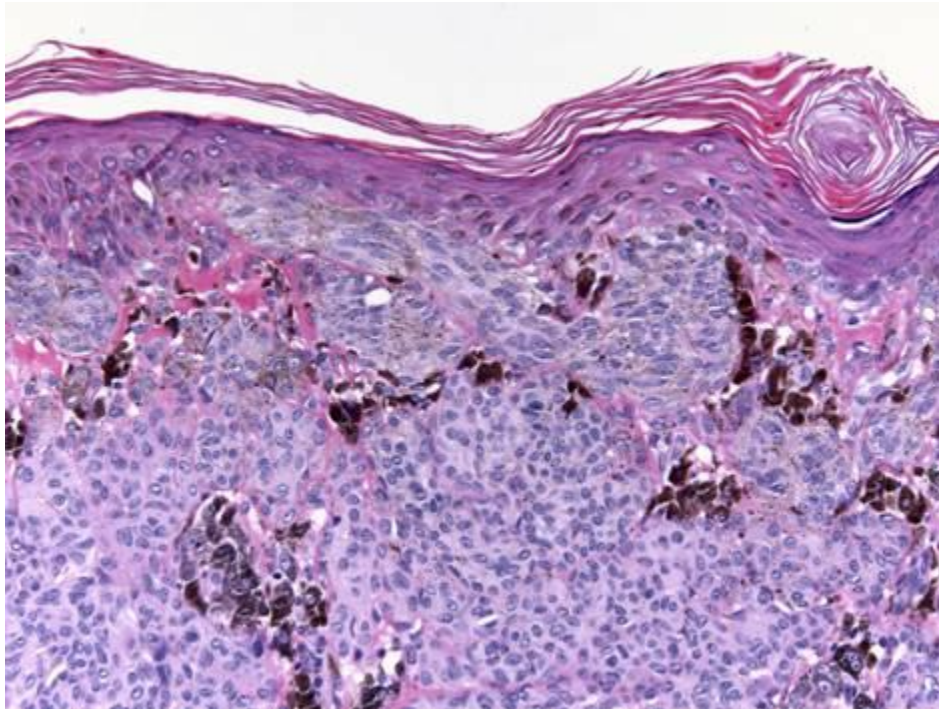
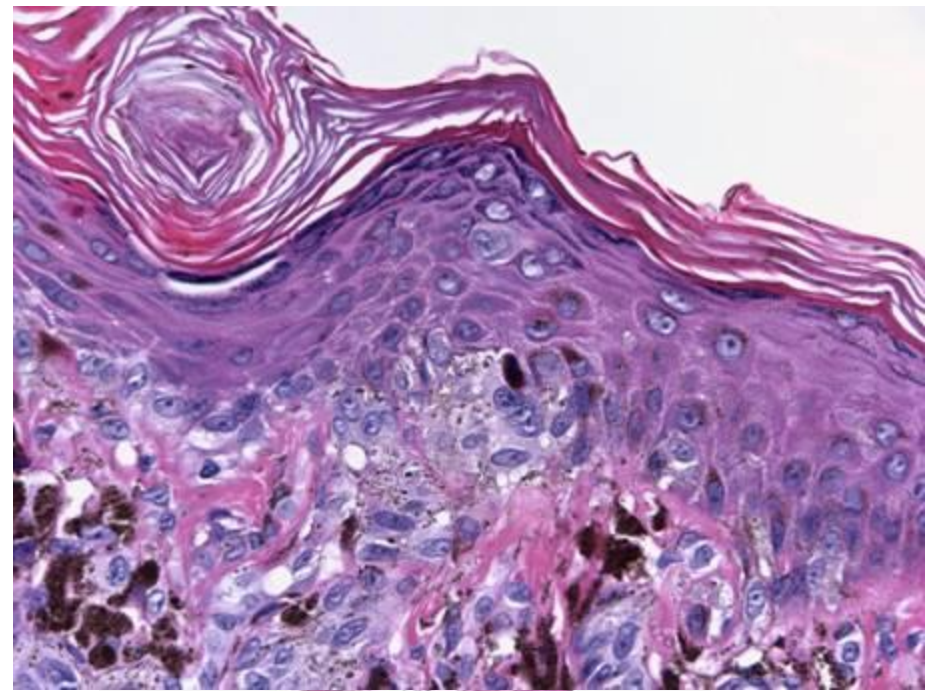
- Symmetrical
- Bridging nests
- Fibroplasia





# Breast Skin Nevus

- Large nests
- Large cells
- Maturation



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# Your Diagnosis?

Nevus?

Melanoma?

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# Your Diagnosis?

Dysplastic?

Non-dysplastic?

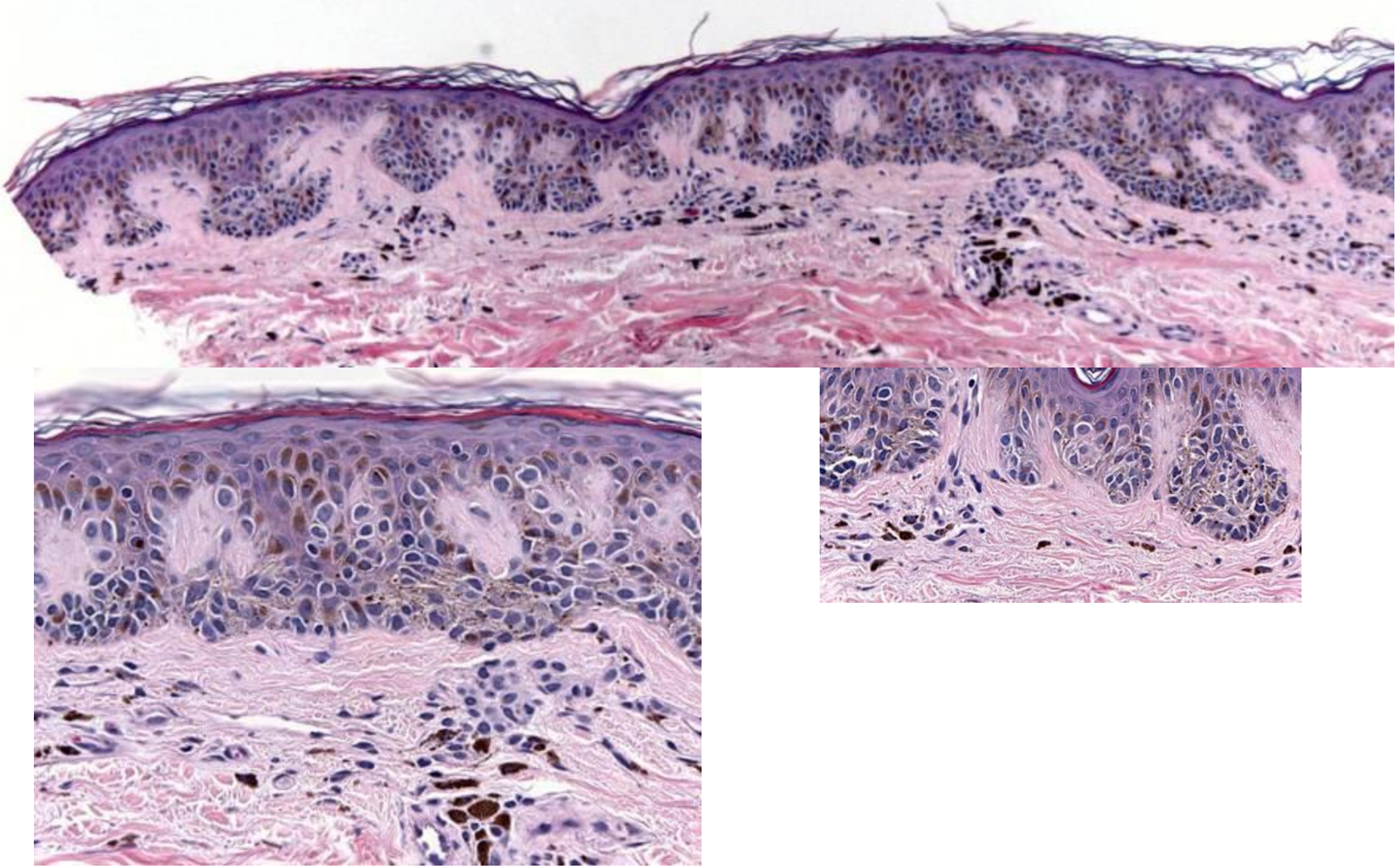
(e.g. special site nevus)

# Diagnosis

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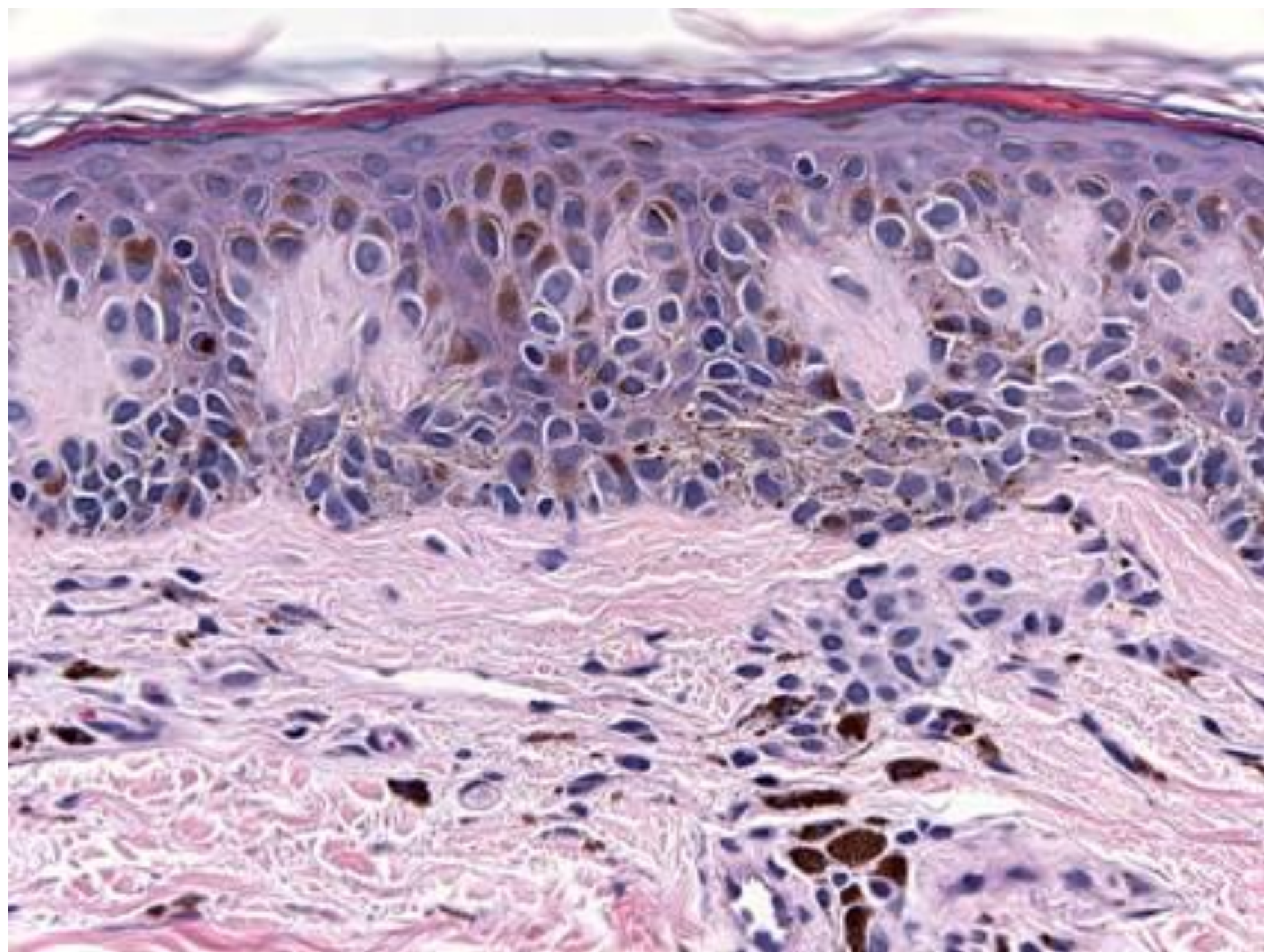
- F 11, nevus of breast
- Compound nevus with superficial atypical melanocytic proliferation of uncertain significance (SAMPUS), most c/w compound nevus with severe dysplasia.
- Comment: Differential diagnosis includes a “nevus of special site” of the breast. Especially if patient has other clinically dysplastic nevi or a family or personal history of melanoma, additional evaluation and possible surveillance may be indicated.
  - If not, the diagnosis of SSN could be supported





“Nevus” of the breast in a 43 year old woman







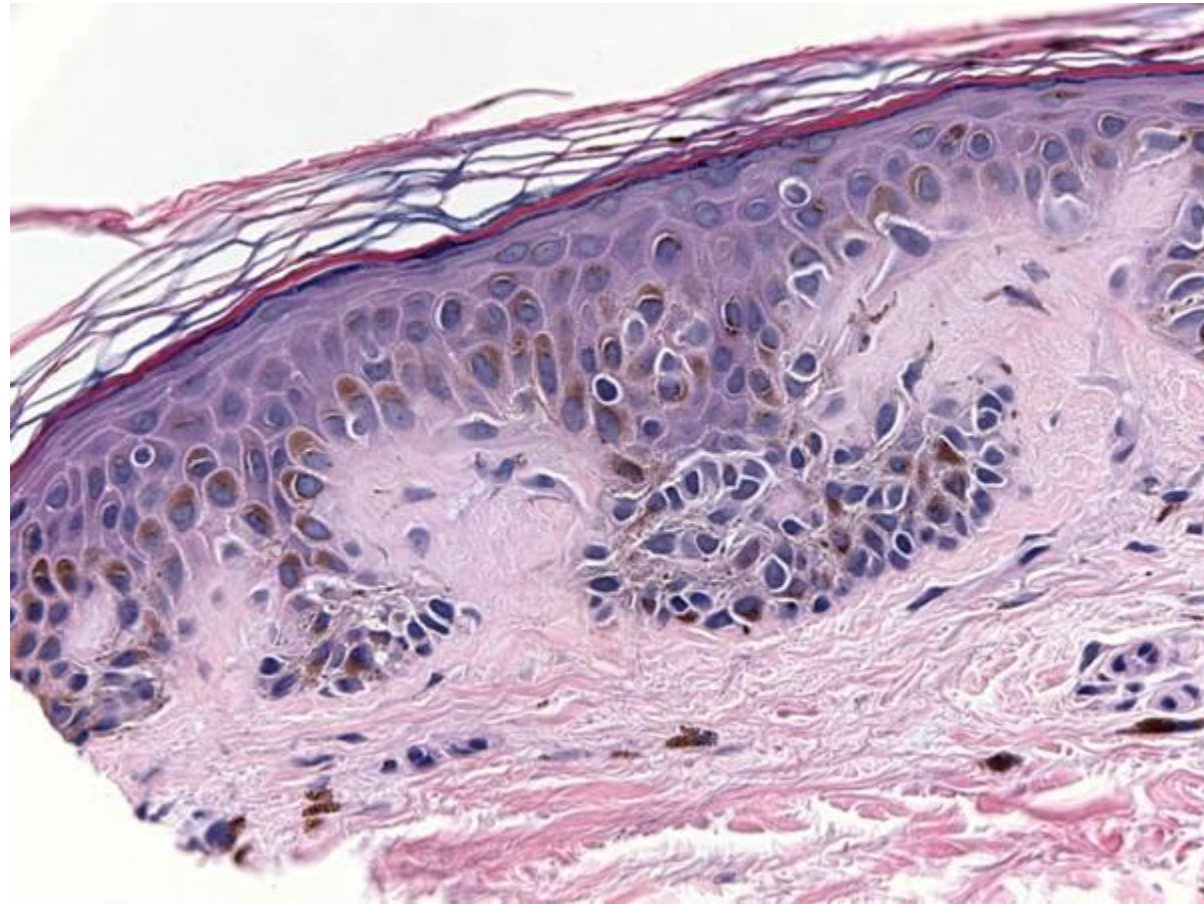
# Nevus of the Breast in a 43 year old Woman

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Diagnosis:

Compound nevus  
with melanocytic  
dysplasia

- Mild cytologic atypia
- Moderate to severe architectural disorder.



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# Your Diagnosis?

Nevus?

Melanoma?

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# Your Diagnosis?

Dysplastic?

Nondysplastic?

# Nevus of the Breast in a 43 year old Woman

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- Diagnosis: Compound nevus with moderate to severe melanocytic dysplasia.
- Additional history:
  - Patient had a melanoma on her back.
  - She is a member of a melanoma-prone family, with three melanomas in her 19-year-old brother and one melanoma in her 37-year-old sister
  - Recognition of a dysplastic nevus in any family member can trigger investigation that ultimately leads to identification of high risk family members.
  - Diagnosis of “nevus of special site” does not trigger such investigation.

# Nevus of Genital Skin

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- Benign nevi of genital skin most often seen on the vulva of young (pre-menopausal) women.
- A few lesions have histologic features imperfectly simulating dysplastic nevi and melanomas, including:
  - large and sometimes confluent nests, large cells, nucleoli, and a lymphocytic infiltrate.
  - Friedman RJ and Ackerman AB: Difficulties in the histologic diagnosis of melanocytic nevi on the vulvae of premenopausal women. Pathology of Malignant Melanoma. Edited by Ackerman AB. New York, Masson, 1981, pp. 119-127
  - Christensen WN, Friedman KF, Woodruff JD, Hood AF: Histologic characteristics of vulval nevocellular nevi. J Cutan Pathol 1987, 14: 87-91
  - Maize JC, Ackerman AB: Pigmented lesions of the skin. Clinicopathologic correlations. Philadelphia Lea & Febiger, 1987
  - Jampel RM, Friedman KF, Woodruff JD, Hood AF, Clark WHJr: Atypical melanocytic lesions of the vulva. J Cutan Pathol 1989
  - Rock B, Hood AF, and Rock JA: Prospective study of vulvar nevi. J Am Acad Dermatol 1990, 22: 104-106

# Clinical Features of Genital Nevi

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- Clinically benign nevi often removed incidentally.
- Certain histologic features arouse a suspicion of melanoma.
  - These atypical changes are rare in vulvar nevi; in a histologic study of 85 vulvar lesions, all but 3 were indistinguishable from control nevi of non-vulvar skin (Christensen et al, J Cutan Pathol 1987) .
  - Vulvar nevi themselves are quite uncommon; in a study of 301 new patients in a gynecology practice, the prevalence of melanocytic nevi on vulvar skin was only 2.3%. (Rock et al, J Am Acad Dermatol 1990).
- Atypical features seem to have no clinical significance except possibility of diagnostic error.
- Prudent to recommend complete excision so that the whole lesion can be examined and to prevent recurrence

# Nevus of Genital Skin Microscopic Features:

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- Architectural features:
  - a small, well-circumscribed papular lesion
  - large nests in epidermis, may vary in size and shape, tend to become confluent
  - no extension of junctional component into shoulder
  - no extensive continuous basal or high level pagetoid proliferation of atypical melanocytes in the epidermis
- Cytologic Features
  - cells larger than most usual nevus cells, often with eosinophilic nucleoli, especially superficially
  - cells mature with descent into the dermis.
  - no mitotic activity, ulceration, necrosis



## Nevi of Special Sites – Genital Skin

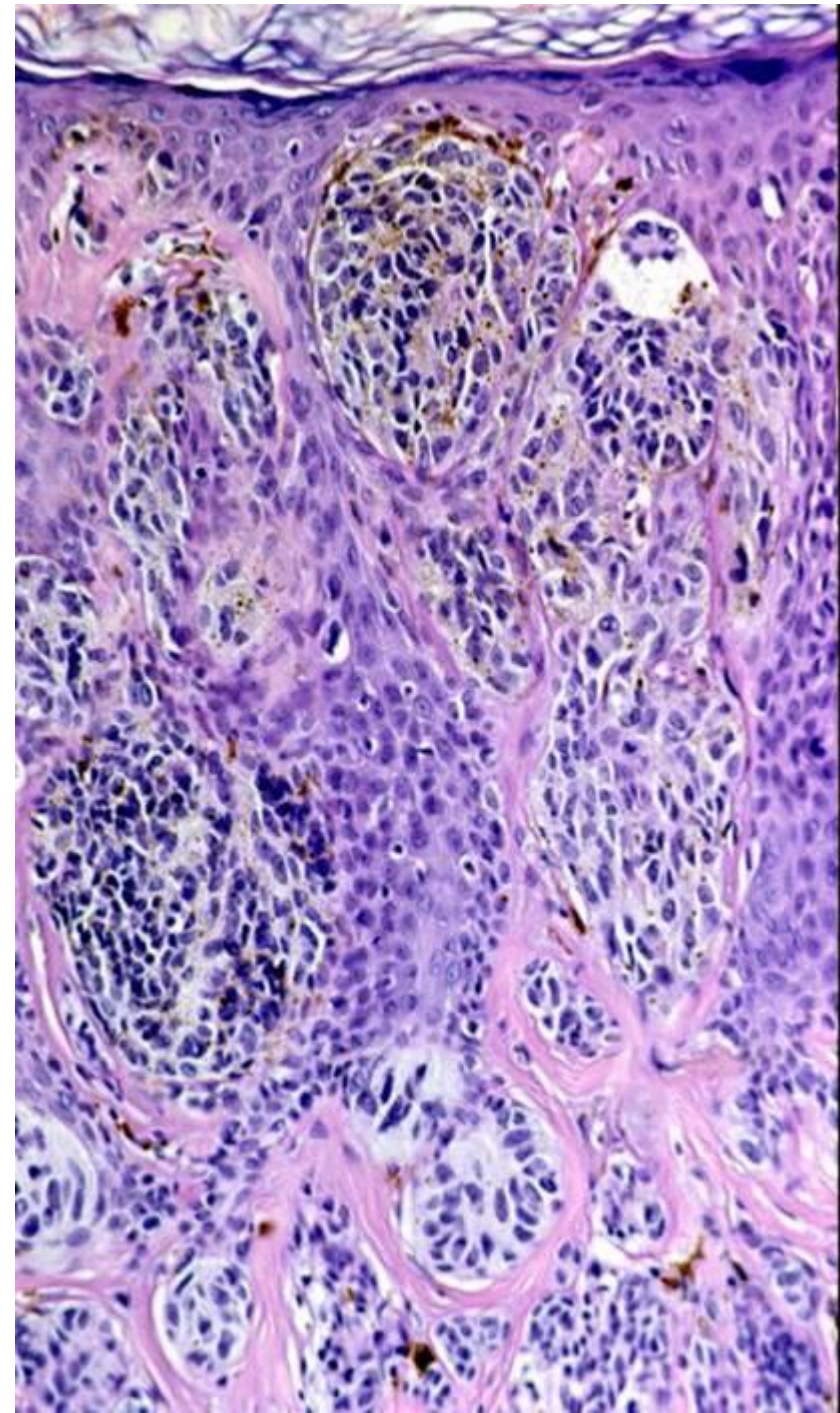
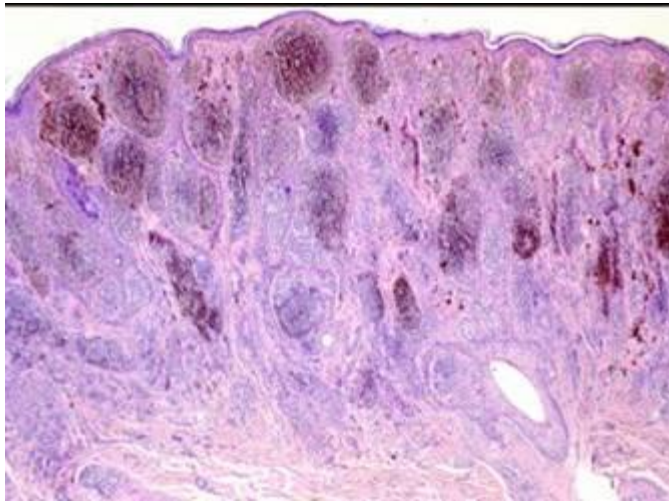
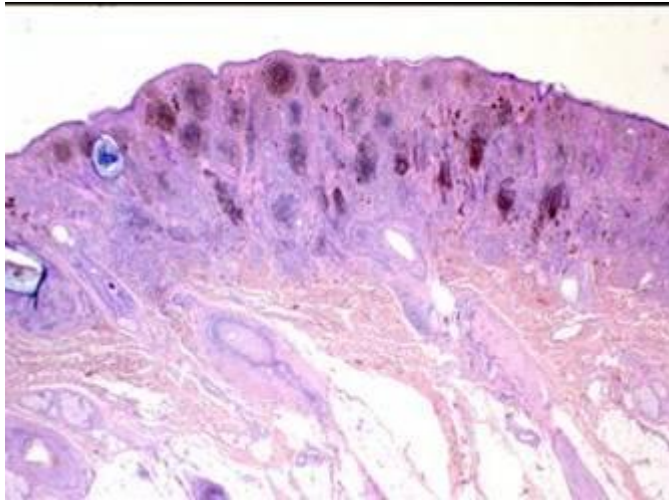
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- Premenopausal women or girls
- Symmetrical lesions, benign clinically
- Melanoma rare premenopausally, but occasionally occurs
- Similar lesions may be seen in males



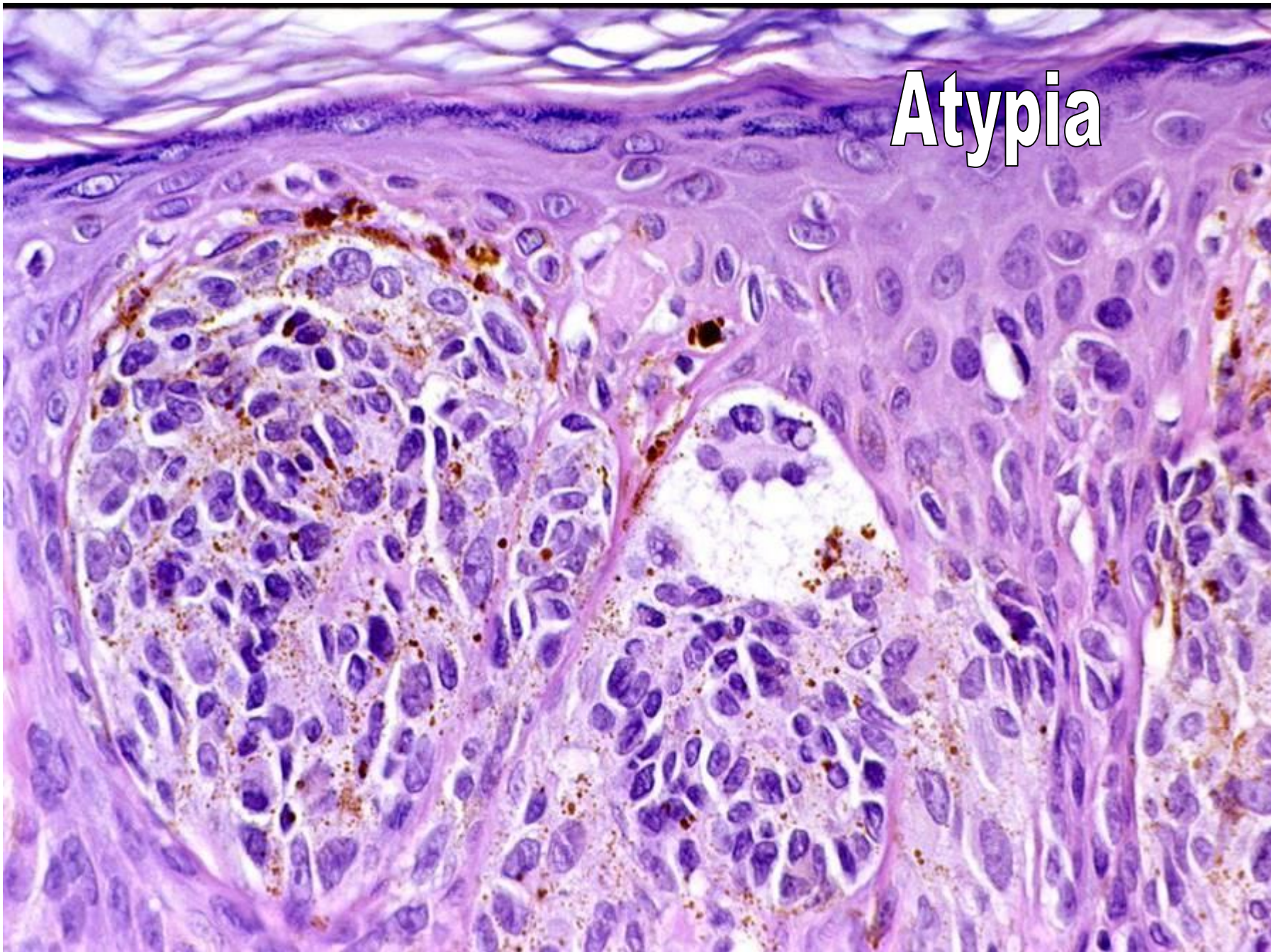
# Special Site Nevus

## Vulvar Skin, F28

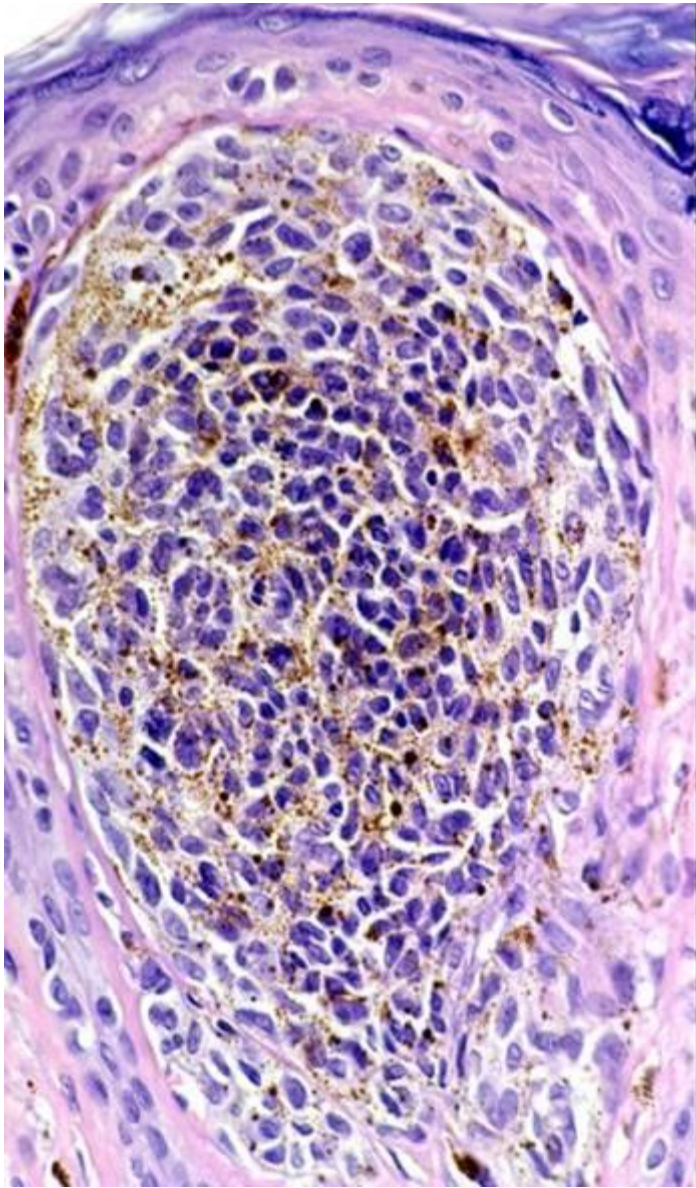




Atypia

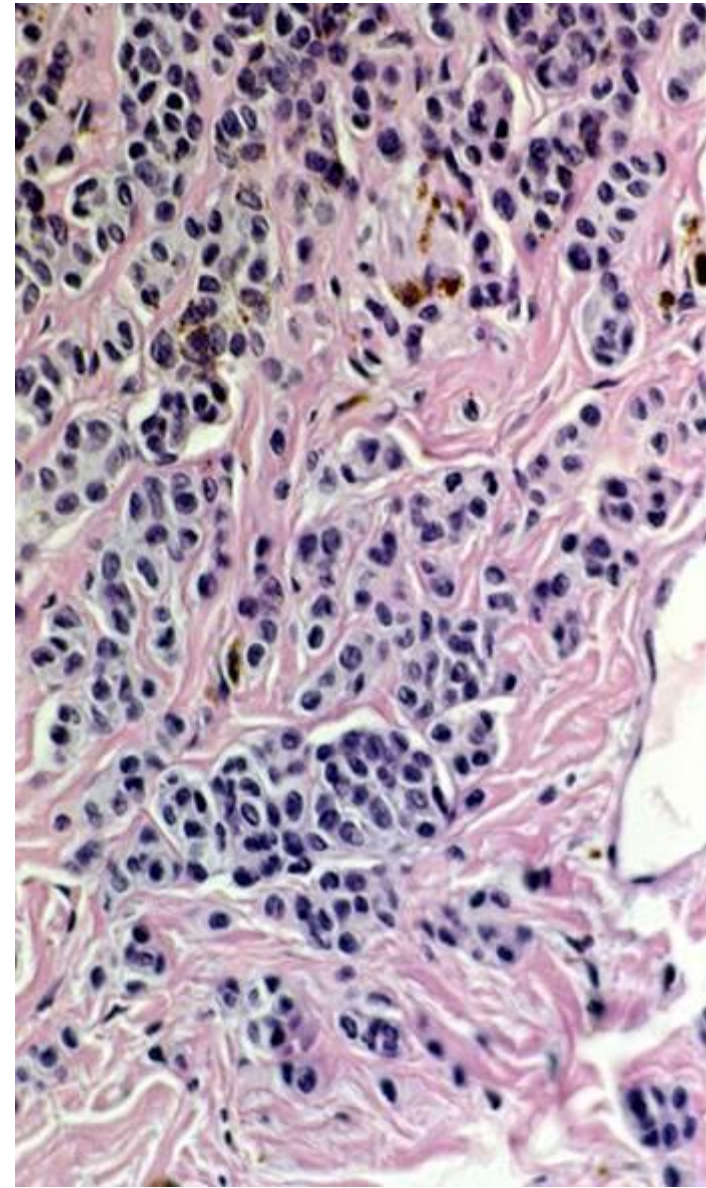






Top of Lesion

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Bottom

# Special Site Nevi

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- Summary 1
  - nevi in special sites may exhibit special features
  - as a rule of thumb, atypia tends to be greatest in genital nevi, least in flexural nevi, intermediate in breast nevi (A Hood)
  - cytologic atypia is not usually high grade
  - maturation is present
  - mitotic rate/Ki-67 rate is low

# Special Site Nevi

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- Summary 2
  - dysplastic nevi and melanomas can occur in all of the “special” sites and should not be under-called
  - uncertainty should be expressed directly with a differential diagnosis
    - superficial atypical melanocytic proliferation of uncertain significance – SAMPUS – for lesions with atypical nontumorigenic components
    - melanocytic tumor of uncertain potential – MELTUMP – for lesions with atypical tumorigenic components
  - Patients should be informed and offered management appropriate to the differential diagnosis

# Possible Management for SAMPUS

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1. SAMPUS – e.g. Nevus vs. Dysplastic Nevus (LG or HG)
  - Many SAMPUS lesions are seen in high risk populations that are being followed (e.g. pigmented lesion clinic patients)
    - For them the threshold for re-excision for close margins can be lower because of their close follow-up and high motivation
  - For a patient with a single lesion, close follow-up is not likely to be obtained through life, and a conservative re-excision should be considered



# Possible Management for SAMPUS

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SAMPUS, e.g. Dysplastic/Atypical Nevus, vs. T1a MM

Management according to the “worst case scenario” should be discussed, i.e. wide(r) complete local excision.

It is not possible to resolve all uncertainty in medicine, including pathology!

# Possible Management for MELTUMP

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MELTUMP, e.g. T2-4 Melanoma vs Atypical Nevus e.g. Spitzoid Tumor

Management according to the “worst case scenario” should be discussed, i.e. wide(r) complete local excision.

Consider adjuvant treatment – possible serious complications

It is not possible to resolve all uncertainty in medicine, including pathology!



Up the Creek without a Paddle?