

 #WCD2019

AEDV

HIGHLIGHTS

24th World Congress of Dermatology (WCD)

10-15
JUNIO
2019

Milán



Patrocina:

janssen  Immunology
PHARMACEUTICAL COMPANIES OF 

Organiza:



AEDV

HIGHLIGHTS

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Milán



Psoriasis and inflammatory dermatosis

psoriasis comorbidity

biological therapies in ichthyoses

Mar Llamas Velasco

Patrocina:



Organiza:



Topics to cover

- Investigation and management of psoriasis associated comorbidity. SPACE 4
- Psoriasis biological therapy: applications to other diseases.
 - Ichthyoses and keratodermas





Comorbidity of psoriasis



Old story
But new chapters



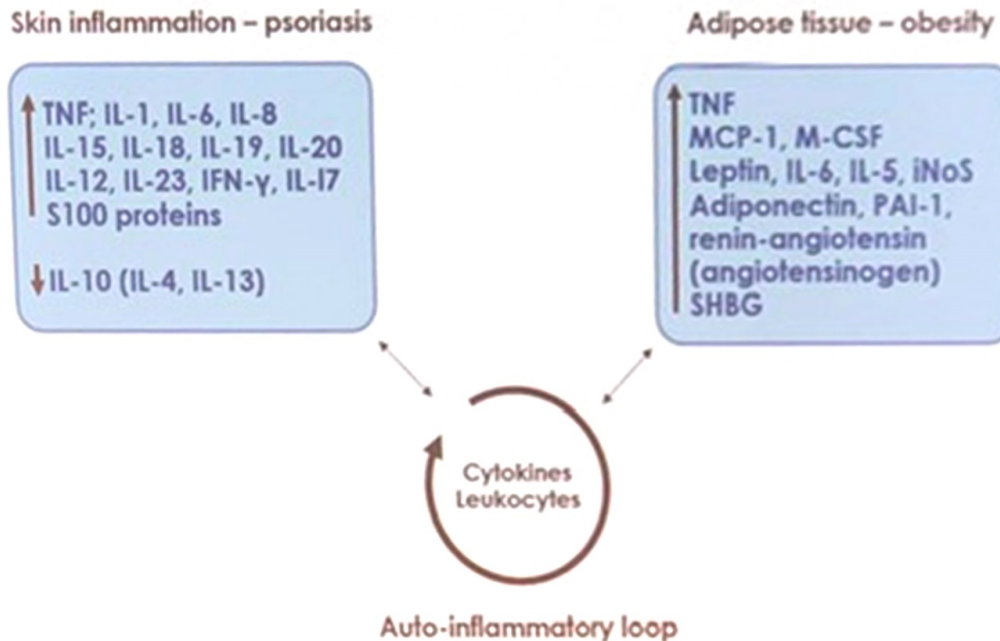
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Comorbidities in psoriasis

- PSORIASIS-OBESITY-NFLV and CV risk factors as a vicious cycle of systemic inflammation.

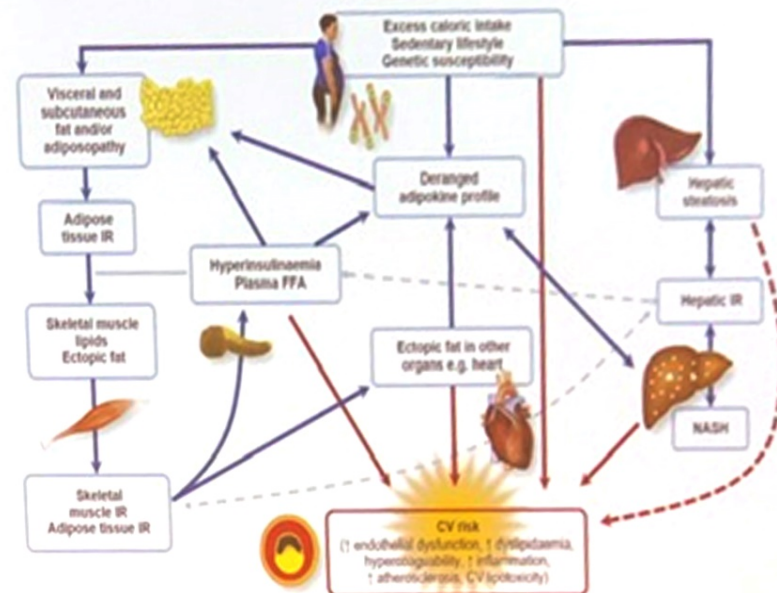
Psoriasis and obesity: a vicious cycle of systemic inflammation



COMORBIDITIES IN PSORIASIS

- Obesity is pro-inflammatory as adipose tissue is an immune and endocrine organ.
 - Increased BMI is associated to increase of TNF, IL6 and PAI-1
 - This increase insulin resistance and platelet adherence and atherosclerosis.
- NAFLD is a risk factor for CVD
- Psoriasis is associated to NAFLD (59% vs 20-30%)

NAFLD is a CV disease risk factor



Comorbidities in psoriasis

- Lost of weight improves the treatment response of patients with psoriasis when treated with ciclosporine.
- PSO care and Biobadaderm has demonstrated BMI as risk factor for therapy withdrawal.

Incidence and Prognosis of Psoriasis and Psoriatic Arthritis in Patients Undergoing Bariatric Surgery

Egeberg A, Sørensen JA, Gislason GH, Knop FK, Skov L.
JAMA Surg. 2017 Apr 1;152(4):344-349

- 12 364 gastric bypass
 - Adjusted HRs:
 - psoriasis 0.52 (95% CI, 0.33-0.81)
 - progression to severe psoriasis 0.44 (95% CI, 0.23-0.86)
 - psoriatic arthritis 0.29 (95% CI, 0.12-0.71)
- 1071 gastric banding
 - Adjusted
 - psoriasis 1.23 (95% CI, 0.40-3.75)
 - progression to severe psoriasis 1.18 (95% CI, 0.12-11.49)
 - psoriatic arthritis 0.53

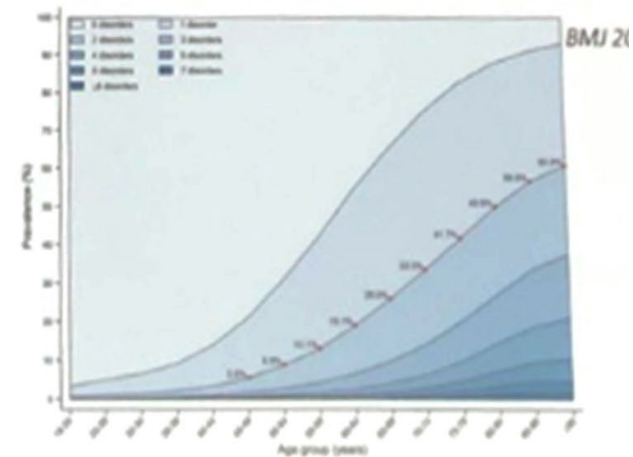
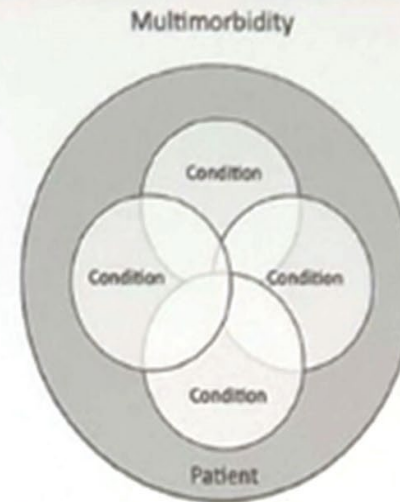
CONCLUSIONS:

- Gastric bypass was associated with a significantly reduced risk and improved prognosis of psoriasis and psoriatic arthritis, gastric banding was not.
 - This finding may be caused by the postoperative differences in nutrient intake and/or weight loss as well as differences in the secretion of hormones that potentially modulate inflammation.

PLENARY SESSION. JONATHAN BARKER

Co- vs Multi- morbidity

- **Co-morbidity:**
 - Co-occurrence of additional conditions alongside a primary, or index, condition
- **Multi-morbidity:**
 - Combination of chronic conditions, which could encompass diagnosed and undiagnosed physical, infectious, and mental health conditions
- **WHO:** 'is connected to psoriatic arthritis and increases the risk of various **co-morbid** diseases'



COMORBIDITIES IN PSORIASIS: REGISTRIES

- Psobest. Registry with all systemics with 15 year-follow up. N= 10,453
- A summary of many articles of the danish psoriasis cohort showed:
 - 20% of patients with psoriasis developed at least one imid. Fivefold increased risk compared with general population.
 - Most imids occurred before the diagnosis of psoriasis
 - Psoriasis was significantly associated with having multiple imids (or 15.2; 95% ci 11.6-67 20.0)

Growing number of comorbidities

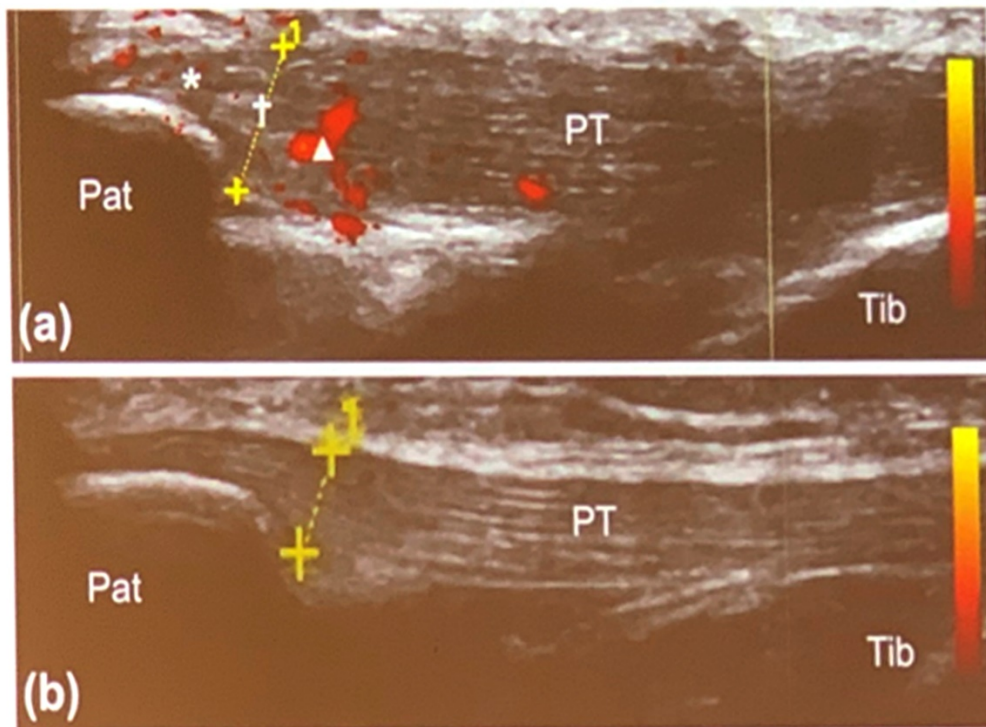
A need to check critically data sources and methods

A need to reference normal population



COMORBIDITIES IN PSORIASIS: PSORIATIC ARTHRITIS

Regression of Peripheral Subclinical Enthesopathy in Patients Treated With Ustekinumab for Moderate-to-Severe Chronic Plaque Psoriasis: A Fifty-Two-Week, Prospective, Open-Label Study



- 23 patients with psoriasis whose ultrasound results showed inflammatory changes were treated with ustekinumab for 52 weeks.
- With treatment, the mean inflammation scores decreased significantly by 42.2% from week 0 to week 24
- Enteseal structural abnormalities did not change significantly during treatment.

Topics to cover

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- Psoriasis biological therapy: applications to other diseases.
 - Ichthyoses and keratodermas



Ichthyoses and keratodermas (yellow 2)

Genes altered in most common Orphan Forms of Ichthyoses

- **Suprabasal keratinopathies:** epidermolytic ichthyosis and ichthyosis en confetti
- **Netherton syndrome:** Deficiency in serine protease inhibitor LEKTI
- **Autosomal recessive congenital ichthyosis (ARCI):** Spectrum from lamellar ichthyosis/LI (TGM1) to congenital ichthyosiform erythroderma/CIE (11 genes with biallelic variants)

What pathways translate gene change into scaling and inflammation?

With better understanding, can we target alterations in pathways towards improved and personalized therapy?



Ichthyoses and keratodermas (yellow 2)

Analysis of Clinical vs. Gene Expression Patterns in Ichthyoses



Lamellar ichthyosis/LI

Congenital ichthyosiform erythroderma/CIE

Epidermolytic ichthyosis/EI

Netherton syndrome/NS

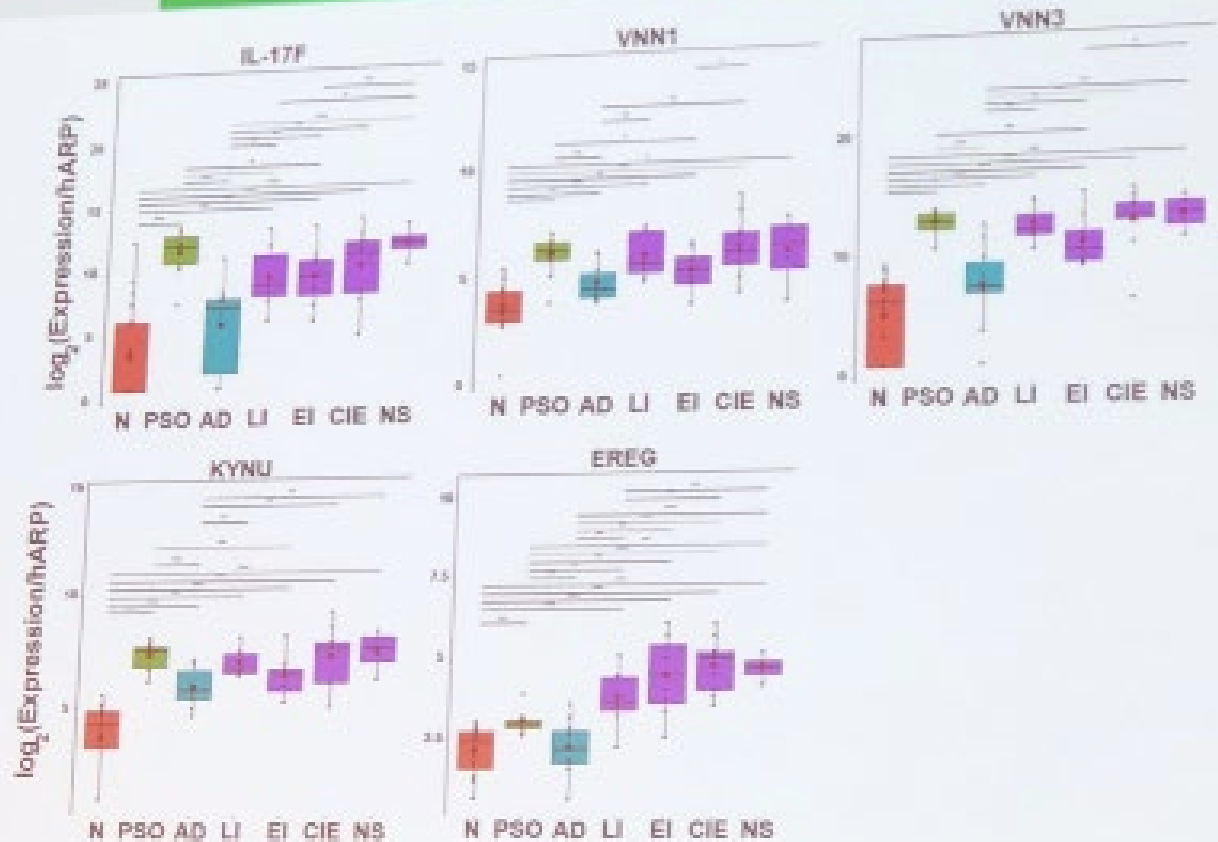
Skin biopsy assessments

- qRT-PCR of (45 markers, 21 patients)
Paller et al. JACI 2017;139:152
- Gene arrays (47K transcripts, 29 patients)
Malik et al. JACI 2019;143:604
- RNA-Seq (32K genes, 60 patients: more extensive subsets) Unpublished data

Icthyosis and psoriasis: shared partners

Amy Paller

Increased expression of other IL-17/TNF α synergistic pathway genes: also increased in psoriasis



Malik et al. JACI 2019;143:604



Ichthyosis and psoriasis: shared partners



ANTI IL17, ANTIP40 Y ANTIIL23: POTENTIAL TREATMENTS FOR ICTHYOSES PATIENTS

Amy Paller

DSP variants treated with ustekinumab

Followup pictures at 12-16 weeks

Both continue to be almost clear 18-24 months after initiation: life-changing

Paller et al. J Am Acad Dermatol 2018;78:498

Keith Choate

Genetics Informs Clinical Care

2/8/19: Rapid genetic diagnosis via WES identifies canonical EKC mutation

2/10/19: We direct initiation of IL12/23 inhibition

2/18/19: Extubated 2/27/19 3/11/19, off transplant list

Cutaneous findings resolved, cardiac function normalized.
Suggests that inflammation may play a role in cardiomyopathy.

Amy Paller

Clinical trials of targeted psoriasis therapy for ichthyosis

- Secukinumab trial in adults: 300 mg monthly vs placebo x 16 wks, then open label through end of year
- Five of 18 patients found drug to be "life-changing" and are continuing drug

Baseline 16 wks Baseline 16 wks Baseline 16 wks

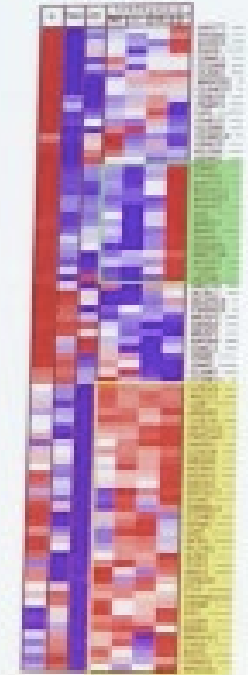
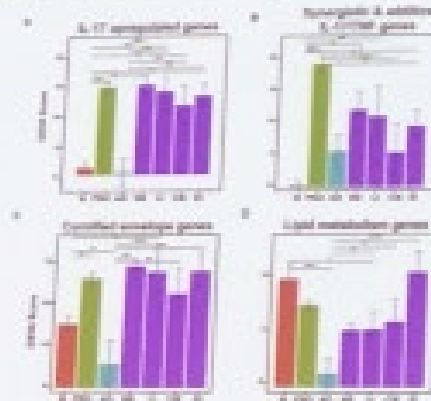
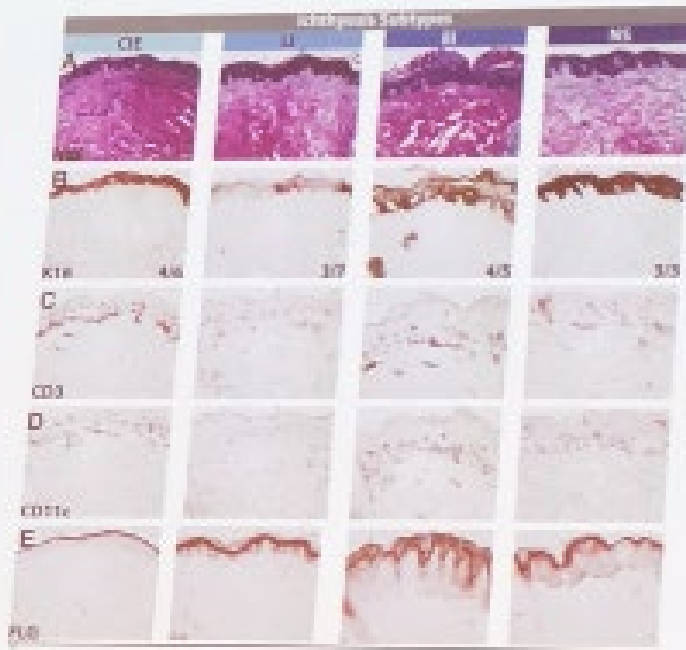
CIE/ NIPAL4 variant



IL-17 dominant immune profile in orphan ichthyoses

Paller et al JACI 2017; Malik et al JACI 2018 : IL17F & IL36B1G

Clinical implication: The link between increased expression of T_H17 pathway cytokines and clinical disease severity raises the possibility of a new therapeutic paradigm of targeted IL-17/IL-23 intervention for patients with ichthyosis.





Milàn

