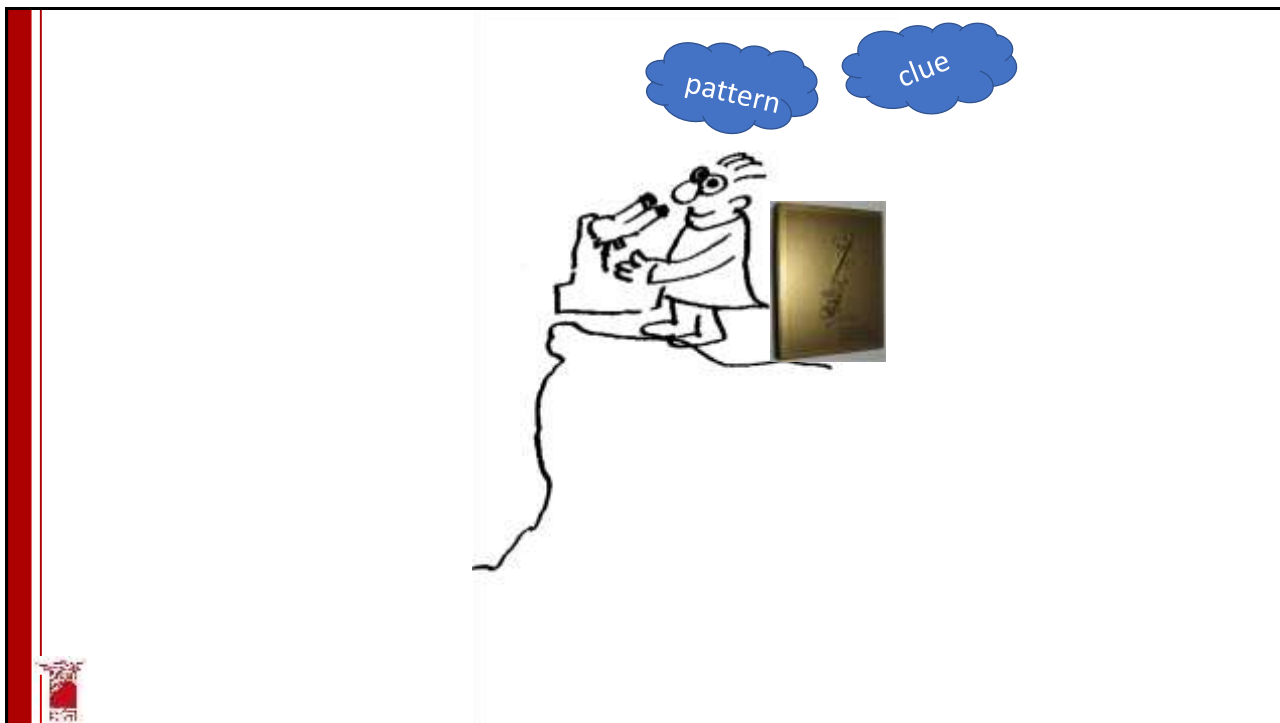


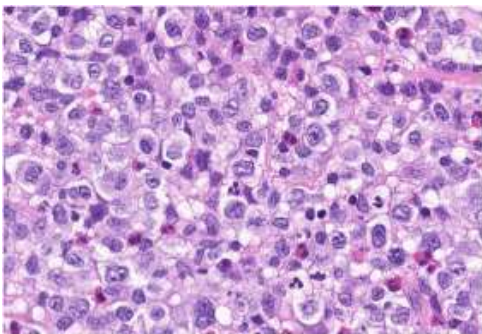
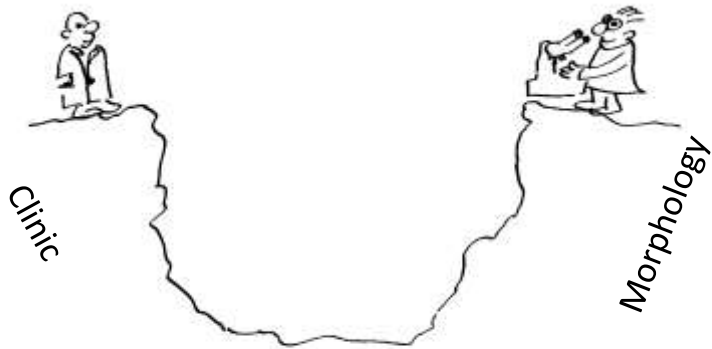
Advanced course 18-4-2023  
VBS dermatopathology

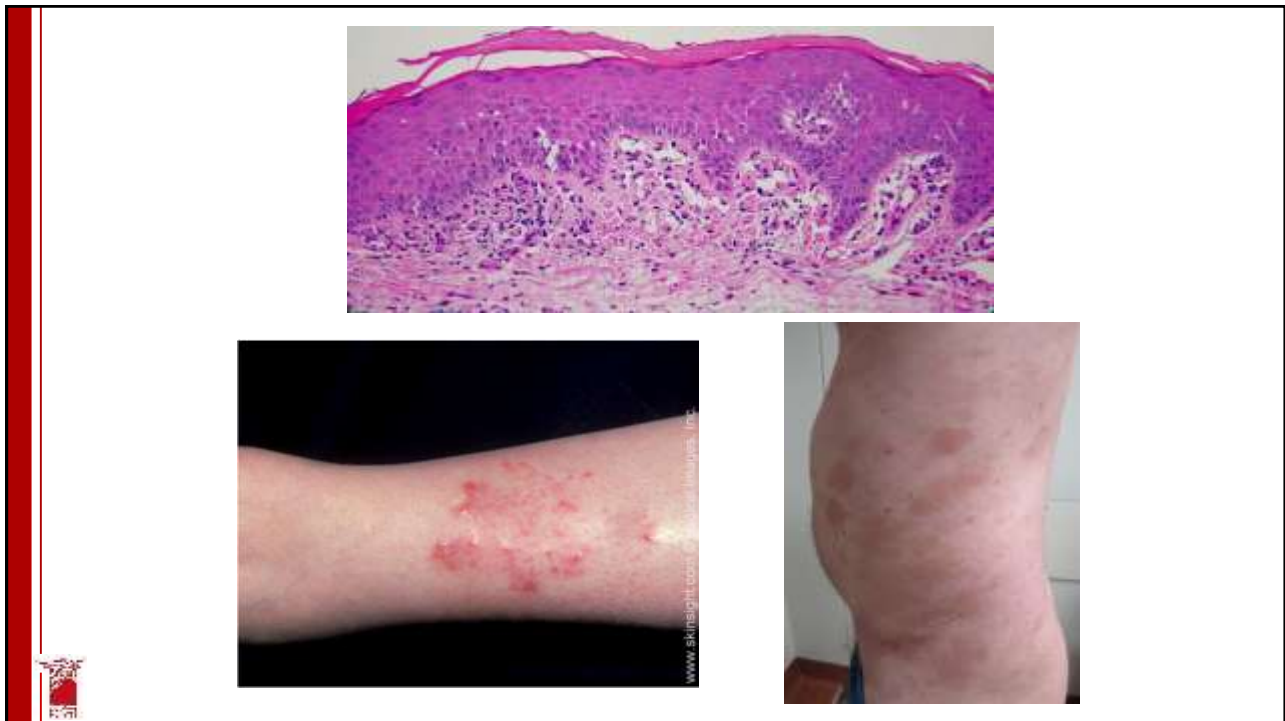
WHEN (MICROSCOPY)(CLINIC)  
CLEARS UP  
(CLINIC)(MICROSCOPY)

Marc Haspeslagh



# Clinical information





## Dermatopathologist?



Dermatopathologist Character? Curious, associative, creative, *scientific*

The image shows the evolution of dermatopathology textbooks. On the left is the cover of "HISTOPATHOLOGY OF THE SKIN" by Walter F. Lever, M.D., published in 1949 by Lippincott Company. In the center is a photograph of a green book. On the right is the cover of "Histopathology of the Skin" by Ackerman, published in 1978. A blue arrow points from the 1949 book to the 1978 book. The 1978 book cover features illustrations of birds at the top and bottom.

1949 LEVER

1978 ACKERMAN

Recognize and take into account increased complexity  
Sub(sub)speciality is mandatory

The diagram illustrates the increasing complexity and sub-specialization in dermatopathology. It starts with a simple tree on the left and branches out into various sub-specialties on the right. A blue arrow points from the simple tree to the complex branching structure.

- oral
- vulvar
- CUTANEOUS ADNEXAL TUMORS
- Cutaneous Adnexal Neoplasms
- Histological Diagnosis of Nevi and Melanoma
- Pigment cell lesions
- ORAL PATHOLOGY
- Vulvar Pathology
- Hair
- An Atlas of Hair Pathology with Clinical Correlations, Second Edition
- SKIN LYMPHOMA
- (Pseudo)Lymphomas
- Histopathology of the Nail
- Nail

# Epidermal hyperplasia

Am J Dermatopathol  
Volume 38, Number 1,  
January 2016  
Fernandez Flores



WHEN (MICROSCOPY)(CLINIC)  
CLEARS UP  
(CLINIC)(MICROSCOPY)



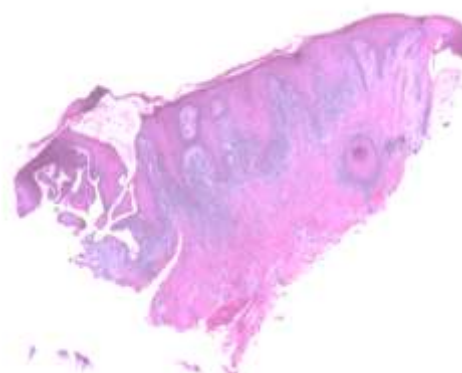
Recent consecutive 15 cases from Dermat with pseudoepitheliomatousepidermal hyperplasia as a main histologic finding (coded as 56PS)







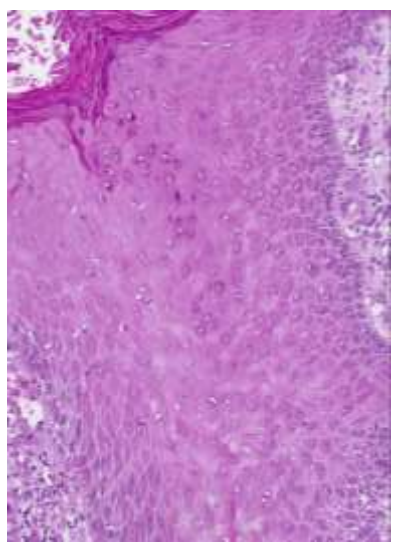
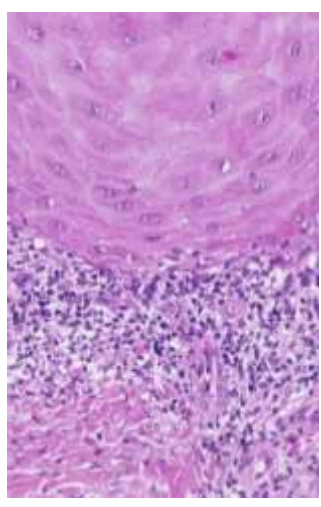
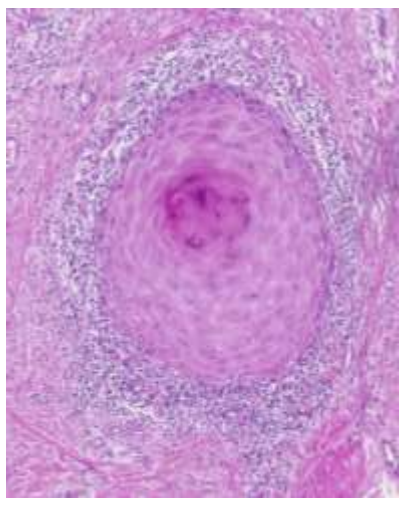
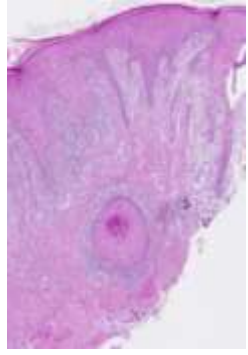
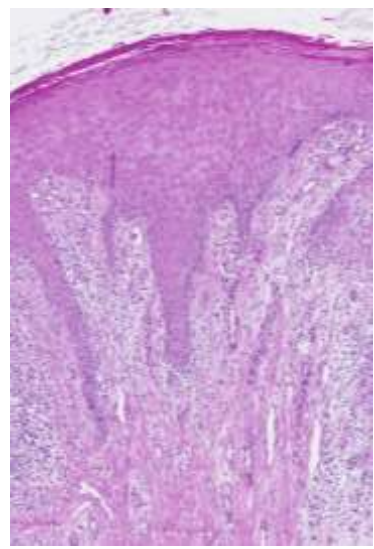
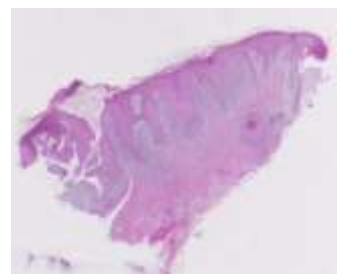
2302-50323

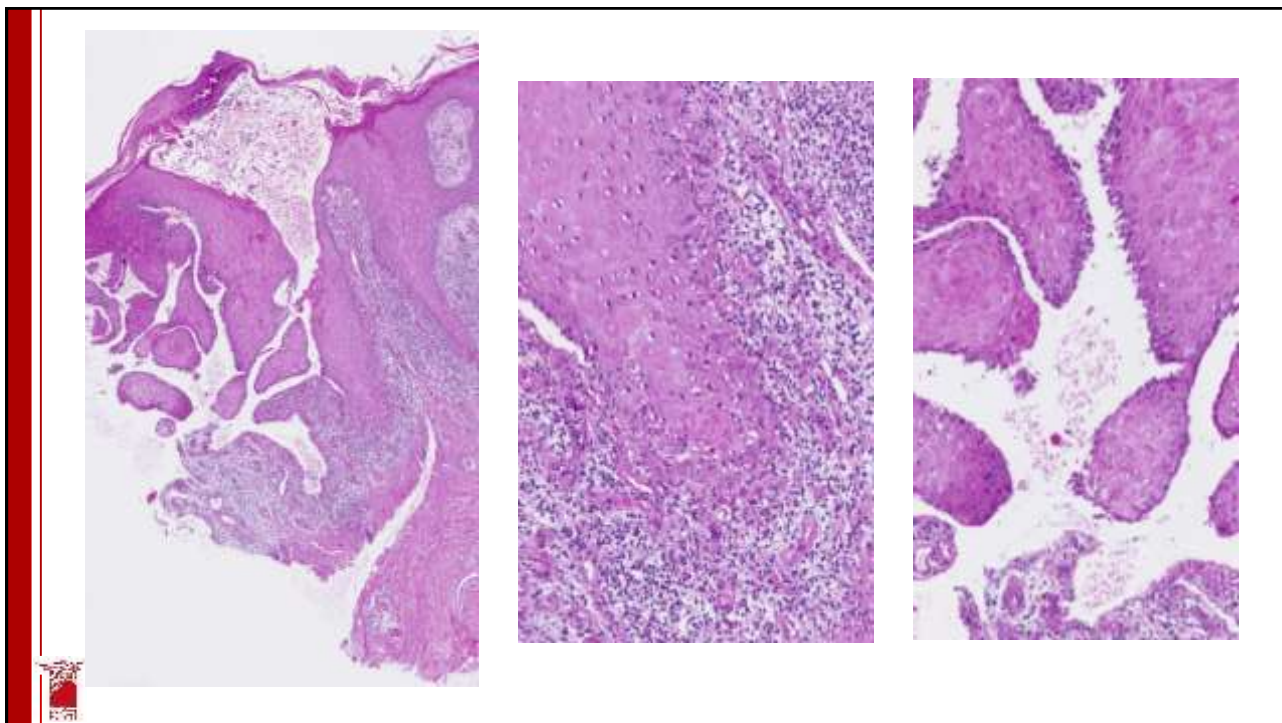


Right shin, large red plaque, infiltrated, enlarging  
Since 2 years present  
Dd carcinoma, Bowen, baso , (necrobiosis  
lipoidica, sarcoidosis, mycosis fungoides,  
granulomatous pathology, sarcoidosis)  
20/11/1953 M



2302-50323





Skin right shin : superficial bandlike infiltrate with variable lichenoid, vacuolopathic, apoptotic dermatitis with pseudoepitheliomatous hyperplasia, compatible with hypertrophic form of lichen planus. No carcinoma in this biopsy,



Clinical and histologic features helpful for differentiating hypertrophic lichen planus from squamous cell carcinoma

**Clinical**

- Hyperkeratotic plaque(s) on the distal extremities, especially the shins
- Presence of multiple plaques with follicular accentuation
- Pruritus
- Wickham striae
- Typical lichen planus affecting oral mucosa, nails, and skin elsewhere
- Negative history of sun damage
- No predisposing factors for multiple SCCs



**Histologic**

- Hyperorthokeratosis, wedge-shaped hypergranulosis, and irregular psoriasiform hyperplasia of the epidermis
- Lichenoid dermatitis with eosinophils
- Classic features of pseudoepitheliomatous hyperplasia
- No cytologic atypia
- Absence of marked solar elastosis, no perforating elastic fibers
- No deep extension beyond the superficial dermis
- No lymphovascular or perineural invasion



**No increased frequency of SCC in patients with cutaneous LP !**

**Squamous Cell Carcinoma Arising in Hypertrophic Lichen Planus: A Review and Analysis of 38 Cases**

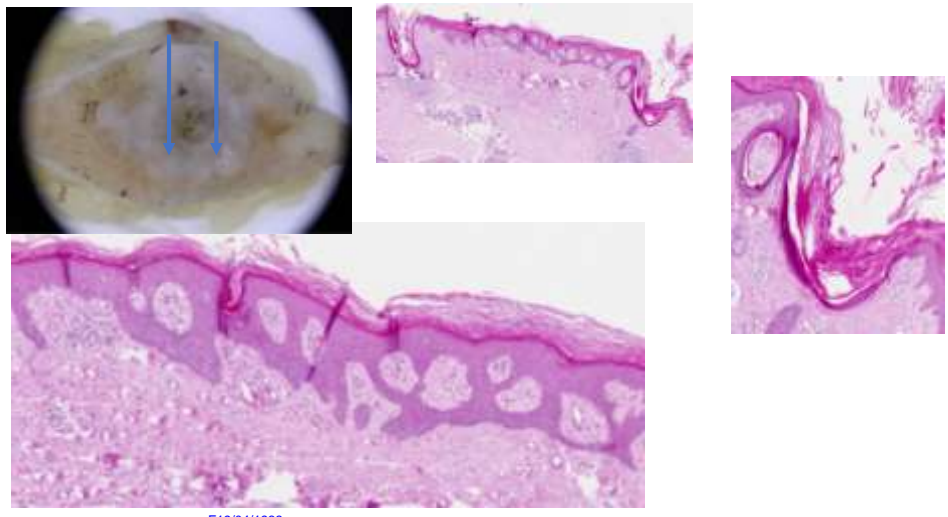
THOMAS J. KNACKSTEFT, MD,<sup>1</sup> LINDSEY K. COLLINS, MD,<sup>2</sup> ZHONGZEE LI, MS,<sup>1</sup> SHAOFENG YANG, MD, PhD,<sup>1\*</sup> AND FARHAKH H. SAMIE, MD, PhD<sup>1\*</sup>

In this population-based study, oral but not cutaneous disease was established as a precursor for intralesional malignancy with a morbidity ratio of 5.94 and incidence of 1.3%. 37 In a subgroup analysis, cutaneous SCC was found to occur predominantly in the hypertrophic variant of LP. Subsequently, an incidence of 0.4% for malignant transformation of cutaneous LP has been reported.



Figure 2. Squamous cell carcinoma from patient 1. (A) Clinical photograph of SCC arising in resolving HLP. (B) Hematoxylin and eosin-stained section of skin biopsy showing well-differentiated SCC (20x).

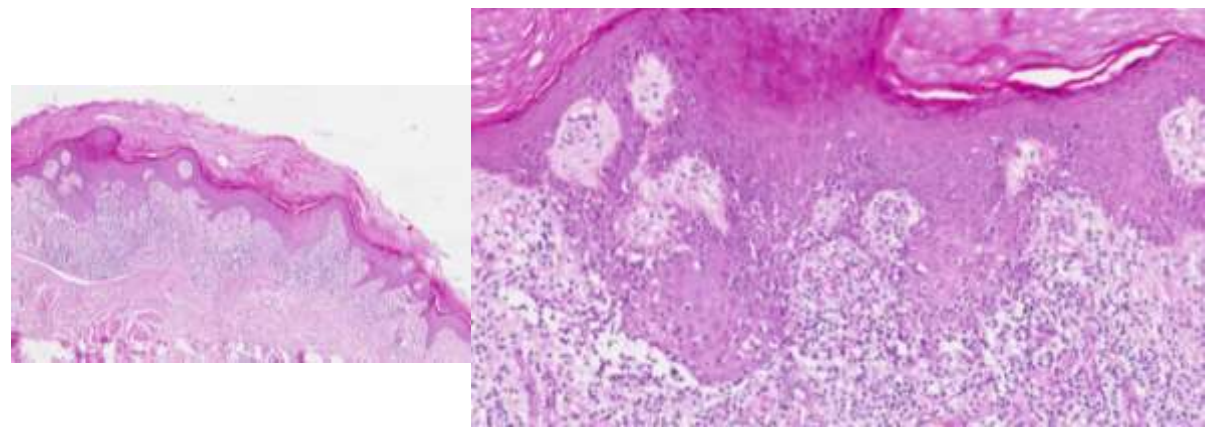




F19/04/1938

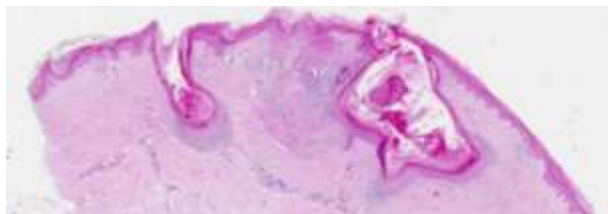
1903-51402

skin right lower leg  
Itching, erythematous papules with central plug : prurigo?  
Cancer? Verruciform keratosis?

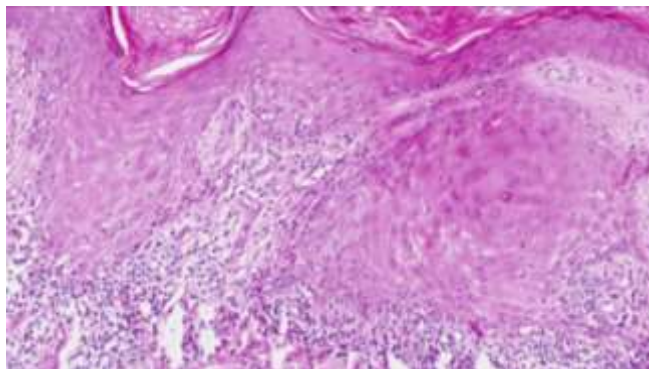
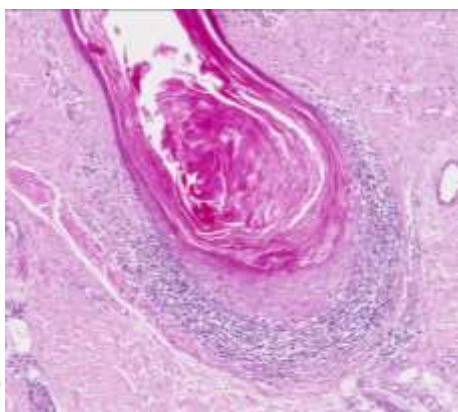


1903-51402

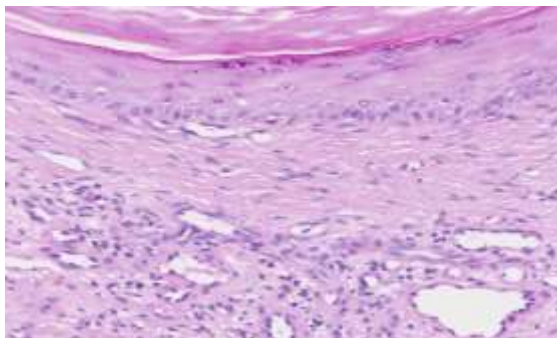
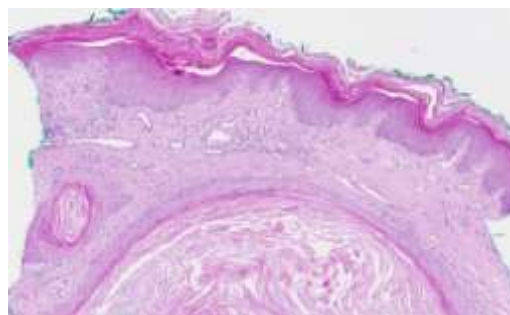
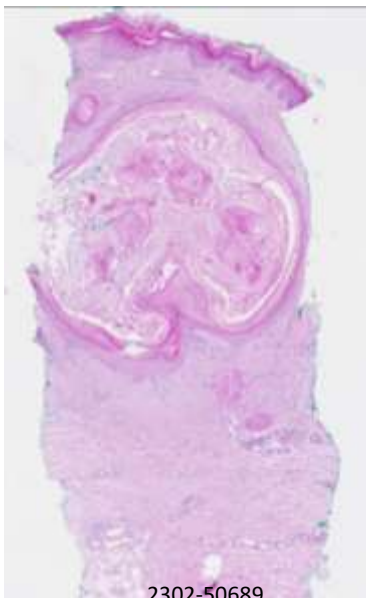




Skin right lower leg : biopsy  
of form of hyperkeratotic to  
verrucous lichenoid  
dermatitis  
No atypia in this fragment.



New biopsy : Verrucous lesions in past,  
diagnosed as verrucous lichenoid lesions  
4 years later, please exclude malignancy

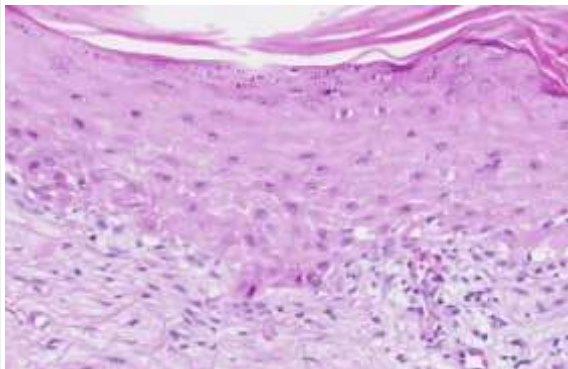
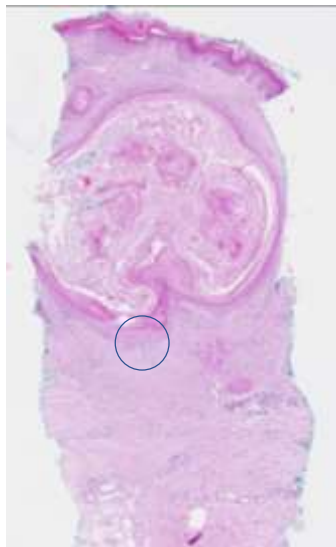


2302-50689



2302-50689

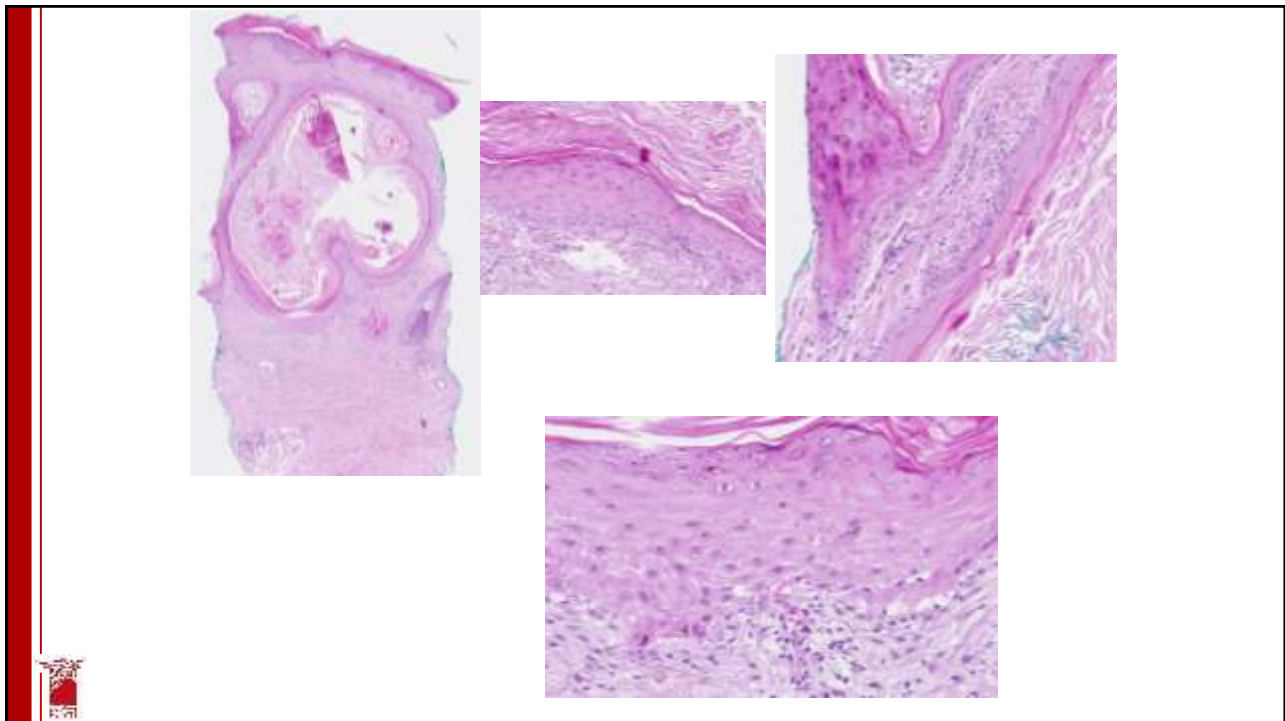
Verruceuze letsels in het verleden als prurigo / verruceuze lichen geïnterpreteerd. Graag uitsluiten maligniteit.



2302-50689







Skin leg right and left  
Lichenoid interface dermatitis with  
premature differentiation and  
formation of infundibulocystic  
structures, compatible with  
**hypertrophic lichen planus with cyst  
formation**





Lichen planus  
follicularis tumidus

#### Clinical type of lichen planus

---

- Classical lichen planus
- Atrophic lichen planus
- Hypertrophic lichen planus
- Eruptive lichen planus
- Lichen planus pigmentosus
- Actinic lichen planus
- Blaschkoid lichen planus
- Zosteriform lichen planus
- Linear lichen planus
- Erosive lichen planus
- Oral lichen planus
- Genital lichen planus
- Lichen plano pilaris
- Plantar lichen planus



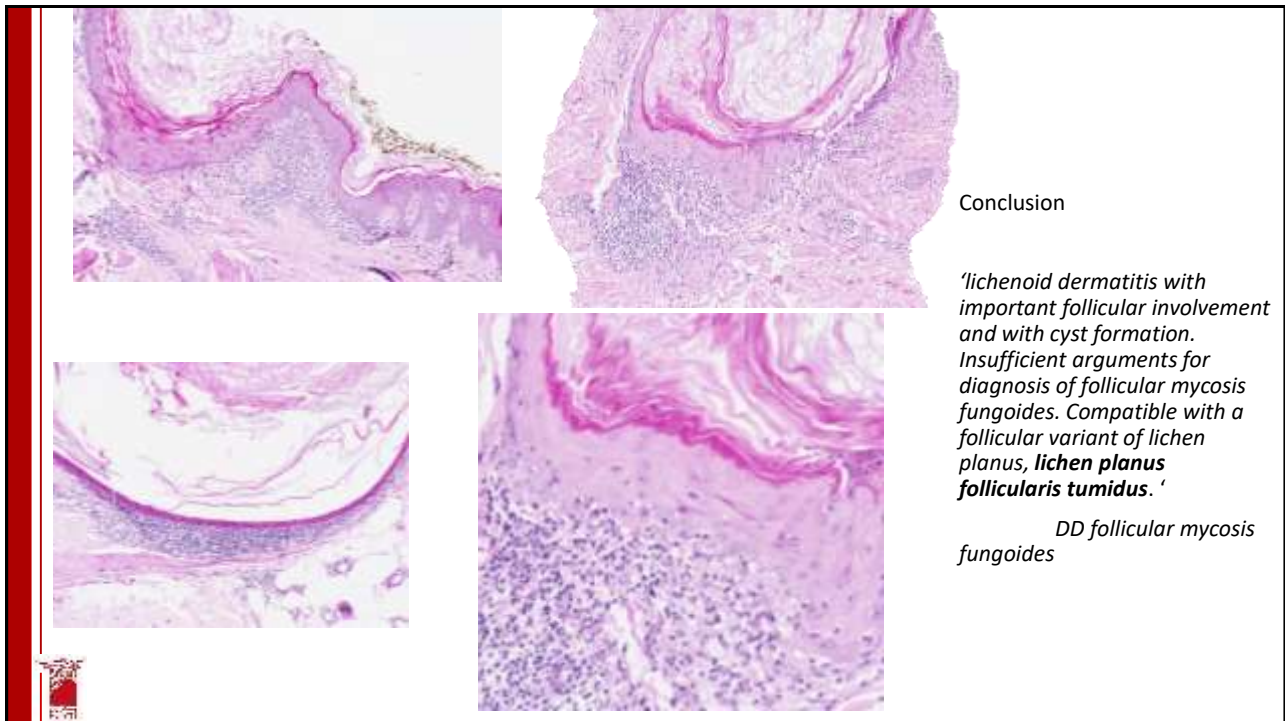
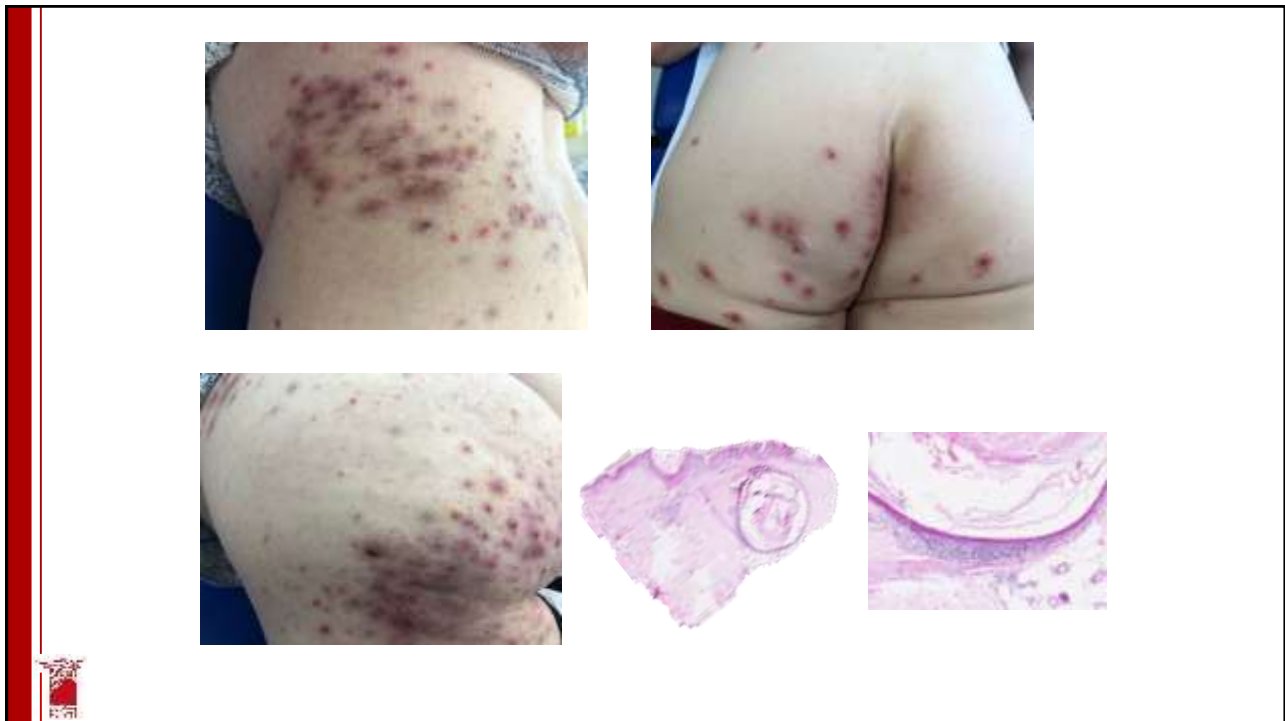
2004-50289

1948 F

- personal history of rheumatoid arthritis
- biopsy gluteus April 2020

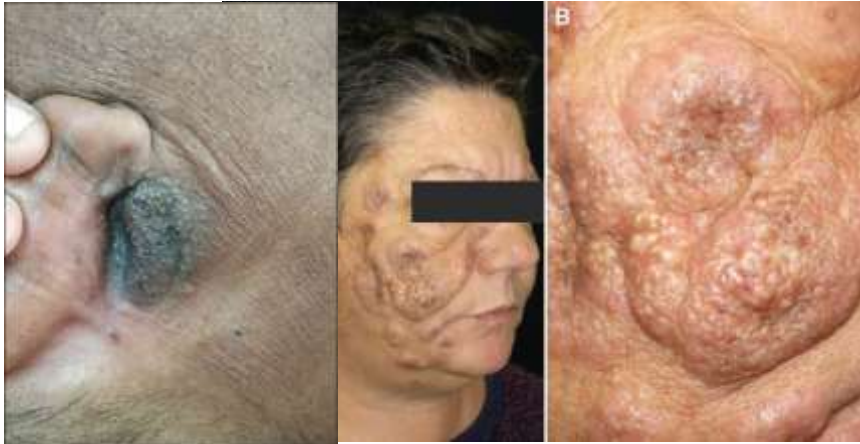
Abcedation and inflammatory nodules, comedo like lesions Kyrle?



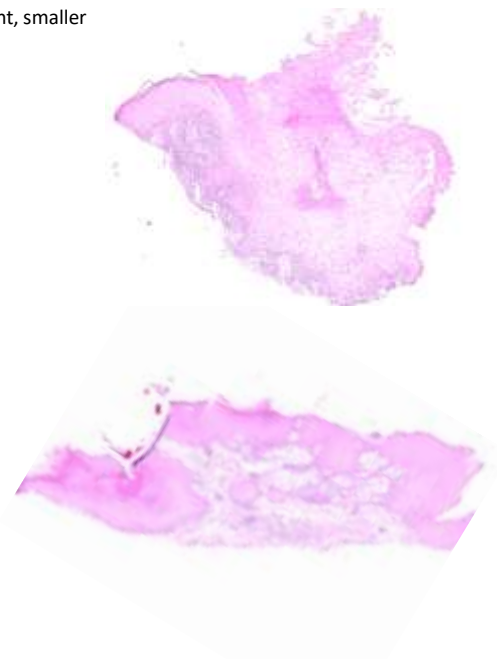


Lichen planus follicularis tumidus

- rare variant of lichen planus
- retroauricular region, the ears, the eyelids, the cheeks, the chin, the nose and the scalp



2302-50825 1927 F right shin  
Central lesion oval fragment, smaller  
fragment from periphery



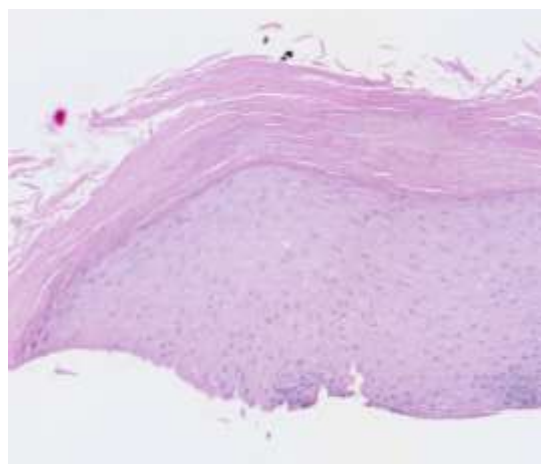
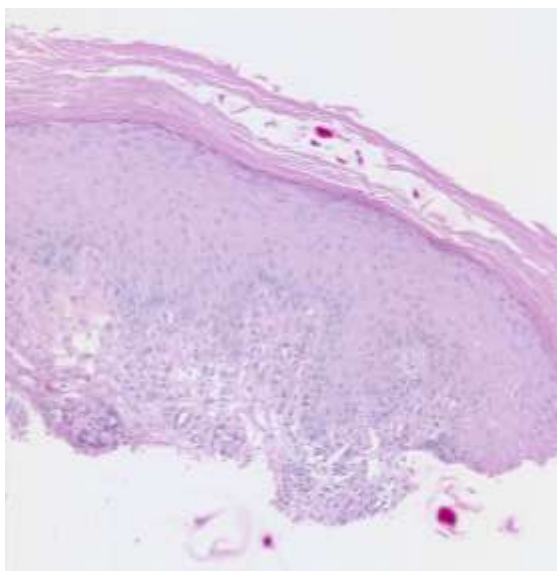
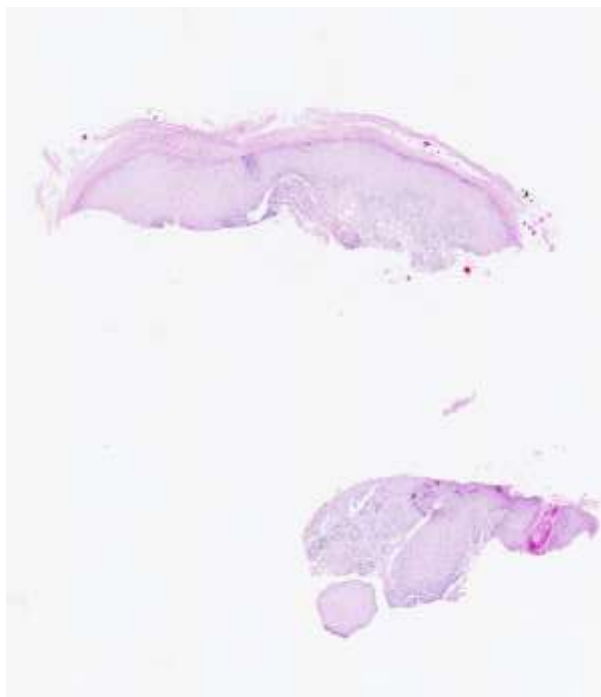
2302-50825

Huid onderbeen.

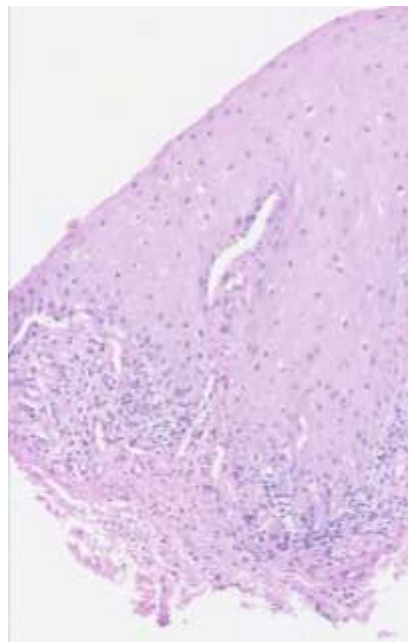
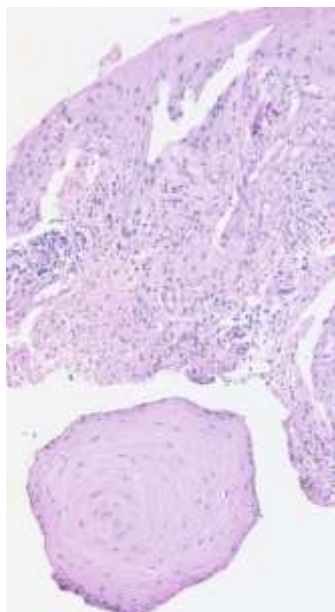
Prior biopsy 1612-50256

Revision shows hyperplasia, less important  
with also some interphase damage?

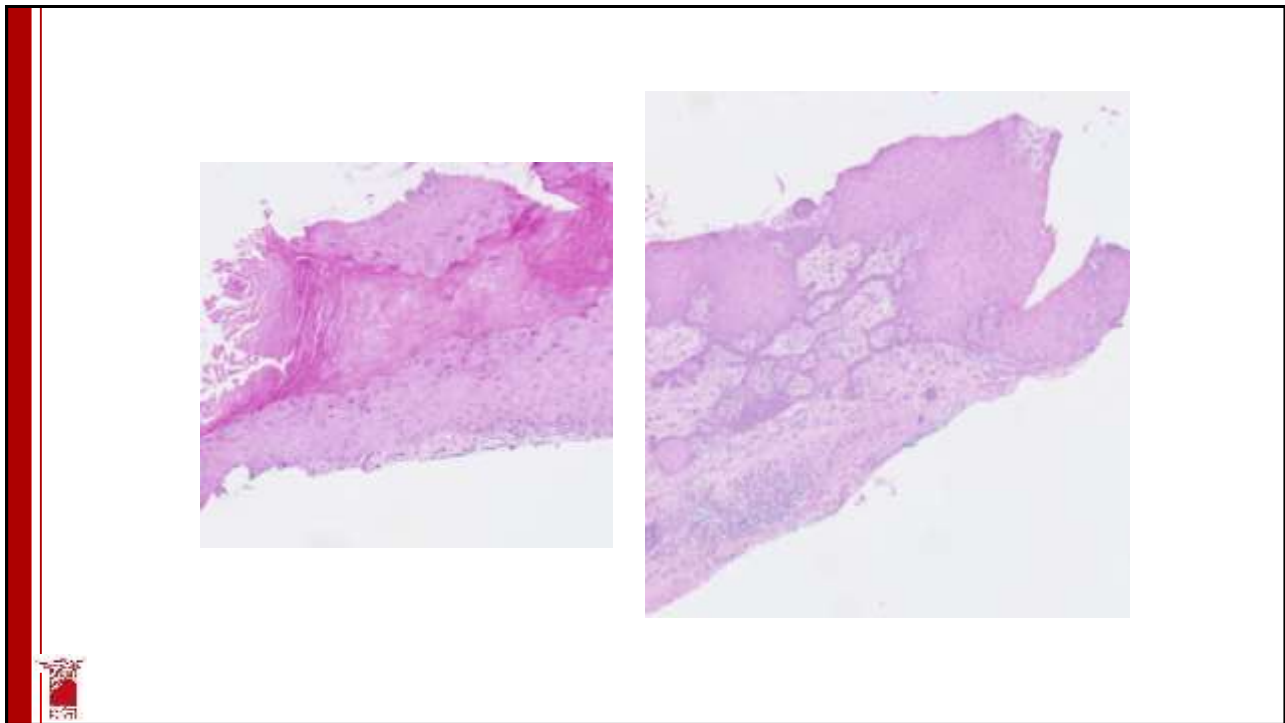
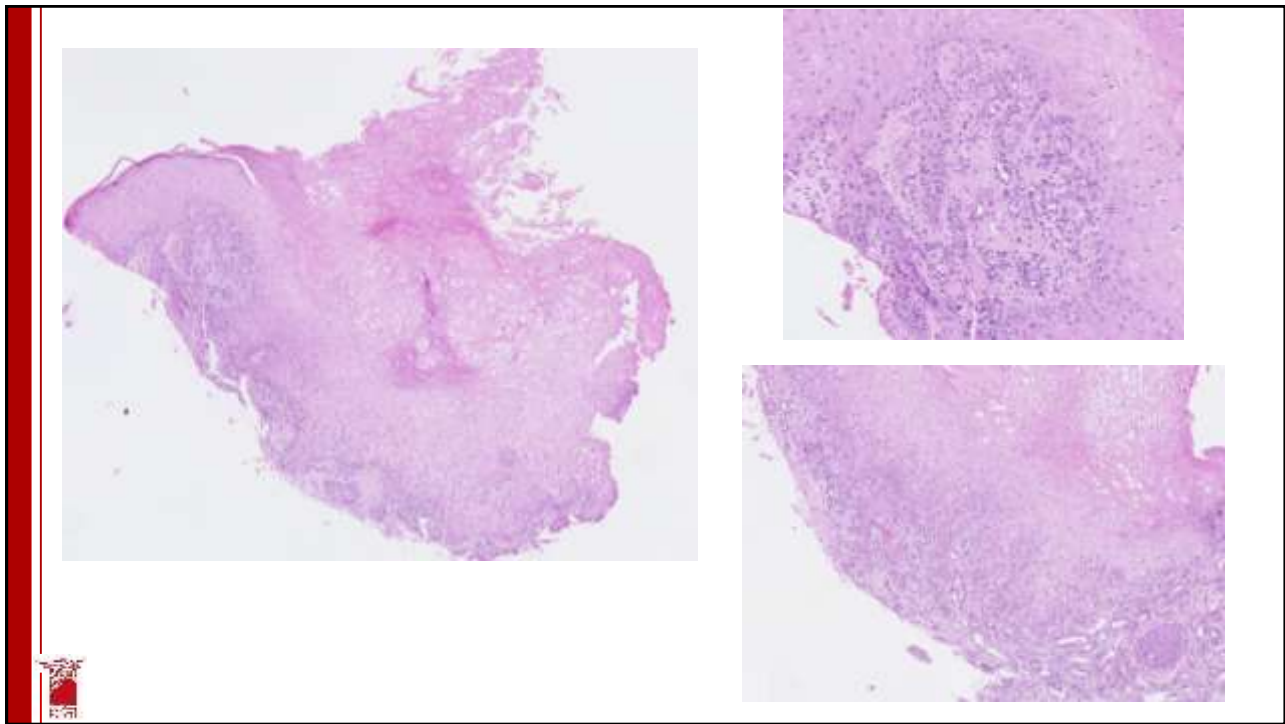
Phone contact: not clear if the  
previous biopsy comes from same  
lesion

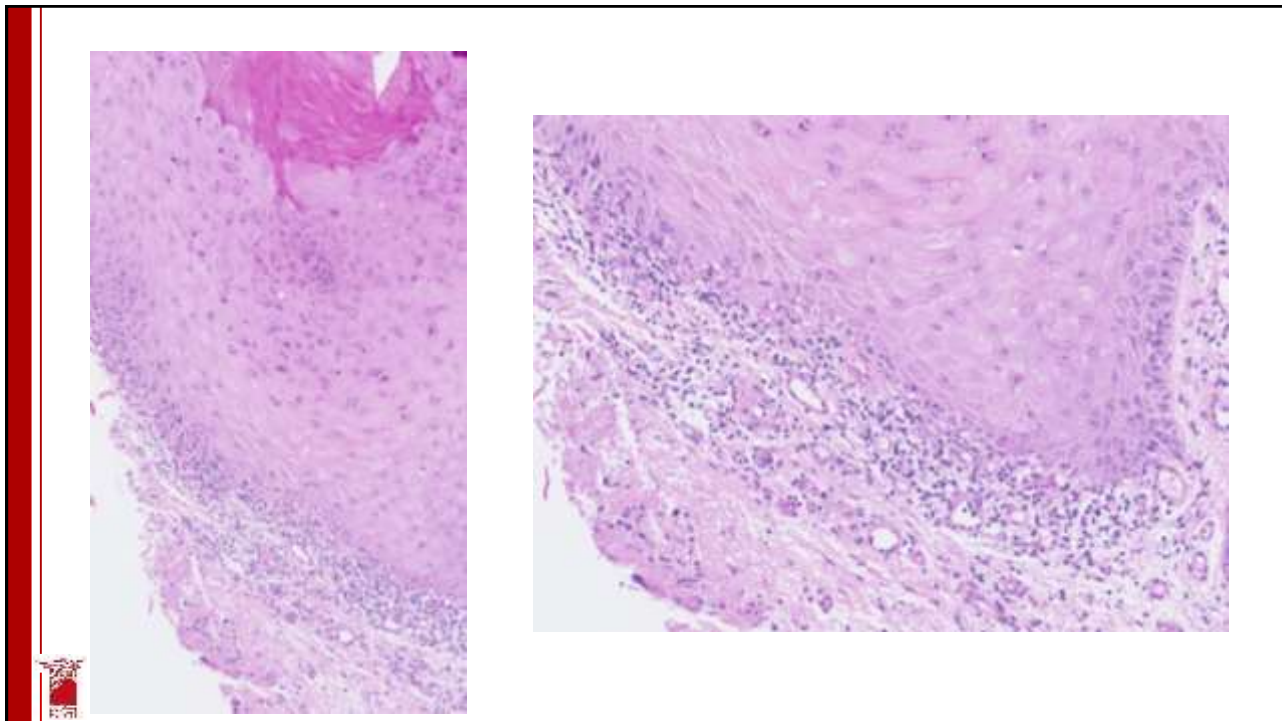


Biopsy lower leg : biopsy from hypertrophic lichenoid processn no squamous cell carcinoma in these sections









## Differential diagnosis

Lichen planus hypertrophicus/lichenoid keratosis

Kerato acanthoma type SC

Squamous cell carcinoma

Chronic irritative NOS

**Inconclusive Deeper-larger biopsy !!!**

2 superficial fragments with  
irregular epithelial hyperplasia and  
focal lichenoid inflammation

Not diagnostic

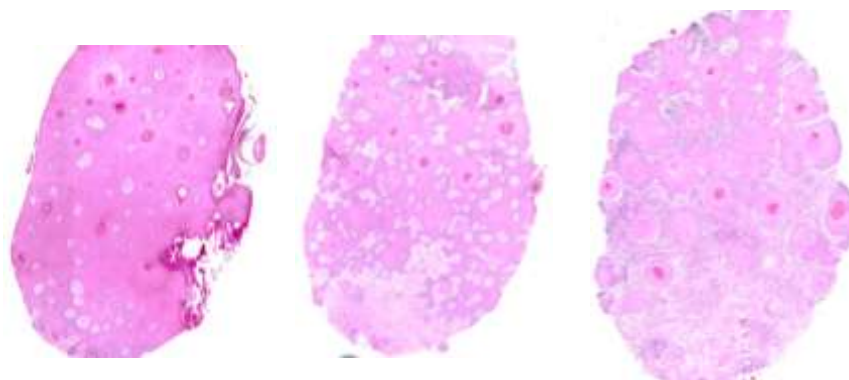
New biopsy to further exclude SCC  
(kerato anthoma type lesion).

2302-50825

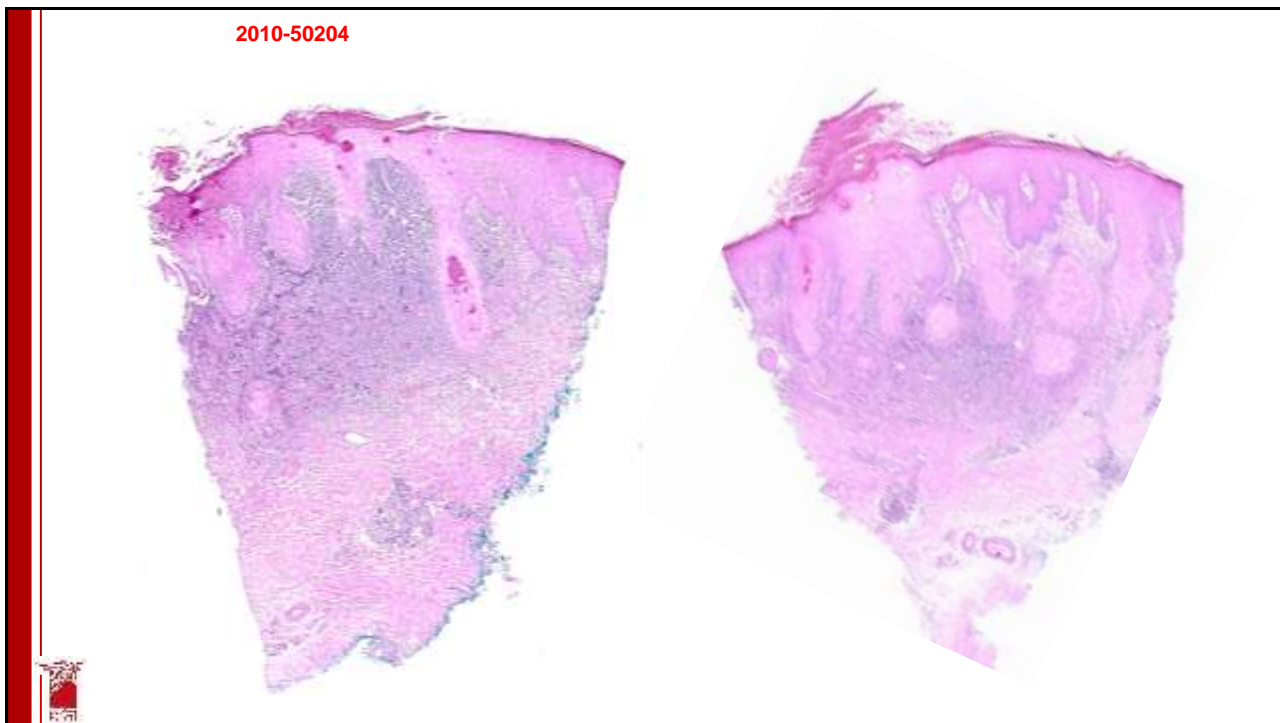
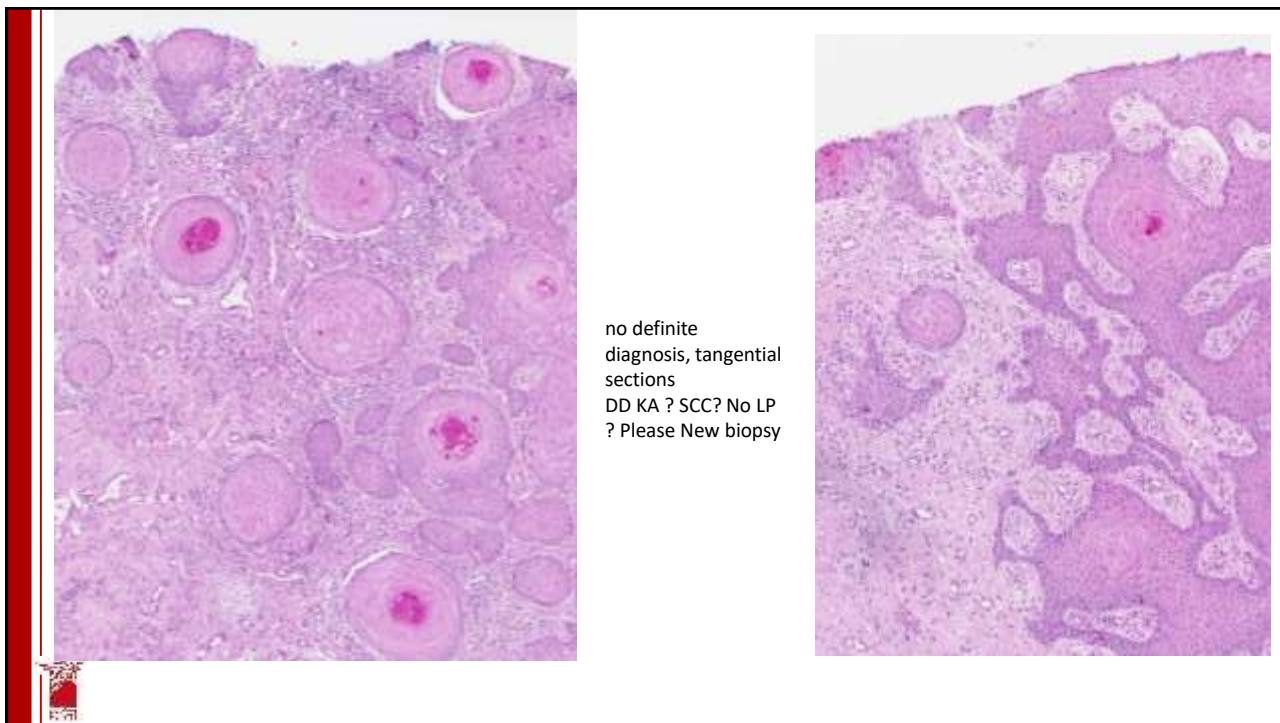
Ankle left : painfull verrucous lichen  
planus, severe lichenification

2009-50786  
1939 F

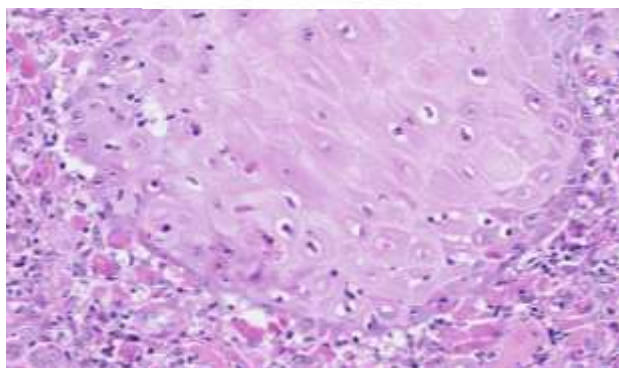
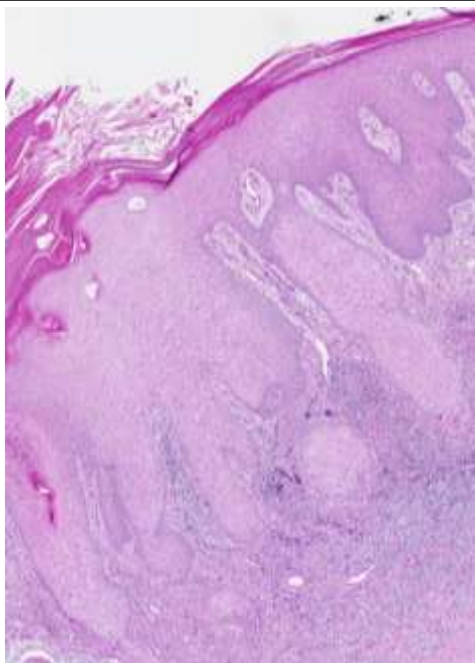
DD/ SCC?



2009-50786







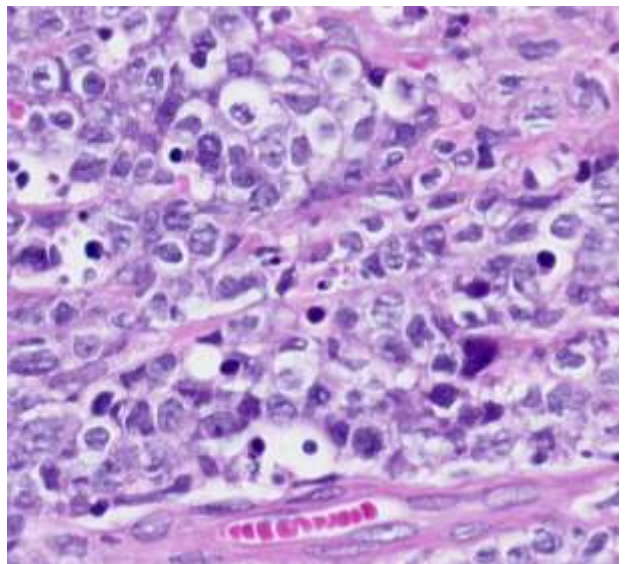
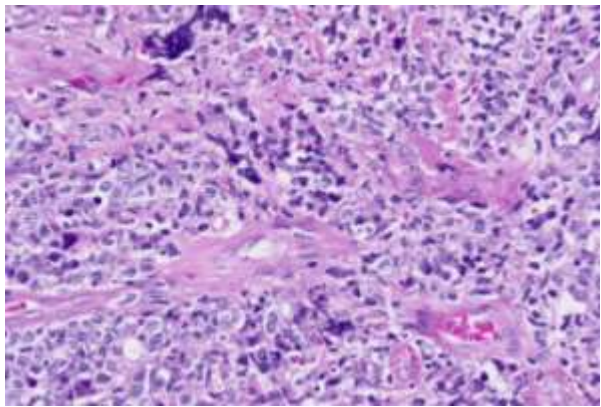
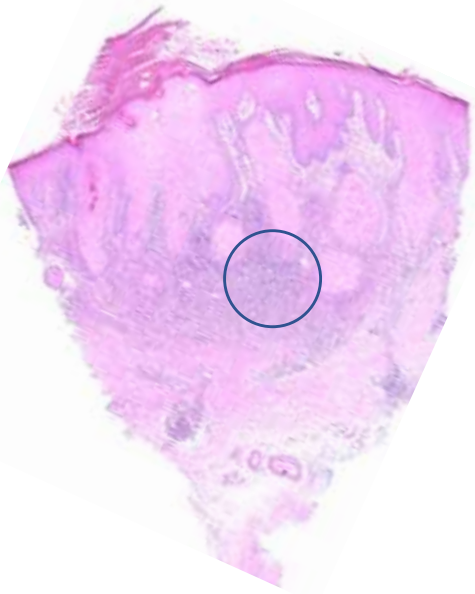
Kerat acanthoma type lesion?

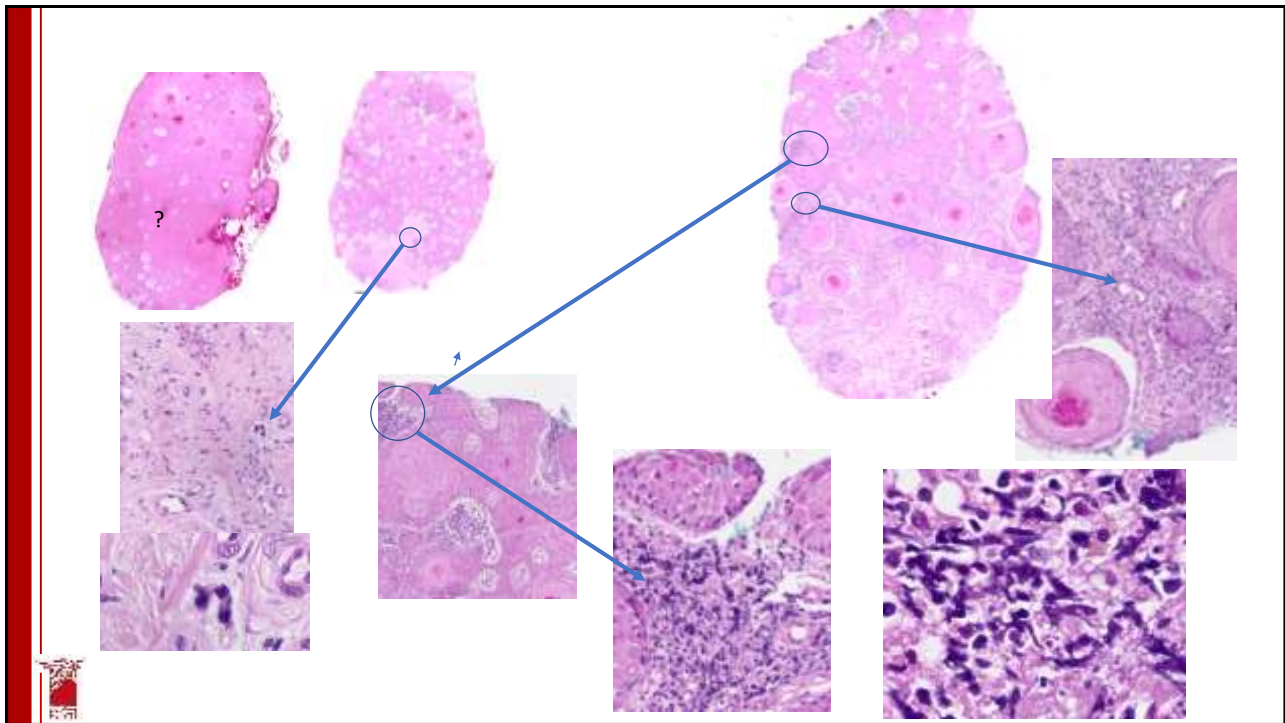
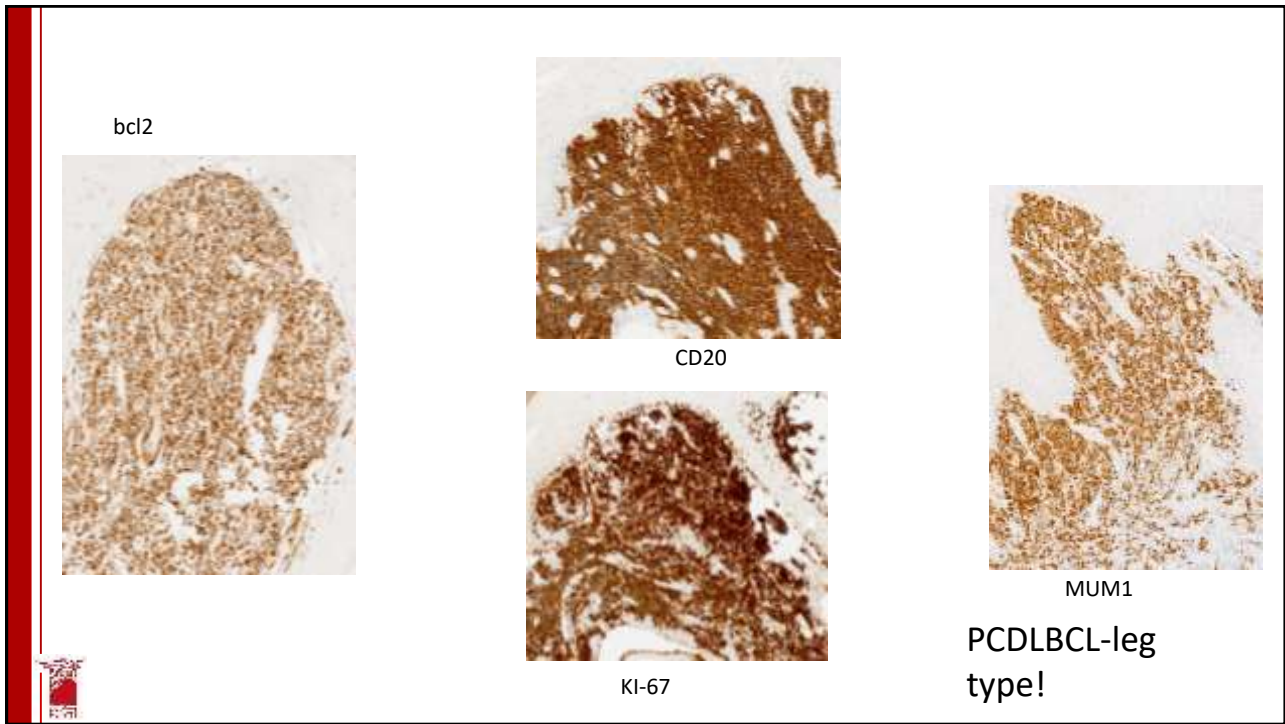


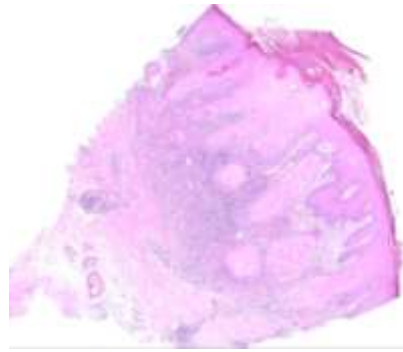
Kerato acanthoma type lesion?



2010-50204







Lower leg left : Primary cutaneous diffuse large cell B cell lymphoma leg type with pseudoepithelial hyperplasia, Secondary localisation of blastic B cell lymphoma has to be excluded



PSEUDOEPITHELIOMATEUZE HYPERPLASIE

Neoplastic conditions

Basal cell carcinoma

Lymphoproliferative disorders

Nasal NK/T lymphoma

Anaplastic Large Cell Lymphoma

Mycosis fungoides

Lymphomatoid papulosis

Granular cell tumor

Melanoma

Spitz nevus

Infections

Mycobacterial

*M. marinum*

*M. tuberculosis*

Leprosy

Deep fungal

Blastomycosis

Paracoccidioidomycosis

Sporotrichosis

Chromomycosis (chromoblastomycosis)

Coccidioidomycosis

Aspergillus

Viral

Genital and perianal herpes simplex in patients with AIDS

Chronic verrucous varicella zoster virus infection in patients with AIDS

Bacterial

Blastomycosis-like pyoderma

Bacillary angiomatosis

Actinomycosis

Granuloma inguinale

Osteomyelitis

Protozoal

Leishmaniasis

Spirochetal

Gammas



Chronic inflammation/irritation

Prurigo nodularis

Halogenoderma

Hypertrophic lichen erythematosus

Hypertrophic lichen planus

Perianal pseudomycosis papules and nodules in children

Elephantiasis nostras verrucosa

Chronic cutaneous wounds

Chondrodermatitis nodularis heliica

Lichen sclerosus

Meloiderplakia

Pyodermitis pyostomatitis vegetans

Periphagus vegetans and periphagoid vegetans

Miscellaneous

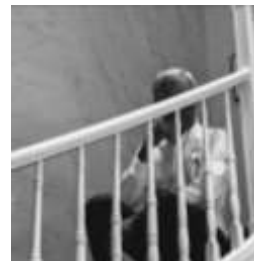
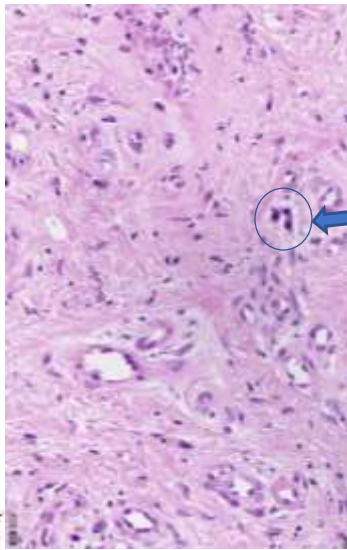
Tattoo

After Mohs surgery





Look to the negative spaces ! Think out of the box

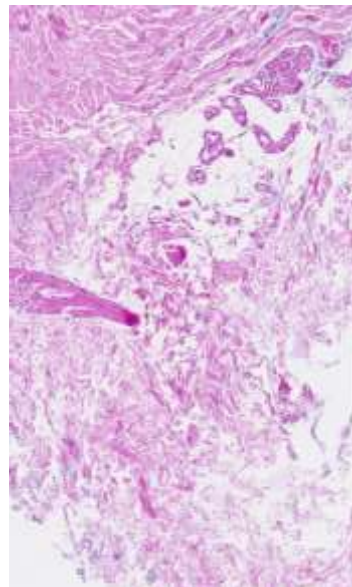
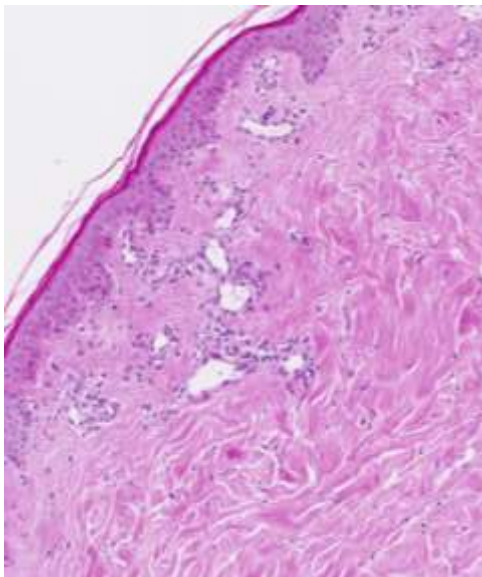
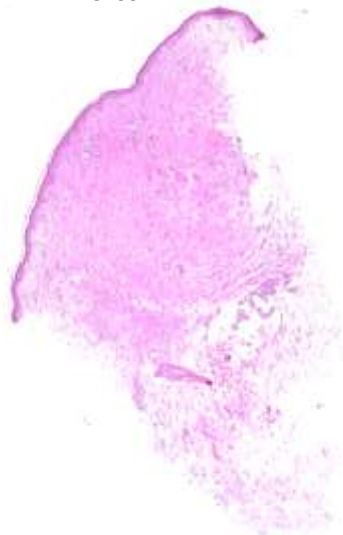


Since many years recidivating crustae, itchy, presternal in actinic back ground  
Response to steroids local but recidives after stopping steroids  
AK? Form of inflammatory disease? seborhoic eczema? grover?

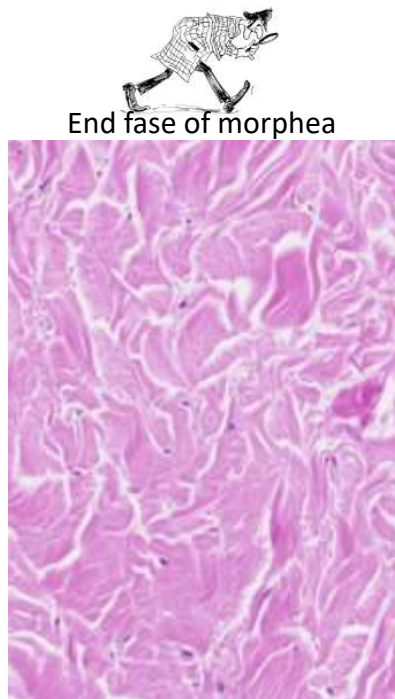
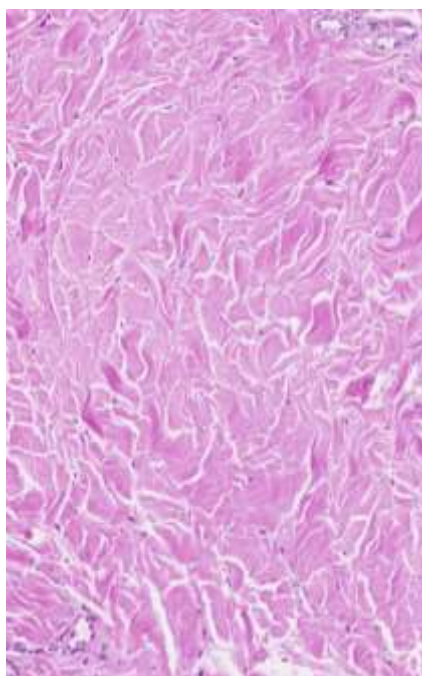
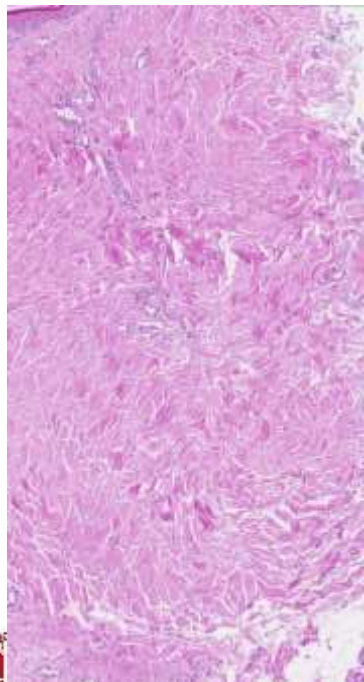


2212-51552

2212-51552



Discrete non diagnostic changes?

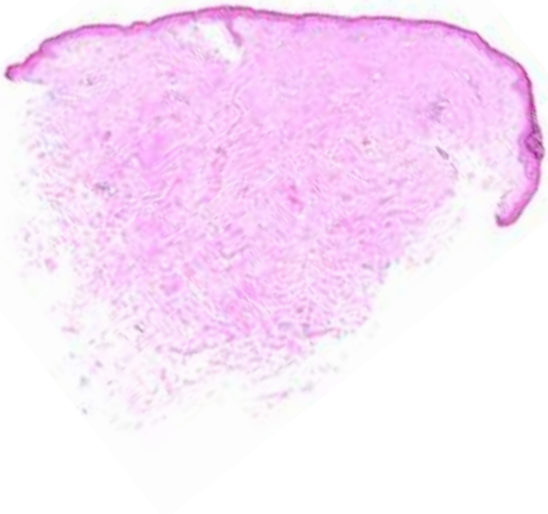


End fase of morphea





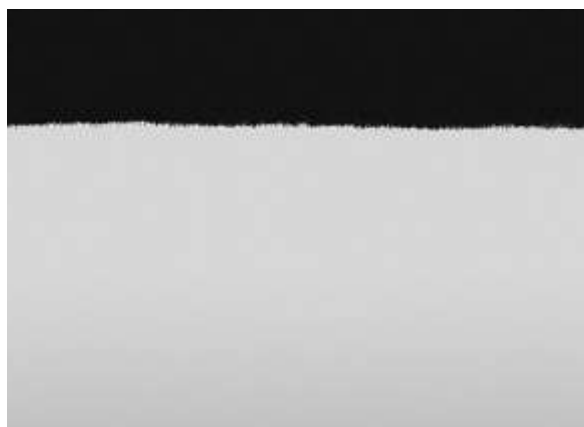
Minor changes on a skin biopsy do not mean it is disease free.  
Absence of skin structures can be diagnostic



**Invisible dermatosis**

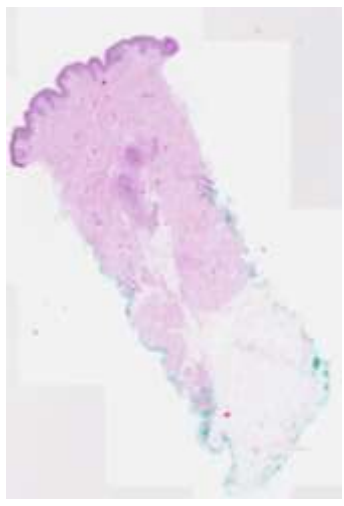
- TMEP
- Mucinosis
- Morphea
- Becker
- Vitiligo
- Mycosis fungoides
- urticaria
- amyloidosis
- pityriasis versicolor
- pityriasis alba
- pigmented purpuric dermatitis

proper clinicopathological correlation is fundamental for a precise diagnosis

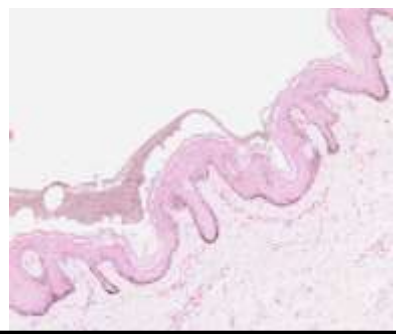


Left flank : sharply delineated, hyperpigmented lesion without hypertrichosis, continuously from abdomen to flank

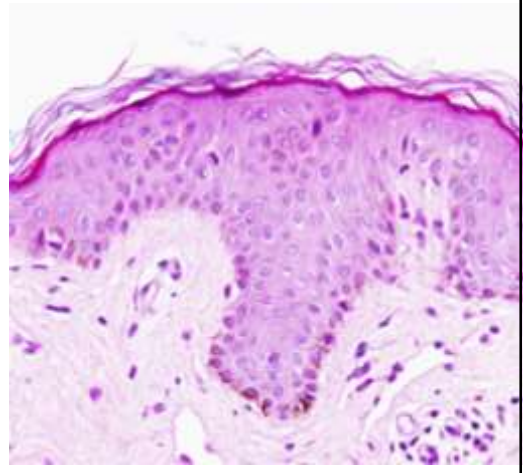
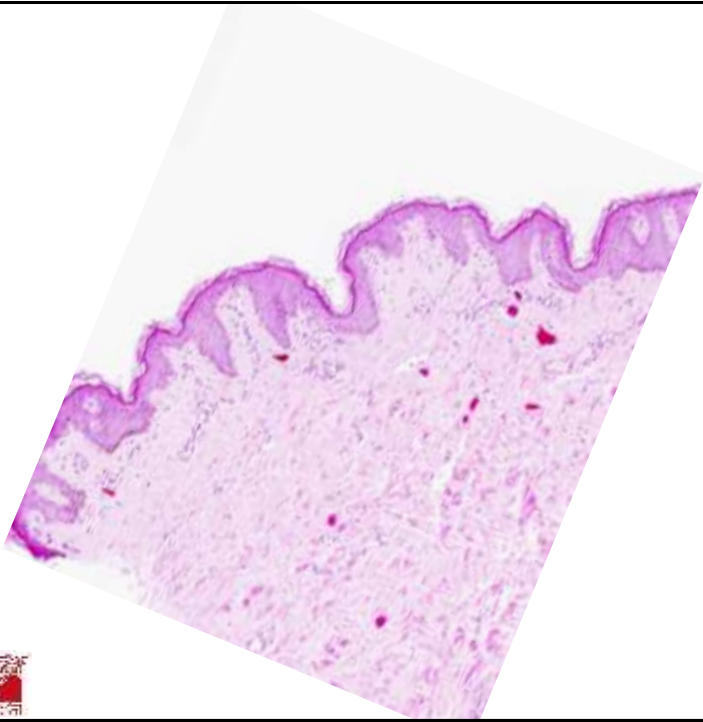
2208-51218 M 2002

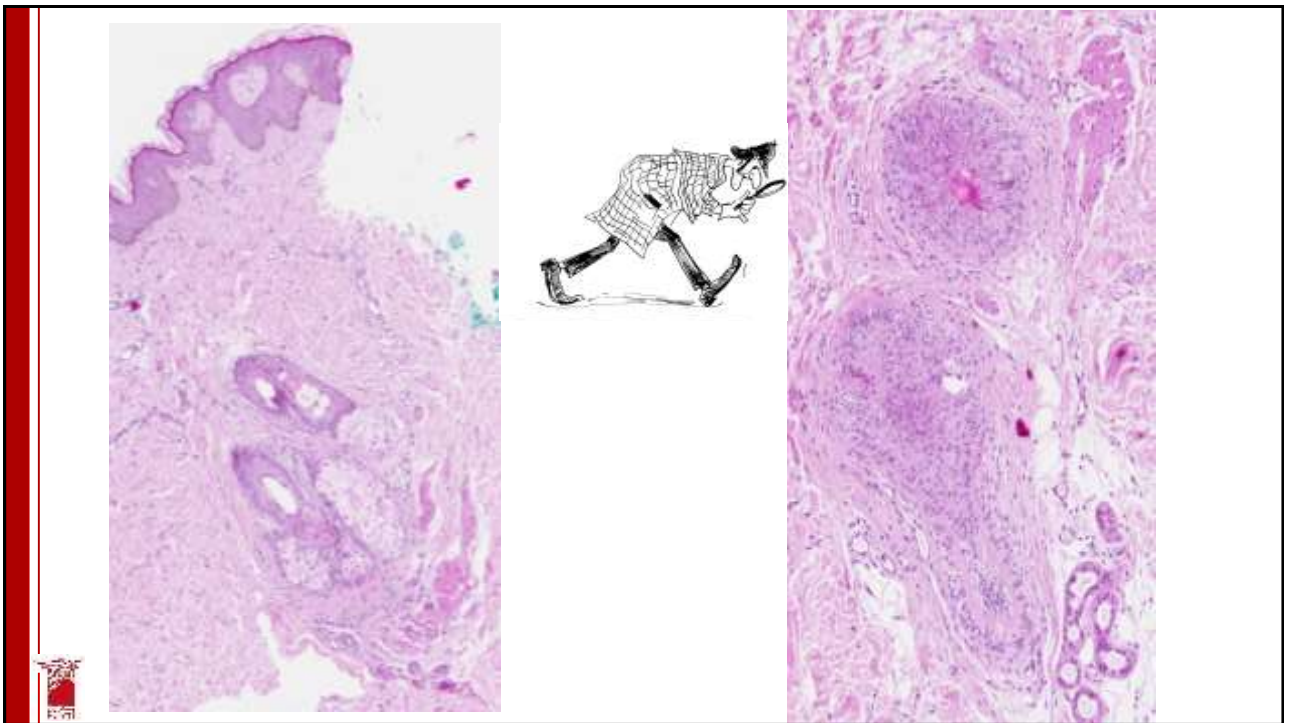
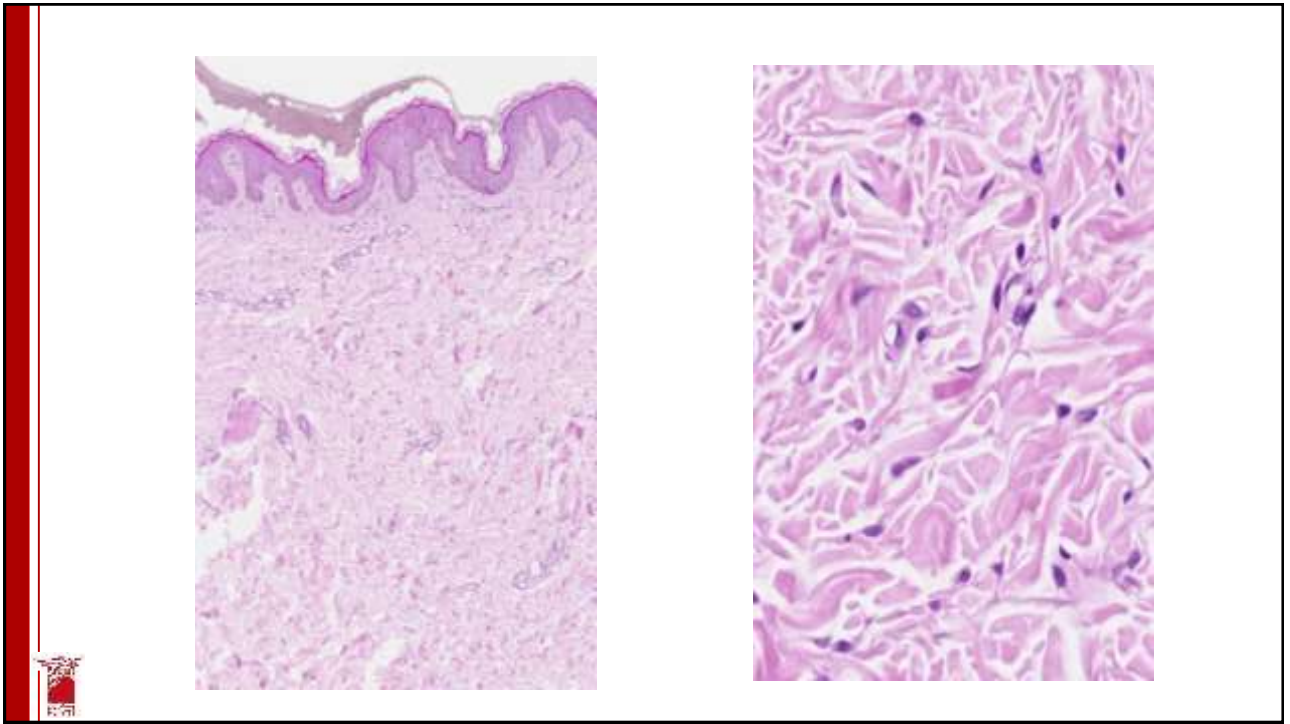


SOX10



FM

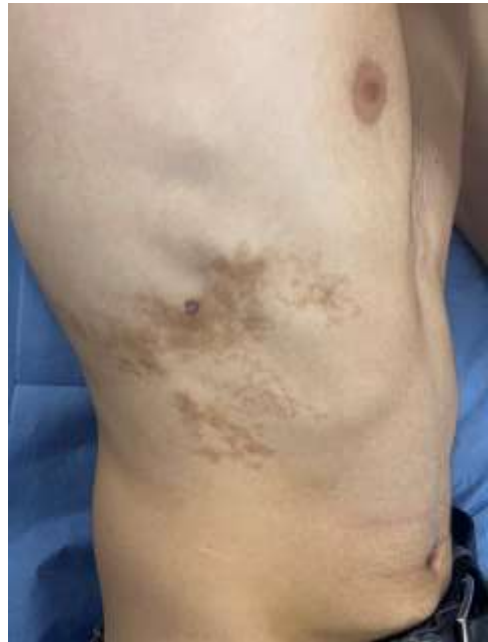
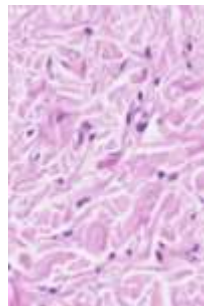
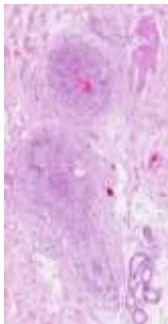
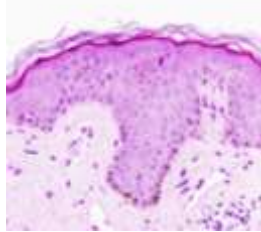




Left flank : sharply delineated, hyperpigmented lesion without hypertrichosis, continuously from abdomen to flank  
Dd naevus of Becker, postinflammatory hyperpigmentation, lichen aureus? Quid?  
29/7/2002 M

BECKER NAEVUS!

postzygotic *ACTB* mutations



Invest in a lab culture  
that focuses on  
Quality and  
Representativity of  
slide





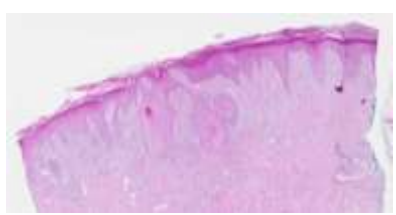
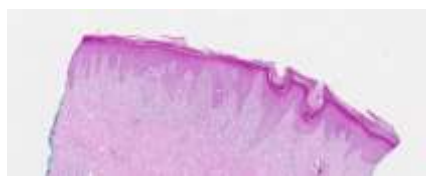
Standard method

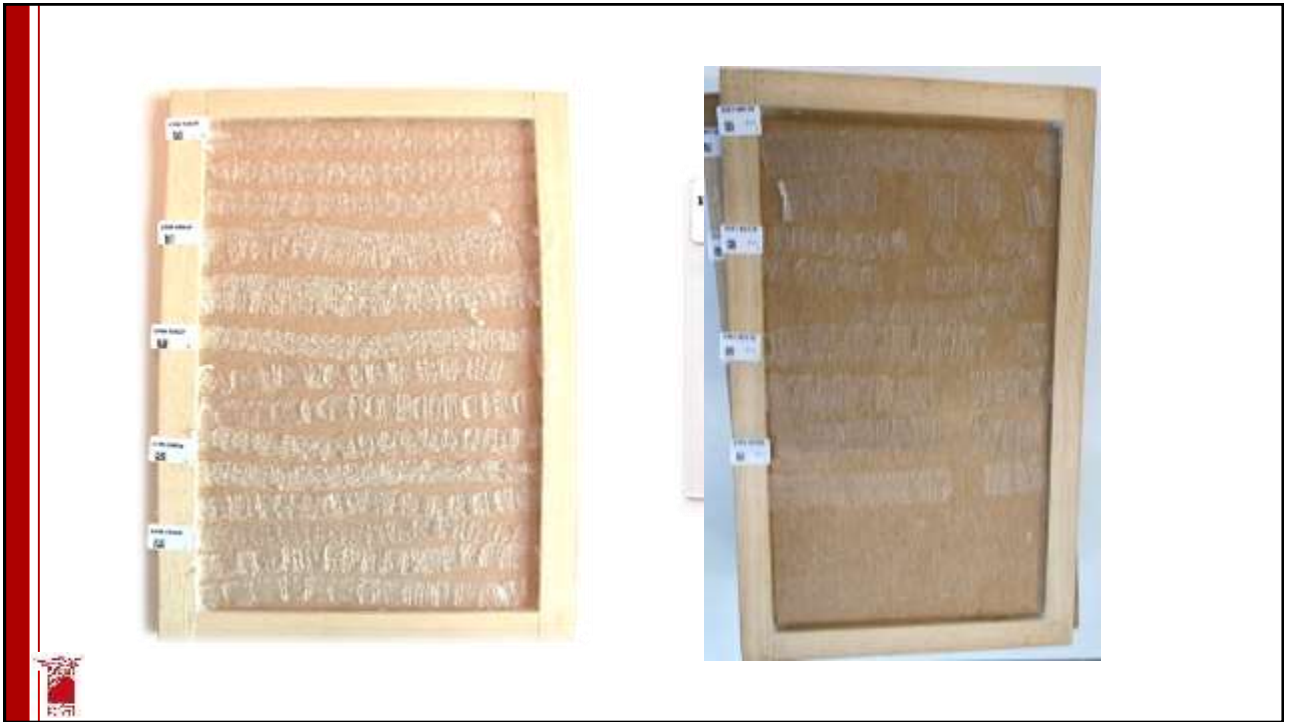
EVD with DD

Punch biopsy

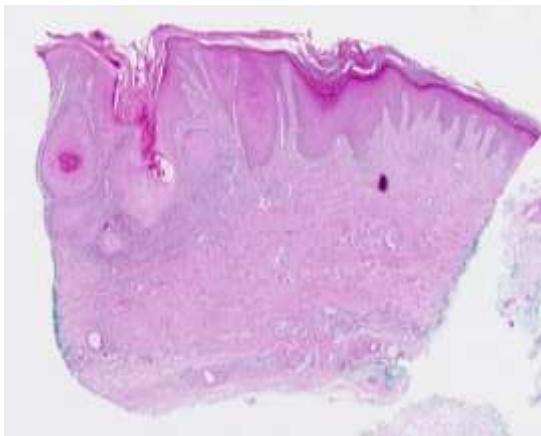
Random cuts give no central information, focal lesions may be missed. Block can be exhausted for eventual additional stains.

Three depths with marked central section and residual tissue for deeper sections. Marked section of focal lesions.

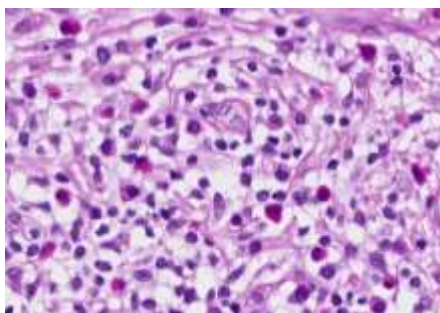
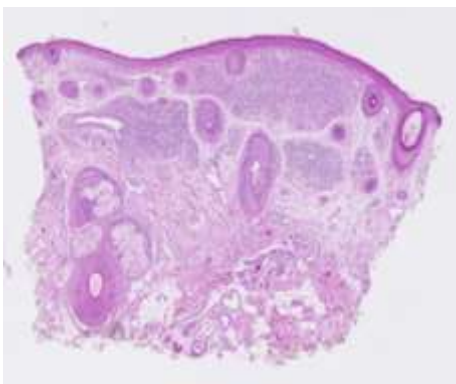




New slides from 3 level cuts

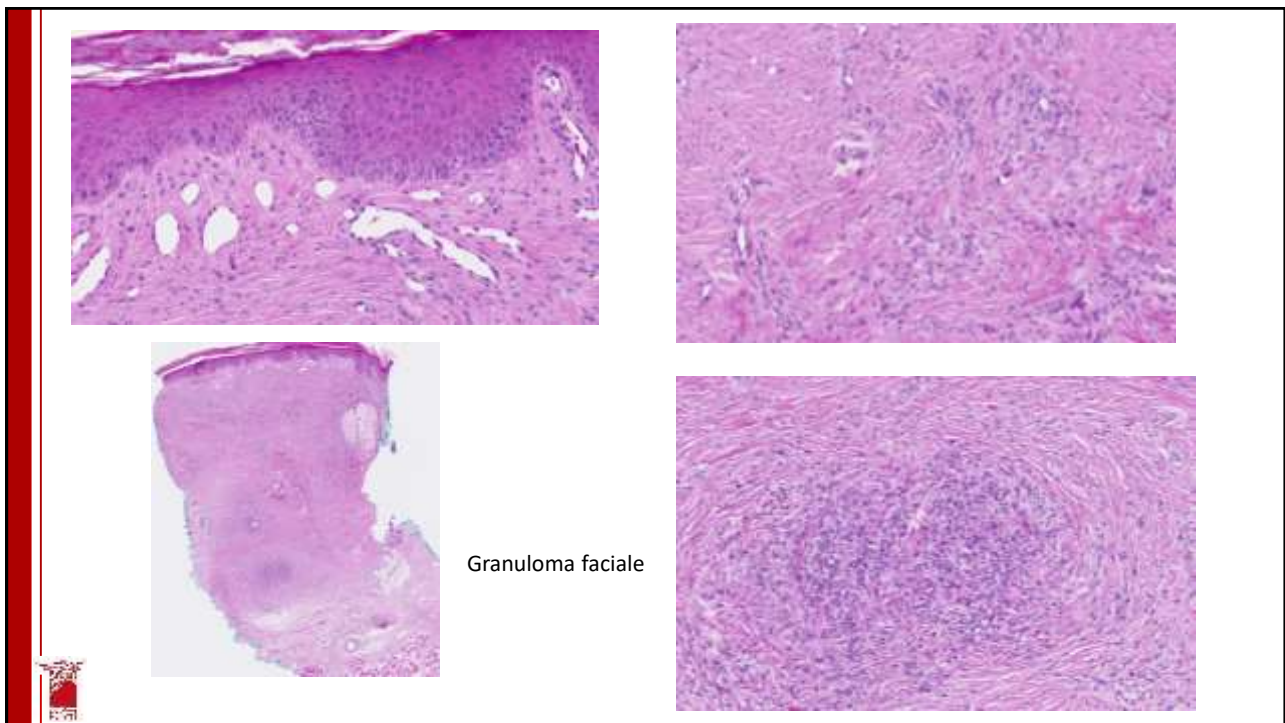


## Take in account the Life of a lesion



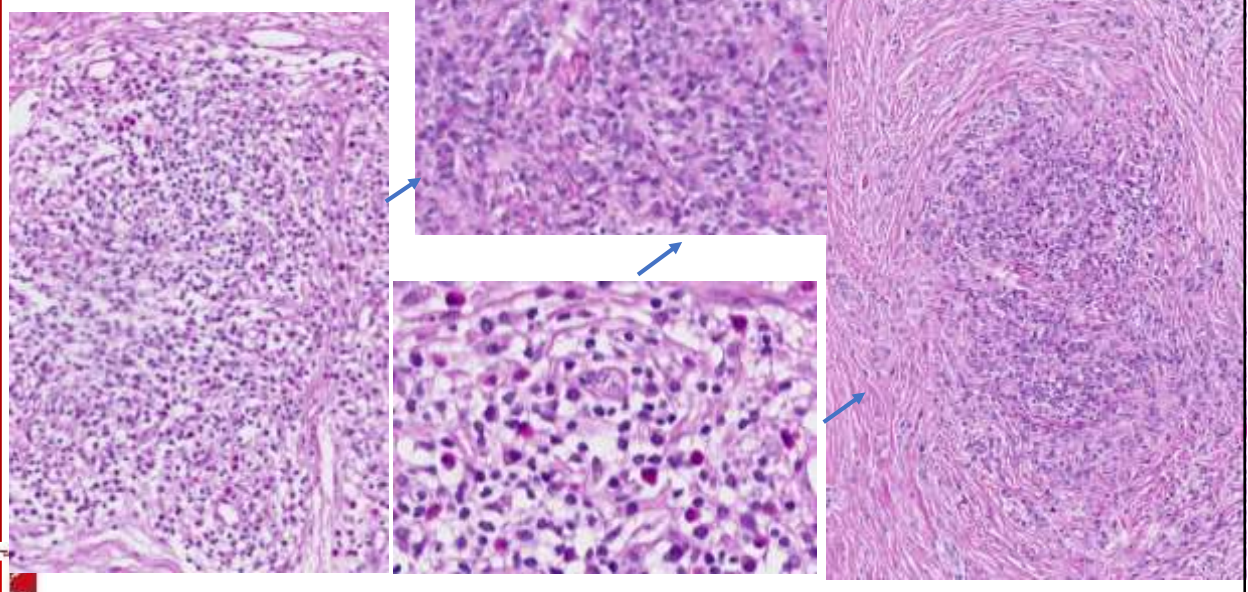
Granuloma faciale







Granuloma Faciale

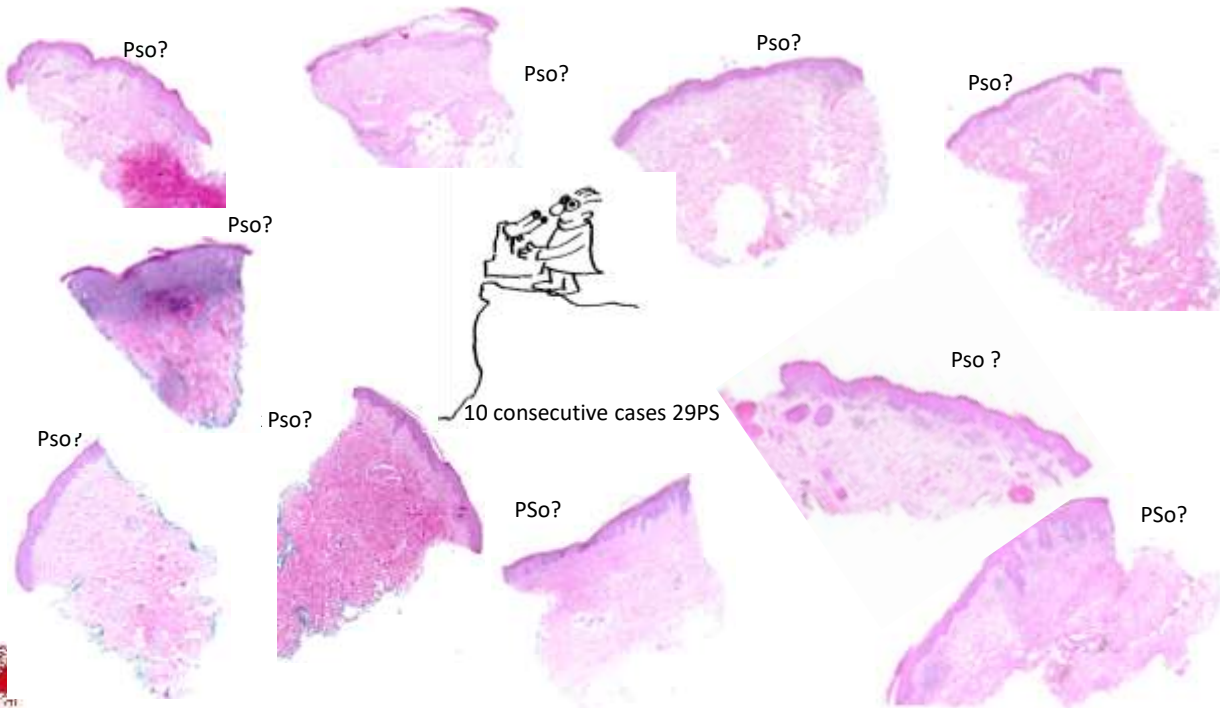


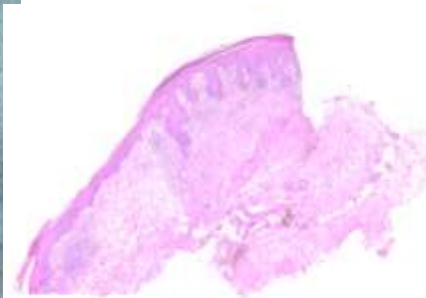
2204-51249

Erythema elevatum diutinum



Be ambitious and try to go step further than descriptive dermatopathology





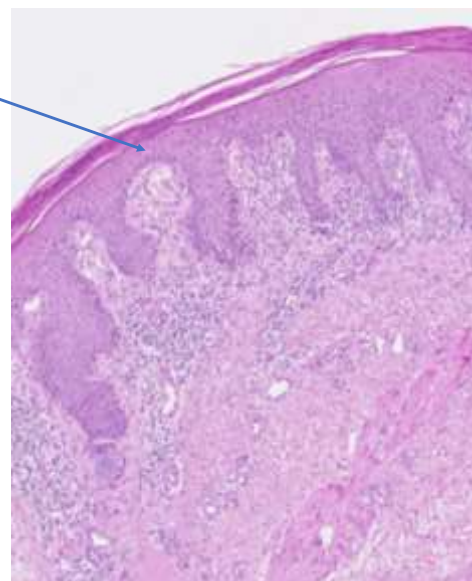
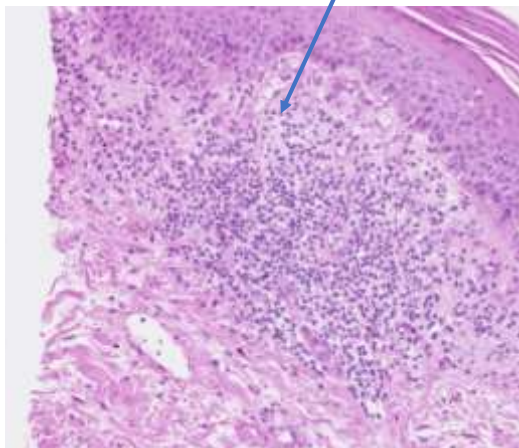
**2303-50018**

Plaques onderbeen rechts en links  
Erythematosquameus, sharp



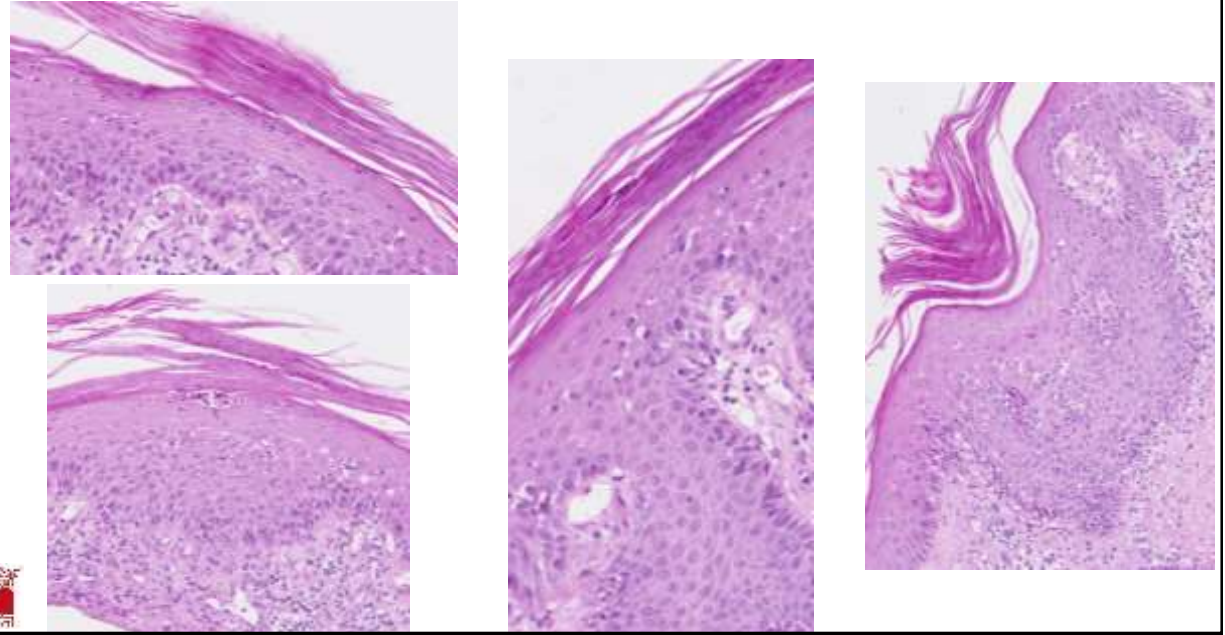
Plaques onderbeen rechts en links  
erythematosquameus  
DD PSO?

13/08/1939 **2303-50018**



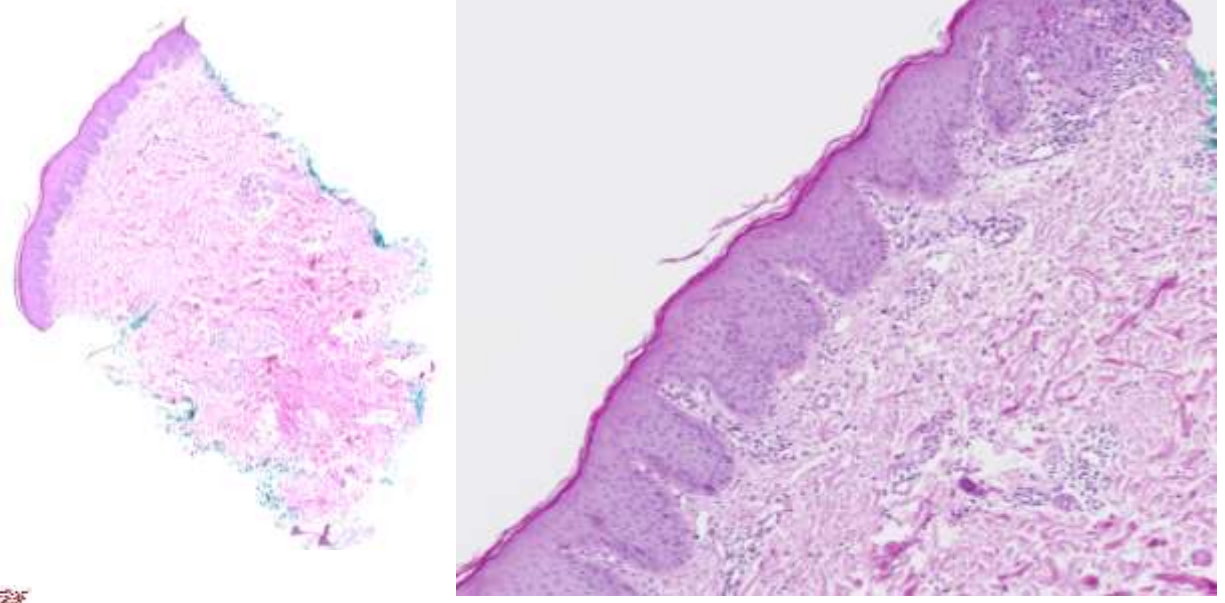


Left Lower leg : acanthotic, parakeratotic dermatitis with intraepidermal neutrophils and prominent papillary capillaries, fitting very well with your clinical diagnosis of psoriasis



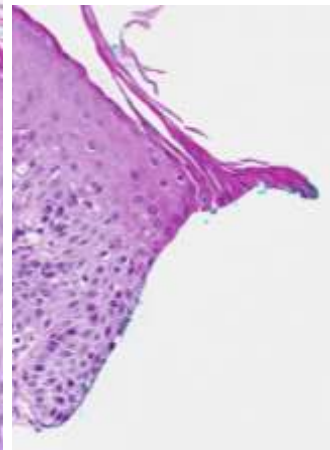
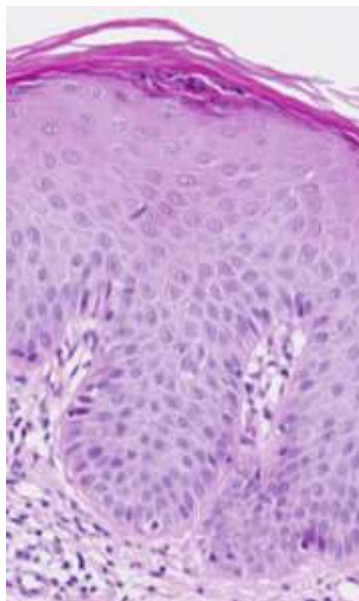
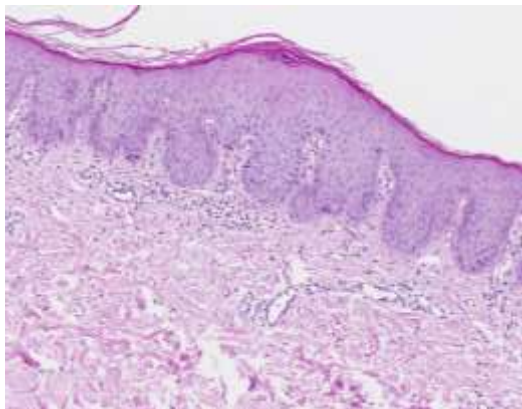
2303-51708 08/01/1989

Right Flank





2303-51708 08/01/1989



Histology very suggestive for Psoriasis



Unilateral psoriatic dermatosis with blaschko linear presentation



### Blaschkoid Psoriasis



BPso, an exceedingly rare variant of psoriasis, was first reported in 1951. It is characterized by linear distribution of psoriasis along Blaschko lines. The pathogenesis of BPso is unclear, but may be explained by genetic mosaics.

The diagnosis of BPso is usually challenging for clinicians and should be differentiated from other dermatoses with similar blaschkoid distribution pattern including inflammatory linear verrucous epidermal nevus, blaschkoid lichen planus, lichen striatus, and linear lupus erythematosus. Skin biopsy plays an important role in making a correct diagnosis.

**Blaschkoid psoriasis: An unusual variant of psoriasis that needs to be diagnosed early and treated aggressively**

[Yang Lo, Tse-Yuan Liaw](#)

First published: 22 October 2019

<https://doi.org/10.1002/kjm2.12141>



Non-pustular psoriasis

Psoriasis vulgaris (early and late onset)

Guttate psoriasis

Erythrodermic psoriasis

Palmoplantar psoriasis

Psoriatic arthritis (PSA)

Inverse psoriasis

Pustular psoriasis

Generalized pustular psoriasis (von Zumbusch type)

Impetigo herpetiformis

Localized pustular psoriasis

•- Palmoplantar pustular psoriasis (Barber type)



Blaschkoid psoriasis



Plaque Psoriasis

Guttate Psoriasis

Pustular Psoriasis

Inverse Psoriasis

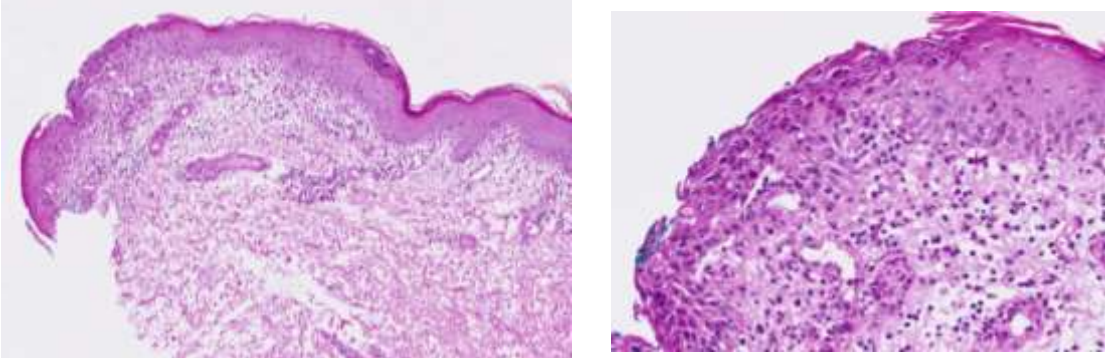
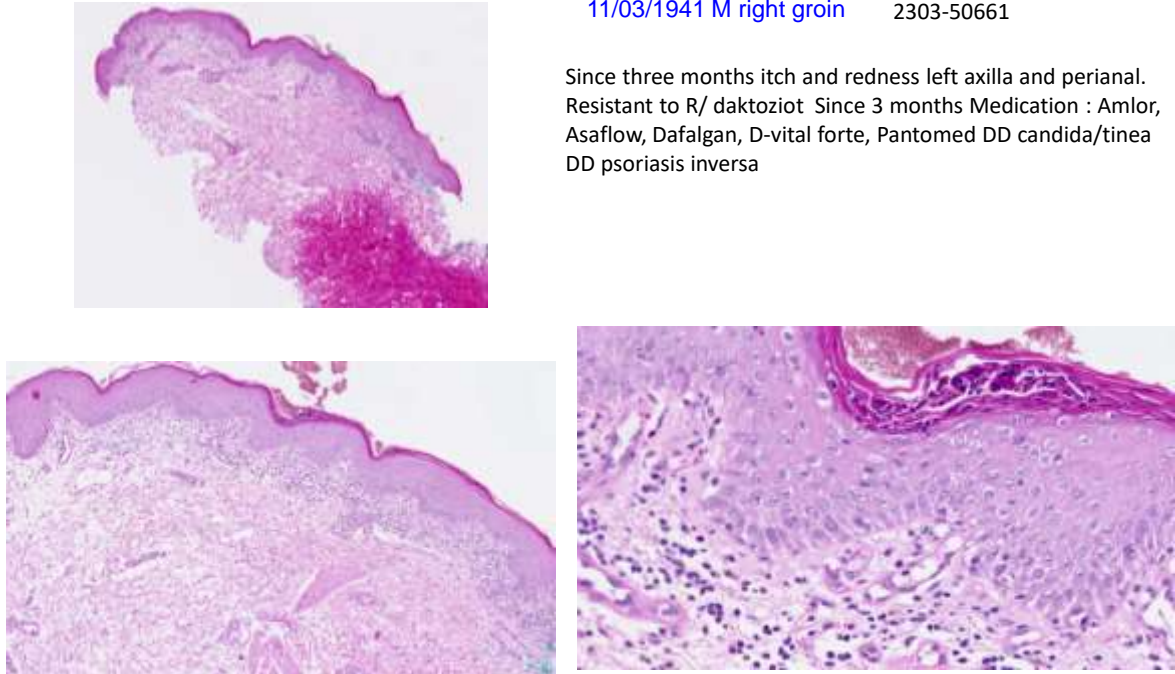
Nail Psoriasis

Psoriatic Arthritis



11/03/1941 M right groin 2303-50661

Since three months itch and redness left axilla and perianal.  
Resistant to R/ daktoziot Since 3 months Medication : Amlor,  
Asaflow, Dafalgan, D-vital forte, Pantomed DD candida/tinea  
DD psoriasis inversa



PAS neg, culture neg - preference Pso inversa



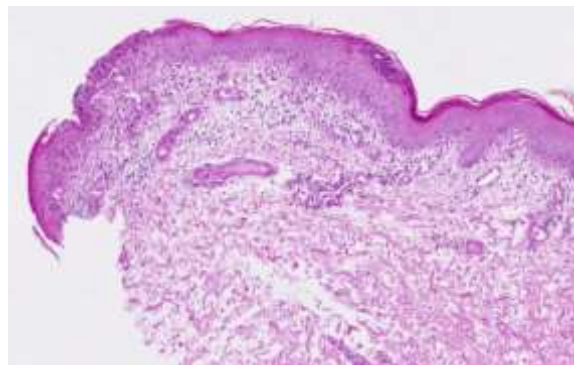
2303-50661

Left axilla : very sharp erythema with some satellite lesions and groins with confluent erythema with colarette flakes and also some satellite lesions



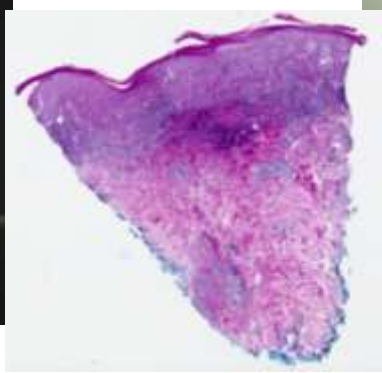
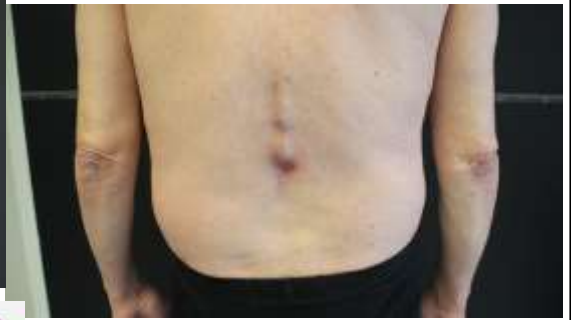
#### PSO INVERSA

it is not unusual for inverse psoriasis to show features considered atypical for plaque psoriasis such as dermal eosinophils, epidermal spongiosis, and focal serum in the scale.

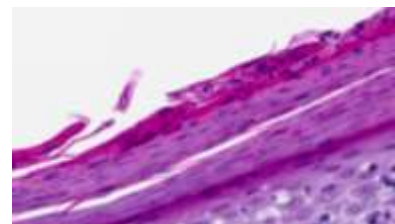
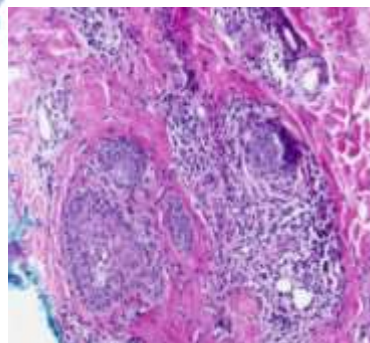
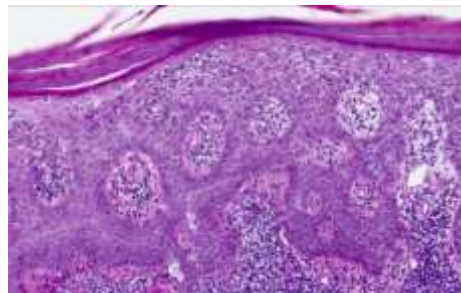
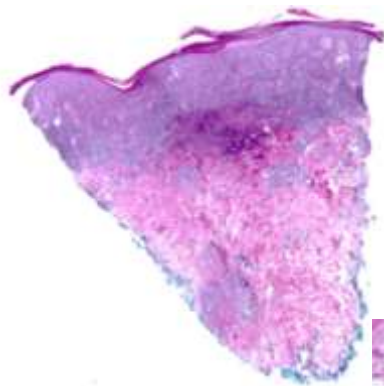




M 1967 atopic eczema  
Since 2021 dupilumab  
therapy  
New plaque on back  
Dermoscopic aspect :  
glomeruloid capillaries  
Bowen?



23b6721

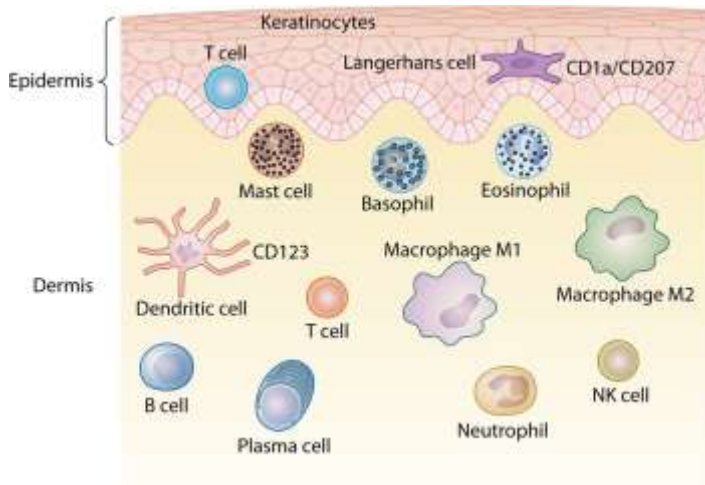


Very dense lymphoid infiltrate  
Exocytotic  
Also deep periadnexal  
involvement  
Superficial changes very  
psoriasiform

DUPIUMAB=monoclonal antibody blocking interleukin 4 and 13 (TH2 reaction)

### Skin associated Lymphoid tissue

innate and adaptive immunity mechanisms



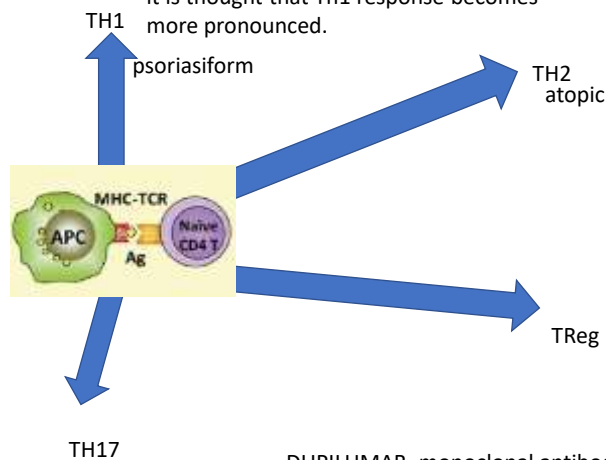
Th1 cells produce a cell-mediated immune response to kill intracellular pathogens.

- Th1 cells produce IFN- $\gamma$  and can activate macrophages and stimulate NK cells.
- Th1 cells play a role in the pathogenesis of [psoriasis](#).

Th2 cell activation leads to B cell stimulation and antibody production.

- Th2 cells produce cytokines IL-4, IL-5, IL-6 and IL-10.
- They can stimulate eosinophil activation.
- Th2 cells are involved in [atopic eczema](#), [allergic responses](#).

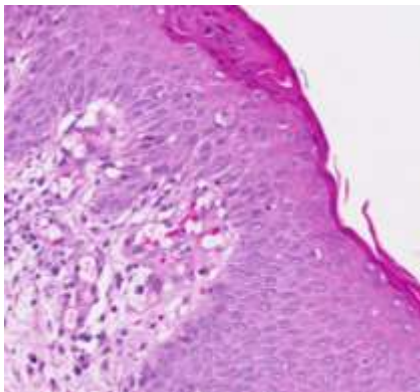
In the acute phase, atopic dermatitis is primarily a Th2 disease, but with time there is a partial shift to Th1. Adding the Th2 inhibition from dupilumab, it is thought that Th1 response becomes more pronounced.



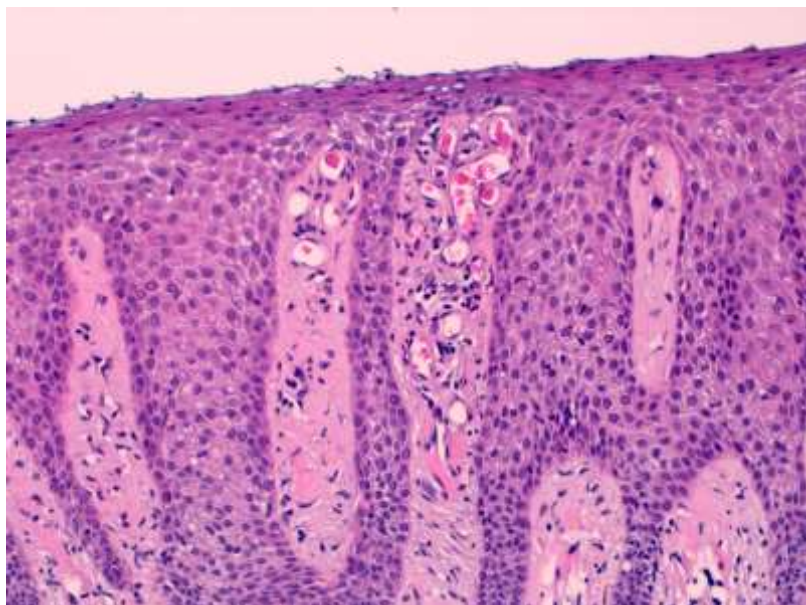
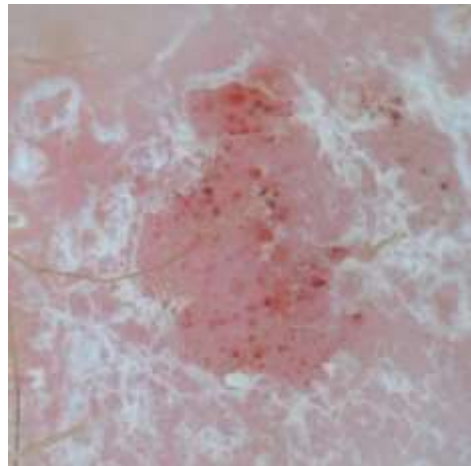
Biologicals for neoplasia or autoimmune diseases can elicit a spectrum of cutaneous reactions that go beyond the classical eosinophilic-rich hypersensitivity reaction and may closely mimic primary dermatitis as lichen, seborrheic dermatitis and psoriasis or produce new complex inflammatory reactions.

DUPILUMAB=monoclonal antibody blocking interleukin 4 and 13 (TH2 reaction)

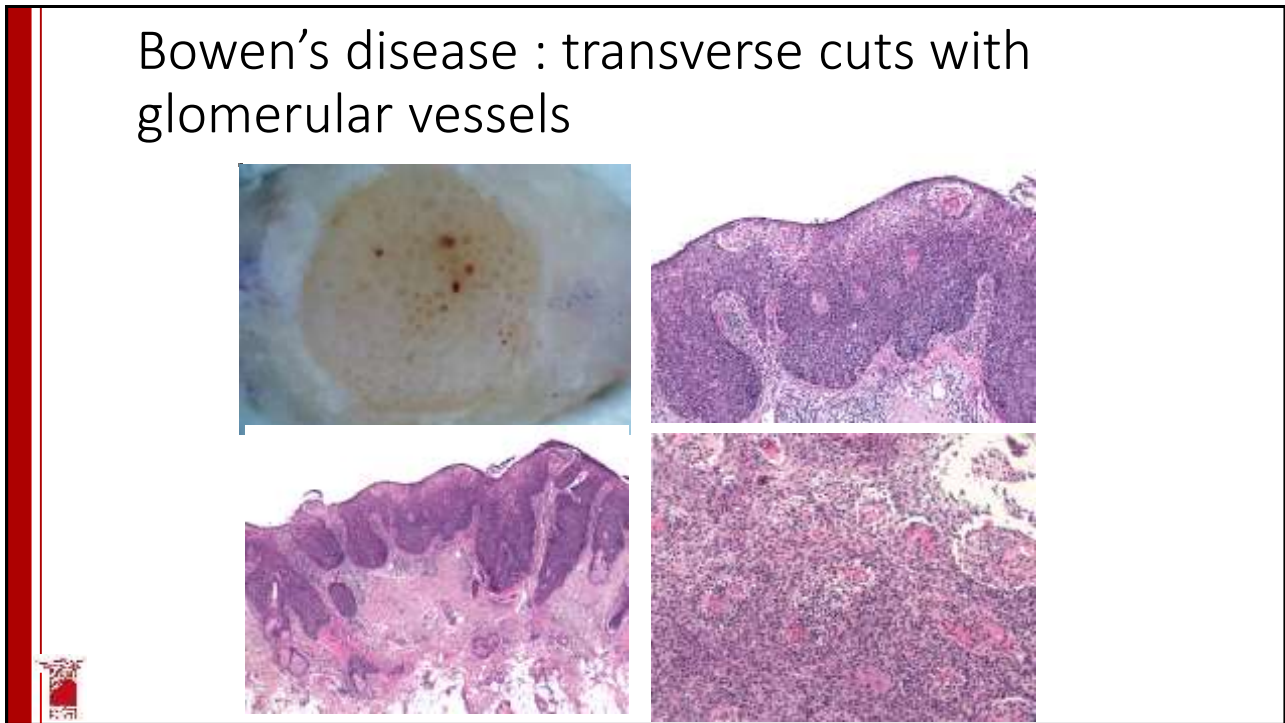
M 1967 atopic eczema  
Since 2021 dupilumab  
therapy  
New plaque on back  
Dermoscopic aspect :  
**glomeruloid capillaries**  
**Bowen?**



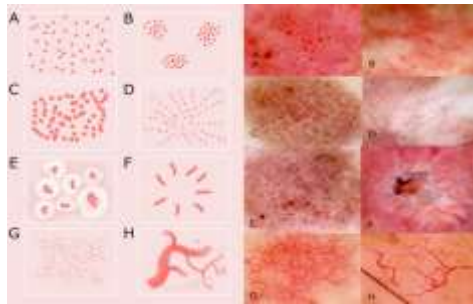
Dotted vessels represent the most frequent  
dermoscopic feature of Psoriasis, being  
present in every single psoriatic plaque.



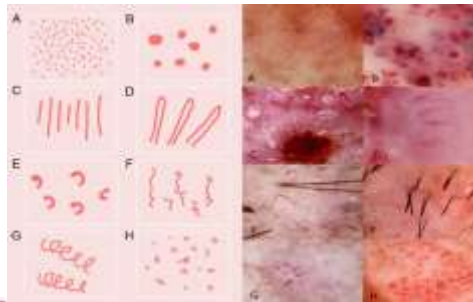








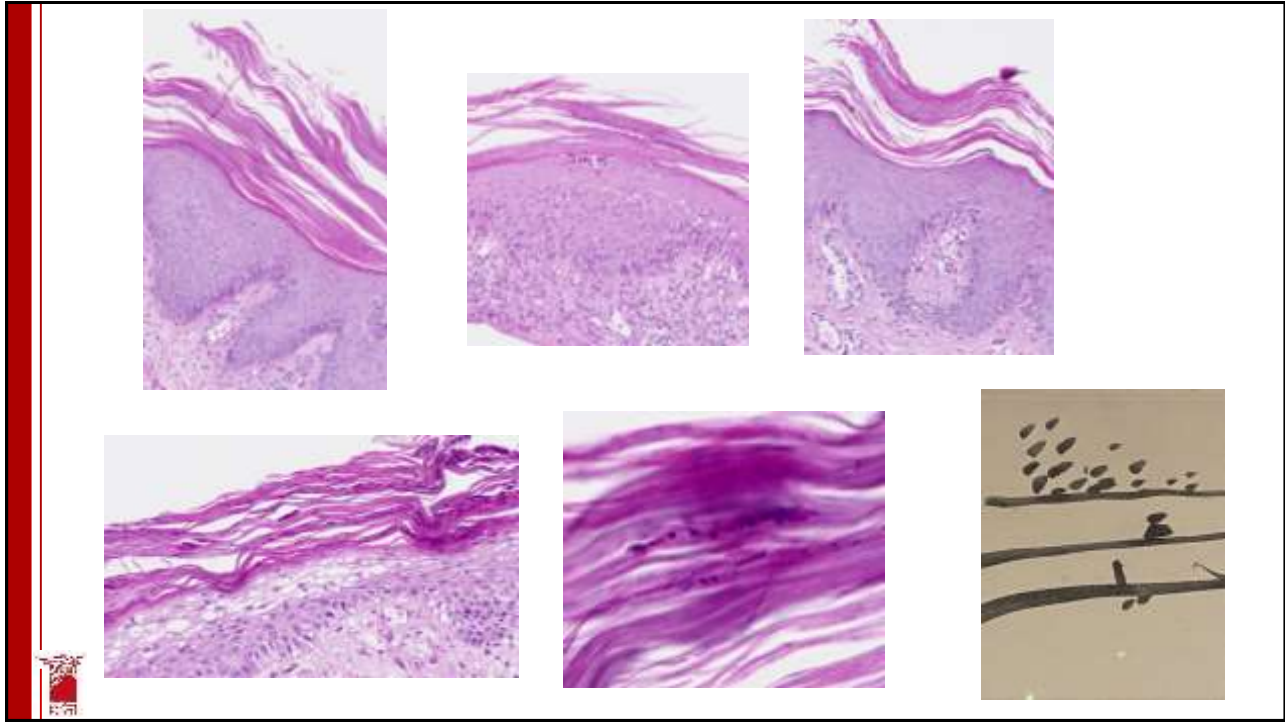
Learn basics of  
dermoscopy  
Its the language of  
your dermatologist!

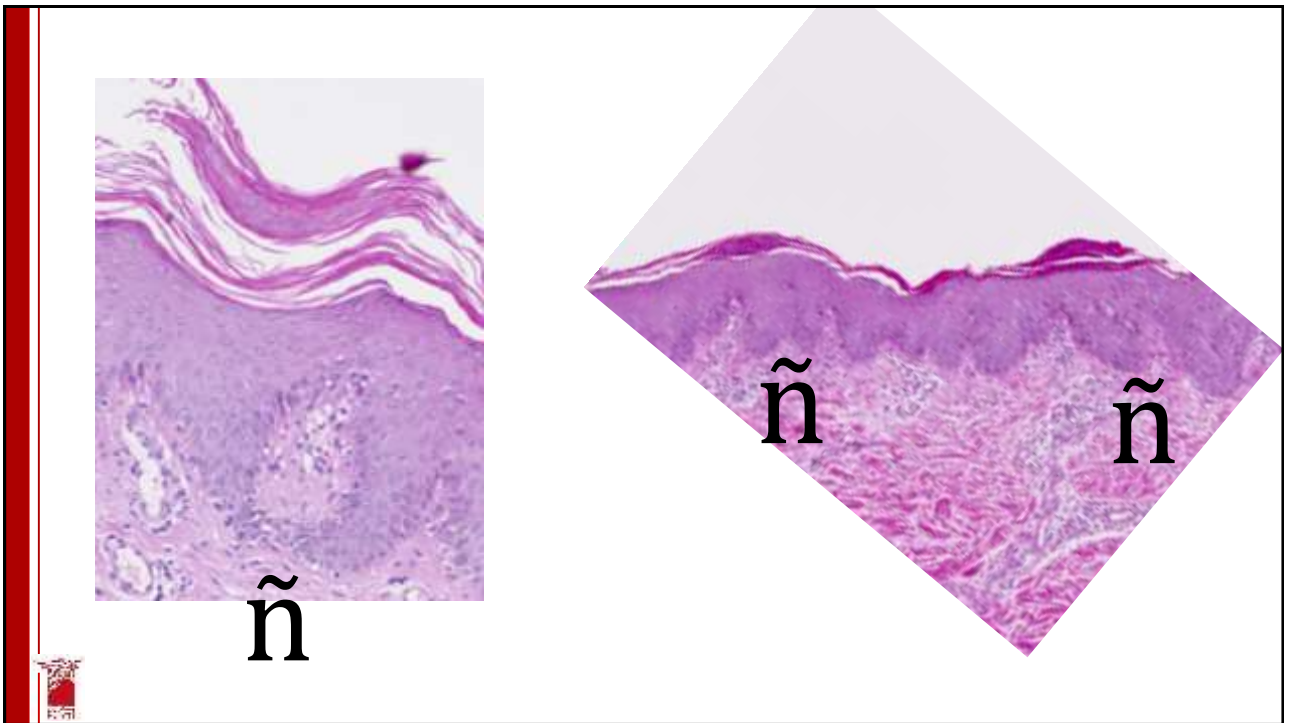


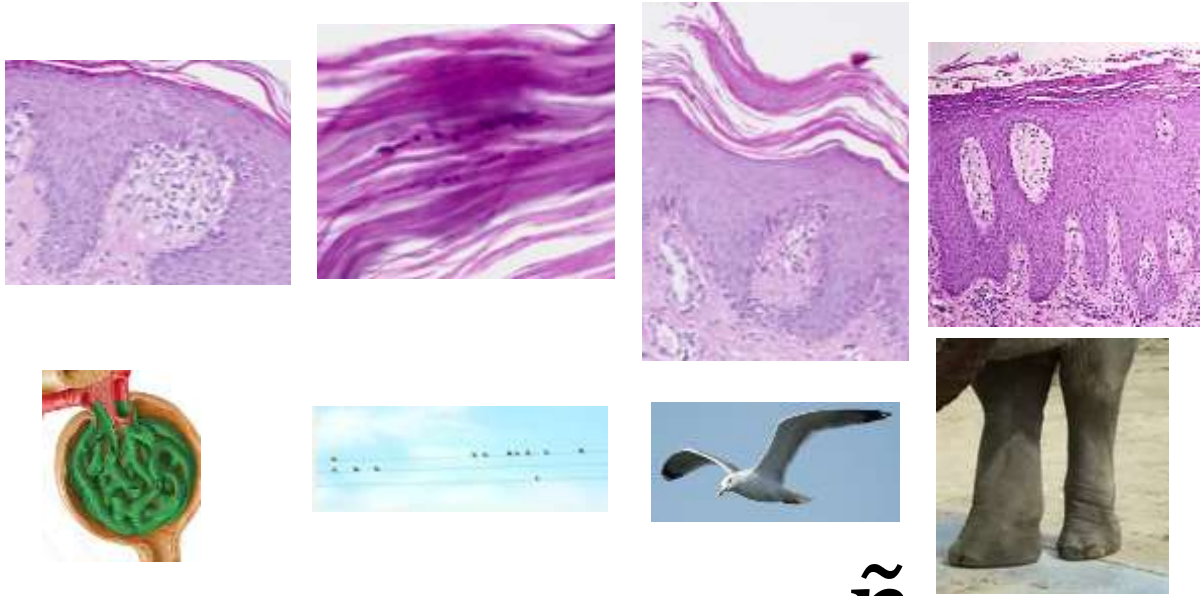
In dermatopathology, the diagnostic process is based on the recognition of **histologic patterns and their correlation with clinical data**. Visual recognition in dermatology and dermatopathology is often **instantaneous**, as the brain of experienced physicians can process large amounts of information **rapidly and effortlessly**. This cognitive phenomenon is part of so-called system 1 (**automatic, effortless, unconscious, experience-based**) thinking.<sup>2</sup>

When first-sight recognition is not possible, system 2 (slow, **conscious, effortful, consequential**) thinking is activated. In these cases, mnemonics are useful.<sup>3</sup> There are **visual clues** (so-called pearls or tips) that can facilitate reaching a final diagnosis in dermatopathology.<sup>4,5</sup> These mnemonic devices are often easily recognizable at first glance, even for individuals with less experience, and they can be extremely useful in daily clinical practice.

Kahneman, D. (2011). *Thinking, fast and slow*. Farrar, Straus and Giroux








Approach Psoriasis as a puzzle full of clues!

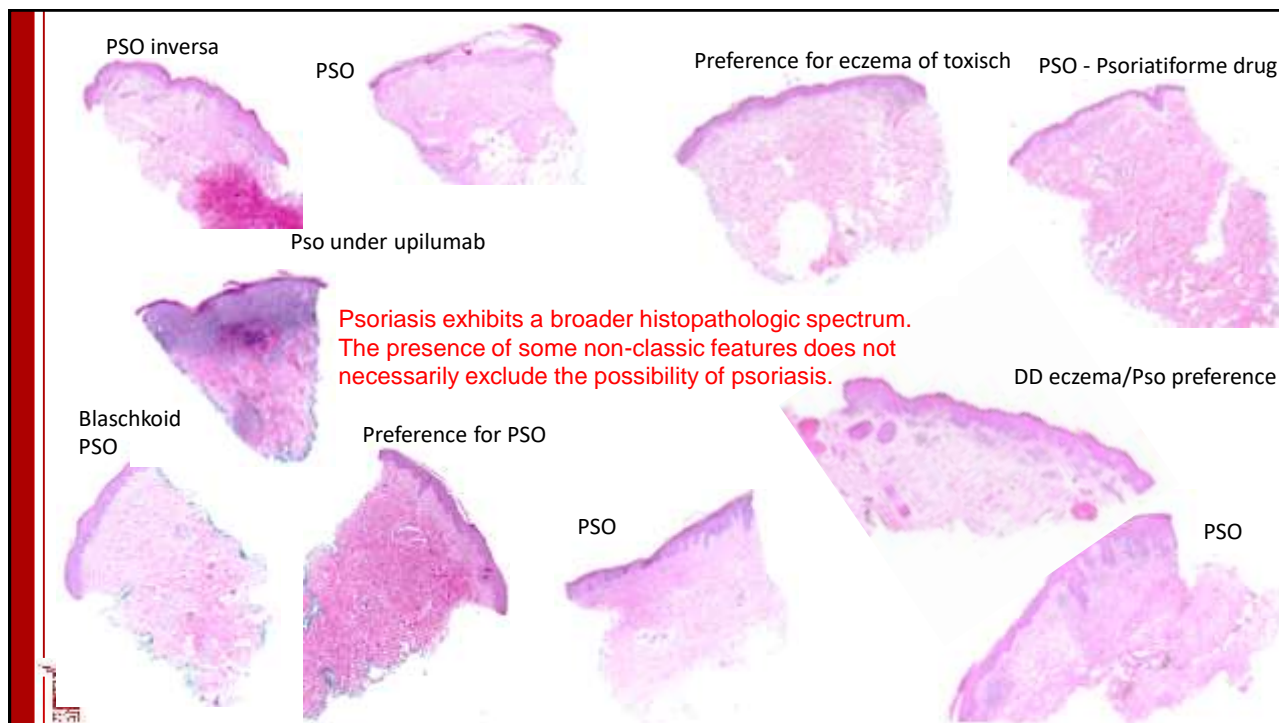
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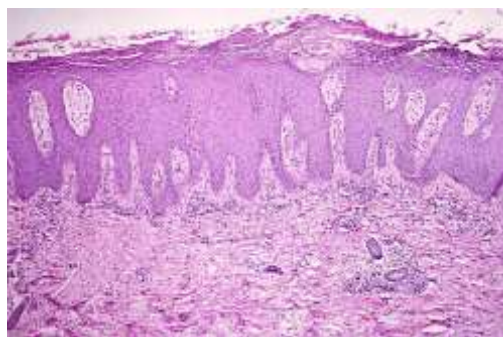
**PSORIASIS**





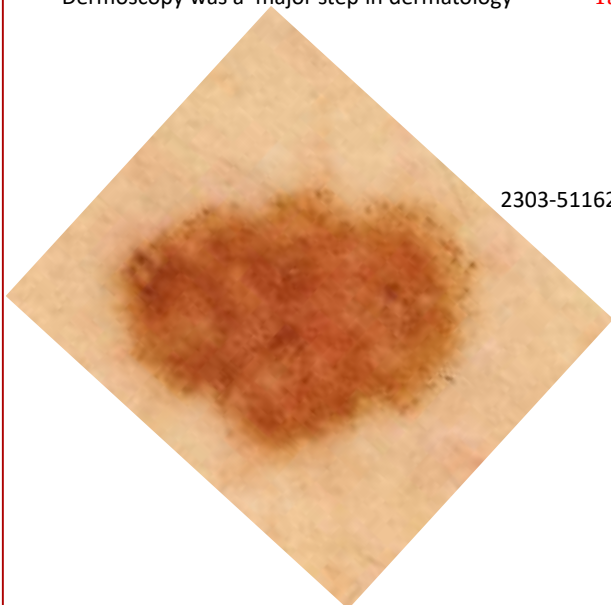
## Psoriatic Lessons learned

- Biopsied inflammatory diseases (psoriasis) rarely full blown text book histology
- Take into account the live of lesions from early guttata to neurodermised plaques and inverse forms
- Psoriasiform dermatitis as side effect in biologicals shifting the interleukin balance between eczema and psoriasis
- Clinicopathologic correlation!!!



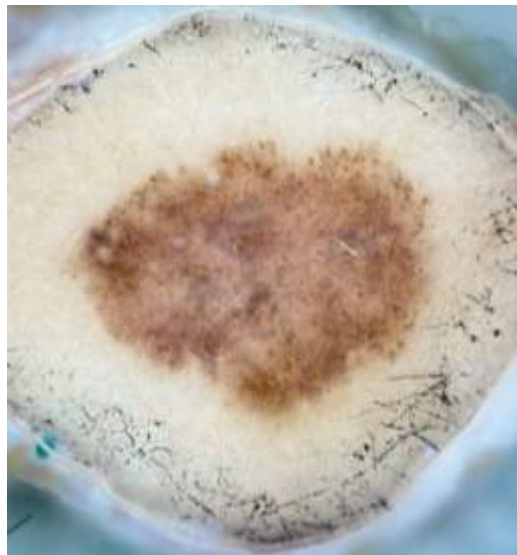
Dermoscopy was a major step in dermatology

Taking into account the heterogeneity of lesions



2303-51162

IN VIVO



EX VIVO

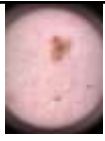


Evolution to lesion specific processing and lesion specific examination

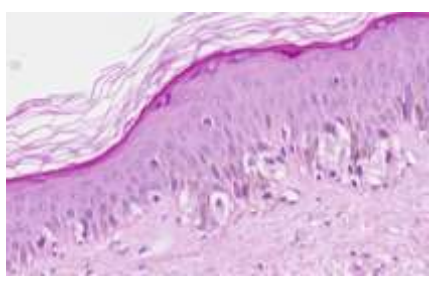
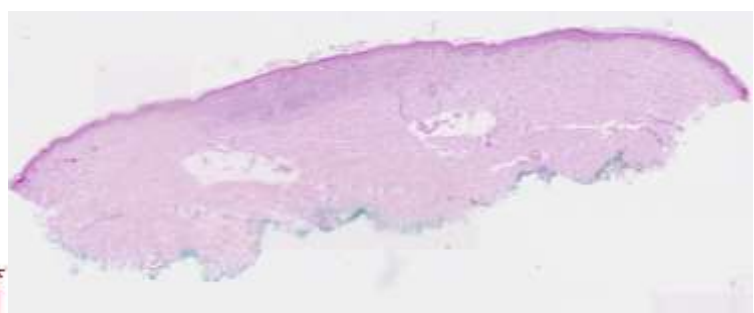
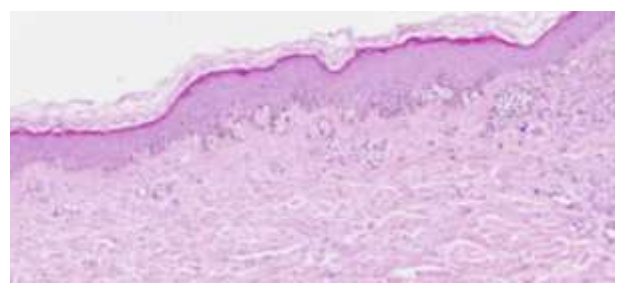
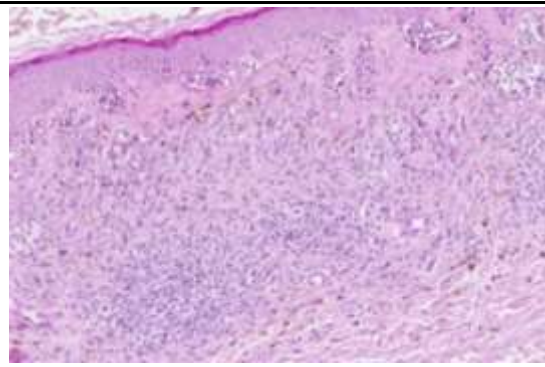


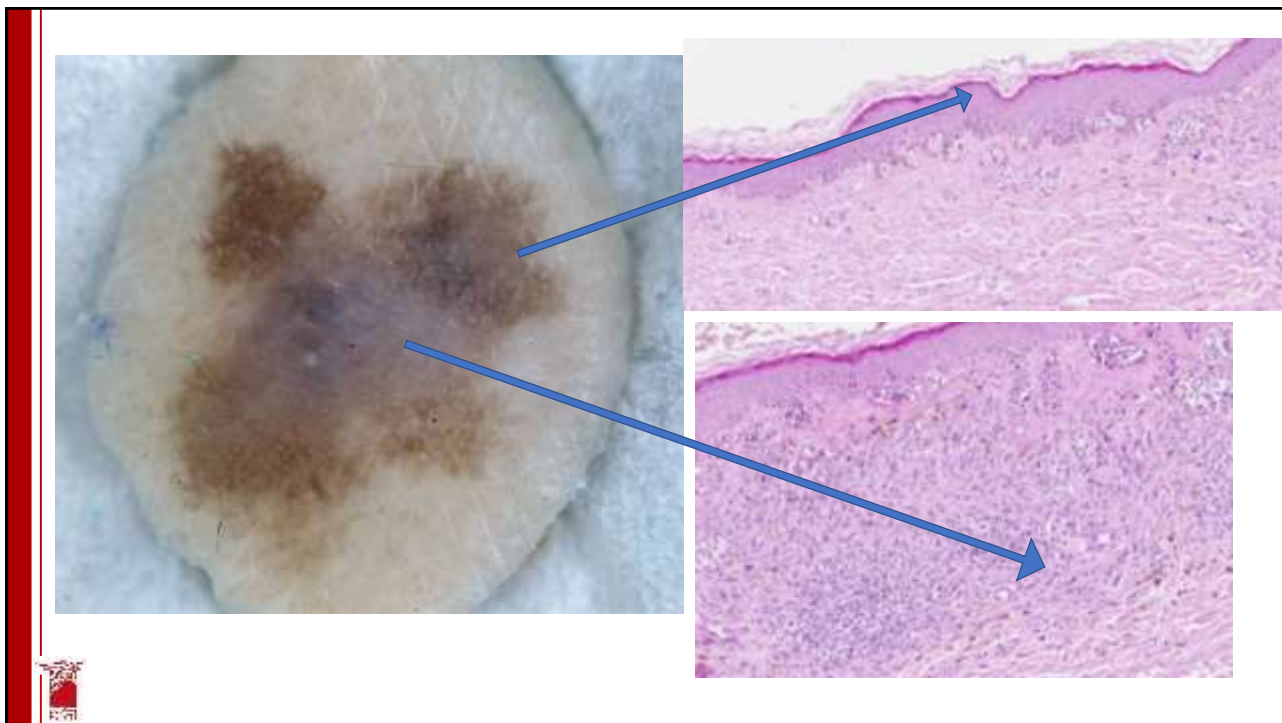
2303-51019





2303-52218  
Asymmetric brown macula with network and central blue blotch  
16/09/1965 F Re kuit

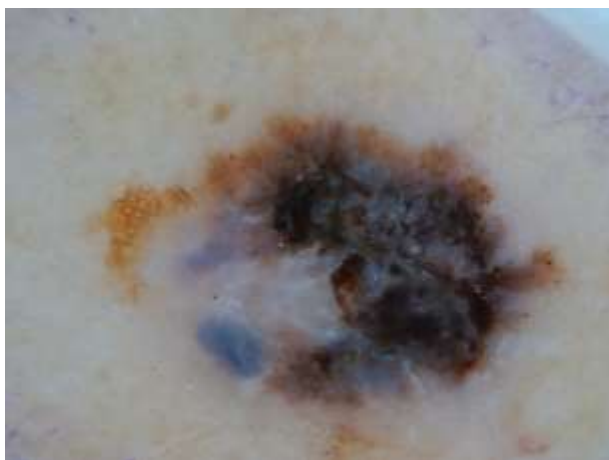




Collision

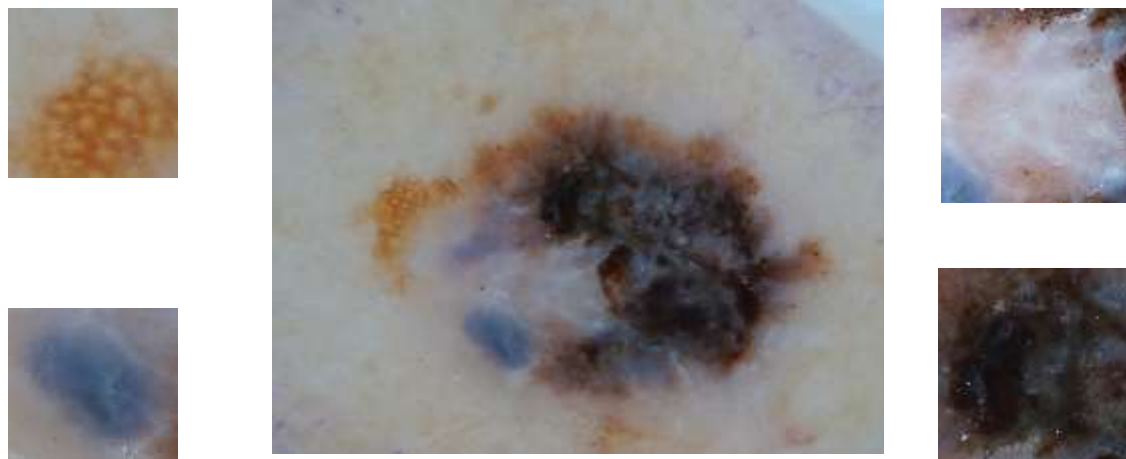


Heterogeneity

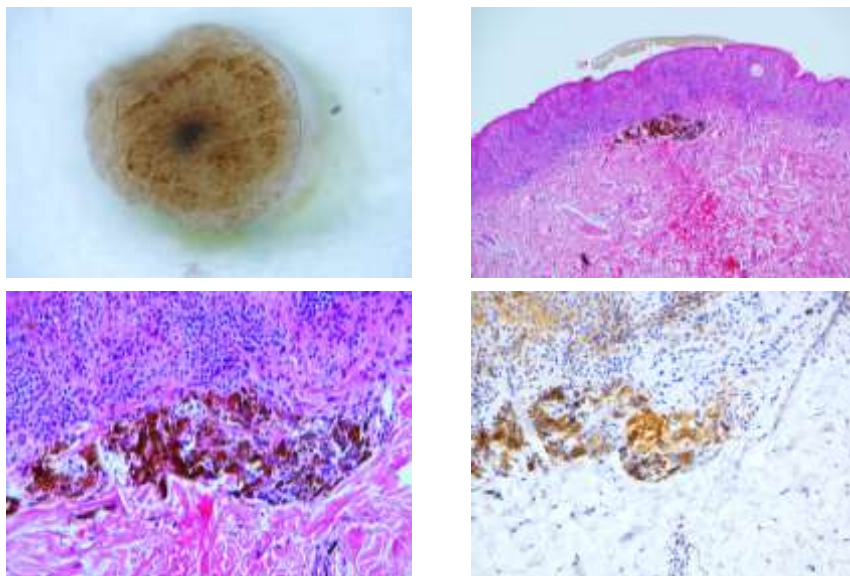




Heterogeneity: prognostic



Naevi with blue dot: focal pigmented epithelioid differentiation with beta catenin= mini DPN?



Subtype of naevus with phenotypic heterogeneity (combined naevus): melanocytoma of WNT pathway



## Taking into account the heterogeneity of lesions

- Heterogeneity within a biopsy: collision of lesions
  - Incidental benign collision of lesions
  - Collision with diagnostic importance
- Heterogeneity within a lesion:
  - Explanatory of dermoscopic image and excision of lesion leading to more diagnostic confidence
  - Implications for Prognosis of lesion
    - identification of exact thickness of melanomas and grading of atypical naevi and (naevus-associated) melanoma
  - Is morphologic expression of molecular heterogeneity
    - identification of melanocytomas, atypical spitzoid tumors, driver mutations of lesions



## Genomic Landscape of Melanoma



Melanoma is not one disease but group of different molecular potentially progressive pathways with intermediate stages and different biological behaviour



WHO Classification of Tumours of the Skin

1. Overview and introduction

2. Melanocytic neoplasms

### 3. Melanocytic neoplasms

Introduction

Genomic landscape of melanoma

#### Melanocytic neoplasms in intermittently sun-exposed skin

Naevi

- Junctional, compound, and dermal naevus
- Simple lentigo and lentiginous melanocytic naevus
- Dysplastic naevus
- Naevus spilus
- Special-site naevi (of the breast, axilla, scalp, and ear)
- Halo naevus
- Meyerson naevus
- Racemose naevus
- Spitz naevus
- Melanocytomas**
- Very superficial, deep penetrating/juxtiform melanocytoma (naevus)
- Pigmented epithelial melanocytoma
- BAP1-inactivated melanocytoma
- MTF pathway-activated melanocytic tumours

Melanoma in intermittently sun-exposed skin

- Low-CSD melanoma (including superficial spreading melanoma)

#### Melanocytic neoplasms in chronically sun-exposed skin

- Melanoma in chronically sun-exposed skin
- Lentigo maligna melanoma
- Desmoplastic melanoma

#### Spitz tumours

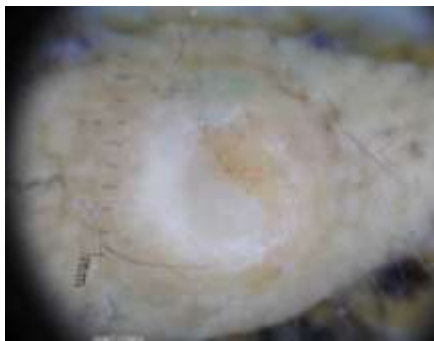
- Spitz naevus
- Pigmented spindle cell naevus (Reed naevus)
- Spitz naevus
- Spitz melanocytoma
- Spitz melanocytoma (Atypical Spitz tumour)
- Spitz melanoma
- Spitz melanoma

#### Melanocytic tumours in acral skin

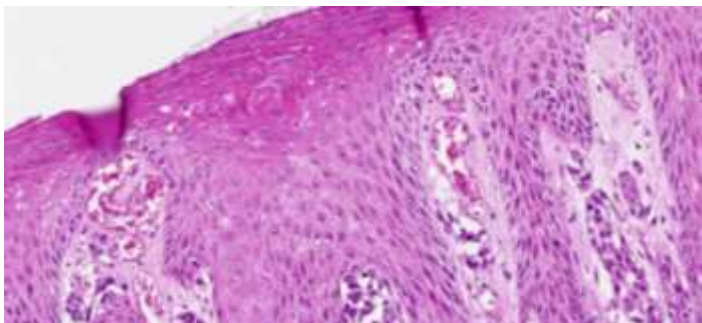
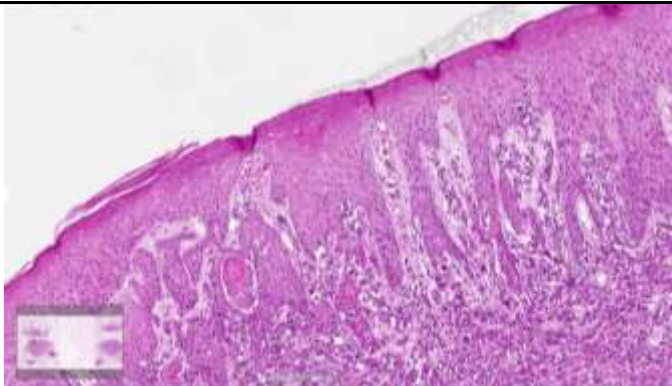
F 16 y  
right upper arm, dermatofibroma?



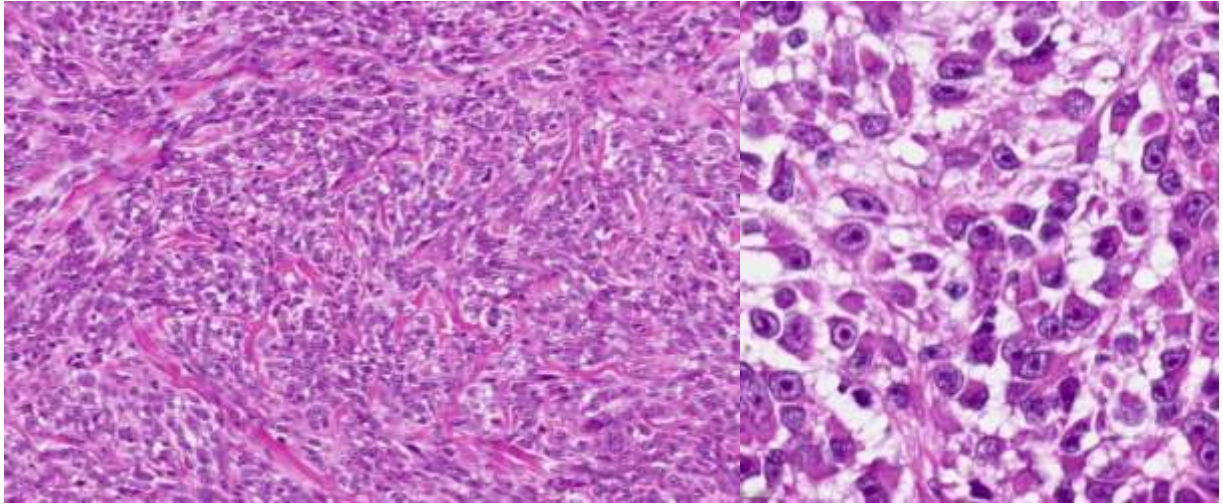
2205-50180



2205-50180



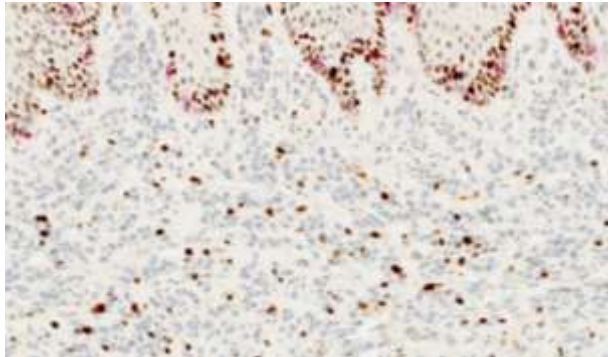




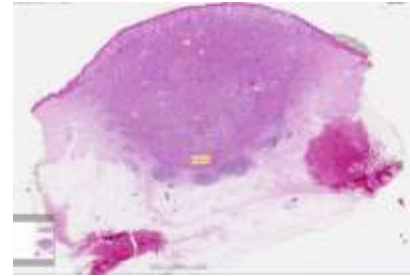
Mitotische activity: 2/mm<sup>2</sup>

DD

- Spitz tumor
  - Atypical Spitz tumor/Spitz melanocytom
  - malignant Spitz tumor/Spitz melanoma
- Melanoma, spitzoid type
- (clear cell sarcoma)
- (CTRC-TRIM11 fused tumor)



MelanA neg /Ki-67 (+-10%)



Dikte: 5 mm



SOX10 and MITF +

## Moleculaire analyse- UGent

- **DNA NGS mutation analysis panel** van 73 genes (SNV&indels) (KAPA HyperCap Roche)

AKT1, **ALK**, APC, AR, ARID1A, ATM, **BAP1**, **BRAF**, BRCA1, BRCA2, CCND1, **CDK4**, CDK6, CDK12, **CDKN2A**, CDKN2B, **CTNNB1**, DICER1, DPYD, EGFR, ERBB2, ERBB3, ESRI, FBXW7, FGFR1, FGFR2, FGFR3, FGFR4, FOXL2, FRK, GATA3, **GNAI1**, **GNAQ**, GNAS, H3F3A, H3F3B, HIST1B3, HIST1H3C, HNF1A, **HRAS**, IDH1, IDH2, IL6ST, JAK1, JAK2, KEAP1, **KIT**, KRAS, MAP2K1, MET, MYOD1, **NRAS**, NTRK1, NTRK2, NTRK3, PDGFRA, PDGFRB, PIK3CA, PIK3R1, POLE, **P TEN**, RBI, RET, RNF43, ROS1, SMAD4, SMO, SPOP, STAT3, STK11, **TERT**, **TP53**, VHL

>>> 1 **VUS**, no variants in **BRAF**, **NRAS**, **KIT** en **TERT** promotor

- **RNA NGS fusion panel**: 26 genen van solid tumor panel (Archer FusionPlex)

**ALK**, **BRAF**, EGFR, ERG, FGFR1, FGFR2, FGFR3, KRAS, **MET**, MYB, MYBL1, MYC, NRG1, **NTRK1**, **NTRK2**, **NTRK3**, PPARG, PRKCA, RAF1, RELA, **RET**, **ROS1**, RSP02, RSP03, TMRSS2, YAPI

- RNA NGS fusion panel: 55 gene from sarcomas RNA NGS panel (ArcherFusionPlex)

ALK, BCOR, BRAF, CAMTA1, CIC, CSF1, CTNNB1, EGFR, EPC1, ERG, ESRI, **EWSR1**, FGFR1, FGFR2, FGFR3, FOS, FOSB, FOXO1, FUS, GLI1, HMG2, JAZF1, MDM2, MEAF6, MET, MGEA5, MKL2, MYOD1, NCOA1, NCOA2, NR4A3, NTRK1, NTRK2, NTRK3, NUTM1, PAX3, PDGFB, PPH1, PLAG1, PRKCA, PRKCB, PRKCD, RAF1, RET, ROS1, SS18, STAT6, TAF15, TCF12, TFE3, TF6, USP6, VGLL2, YAPI, YWHAE

>>> no fusion or splice variants

- **CNV sequencing**

>>> **monosomie 1**

## Arnaud de la Fouchardière - CLB Lyon

- **RNA sequencing --> Med15-ATF1 fusie**
  - Med15: partner in Med15-TFE3 fused renal cell carcinoma
  - ATF1: partner in EWSR1-ATF1 clear cell sarcoma
    - Part of ATF1/CREB1/CREM family
  - Fusion peptide --> MITF activation
    - master regulator of melanine synthesis and melanosoom biogenesis
- **Clustering with clear cell sarcoma (like) lesions**
  - other tumors of the spectrum of MITF activation pathway
    - CRTC-TRIM11
    - MITF-CREM
    - ACTIN-CREM
  - Clear cell sarcomas
    - EWSR1-ATF1
    - EWSR1-CREM



## Conclusion and approach

- To consider and treat as a clear cell sarcoma
- Prognosis like clear cell sarcoma
  - Tendency for local recidivation and late metastatic behaviour
  - Cutaneous CCS smaller lesions better outcome
  - MR (local staging): negative
- PET-CT: negative
- Follow-up



## lessons learned

- Invest in a lab culture that invests in the **quality** and **representativity** of section and **Lesion specific** processing and lesion specific examination
- Take into account the frequent **Heterogeneity** of lesions, value of (ex vivo) dermoscopic information (rule in pigment lesions)
- Follow the **Life** of the lesion
- **minor changes** on a skin biopsy do not mean it is disease free.
- Look to the **negative spaces, think out of the box**
- Do not expect to see the **Full blown Histologic** characteristics of lesions because these lesions are often clinically diagnostic and are not biopsied
- Be aware of **complexity of new inflammatory patterns** often related to **biologicals**
- **Diagnosing atypical pigment lesions is rapidly evolving to a subspecialty with an integrated dermoscopic-histologic-molecular approach**
- Sufficient **Clinical dermatology knowledge** is mandatory
- An **active liaison with the referring dermatologists** is invaluable, learn basics of **dermoscopy**
- Be ambitious and **go a step further than descriptive dermatopathology**
- Open creative mind and peer consultation **elevate dermatopathology** to a unique specialism with an important contribution to the well-being of the patient



THANK YOU !



Curious, associative, creative, *scientific*,

