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The MPATH-Dx reporting schema for melanocytic proliferations and melanoma

Michael W. Piepkorn, MD, PhD[a,b,c], **Raymond L. Barnhill, MD**[d], **David E. Elder, MBChB, FRCPA**[e], **Stevan R. Knezevich, MD, PhD**[f], **Patricia A. Carney, PhD**[g], **Lisa M. Reisch, PhD**[b], and **Joann G. Elmore, MD**[b] ***(A NIH founded group)***

Consensus: *Carney PA et al 2016*

Cat 1: No risk	95%	Benign, (mild atypia)	No further treatment.
Cat 2: Low risk recurrence	64%	Moderate atypia	Complete excision.
Cat 3: Risk local progression	84%	Severe atypia	5mm re-excision.
Cat 4: Risk loco-regional progression	88%	pT1a, (pT1b)	Wide excision (SN)
Cat 5: Risk progression & metastases	100%	pT2 and higher	Wide excision and more

Discussions:
In some cases: compromise rather than consensus.
Descriptive Diagnoses.

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DiagnostIc Categorisations on review

Atypical intraepidermal melanocytic proliferation (AIMP. IAMPUS):

Categories: 2 or 3.

Disordered lentiginous and/or junctional nested to focally pagetoid without sufficient criteria for *melanoma in situ*.

Pagetoid intraepidermal melanocytic proliferation (PIMP. IAMPUS):

Categories: 2 or 3.

As AIMP , with prominence of *in situ pagetoid spread*.

Superficial atypical melanocytic proliferation of uncertain significance (SAMPUS):

Categories: 2,3 or 4/*pT1a*

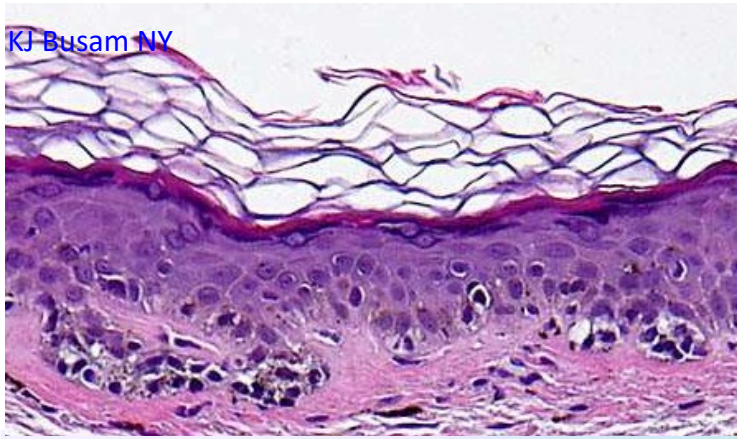
As AIMP, with melanocytic cells in the papillary dermis having cytological abnormalities insufficient for *invasive melanoma*.

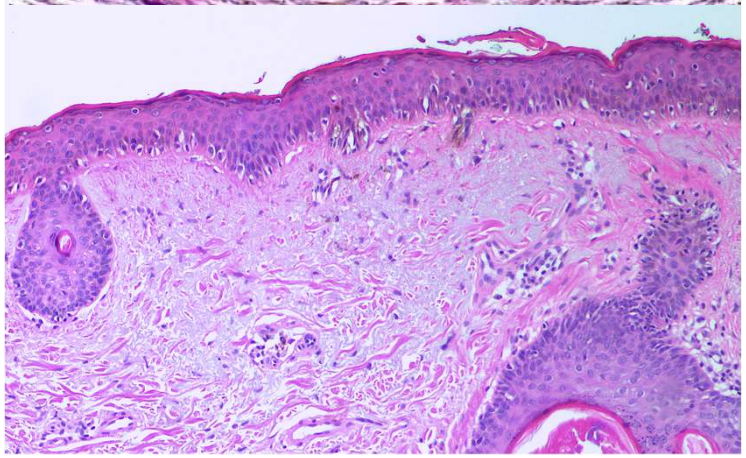
Implies some potential for disease progression in the event of incomplete re-excision.

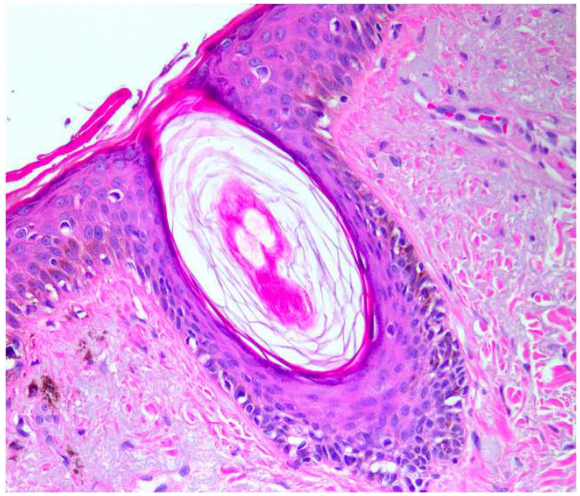
Melanocytic tumor of uncertain malignant potential (MELTUMP):

Categories: 3,4,or 5.

More *substantial dermal involvement*, with or without an intraepidermal component. Cytologic characteristics are unusual but not conclusively those of the *common forms of melanoma*. Unquantifiable, risk for metastatic competence after complete excision.







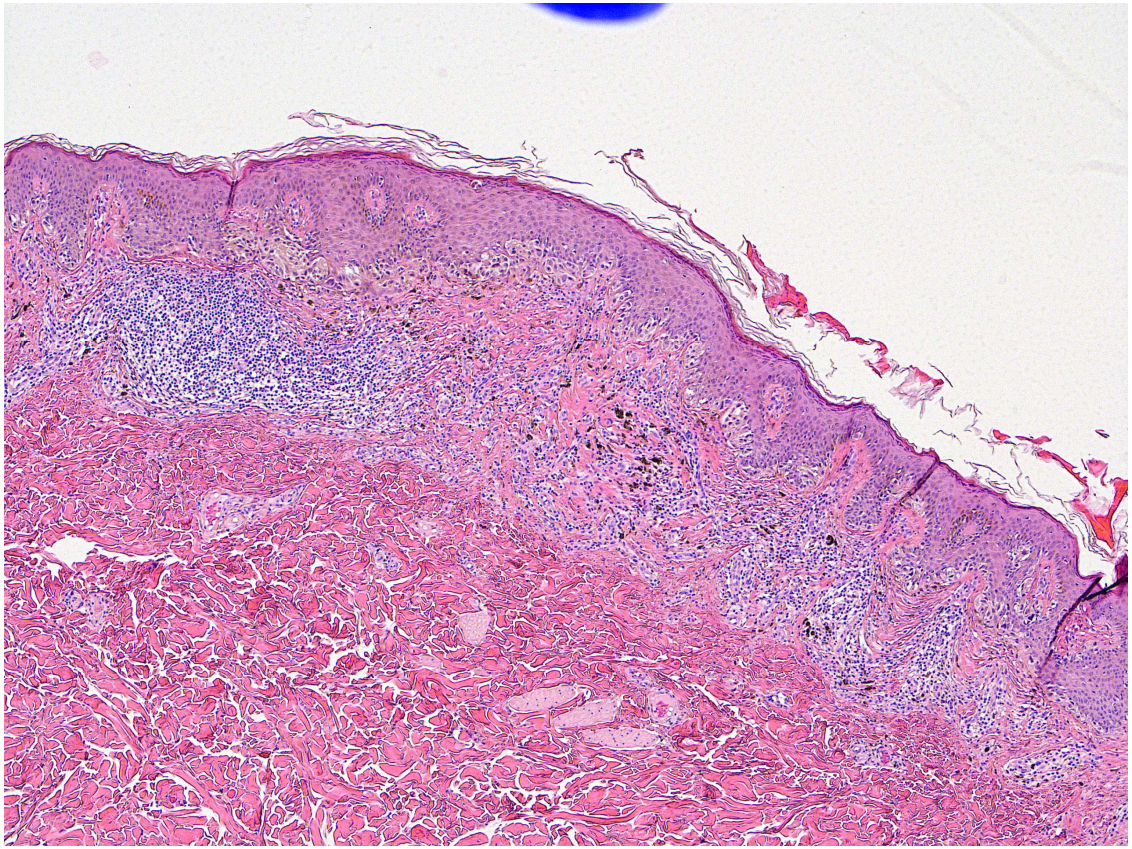
A dysplastic nevus in the skin with actinic damage is usually a melanoma.

Lentigo maligna
Head, neck, ear, bald scalp

No Epidermal hyperplasia.
No rete ridge elongation.
No bridging.
No concentric fibroplasia.

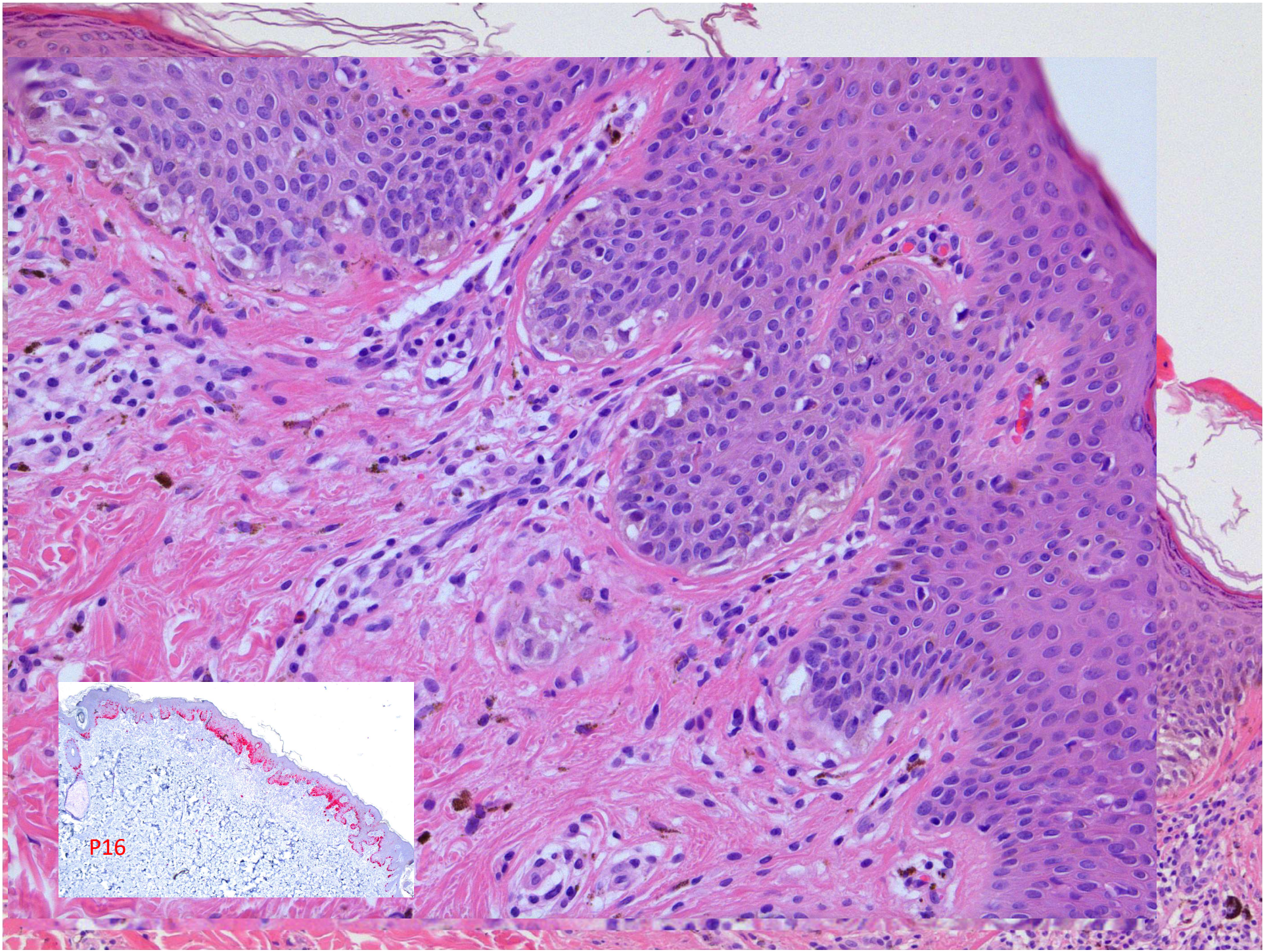
Adnexal Involvement.

Special site nevi (genital, breast, axilla, flexural, acral, scalp, ear)



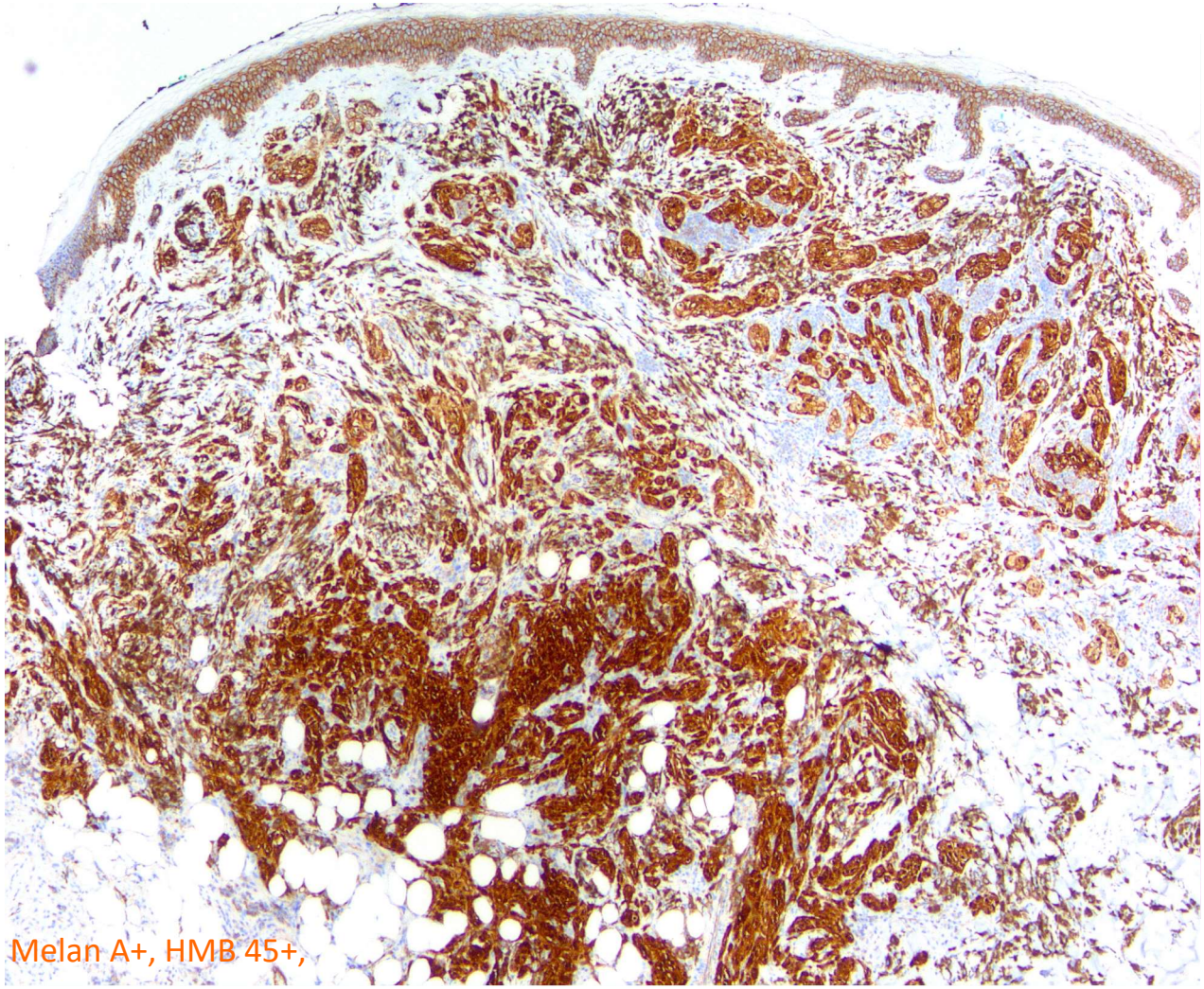
Architectural features that overlap with dysplastic nevi and melanoma. (*WHO 2018)*

15 yr. old girl with
bilateral moles in the skin of the breast
and
history of dysplastic nevi.


P16

Differential. Melanocytic tumor of uncertain malignant potential (MELTUMP):

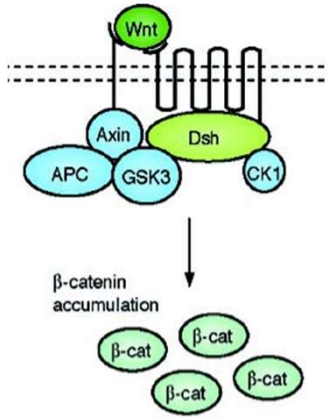
Deep penetrating nevus



Melan A+, HMB 45+,

BRAFV600E or HRAS

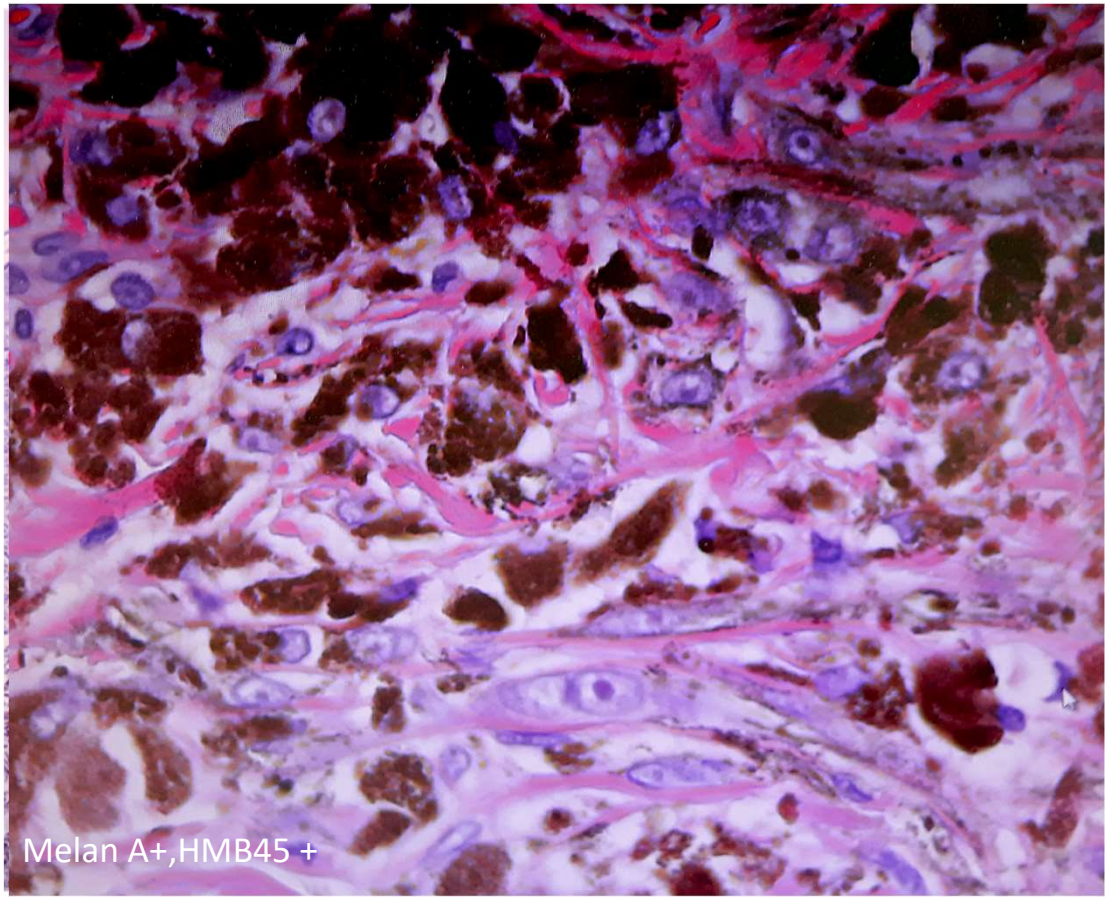
Wnt



Differential. Melanocytic tumor of uncertain malignant potential (MELTUMP):

Pigmented epithelioid melanocytoma

(Epithelioid blue nevus)



Pigmented
dendritic & epithelioid melanocytes.
Melanophages.

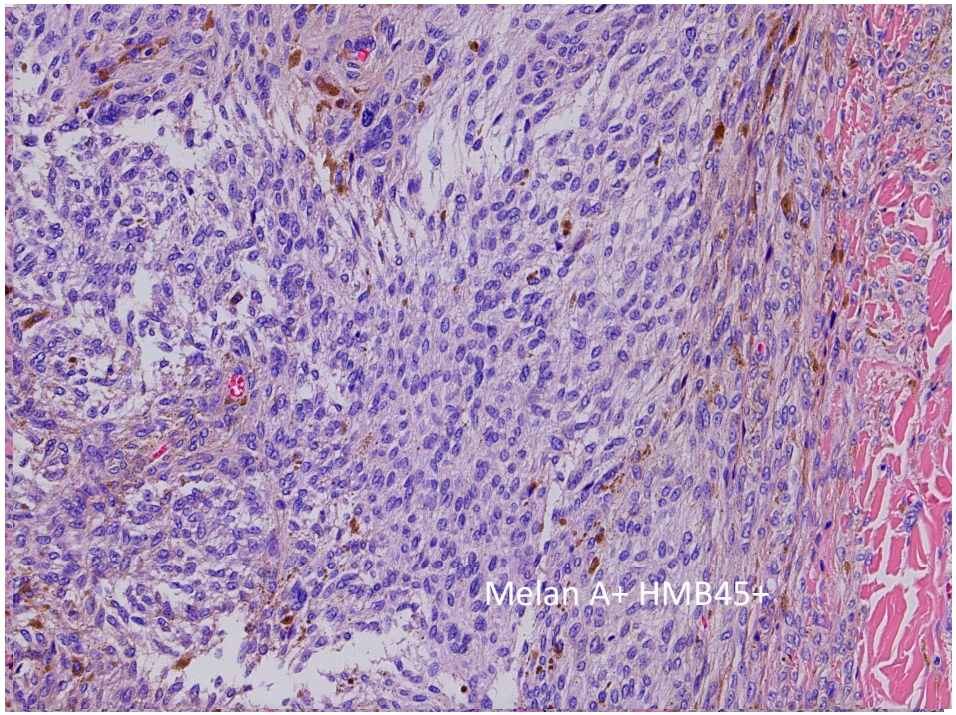
BRAF and PRKAR1A-alterations
PRKAR1A loss in the epithelioid cells

PRKCA fusions (subset spitz related)

GNAQ mutations: 20% (BN related).

Differential. Melanocytic tumor of uncertain malignant potential (MELTUMP):

Cellular blue nevus, Atypical cellular blue nevus
Blue nevus-like melanoma



Young Adults. W> M.
Scalp, back, buttocks.

Pigmented nodules.
Diameter: mm to several cm.

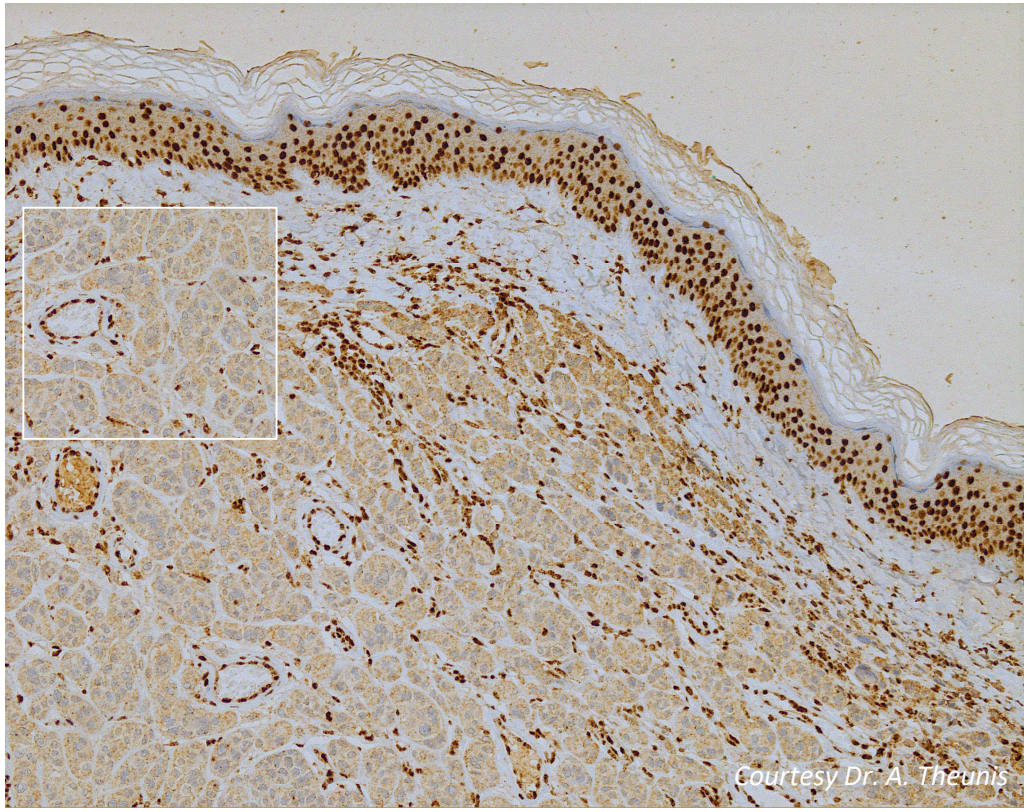
Atypical forms, uncertain behavior.

Bulbous, vertically oriented.
Well defined.
Nests and fascicles.
Fusiform to ovoid cells.
Collagen & melanophages

GNAQ GNA11 mutations

Differential. Melanocytic tumor of uncertain malignant potential (MELTUMP):

Combined BAP1-inactivated nevus/melanocytoma



Children & young adults.
Extremities.
Skin-colored papules.

Sporadic (combined)

Syndromic (multiple lesions)

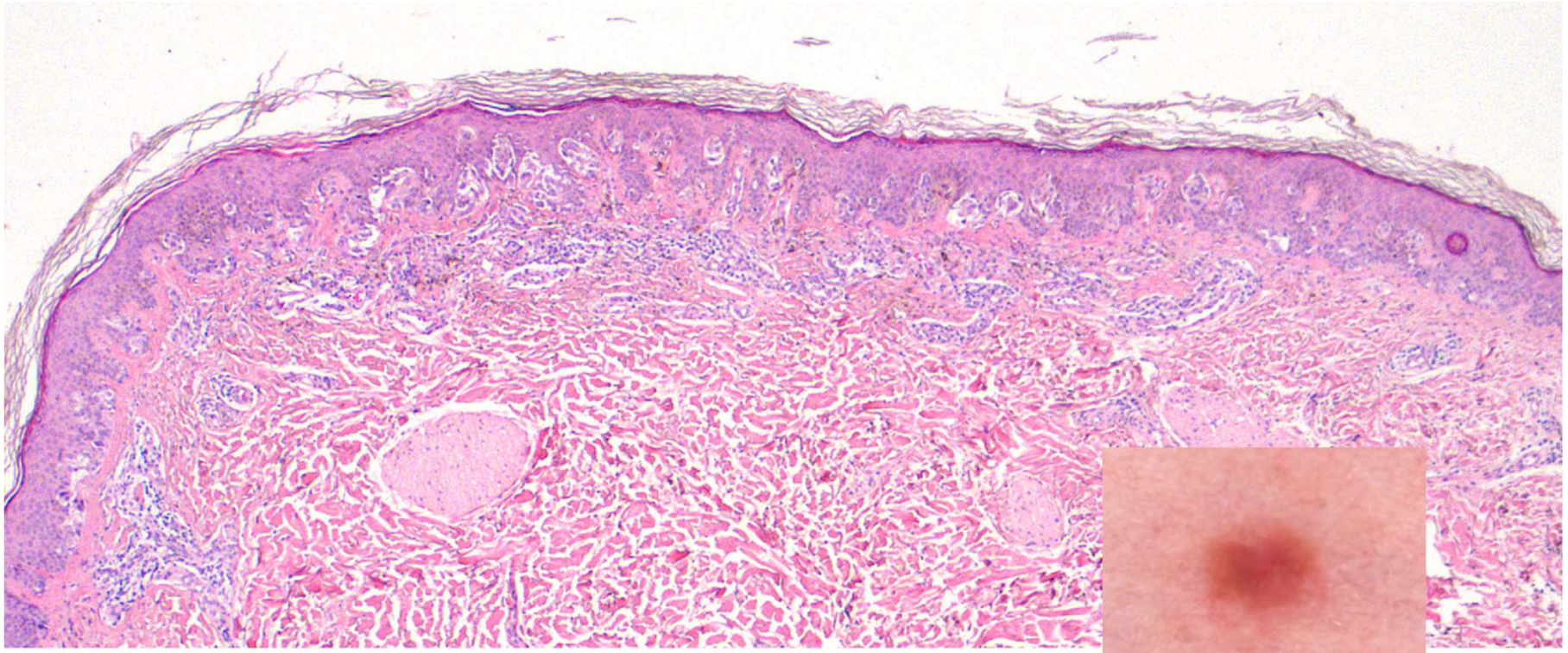
Atypical (melanocytoma variants)
Rare cases SN+
Biologically indeterminate

No acanthosis,clefting & Kamino.
Lymphocytic infiltrate

BAP1 loss
BRAF mutation (unusual in spitz)

Differential. Melanocytic tumor of uncertain malignant potential (MELTUMP):

The Spitz family

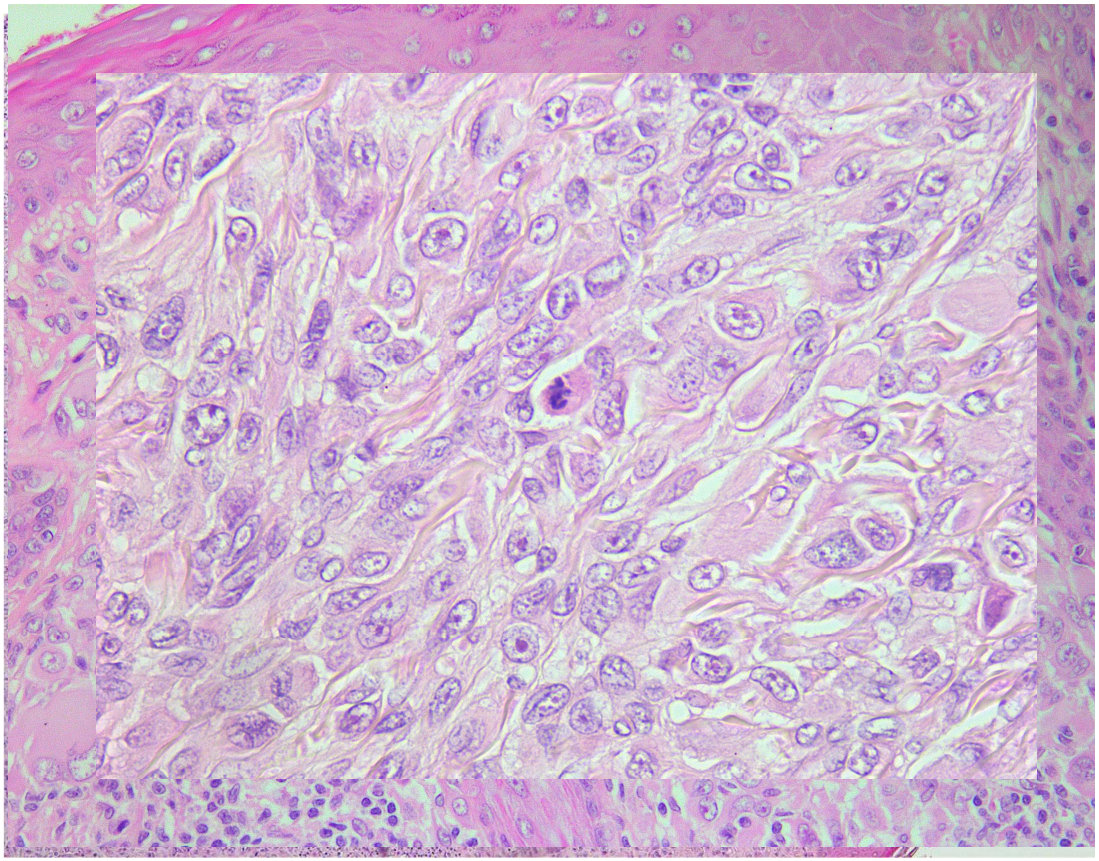


Any age. Adolescents & young adults. Rapid growth.
Lower extremities face trunk.
Prototypical < 6mm.

Courtesy of Dr. M. Jung

Differential. Melanocytic tumor of uncertain malignant potential (MELTUMP):

The Spitz family



Atypical Spitz Tumors are indolent
Diagnosis can be difficult.

Spitz: HRAS mutation: 20%.

Spitz & AST:

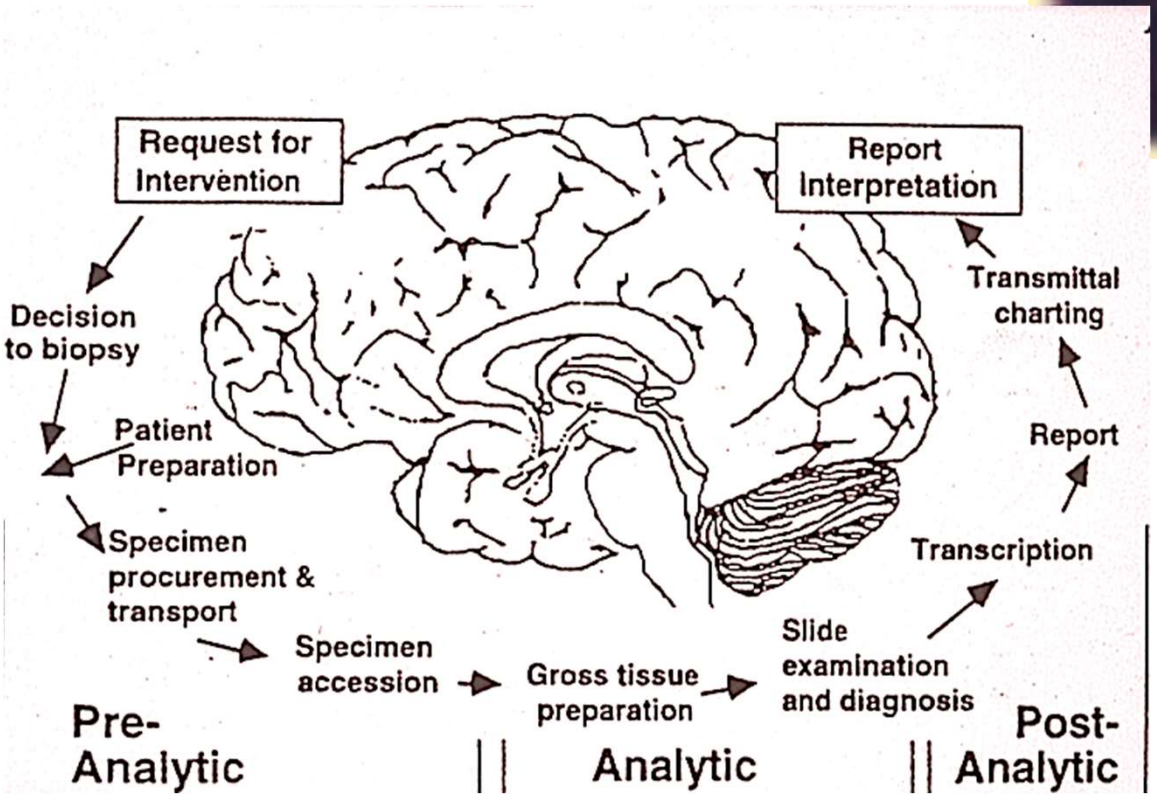
-55% kinase fusions
(rare in melanoma))
ROS1, BRAF, ALK ,NTRK1.
-Absent BRAF and NRAS Mutations.

Malignant Spitz Tumor:

-Rare HRAs, BRAF, NRAS mutations.
-PTEN, TERT promoter mutations.
-Homozygous loss of 9p21.

FISH analysis can be useful.

The Total Test Cycle



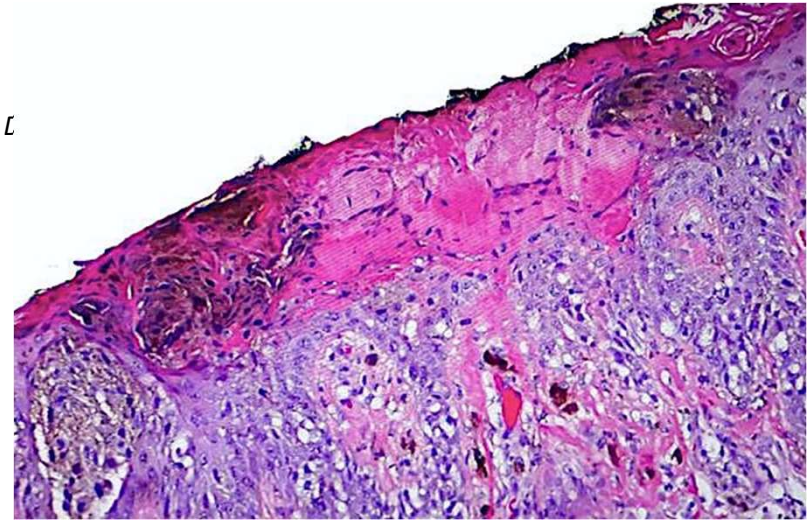
Excisional Biopsies
Family and Personal HX.
Site
Recent trauma
Recent UV exposure

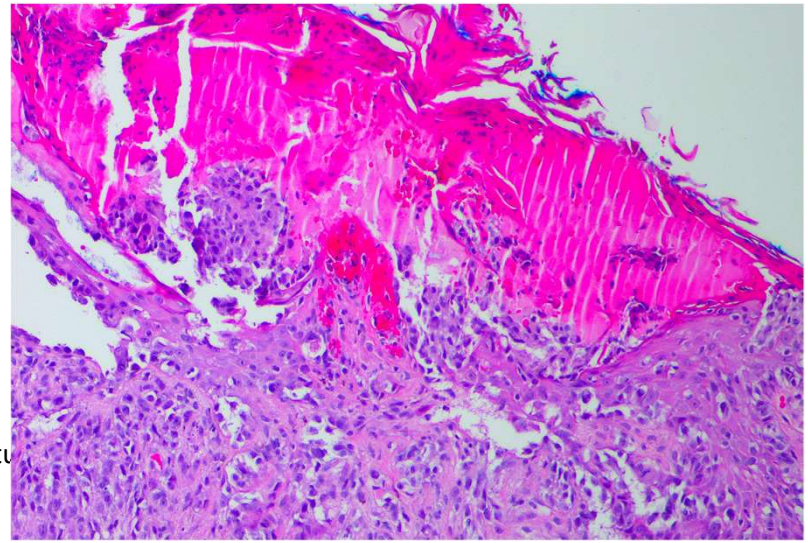
ffeoli & Piruli' 1975

Le référentiel national des mélanomes

Summary of the pathology report

Written by Dr Francesco Feoli (LNS & CHU Saint Pierre, Brussels), reviewed by L (SLDV/HRS) and Dr Joseph Kerger (Institut Jules Bordet, Brussels).





A. Tumor

Melanoma. Specify type and if *in situ* or invasive.

1. Breslow.
2. Ulceration
3. Microsatellites/ satellites
4. Primary tumor mitotic rate
5. Level of invasion (Clark)
6. TIL Tumor-infiltrating Lymphocytes
7. Tumor Regression
8. Lymphovascular Invasion
9. Neurotropism
10. Other TNM Descriptors (if applicable)
    - m: Multiple.
    - r: Recurrent.
    - y: Post Treatment.
11. Margins
    - Biopsies: Distance of the margins from the tumor is optional.
    - Excisions and Re-excisions: Measure their distance from in situ melanoma.

Tissue Examination Requests (TER)

- Terms such as “Atypical Nevus” or “Suspicion of Melanoma” and similar should be clarified in the TER using the ABCDE criteria. The clinicians should also transmit to the pathologists additional relevant data such as the number of clinically detected lymph node metastases, the number of distant metastases, the value of serum LDH, etc. Information from any prior biopsy should be documented in the pathology report for staging purposes. It is also important specifying on the tissue examination requests the indications for SLN biopsy and those for the regional lymphadenectomies.

Quality Control and Quality Assurance

- Selected SNOMED diagnostic codes should be systematically used[23]. The existing procedures of internal and external review should be extended to all the borderline, suspicious and malignant cases. The results should be documented.

Le référentiel national des mélanomes

How many Melanomas?

Which Stage?

How many sentinel nodes?

How many borderline lesions?

How many cases reviewed?

Diagnostic discordance rates?

Melanocytic tumours				pulatio
Invasive		**In situ**		
Acral-lentiginous melanoma	M-87443	Dubreuilh's melanosis	M-87422	
Amelanotic melanoma	M-87303	Lentigo maligna	M-87422	
Desmoplastic (neurotropic) melanoma	M-87453	Melanoma, Clark level 1	M-87202	
Epithelioid cell melanoma	M-87713	Melanoma in situ	M-87202	
Lentigo maligna melanoma	M-87423	Naevus with severe dysplasia	M-87202	
Malignant melanoma, NOS	M-87203	**Benign/borderline lesions**		
Melanoma, regressing	M-87233	Blue naevus	M-87800	
Melanoma arising from blue naevus	M-87803	Cellular blue naevus	M-87900	
Melanoma arising from dysplastic naevus	M-87203	Combined naevus	M-87600	
Melanoma arising in a giant congenital naevus	M-87613	Common blue naevus	M-87800	

fine

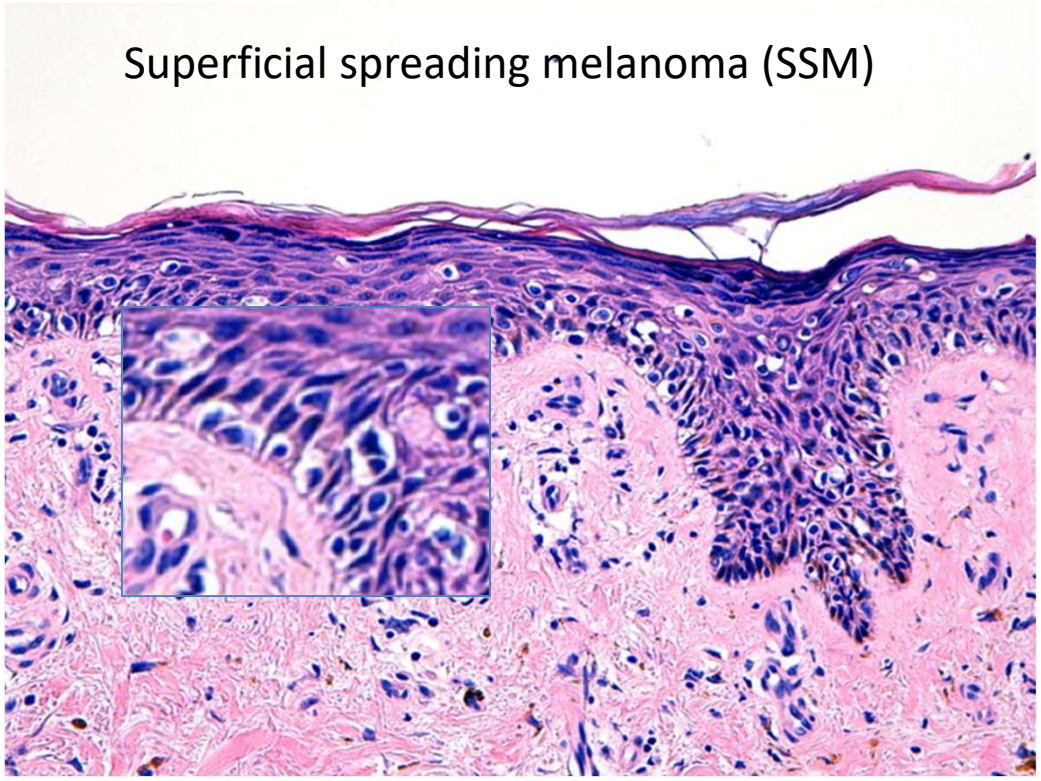
Mitogenic Drivers are different in different types of Melanoma

Localization primary melanoma	*BRAF* 7q34	*NRAS* 1p13.2	*KIT* 4q12	*GNAQ* 9p21	*GNA11* 19p13
Melanoma from CSDS/LMM	8%	15%	28%	1.4%	0
Melanoma from NCSD skin	60%	22%	0%-very low	0	0
ALM	22%	10%	23–36%	0	0
Mucosal melanoma	3–11%	5–24%	16–39%	0	0
Uvea melanoma	0%	0%	0%	45–50%	32%
Melanoma from the CNS	0%	0-low in adults. Frequently mutated in melanoma in context of NCM in children.	0%	30% (adults)	30% (adults)
Sensitive to treatment with	*BRAF* inhibitors	MEK inhibitors. Resistant to BRAFi	Imatinib, nilotinib, sunitinib, dasatinib	(Pre-clinical) MEK inhibitors	(Pre-clinical) MEK inhibitors

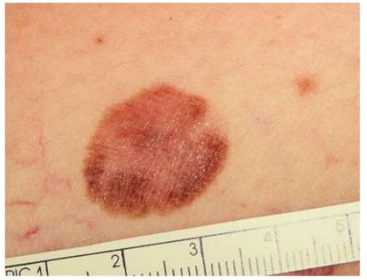
In different studies, there is some variation in reported frequencies (5, 11, 12).
CSDS, chronic sun damaged skin; LLM, lentigo malignant melanoma; ALM, acrolentiginous melanoma; CNS, central nervous system.

van Engen-van Grunsven ACH et al. 2014

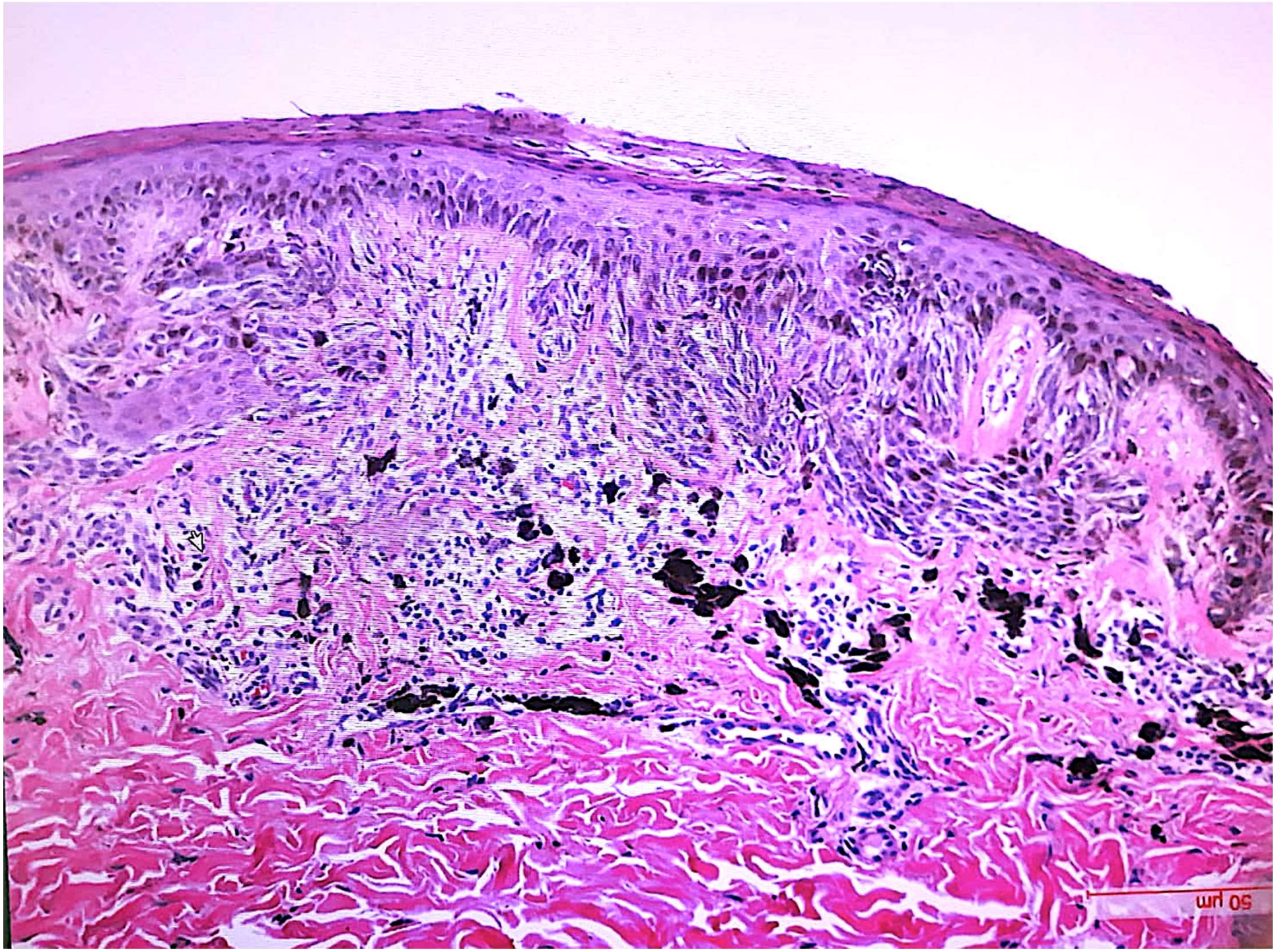
Superficial spreading melanoma (SSM)



The most common type of melanoma.
Radial growth phase for months-decades.
Invasion: unknown proportion.



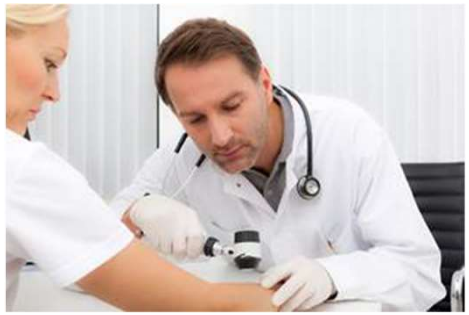
ABCDE rule:
Diameter: > 6 mm (often 1–2 cm),
Asymmetry, Border irregularity,
Colour variationEvolving.


50 µm

OncologyNurseAdvisor

Bryant Furlow
September 19, 2018

Skin Cancer Screening Programs: Are They Effective?



2006-2015:US Melanoma incidence rose by 1.5% a year.
Mortality rates declined by 1.2% per year.

47% with clinically diagnosed melanoma would not have otherwise seen a doctor for a skin examination

Cancer Stat Facts: Melanoma of the skin. National Cancer Institute website. 2018.

Stang A et al: The German skin cancer screening programme. *Eur J Cancer.* 2016;64:83-88.