BIODERMA CONGRESS REPORTS

WCPD 2025

Reports written by Dr Maria Florencia Martinez (Pediatrician & Pediatric dermatologist, Argentina)

Trichology

Psoriasis and seborrheic dermatitis

Speaker: Enrique Salvador Rivas Zaldivar (Guatemala)

Introduction

- The talk focused on the **clinical and dermatoscopic differentiation** between **scalp psoriasis** and **seborrheic dermatitis** in **children and adolescents**, both **common diagnoses** seen in pediatric dermatology.
- Special attention was given to **scalp hyperkeratosis**, which is frequently encountered and may represent various underlying conditions:
    - Most commonly: **Atopic dermatitis** and **seborrheic dermatitis**
    - Other considerations: **Scalp Psoriasis** and **Tinea capitis**
    - Less frequent but important systemic diseases: **Dermatomyositis** and **Langerhans cell histiocytosis**

Clinical Features: Psoriasis vs. Seborrheic Dermatitis

Feature	Psoriasis	Seborrheic Dermatitis
Scale	Silvery-white, thick	Oily, yellowish, or dry

Feature	Psoriasis	Seborrheic Dermatitis
Plaque	Well-demarcated	Poorly defined
Erythema	Prominent, especially beyond hairline	Less well-defined, more subtle
Itching	Present	Also present → may cause scratching lesions
Retroauricular Involvement	Common	Less frequent
Peripheral Scaling	More in SD, scaling follows hair shafts	Seen in SD, rarely in psoriasis

Note: Both diseases may present **erythema and scale**, making clinical diagnosis difficult in isolation.

Histopathology Overview

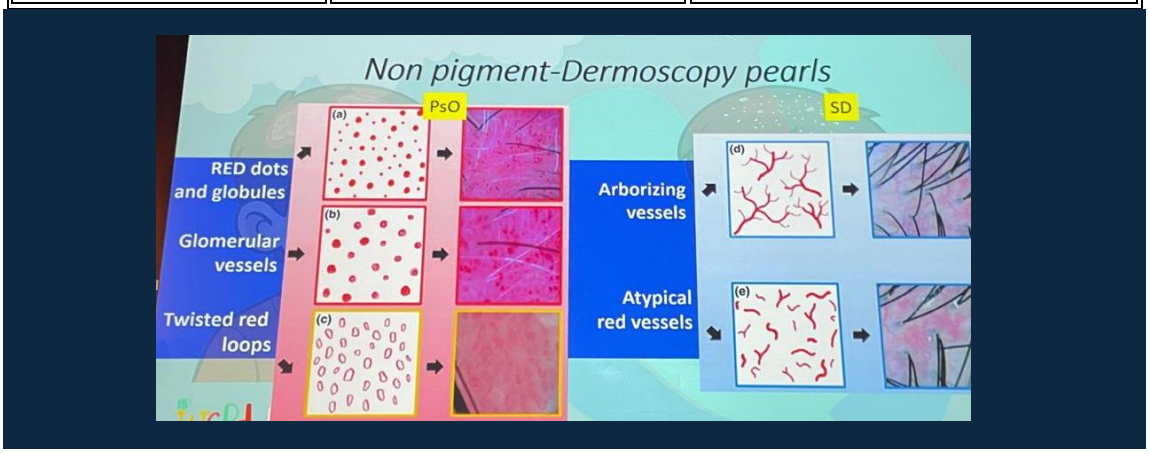
- Psoriasis:
  - Hyperkeratosis
  - Parakeratosis
  - Acanthosis
  - Elongated dermal papillae with dilated capillaries
  - Perivascular lymphocytic infiltrate
- Seborrheic Dermatitis:
  - Spongiosis (eczema-like)
  - Parakeratosis
  - Superficial perivascular inflammation
  - Lymphocytic exocytosis

Even histology can be inconclusive in some overlapping presentations. That's where dermatoscopy (trichoscopy) becomes essential.

Trichoscopy: A Non-Invasive Diagnostic Aid

Vascular Patterns – The Key Differentiator:

Dermatoscopic Finding	Psoriasis	Seborrheic Dermatitis
Vessel Type	Red dots, glomerular vessels, twisted red loops	Arborizing blurry vessels, atypical patterns
Localization	Superficial dermal capillaries	Deeper and less defined vessels
Scale Appearance	Thick, dry, White	Yellowish, greasy



- **Zoom level matters**: 10x is often not enough to see vessels clearly, **50x magnification** is preferred.
- **Gel application (e.g., ultrasound gel)** is recommended to avoid **flush artifacts** that may distort vascular visualization.

Classification of Scalp Psoriasis Patterns

(*Bruni* et al*., 2021*)

1. **Plaque Psoriasis** – Classic well-demarcated red plaques with scaling

2. **Thin Scale Psoriasis** – Subtle erythema, fine scale
3. **Sebopsoriasis** – Overlap appearance with greasy scale
4. **Psoriatic Cap** – Thick scale buildup without overt erythema
5. **Pityriasis Amiantacea Type** – Common in children, adherent scales surrounding hair shafts
6. **Cicatricial Psoriasis** – Rare, with scarring features
7. **Pustular Psoriasis** – Very rare in the pediatric scalp

Clinical Subtypes of Seborrheic Dermatitis by Age

- **Infants**: Cradle cap
- **Younger children**: Fold involvement (retroauricular, perioral)
- **School-aged**: Often associated with **atopic dermatitis**
- **Adolescents**: Often worsened by **acne**, **hormonal changes**, and **oily skin**

Contributing factor: *Malassezia spp.* overgrowth in all age groups

Study Reference: Prof. Kim (Korea, 2011)

- Validated the use of **vascular pattern analysis** via **trichoscopy** to distinguish between psoriasis and SD.
    - Psoriasis: red dots and globules, glomerular vessels, twisted red loops
    - Seborrheic Dermatitis: arborizing vessels, atypical red vessels

Take-Home Points

- **Scalp psoriasis and seborrheic dermatitis can be hard to distinguish clinically**, especially in children.
- **Trichoscopy is a key tool** to avoid misdiagnosis and reduce unnecessary **biopsies**.
- **Main differentiator = Vascular pattern**:
    - Psoriasis → glomerular, regular red dots

    - SD → blurry, arborizing vessels
- Always consider **extra-scalp clues**: nail changes, extensor plaques (psoriasis), facial fold involvement, and AD background (SD).

References:

- Bruni F, *et al.* Clinical and trichoscopic features in various forms of scalp psoriasis. J Eur Acad Dermatol Venereol. 2021 Sep;35(9):1830-1837.

- Silverberg NB. Scalp hyperkeratosis in children with skin of color: diagnostic and therapeutic considerations. Cutis. 2015 Apr;95(4):199-204

- Waśkiel-Burnat A *et al.* Differential diagnosis of red scalp: the importance of trichoscopy, Clinical and Experimental Dermatology, 2024, Setp; 49 (9): 961–968

- Kim GW *et al.* Dermoscopy can be useful in differentiating scalp psoriasis from seborrhoeic dermatitis. Br J Dermatol. 2011 Mar;164(3):652-6

Tinea capitis and pediculosis

Speaker: Arturo Lopez Yañez Blanco (Mexico)

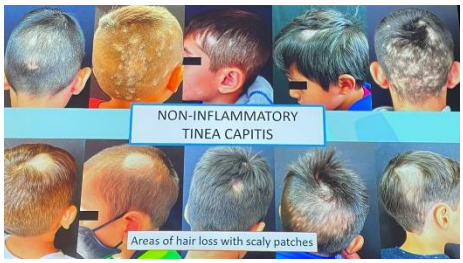
Tinea capitis

The speaker began with a general overview of tinea capitis emphasizing that it's a fungal scalp infection mainly affecting children (98%), caused by dermatophytes of the Trichophyton and Microsporum genera.

Epidemiology & Clinical Forms

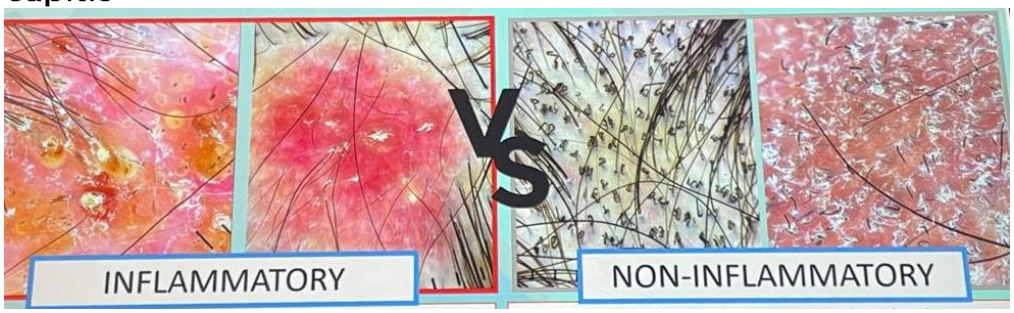
The etiological agents vary by region: **M canis, T tonsurans**, M audouinii, T mentagrophytes, T verrucosum.

Two main clinical forms:

Inflammatory tinea capitis	Non-inflammatory tinea capitis
	
Tender plaques with pustules and crust	Single or multiple hair loss patches
Painful abscess	Scaly patches
Lynphadenopathy	Pruritus

Diagnostic Tools

- Clinical examination
- Microscopy
- Wood's lamp
- Molecular methods
- Trichoscopy (important tool emphasized throughout):

Inflammatory tinea capitis	Non-inflammatory tinea capitis
	
Follicular pustules	Corkscrew hairs
Crusts	White sheaths
Perifollicular scaling	Perifollicular and diffuse scaling
Linear vessels	Black dots
Erythema	Morse code-like hairs
Comma hairs /Zigzag hairs	

Triad of signs (hair loss, scaly patches, peritoneal involvement) = high predictive value (95%).

Differential Diagnosis:

- Lupus
- Alopecia areata
- Seborrheic Dermatitis
- Dissecting cellulitis

Treatment Recommendations

→ Systemic antifungals are essential.
→ Griseofulvin (20-25 mg/k/d during 8-12 weeks longer is culture is positive) and Terbinafine (3-6 mg/k/d during 4 weeks (Tricophyton) to 8-12 weeks (Microsporum)) recommended first-line.
→ Choice depends on fungal culture result and drug availability.
→ Topical agents recommended as adjuvant therapy (twice weekly).
→ Remove fomites

→ Household screening and treatment are crucial to prevent recurrence.

Common parental questions addressed:

≈ School return: after treatment initiation.
≈ No need for haircuts or use of hats.
≈ Tracing contact in school is essential.
≈ Measures at home: avoid sharing personal items, boil and sanitize possible fomites for 5 minutes, pets should be examined.

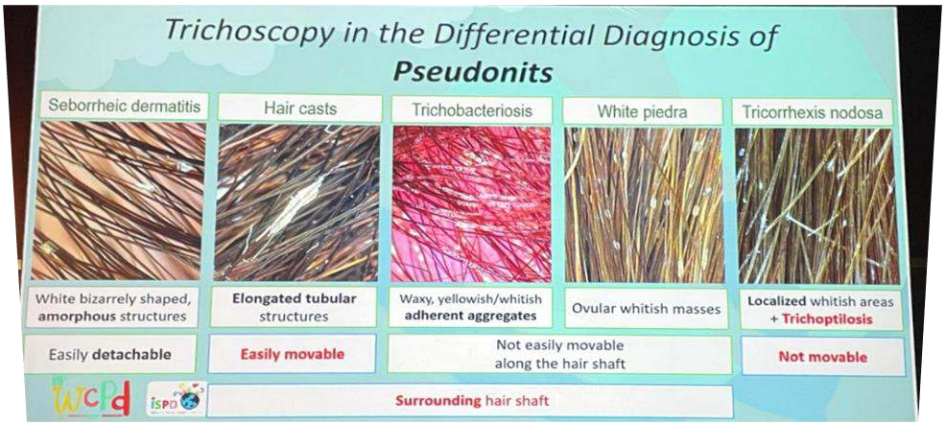
Pediculosis capitis

Introduction

- **Ectoparasitic** infection of the hairs and scalp
- Public global health problem
- Affects children **aged 6–12 years**.
- **Females** more affected.
- Transmission: **direct contact** (lice don't jump or fly).
- Examination revealed white nodes, prompting evaluation for nits vs. pseudo-nits.

Differential Diagnosis

Nits: contains vital nymhps
Pseudonits can resemble lice eggs, found in:
Seborrheic dermatitis: white bizarrely shaped, amorphous structures, easily detachable.
Hair casts: elongated tubular structures, easily movable.
Trichobacteriosis: waxy, yellowish/whitish adherent aggregates, not easily movable
White Piedra: ovular witish masses, not easily movable
Trichorrhexis nodosa: whitish areas + trichoptilosis. Not movable



Trichoscopic Differences

True nits: brown with oval heads.

Pseudonits: translucent, grayish, black tips.

Clinical Signs

→ Occipital/cervical **pruritus**
→ **Lymphadenopathy**
→ Fast-moving lice, difficult to spot (can move ~23 cm/min)
→ May co-occur with other scalp conditions (e.g., alopecia areata)
→ Complications: secondary bacterial infection

Treatment

No major new treatments. **Conventional therapy** remains effective.

Education for parents about lice behavior and contagion is essential.

THERAPY	PRESCRIPTION
PERMETRIN	LOTION 1%. Apply and washep up the hair after 10 min, repeat in 1 week
MALATHION	LOTION 0,5%. Apply and washep up the hair after 8-12hs, repeat in 1 week
BENZYL ALCOHOL	LOTION 5%. Apply and washep up the hair after 10 min, repeat in 1 week
IVERMECTIN	LOTION 0,5%. Apply and washep up her hair after 10 min, repeat in 1 week ORAL TABLETS: 0,2 mg/k/d 2 days, repeat in 1 week
TMS	ORAL: 10 mg/k/d 3 days BID, repeat in 1 week

References:

- Vargas-Navia N et al. Tiña Capitis en niños. Revista chilena de pediatría. 2020:91(5), 773-783
- Kinoshita-Ise M, et al. Update on trichoscopy: Integration of the terminology by systematic approach and a proposal of a diagnostic flowchart. J Dermatol. 2022 Jan;49(1):4-18.
- Aqil N, et al. A prospective study of tinea capitis in children: making the diagnosis easier with a dermoscope. J Med Case Rep. 2018 Dec 28;12(1):383
- Lacarrubba F, et al. Trichoscopy in the Differential Diagnosis of Pseudonits. Skin appendage disorders. 2019: 5; 142-145

Effluvium in pediatric population

Speaker: Cecilia Navarro Tuculet (Argentina)

Pediatric telogen effluvium – causes, diagnosis, and management

Introduction:

- **Telogen effluvium (TE)** is a form of diffuse non-scarring hair loss caused by an abnormal shift in follicular cycling leading to premature shedding.
- **Incidence in Children:** Data on pediatric TE is limited; most studies have been conducted on adults. **Point prevalence** of TE in children is 2.7%.

Types of Telogen Effluvium:

1. **Acute TE**
    - Develops within 2-3 months of the inciting factor.
    - Self-limited and resolve within 3 months.
2. **Chronic TE**
    - Persistent shedding for over 6 months.

Common Triggers of Telogen Effluvium in Children:

- **Emotional Stress**
- **Chronic illness** (e.g., rheumatic, collagen, vascular diseases)
- **Acute Illness** (e.g., viral infections, febrile conditions)

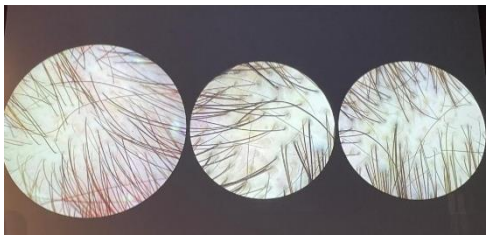
- **Nutritional Deficiencies** (low ferritin, zinc, vitamin D)
- **Endocrine Disorders** (thyroid disease, androgen excess)
- **Medications** (e.g., anticoagulants, beta-blockers, retinoids)
- **Infectious Diseases** (e.g., post-COVID, dengue outbreak)
- **Inflammatory Scalp Conditions** (e.g., seborrheic dermatitis)
- **Eating Disorders** (e.g., rapid weight loss)

Prevalence in Pediatric Population:

- Acute TE: Common after viral infections like **COVID-19** and **dengue**.
- Chronic TE: Frequently triggered by **nutritional deficiencies**, especially **low ferritin** and **zinc**.

Diagnosis and Evaluation:

1. **History and Physical Exam:**
    - Assess **duration**, **rate**, **location**, and **extent** of hair loss.
    - **Associated symptoms**: pain, tenderness, pruritus.
    - **Hair care behavior**: grooming or use of hair care products.
    - Differentiate **hair shedding** from **breakage**.
2. **Scalp Exam**:
    - **Evaluate**: erythema, scales, pustules, papules, erosions, excoriations.
    - Hair **Pull test**
    - Hair loss **pattern** is typically **diffuse**, especially in the **bitemporal area**.
    - **Dermoscopy**: Empty follicles and upright regrowing hairs of normal thickness; differentiation from androgenetic alopecia using **hair shaft diameter variability**.



3. Additional Tests:
    - Scalp Biopsy: To distinguish TE from other conditions (e.g., alopecia areata).
    - Trichogram: To assess the proportion of telogen vs. anagen hairs.
    - Hair Collection: Useful to quantify and track the hair loss over time.

Differential Diagnosis:

- Anagen Effluvium: Hair loss from chemotherapy or toxins (over 80% of scalp hair).
- Androgenetic Alopecia: Characterized by miniaturized hairs.
- Diffuse Alopecia Areata: Diffuse hair thinning with possible exclamation-point hairs.
- Loose Anagen Syndrome: Easily extracted hair, typically in blonde females.
- Structural hair disorders: weakening of the hair shafts.

Management:

1. Reassurance and Avoidance of Triggers:
    - TE is usually **self-limiting** and requires removal of inciting factors.
    - Psychological Support for emotional distress is crucial.
2. Treatment Options:
    - Minoxidil: Its use in children is uncertain. Not first-line therapy.

    - TE typically resolves after 2-3 months of active shedding, followed by **stabilization** and **regrowth** within 6-12 months.
3. **Prognosis**:
    - TE is generally **self-limiting**. Once triggers are addressed, hair regrowth is typically seen within **6-12 months**.

Take-Home Messages:

1. **Key Triggers**: Emotional stress, febrile illness, and nutritional deficiencies.
2. **Patient Evaluation**: Inquire about hair styling and rule out **traction alopecia**.
3. **Diagnosis**: Use **dermoscopy** to differentiate between TE and other forms of alopecia.
4. **Management**: Provide **reassurance**; minimize trigger exposure and offer **psychosocial support**.
5. **Prognosis**: TE is self-limiting; improvement expected within **6-12 months**.

References:

- Chen V, et al. Etiology, management, and outcomes of pediatric telogen effluvium: A single-center study in the United States. Pediatric dermatology. 2023; 2023 (1): 120-124
- Thomas M, et al. A Single Centre Retrospective Review of Nutritional Deficiencies Associated With Telogen Effluvium in the Paediatric Population in Canada. J Cutan Med Surg. 2022;26 (4): 420-421
- Kim HS, et al Braids or Pony-Tail-Associated Traction Alopecia in Female Children. Ann Dermatol. 2019 Feb;31(1):117-119.

Loose anagen syndrome versus short anagen syndrome

Speaker: Arturo Lopez Yañez Blanco (Mexico)

Introduction:

- Although both SAS and LAHS are present with short hair in children, they are distinct disorders.
- They may appear similar but differ **in pathophysiology, clinical findings, and diagnostic features.**

Short Anagen Syndrome (SAS)

Definition:

- Benign disorder due to **shortened anagen phase.**
- It leads to **an inability to grow long scalp hair.**

Epidemiology:

- Primarily affects **Caucasian females**, aged **2–6 years.**

Pathophysiology:

- **Shortened anagen phase** → hair does not grow long before transitioning to telogen.
- **WNT10A gene** mutation in ~40% (suggestive of autosomal dominant pattern).

Clinical Features:

- Hair appears short, sparse, and thin.
- Often, it affects bilateral frontoparietal scalp.
- May be associated with:
  - Inner scleroderma
  - Nail changes (e.g. micronychia)
  - Trichodysplasia síndromes
- No hair fragility or breakage.
- It can significantly impact psychosocial well-being.

Diagnostic Findings:

- Pull test: Negative or mildly positive.
- Trichoscopy: Normal.
- Haircut test: Conical tips.

- Trichogram: Increased telogen hairs, anagen:telogen ratio reversed (e.g. 1:2).
- Microscopy: Normal anagen hairs.

Loose Anagen Hair Syndrome (LAHS)

Definition:

- Hair shedding disorder due to **defective anchoring** of anagen hairs in the follicle.

Epidemiology:

- Typically affects **female children**, ages **6–10 years**.
- May be underdiagnosed in **males**.

Pathophysiology:

- **Defective keratinization** of the inner root sheath.
- Poor adhesion between outer and inner root sheaths.
- Linked to **keratin gene mutations**.

Clinical Features:

- **Diffuse hair loss**, especially in **occipital and parietal areas**.
- **Hair easily and painlessly extracted**.
- Associated conditions: Noonan syndrome, trichorhinophalangeal syndrome.
- May lead to **psychological distress**.

Diagnostic Findings:

- **Pull test**: Positive and painless.
- **Trichoscopy:**
  - Vellus hair and slightly pigmented hairs
  - Dirty dots
  - Scalp scales
  - Cadaveric hair
  - Granular rectangular structures
- **Trichogram**: Loose anagen hairs with **ruffled cuticles**, "pockey stick" morphology.
- **Microscopy**: Confirms **disrupted inner root sheath.**

Differential Diagnosis:

- SAS (normal or thin hair diameter)
- Telogen effluvium (regrowing hairs, single hair follicular units)

- Diffuse alopecia areata (black and yellow dots, broken hairs)
- Androgenetic alopecia (anisotrichosis, vellus hairs, single hair follicular units, perifollicular pigmentation)

Treatment and Management (Both Conditions):

- **Reassurance** and education of parents.
- **Spontaneous improvement** often occurs with age.
- For selected cases with psychosocial impact:
  - **Topical minoxidil** 2–5%,
  - **Oral minoxidil:** max 0.02 mg/kg/day
- Supportive care:
  - Gentle grooming
  - Camouflage
  - Counseling

Comparison Table: SAS vs. LAHS

Feature	SAS	LAHS
Age at diagnosis	2–6 years	6–10 years
Sex predominance	Female	Female > Male
Hair appearance	Short (<10cm), sparse, fine	Fine, short (>20cm), easily pulled
Pull test	Negative or mildly positive	Positive, painless
Trichoscopy	Normal	Rectangular/circular black dots, dirty dots

Feature	SAS	LAHS
Trichogram	↑ Telogen hairs	Anagen hairs (70%) distorted bulbs and roots
Microscopy	Normal hair shafts	Disrupted inner root sheath
Pathophysiology	Shortened anagen phase	Poor anchoring of anagen hairs
Genetic component	WNT10A mutation (40%)	Keratin gene defects
Associated syndromes	Scleroderma, micronychia, etc.	Noonan syndrome, TRPS
Prognosis	Benign, improves with age	
Minoxidil use	Possible if psychosocially indicated	

Take-Home Messages:

- SAS and LAHS are frequent yet distinct causes of short hair in pediatric patients.
- SAS: Due to shortened anagen phase; LAHS: Due to defective anchoring of the anagen hair.
- Diagnosis is clinical, supported by trichoscopy and trichogram.
- Both are benign and may be resolved with age but require individualized care when psychosocially impactful.

References:

Cranwell WC, et al. Loose anagen hair syndrome: Treatment with systemic minoxidil characterised by marked hair colour change. Australas J Dermatol. 2018;59(4):e286-e287.

Lemes LR, et al. Topical and oral minoxidil for hair disorders in pediatric patients: What do we know so far? Dermatol Ther. 2020;33(6):e13950.

Starace M, et al Short anagen syndrome: A case series and algorithm for diagnosis. Pediatr Dermatol. 2021;38(5):1157-1161

Cicatricial alopecia in children

Speaker: Miguel Marti (Argentina)

Epidemiology

- **Cicatricial alopecia in adults** represents ~7% of all alopecia cases.
- **Pediatric data is lacking**: only 29 articles in PubMed over the last 5 years.
- Lack of data and research in pediatric populations underlines the need for awareness and early recognition.
- More frequent in **female children**

Most common diagnoses:

- **Primary cicatricial alopecia** (most frequent overall)
    - **Lichen planopilaris (LPP)**
    - **Central centrifugal cicatricial alopecia (CCCA)**
- **Secondary causes:**
    - **Tinea capitis**
    - **Lupus erythematosus**

Common symptoms:

- Itching
- Pain
- Flaking

Clinical signs:

- Loss of follicular openings
- Peripilar casts
- Follicular fusion

Focus: Pediatric Lichen Planopilaris (LPP)

- Limited clinical trials or prospective studies on LPP in children.
- It can occur in **children and adolescents**.

Clinical presentation:

- Scarring alopecia
- Perifollicular erythema
- Scaling
- Atrophic areas
- Follicular hyperkeratosis
- Predominantly in **vertex** and **parietal regions**

Treatment:

Treatment Modality	
Topical corticosteroids	First-line therapy
Intralesional corticosteroids	Effective in localized disease
Systemic corticosteroids	In more severe cases
Hydroxychloroquine, methotrexate	Reserved for refractory cases

Secondary Cicatricial Alopecia – Hair Transplantation

- Study included **13 children** with **post-burn scalp alopecia** (10 males, 3 females).
    - Hair transplantation shown to be **Safe** and **effective** for secondary cicatricial alopecia

Differential Diagnosis: Congenital Triangular Alopecia (CTA)

- A **non-cicatricial** and **benign** alopecia, usually first noted in **infancy or early childhood**.
- Can mimic cicatricial alopecia due to trichoscopic overlap.

Clinical characteristics:

- Triangular, oval, or lancet-shaped patches
- Apex typically oriented toward the vertex

Take-Home Messages

- **Early diagnosis** is essential to prevent progression and improve long-term outcomes.
- **Lichen planopilaris (LPP)** is the most frequent primary cicatricial alopecia in pediatric populations (~11 years average age).
- **Secondary alopecia**, especially post-burn, can be managed with **hair transplantation**.
- Conditions like **congenital triangular alopecia** must be considered in differential diagnosis to avoid mismanagement.
- More **clinical and epidemiological studies** are needed in the pediatric population.

References:

- Carmichael AR, et al. Cicatricial Alopecia in the Pediatric Population: A Case Series and Review of the Literature. Pediatr Dermatol. 2025 Jan 29. doi: 10.1111/pde.15864. Epub ahead of print
- Papierzewska M, et al. Lichen Planopilaris in Children: A Systematic Review. Pediatr Dermatol. 2025 Jan-Feb;42(1):22-30.
- Wang J, et al. Application of Autologous Hair Transplantation Technique in Children with Cicatricial Alopecia. Adv Ther. 2023 Sep;40(9):4024-4031.
- Starace M, et al. Atypical Presentation of Congenital Triangular Alopecia: A Case Series in Italy. Dermatol Pract Concept. 2020 Oct 26;10(4):e2020122

My most challenging cases

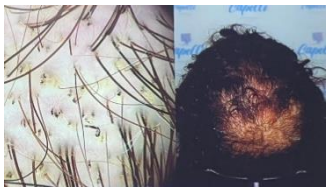
Speaker: Lizet Rojano Fritz (Colombia)

Case 1: Tinea Capitis + Trichotillomania

Patient	**8-year-old female.** No relevant personal or familiar medical history
Initial Dx	Alopecia areata (Dec 2024)
Treatment	Clobetasol + Prednisone → No response
Culture	Positive for *Microsporum canis*
Treatment 1	Terbinafine x 3 months

Patient	**8-year-old female.** No relevant personal or familiar medical history
Follow-up	Persistent central alopecia → repeat trichoscopy: black dots, broken hairs
Culture	Still positive
Treatment 2	Griseofulvin x 6 months
Observation	Vertex with poor regrowth, trichoptilosis, fine hairs
Final Dx	Tinea capitis + **Trichotillomania** (Patient admitted to hair pulling at night)

Key Point:



Consider **dual diagnoses** in pediatric alopecia. Always confirm tinea capitis via **culture**.

Trichoscopy – Findings by Condition

Feature	Trichotillomania	Tinea Capitis
Broken hairs Black dots	✅ ✅	✅
Trichoptilosis Flame hairs Tulip hairs V sign Microexclamation hairs	✅	❌
Yellow dots	✅/❌	❌

Case 2: Inactive Linear Morphea – Hair Transplant

Patient	**8-year-old female**
History	5 years of linear facial plaque from vertex to forehead/eyebrow
Symptoms	Social withdrawal, no medical history
Biopsy	Linear morphea
Trichoscopy	Loss of Follicular openings, broken hairs, black dots, pink areas, pili torti.
MRI	Thinning of subcutaneous tissue (scalp & facial region)
Autoimmune panel	Negative
Treatment	Hair transplant after 4 years of inactive lesion
Result	Successful regrowth, improved self-esteem

Key Point:

Hair transplantation can be effective in **inactive morphea** with no ongoing inflammation.

Case 3: Trichorhinophalangeal Syndrome Type I (TRPS I)

Patient	**15-year-old female**
Hx	Congenital hypotrichosis
Trichoscopy	Normal
Trichogram	Dystrophic anagen bulbs
Phenotypic Features	Bulbous nose, cone shaped epiphyses hands and feet, maxillary prognathism, thin upper lip
Genetic Test	Deletion at chromosome 8q24.12

Patient	15-year-old female
Dx	TRPS Type I
Treatment	Topical minoxidil → Good hair density at 6 months

Key Point:

In congenital hypotrichosis, always **assess for syndromic features** and **genetic testing**.

Final Clinical Takeaways

- **Multiple pathologies** may coexist in pediatric alopecia (e.g., tinea + trichotillomania).
- **Culture** remains the gold standard for **Tinea capitis** diagnosis.
- **Hair transplantation** is a valid treatment for **inactive linear morphea**.
- **Genetic evaluation** is critical when hair loss presents dysmorphic features.

References:

- Rudnicka L, et al. Atlas of Thrichoscopy.
- Sonthalia S, et al. Linear Patch of Alopecia in a Child: Trichoscopy Reveals the Actual Diagnosis. Skin Appendage Disord. 2019 Nov;5(6):409-412
- Saceda-Corralo D, Tosti A. Trichoscopic Features of Linear Morphea on the Scalp. Skin Appendage Disord. 2018 Jan;4(1):31-33.
- Glaser DH, et al. Linear Scleroderma of the Head - Updates in management of Parry Romberg Syndrome and En coup de sabre: A rapid scoping review across subspecialties. Eur J Rheumatol. 2020 Feb;7(Suppl1):S48-S57

Androgenetic alopecia

Speaker: Luis Sanchez Dueñas (Mexico)

General Overview

- **Pathophysiology:** Miniaturization of hair follicles due to susceptibility to androgens (not elevated serum androgens).
- **Paradox:** Androgens promote terminal hair in some regions (beard, axilla, etc.) but cause miniaturization in scalp due to receptor sensitivity
- **Key areas of scalp involvement:**
    - **Males:** Frontal-temporal and vertex
    - **Females:** Crown

In Children & Adolescents

- Onset after adrenarche (ages 6–9) due to adrenal androgen (DHEA) production
- Clinical pattern in **males** often resembles **female pattern (MAGA-F)**
- Inflammation may be more frequent in pediatric biopsies
- Trichoscopic features mirror adult patterns but with earlier onset

Trichoscopy

Feature	Frequency
Hair diameter variability	100%
Vellus hairs	High
Yellow dots	Occasional
Peripilar sign	Common
Wavy hairs	Present
Focal atrophy	Rare

- **Main differentiator:** Hair diameter variability (not seen in telogen effluvium or alopecia areata)

Epidemiology & Clinical Data

≈ Youngest reported case: 6 years old
≈ Sex distribution: Male predominance overall
≈ Family history: Present in ~75% of pediatric cases
≈ Common comorbidity: Acne, insulin resistance

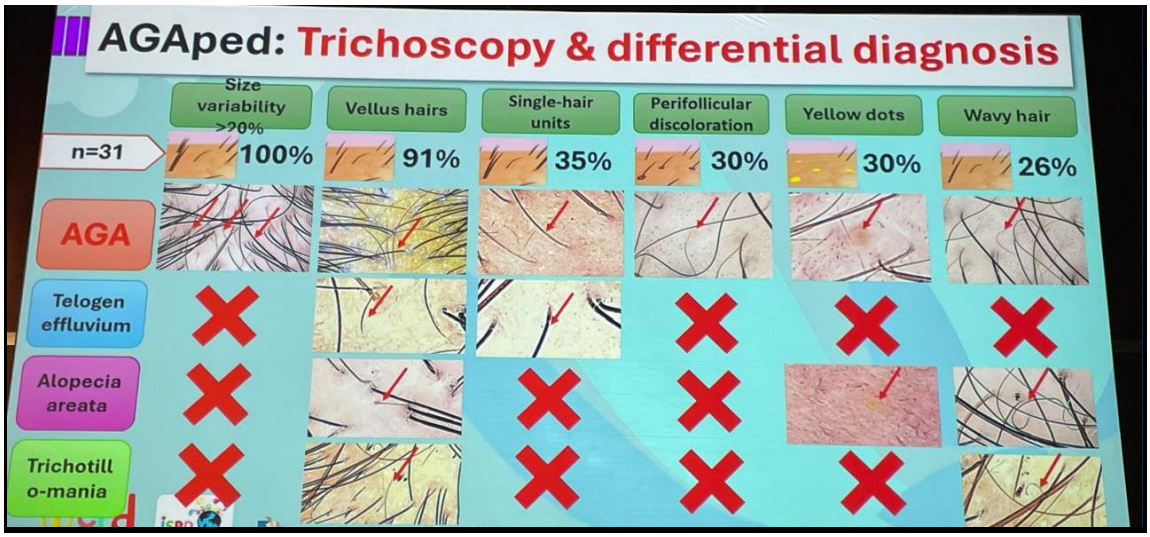
Associated Conditions (Comorbidities)

- **Endocrine:**
  - Non-classical congenital adrenal hyperplasia
  - Insulin resistance (frequent)
  - Thyroid dysfunction
- **Metabolic:**
  - Obesity
  - Metabolic syndrome
- **Mental Health:**
  - Depression
  - Anxiety
  - Social withdrawal
- **Cutaneous:**
  - Acne
  - Seborrhea
  - Hirsutism

Referral & Workup Recommendations

Indication for Referral	Recommended Action
Pre-pubertal onset	Endocrine referral
Male with female pattern hair loss	Hormonal panel
Female with signs of hyperandrogenism	Hormonal panel
Suggested labs	Testosterone, DHEA-S, SHBG, LH/FSH, Vitamin D, Glucose, Insulin

Differential Diagnosis: Telogen effluvium, Alopecia areata, trichotillomania



Treatment Algorithm (Not Officially Approved)

First-line (Both sexes):

- Topical Minoxidil 2% - 5%

If partial response:

- Add low-dose oral minoxidil:
  - **Females:** 0.25–0.5 mg/day
  - **Males:** 1–2.5 mg/day

Adjuncts:

- Topical/oral Finasteride (Males/Females)
- Oral Spironolactone (Females only)

Advanced therapy (if poor response):

- **Females:** Oral Finasteride 2.5 mg
- **Males:** Oral Finasteride 1 mg

	FEMALE	MALE
PREPUBERAL	TOPICAL MINOXIDIL 2%	
PUBERAL	TOPICAL MINOXIDIL 5%	
PARCIAL IMPROVEMENT	Oral minoxidil 0,25-0,5 mg/d Topical Finasteride Topical/Oral Espironolactone	Oral minoxidil 1-2,5 mg/d Topical Finasteride
LIMITED IMPROVEMENT	Oral Finasteride 2,5 mg/d	Oral Finasteride 1 mg/d

Adverse Events Noted

Medication	Event	Action Taken
Oral Finasteride	Gynecomastia (Male)	Stopped → Reversible
Oral Minoxidil	Trichomegaly (Excess lashes)	Dose reduction

Clinical Cases

- **Telogen effluvium** may precede androgenetic alopecia
- Association with acne, dermatitis, and metabolic disorders is frequent
- **Case example:** Insulin resistance aggravates alopecia flare

Take-Home Messages

- AGA in children/adolescents is underdiagnosed and underreported

- Often associated with systemic androgen sensitivity → Requires systemic evaluation
- Trichoscopy is the cornerstone for early diagnosis
- Treat early to prevent irreversible follicular loss
- Strong need for multidisciplinary approach

References:

- Gomes TF, et al. Pediatric androgenetic alopecia: an updated review. J Dtsch Dermatol Ges. 2023 Jan;21(1):19-25.
- Gonzalez ME, et al. Androgenetic alopecia in the paediatric population: a retrospective review of 57 patients. Br J Dermatol. 2010 Aug;163(2):378-85
- Tosti A, et al. Androgenetic alopecia in children: report of 20 cases. Br J Dermatol. 2005 Mar;152(3):556-9
- Griggs Jet al. Pediatric androgenetic alopecia: A review. JAAD. 2021;85 (5): 1267 - 1273

Alopecia areata

Speaker: Sonia Ocampo-Garza (Mexico)

General Overview

- **Type**: Non-scarring, autoimmune alopecia
- **Pediatric onset**: ~20% of cases begin in childhood
- **Course**: Chronic, unpredictable, with high relapse rates
- **Spontaneous regrowth**: ~50% within 1 year
- **Impact**: Significant psychological burden and ↓ quality of life
- **Evidence**: No preventive or curative treatment; limited RCTs

Clinical Classification and Management Strategy

Group	Clinical Pattern	First-line Treatment	Alternative Options
1	<50% scalp, mild activity, with regrowth	Topical corticosteroids + Minoxidil	Anthralin, intralesional triamcinolone, dexamethasone pulses
2	>50% scalp, high activity/resistance/ ophiacean pattern	Oral dexamethasone +	Methotrexate, Cyclosporine, Hydroxychloroquine

Group	Clinical Pattern	First-line Treatment	Alternative Options
		Topical clobetasol or minoxidil	
3	Totalis/Universalis	Contact immunotherapy ± Topical steroids	JAK inhibitors, oral steroids, methotrexate

Topical and Intralesional Corticosteroids

- **Topical**: High-potency (e.g. clobetasol) effective vs. low-potency (hydrocortisone)
  → *Clobetasol: 85% ≥50% regrowth vs. Hydrocortisone: 33% (at 24 weeks)*
- **Intralesional Triamcinolone**:
  - Recommended in **children >10 years** with localized disease
  - Usual doses: 2.5, 5, 10 mg/mL
  - **5 mg/mL** preferred (higher regrowth vs. 2.5 mg/mL)
  - Max: **≤20 mg per session**
  - Injection depth: **Bulb-level**, unlike superficial injection in scarring alopecias

Systemic Corticosteroids

- **Preferred**: Oral dexamethasone or betamethasone **mini pulses**
  - Dose: **0.1 mg/kg**, 2 days/week
  - ↓ Side effects, ↓ relapse vs. daily/oral IM

Minoxidil

Type	Dose	Notes
Topical	2–5%	Widely used
Oral	0.5 mg/day	71% improved in case series (hypertrichosis most common AE)

Methotrexate

- Dose: **0.2–0.4 mg/kg/week** + folic acid
- Age range studied: 8–18 years
- **Response**: 50% regrowth in 5/40 patients
- Discontinue if no response after 6–9 months

Hydroxychloroquine

- Limited evidence
- 9 patients: 5 responders, 4 non-responders
- **Mean SALT score improvement**: 3.2

Topical Immunotherapy

Agents:

- **SACV** (Squaric acid dibutyl ester)
- **DPCP** (Diphenylcyclopropenone)

Protocol:

1. Sensitize with 2% solution on small area
2. After 2–3 weeks: initiate treatment with 0.0001–0.001%
3. Gradual titration to induce mild dermatitis
4. If **there is no regrowth after 6 months**, discontinue

Adverse Events:

- Contact dermatitis, vesicles, lymphadenopathy, edema, pigmentary changes, flu-like symptoms

JAK Inhibitors

Drug	JAK Target	Pediatric Use	Notes
Tofacitinib	Pan-JAK	Off-label	87% response in 31 patients

Drug	JAK Target	Pediatric Use	Notes
Baricitinib	JAK1/2	Off-label	68% SALT reduction
Ritlecitinib	JAK3/TEC	FDA-approved ≥12 years	SALT <20 in 25–50% at 48 wks

- **Recurrence**: High after discontinuation
- **Limitation**: High cost, limited long-term safety data

Treatment Summary by Pattern and Activity

Extent	Activity	Primary Approach	Secondary Options
Localized	Active	Topical corticosteroids + Minoxidil	Anthralin
	Inactive		Immunotherapy
Extensive	Active		Systemic corticosteroids, JAK inhibitors (Ritlecitinib: approved 12 yo), Immunosuppressants
	Inactive		Immunotherapy or JAK inhibitors, Systemic corticosteroids

Take-Home Messages

- Choose therapy based on **age and disease extent**
- Avoid discontinuation before **3–6 months**
- First-line: **Topical corticosteroids + Minoxidil**
- Consider **oral mini pulses** for extensive or rapidly progressing cases
- **JAK inhibitors and immunotherapy**: viable for severe cases
- Limited evidence for pediatric populations — interpret cautiously

References:

- Garnacho Saucedo G, et al. Treatment of alopecia areata in children. Piel. 2016; 31 (8): 582-588
- Lenane P, et al. Clobetasol propionate, 0.05%, vs hydrocortisone, 1%, for alopecia areata in children: a randomized clinical trial. JAMA Dermatol. 2014 Jan;150(1):47-50.
- Chu, T et al. Benefit of different concentrations of intralesional triamcinolone acetonide in alopecia areata: An intrasubject pilot study. JAAD. 2015; 73 (2): 338 – 340
- de Nicolas-Ruanes B, et al. Low-dose oral minoxidil for treatment of androgenetic alopecia and telogen effluvium in a pediatric population: A descriptive study. J Am Acad Dermatol. 2022 Sep;87(3):700-702

Atopic dermatitis PART II

Topical therapy update

Speaker: Lawrence Eichenfield (USA)

Opening Remarks and Clinical Context

Despite recent advances in systemic agents, topical care remains foundational in AD management, even in patients on systemic treatment.

Topical therapy includes:

- General skin care (e.g., moisturization, barrier repair)
- Topical corticosteroids
- Calcineurin inhibitors
- Newer non-steroidal agents

A critical point raised is that **new topical agents are typically studied against vehicles**, rather than active comparators like corticosteroids, and usually as **monotherapy**, which doesn't reflect real-world practice where combination therapy is common.

The speaker's core message to patients is to aim for **long-term disease control**, defined as:

- Minimal rash
- Minimal itch
- Minimal sleep disturbance

Wrestling with Steroid Phobia: The Topical steroid withdrawal phenomenon

Topical corticosteroids remain **first-line treatment** in many cases.

Steroid phobia is discussed with a notable shift from concern about atrophy to a growing belief in "topical steroid addiction" (TSA). The speaker highlights the **video "Skin on Fire"** as an example of this messaging. (*https://www.youtube.com/watch?v=GuaBbsL1qKA)*

While **topical steroid withdrawal syndrome (TSW)** is a recognized phenomenon, particularly in adults (rare in pediatric population) with long-term use, the **concept of widespread topical steroid addiction lacks evidence**.

A **Swedish internet survey** of self-identified TSW patients (recruited via Facebook) reported:

- Common symptoms: burning, pruritus, neuropathic sensations
- Some were still using topical corticosteroids
- High psychosocial burden including school/work absenteeism

Challenges in Comparing Topical Agents

- **Meta-analysis limitations** due to inconsistent outcome measures and population variability
- A **Cochrane network meta-analysis** on topicals identified:
    - **Very potent corticosteroids** are the most effective
    - **Low-dose tacrolimus** surprisingly ranked second, based on a small 30-patient study

Real-World Corticosteroid Effectiveness

Clinical trial data may **overstate perceived effectiveness**. In a study of BID mid-potency corticosteroids for 4 weeks:

- **25%** of patients achieved **clear/almost clear**
- **15%** reached **EASI-90**
- About **one-third** had ≥4-point itch reduction

These results reflect modest short-term efficacy even for traditional agents, reinforcing the need for novel therapies.

Newer Non-Steroidal Topical Therapies

1. Topical Ruxolitinib (JAK1/2 Inhibitor)

- Formulation: 1.5% cream
- Approved in the U.S. for patients **12+ years**, with studies down to **age 2**
- **Rapid antipruritic effect**
- In phase 2, **superior to triamcinolone 0.1%** for IGA success and EASI-75
- Well-tolerated with **low stinging/burning**; systemic absorption limits use to **≤20% BSA**

Pediatric Data: In 2–12-year-olds, ~56% achieved clear/almost clear with BID application.

2. Tapinarof (Aryl Hydrocarbon Receptor Agonist)

- Approved for **ages 2+**
- Mechanism: AHR activation reduces oxidative stress, inhibits T-resident memory cells
- Phase 3 study: ~46% clear/almost clear; mean baseline BSA = 17%
- **Well-tolerated**, even on sensitive skin
- Unique AE: **Follicular events**, possibly due to keratinocyte upregulation

Long-term data:

- 1-year study: 82% reached clear/almost clear with intermittent use
- No systemic absorption; **no BSA restrictions**

3. Crisaborole (Topical PDE4 Inhibitor)

- Approved **≥3 months of age**
- Shown to be **safe and effective for long-term daily use (1 year)**

- Used for mild-to-moderate AD

4. Roflumilast (PDE4 Inhibitor)

Formulation	Indication	Age	Notes
0.3% cream	Psoriasis	≥6	First approval
0.3% foam	Seborrheic dermatitis	Adult	Newer formulation
0.15% cream	Atopic dermatitis	≥6	Recently approved
0.05% cream	AD (age 2–5 study)	2–5	Not yet approved

- In AD studies: ~30% clear/almost clear after **QD for 4 weeks**
- **Extension trial**: Twice-weekly proactive use-maintained remission for ~281 days
- Good tolerability and long-term safety data emerging

5. Delgocitinib (Pan-JAK Inhibitor)

- Approved in some regions for **chronic hand eczema**
- Demonstrates good results in clinical and QoL metrics
- May have broader dermatologic applications in the future

Clinical Implications and Future Direction

Current Topical Options

- **Steroids** remain first-line, but usage varies due to safety concerns and access
- **Calcineurin inhibitors** (tacrolimus/pimecrolimus) remain valuable
- **New non-steroidals** are expanding options, especially for sensitive skin areas and steroid-phobic patients

Cost and Access Challenges

- Many new agents are **cost-prohibitive**, which limits routine use
- Insurance access varies significantly

Combination Therapy and Real-World Practice

- While trials study **monotherapy**, in practice we **combine topical agents**
- There's increasing interest in **proactive therapy** to maintain remission
    - Tacrolimus and roflumilast have data supporting this approach
    - Tapinarof has shown **drug-free remission** lasting 60–80 days in some patients

Closing Thoughts

- The landscape of topical therapy for AD is evolving rapidly
- There is now a **broader armamentarium** of steroid-sparing options with novel mechanisms
- The challenge lies in determining **optimal integration**, balancing:
    - **Efficacy**
    - **Safety**
    - **Cost-effectiveness**
    - **Patient preferences**

References:

- Buethe MG, et al. Topical The rapy fo r A topic Dermatitis. What is New and the New Paradigm. Dermatol Clin. 2024; 42 (4): 569-575
- Kleinman E, et al. What's New in Topicals for Atopic Dermatitis?. Am J Clin Dermatol. 2022;23 (5): 595-603
- Alsterholm M et al. Topical Steroid Withdrawal in Atopic Dermatitis: Patient-reported Characterization from a Swedish Social Media Questionnaire. Acta Derm Venereol. 2025;3:105
- Lax SJ, et al. Topical anti-inflammatory treatnebts for eczcema: network meta-analysis (Review). Cochrane database Syst Rev. 2024;8 (8):Cd015064.
- Simpson EL, et al. Long-Term Safety and Efficacy with Roflumilast Cream 0.15% in Patients Aged ≥6 Years with Atopic Dermatitis: A Phase 3 Open-Label Extension Trial. Dermatitis. 2025. Epub ahead of print.

Systemic treatment: eligibility criteria, medication choice

Speaker: Carsten Flohr (United Kingdom)

While advanced therapies in atopic dermatitis (AD) are gaining prominence, conventional systemic treatments remain foundational. This presentation addresses the strategic use of both conventional and newer systemic treatments, framed through clinical evidence and a detailed case study.

Key Discussion Points

- Indications for **initiating systemic therapy** in AD
- **Selection and practical use** of **conventional** agents (methotrexate, cyclosporine)
- Introduction and positioning of **advanced therapies** (biologics and JAK inhibitors)
- Highlight the importance of **progression and individualization of therapy**.

Pathophysiological Considerations and Disease Burden

Atopic dermatitis is characterized by a **chronic itch-scratch cycle** that perpetuates inflammation. **Exacerbating factors** must be **managed before** initiating systemic therapy:

- Food and respiratory allergies
- Psychological comorbidities (anxiety, depression)
- Recurrent skin infections

Effective management should include:

- Intensive topical therapy
- Multidisciplinary support (including psychological input)
- Education and behavioral interventions
- Consideration of patch testing where indicated

Conventional Systemic Therapies

Methotrexate

- Commonly used as a first-line systemic in UK practice (off-label)
- Mechanisms include folate antagonism and modulation of JAK/NF-κB pathways
- Demonstrated durable efficacy in the TREAT trial
- Dosing: 0.4–0.5 mg/kg/week, without need for test dosing
- Subcutaneous administration can improve efficacy and reduce GI side effects
- Common side effect: nausea (managed with daily folic acid except on dosing day)
- Rare but monitored risk: bone marrow suppression

Cyclosporine

- Offers rapid disease control but limited by rebound and long-term safety concerns
- Mechanism: T-cell inhibition
- Nephrotoxicity and hypertension are primary risks, although recent biomarker studies show no significant renal impact in trial participants
- Often used short-term, with tapering or transition to other agents

Transition to Advanced Therapies

Following suboptimal or complicated responses to conventional agents, advanced therapies may be introduced.

Dupilumab

- Approved for AD and asthma, offering a targeted IL-4/IL-13 blockade
- Strong safety profile
- Notable concern: increased frequency of herpetic infections in a subset of patients

JAK Inhibitors (e.g., baricitinib, upadacitinib, abrocitinib)

- Broader cytokine inhibition, with rapid pruritus control
- Higher risk of infections; patient selection is key
- Flexibility in dosing (e.g., 15 vs 30 mg for upadacitinib) allows for individualized approaches

Evidence-Informed Decision-Making

Network meta-analyses (NMAs) provide comparative efficacy and safety data for systemic treatments. One application of this is the clinical decision-support platform [**EczemaTherapies.com**], designed to:

- Compare therapies on outcomes such as EASI, pruritus NRS, and DLQI/CDLQI
- Present GRADE-based interpretations
- Facilitate shared decision-making with patients

Combination Therapy in Complex Cases

For patients with multifaceted disease courses or limitations to monotherapy, combination regimens may be necessary.

Case Study Overview:

A patient with severe, early-onset AD (EASI >50 at age 10) demonstrated:

- Dependence on potent topical **corticosteroids**
- Recurrent bacterial and viral infections, including HSV
- High comorbidity burden (asthma, allergic rhinitis, psychological distress)
- Partial or unsustained response to **methotrexate** and **cyclosporine**
- Adverse effects limiting conventional therapy use
- After the recurrence of HSV on **dupilumab** monotherapy, treatment was adjusted

- Combined therapy with **dupilumab (200 mg Q2W)** and **upadacitinib (15 mg/day)** was initiated
- Prophylactic **valacyclovir** successfully prevented viral reactivation
- Patient achieved long-term stability and substantial improvement in quality of life

This treatment approach is now published in *Pediatric Dermatology* as an example of advanced therapeutic integration.

Clinical Practice Considerations

- **Methotrexate** remains the preferred first-line systemic option in many settings
- **Cyclosporine** is useful for acute control but has limitations in maintenance
- **Advanced agents** offer greater precision and patient-tailored outcomes but require close monitoring and infrastructure
- **Guidelines and NMAs** support rational sequencing but do not yet provide strict hierarchies; clinical judgment remains essential
- **Combination therapies** may be considered in severe or refractory cases under close supervision

Final Reflection

Optimal management of atopic dermatitis requires a nuanced balance between guideline-based strategies, emerging evidence, and real-world complexities. The therapeutic landscape is expanding rapidly, and with it, the opportunity to tailor interventions based on disease severity, comorbidities, and patient preferences—always with a multidisciplinary approach at the center.

References:

- Noda S et al. The translational revolution and use of biologics in patients with inflammatory skin diseases. J Allergy Clin Inmunol. 2015;135(2):423-336
- Gandhi NA et al. Targeting key proximal drivers of type 2 inflammation in disease. Nat Rev Drug Discov. 2016;15(1): 35-50
- Flohr C, et al. Efficacy and safety of ciclosporin versus methotrexate in the treatment of severe atopic dermatitis in children and young people

(TREAT): a multicentre parallel group assessor-blinded clinical trial. Br J Dermatol. 2023 Nov 16;189(6):674-684
- Wollenberg A, et al. European guideline (EuroGuiDerm) on atopic eczema: part I - systemic therapy. J Eur Acad Dermatol Venereol. 2022 Sep;36(9):1409-1431
- Drucker AM, et al. Systemic Immunomodulatory Treatments for Atopic Dermatitis: Living Systematic Review and Network Meta-Analysis Update. JAMA Dermatol. 2024;160(9):936–944.

Approach to patients with suboptimal response to systemic treatment

Speaker: Elaine Siegfried (USA)

Key Themes:

- Patient selection is critical to avoid treatment failure
- Recognition of phenotype and endotype is essential
- Multiple patient-specific factors affect treatment response
- High complexity in non-responders, often requiring individualized strategies

Initial Evaluation and Patient Stratification

Checklist Prior to Initiating Systemic Therapy:

Consideration	Description
Endotype	E.g., classical AD, contact dermatitis, psoriasis/psoriasiform overlap
Non Atopic Comorbidities	Systemic comorbidities, Sleep disruption, HSV (herpes incognito), recurrent otitis media, pneumonia
Atopic Comorbidities	Especially ocular (risk for dupilumab-induced conjunctivitis)
Corticosteroid Exposure	Topical and systemic
Psychosocial Factors	Adherence barriers, anxiety, needle phobia

Consideration	Description
BMI & Development	Consider nutritional status
Family History	Atopy, autoimmune, immunodeficiency
Access and Cost	May influence therapy selection

Phenotyping & Endotyping

Recognized Subtypes:

- Classical atopic dermatitis
- Contact dermatitis (irritant/allergic/mixed)
- Psoriasis or psoriasiform dermatitis
- Urticarial variants
- Nutritional/immunodeficiency-associated dermatoses

Biomarkers and Labs

Biomarker	Interpretation
Total/Specific IgE	Degree of atopic sensitization
Eosinophil Count	HES if >1500 × 3
Albumin, Total Protein, Globulins	Nutritional and immunologic markers
ANA, Histone	Possible correlation with anti-drug antibody formation
Vitamin D	Often deficient; screen for rickets
Celiac Screening	Especially in failure to thrive
Immunologic Panel	Recurrent infections warrant screening for PID

Defining and Assessing Treatment Response

Clinical Metrics:

Response ➔	Criteria
Optimal ➔	IGA 0 (clear)
Acceptable ➔	IGA 1 (almost clear), stable mild disease
Failure ➔	No meaningful improvement (e.g., <2-point IGA drop)

Common Causes of Treatment Failure

Cause	Note
Psoriasiform Skewing	Poor response to Type 2 inhibitors
Allergic Contact Dermatitis	Difficult to detect, patch testing limited
Non-Adherence	Often underestimated
Needle Phobia	Impacts biologic use. **Management:** Home-based behavioral techniques Topical anesthetics Pharmacologic support Mental health referral
Anti-Drug Antibodies	Not well studied in AD yet
Undiagnosed Infection	May be unmasked post-immunomodulation
Primary Immunodeficiency	Often missed without full immune workup
Hypersensitivity to Excipients	E.g., polysorbates (noted in most biologics) **Polysorbate 80** - Dupilumab, tralokinumab **Polysorbate 188** - Nemolizumab

Treatment Adjustment Strategies

Clinical Clue	Consideration
Persistent inflammation	Increase topical steroid or add systemic
Injection refusal	Oral JAKi or systemic alternatives
Excipient reaction	Switch class if possible (not always feasible)
Long-term JAKi risk	Transition back to biologic when stable
Poor response to dupilumab	Transition to JAKi (e.g., upadacitinib)
Allergic contact dermatitis phenotype	Patch testing, methotrexate
Suspected anti-drug antibody	Switch to a different class (e.g., JAKi)
Psoriasiform phenotype	IL-12/23 blockade (e.g., ustekinumab) may be more effective
Adherence issues	Simpler regimens, oral options

Meta-Analysis Summary

- **JAK inhibitors (high dose)** show superior efficacy compared to low dose and dupilumab
- **Higher efficacy comes with increased adverse effects**
- **Studies vary in duration and population (mostly adult-centric)**

Conclusion

- **Treatment failures** in pediatric AD are multifactorial and require understanding of endotype, phenotype, and patient context.
- **10% of patients account for most time and complexity.**
- A **flexible, personalized, data-informed approach** is essential to optimizing outcomes.

References:

- Talasila S, et al. Analysis of publicly available adverse events reported for pediatric patients treated with Janus kinase inhibitors. Pediatr Dermatol. 2024 Nov-Dec;41(6):1040-1046.
- Fyhrquist N, et al. Endotypes of atopic dermatitis. J Allergy Clin Immunol. 2025 Mar 5:S0091-6749(25)00260-X
- Bieber T. Disease modification in inflammatory skin disorders: opportunities and challenges. Nat Rev Drug Discov. 2023 Aug;22(8):662-680.
- Bieber T. The paradigm shift in drug development for atopic dermatitis: Addressing the variables of the equation leading to disease modification. Ann Allergy Asthma Immunol. 2025 Feb;134(2):144-150.
- Liao Q, et al. Comparative efficacy and safety of dupilumab versus newly approved biologics and JAKi in pediatric atopic dermatitis: A systematic review and network meta-analysis. PLoS One. 2025 Feb 24;20(2):e0319400

The future of atopic dermatitis

Speaker: Amy S. Paller (USA)

Advances and Predictions in Atopic Dermatitis (AD)

1. Topical Therapies: Evolving Options

- **Calcineurin Inhibitors (e.g., Tacrolimus, Pimecrolimus)**
    - ~25 years of clinical use; safety profile well understood
    - Effective for **maintenance** and use in **sensitive areas**
    - **Burning/stinging** can be reduced by:
        - Pre-treatment with topical corticosteroids
        - Use of chilled formulations
- **New Non-Steroidal Topicals:**

Agent	Status	Age Range	Notes
Roflumilast	Emerging	Likely expanding	Minimal stinging/burning
Ruxolitinib	Approved	≥12 years	Potential for younger use in future
Tapinarof	Approved	≥2 years	Low irritation profile

- Microbiome-Based Topicals:
    - Ongoing research into **commensal organisms** (e.g., *S hominis*)
    - Goal: reduce *S aureus* colonization

2. Novel Targets and Pathways

- **OX40/OX40L Inhibitors** (Type 2 immune pathway)
    - Target **T-cell co-stimulation**
    - Potential for **longer remission** post-treatment
    - May enable **less frequent dosing**
- **Multi-Target Biologics (Bispecifics/Trispecifics)**
    - Combining IL-4Rα, IL-13, IL-31, IL-18 targets
    - Greater **efficacy potential** via polycytokine blockade
- **IL-31 Pathway**
    - **Nemolizumab** shows **rapid itch reduction**

3. Drug Delivery Innovations

- **Challenges with Biologics:**
    - Injection pain is a major barrier in pediatrics
    - Strategies for pain reduction:
        - **Distraction techniques** (VR, music, toys)
        - **Cuddling techniques**
        - **Warming or room-temp medication**
        - **Topical anesthetics**
- Emerging Technologies:

Method	Limitation
Microneedles	Not feasible for high-volume biologics

Method	Limitation
Needle-free injectors	Volume limitations (e.g., dupilumab = 2mL)
Sensor-triggered feedback devices	Potential for behavioral intervention

4. Systemic Therapies: Present and Future

- **Dupilumab** (IL-4Rα blocker):
  - Durable responses in some pediatric patients
  - Some maintain remission after stopping therapy
- **Selective JAK Inhibitors (e.g., Upadacitinib, Abrocitinib)**
  - Fast-acting oral options
  - Broader immunosuppressive profile; long-term safety still under investigation
- **Small Molecule IL-23 Inhibitors (e.g., Icotrokinra)**
  - Successful in **psoriasis**; early AD trials ongoing

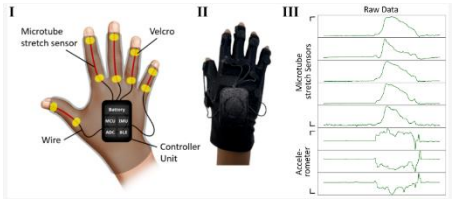
5. Itch as a Therapeutic Frontier

- **Itch Pathways:**

Pathway	Agent or Target
IL-31	Nemolizumab
IL-4/IL-13	Dupilumab, JAK inhibitors
Substance P	Failed trials so far
Proteases (e.g., V8 protease)	Antiplatelet drugs as novel topicals
PAR2 activation	Calocrine inhibition under study

- **Objective Itch Monitoring:**
  - Acoustic and movement sensors to distinguish:

        - Scratching vs. rubbing vs. random motion
    - **Biofeedback wearables** show promise in reducing nocturnal scratching



6. Remote Monitoring & Digital Trials

Remote Clinical Trials:

<u>Feasible with</u>:

➔ Telemedicine

➔ High-res photography

➔ Real-time PROs

➔ Sensorized wearables

Wearable Technology:

<u>Tracks:</u>

➔ Itch/scratch activity

➔ Sleep disturbance

➔ Skin hydration, TEWL, erythema, thickness

➔ Microbial density

Examples:

- **Programmable wearable TEWL sensor**: collects hourly data non-invasively
- **Miniaturized skin sensors** developed at Northwestern University

8. Next-Gen Technologies:

Technique	Application
Proteomics (5,000 proteins)	Serum analysis from small blood volumes
Single-cell transcriptomics	High-resolution skin data
Microbiome swabbing	Genomics and proteomics
Detergent-based epidermal swabbing	Non-invasive immune profiling

- Skin Lipidomics:
    - **Stratum corneum ceramides** as predictors for:
        - Disease development in infants
        - Therapy responsiveness
    - Potential to guide **topical ceramide replacement** or **filaggrin enhancement** therapy

Summary of Future Directions

Area	Future Outlook
Therapeutics	More non-steroidal topicals, pain-free biologics, small molecule inhibitors
Monitoring	Objective wearable sensors, real-time feedback
Access & Equity	Need for cost reduction and global availability
Clinical Trials	Move toward remote, tech-enabled designs

References:

- Puar N, et al. New treatments in atopic dermatitis. Ann Allergy Asthma Immunol. 2021 Jan;126(1):21-31
- Gallo RL, et al. Staphylococcus aureus: The Bug Behind the Itch in Atopic Dermatitis. J Invest Dermatol. 2024 May;144(5):950-953
- Au C-Y, et al. Sensorised Glove to Detect Scratching for Patients with Atopic Dermatitis. Sensors. 2023; 23(24):9782

- Tsoi LC, et al. Noninvasive Tape-Stripping with High-Resolution RNA Profiling Effectively Captures a Preinflammatory State in Nonlesional Psoriatic Skin. J Invest Dermatol. 2022 Jun;142(6):1587-1596
- Rinnov MR, et al. Skin biomarkers predict development of atopic dermatitis in infancy. Allergy. 2023 Mar;78(3):791-802

Nail diseases

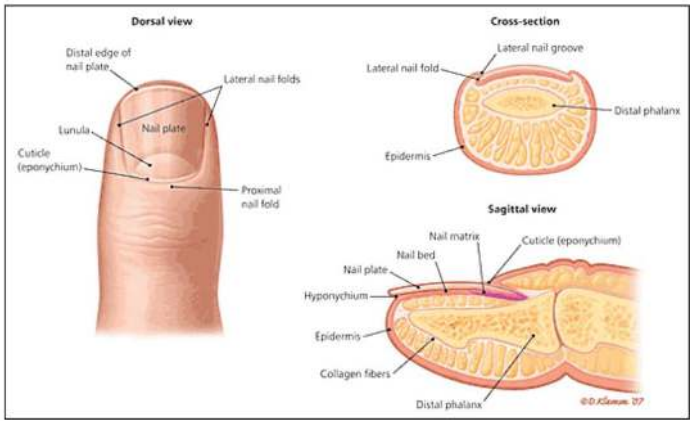
Nail surgery in children: Practical tips for success

Speaker: Jane Bellet (USA)

Key Concepts & Tips

1. Nail Anatomy Review:

- **Know your landmarks**: The *lunula* and *proximal nail fold* overlie the **nail matrix**, the key site for many biopsies.
- Nail matrix is thin—**depth matters**, as you reach bone quickly.



2. When to Biopsy:

- **Same rule as skin lesions**: If you'd biopsy it on the skin (e.g., for diagnostic uncertainty, management guidance, or concern), biopsy it on the nail.
- Don't fear nail dystrophy post-biopsy— "the nail is already abnormal."
- Atypical nail pigmentation should not be ignored (e.g., longitudinal melanonychia).

3. Pediatric Considerations:

- Anatomy is the same as adults, but logistics differ:

    - **Anesthesia is always needed** (often general for younger patients).
    - **Post-op behavior** (kids run, play, etc.).
- Choose digit carefully if optional—avoid thumbs/great toes if possible.

4. Pre-op Planning:

- **Schedule time generously** (1 hour recommended).
- Ensure child eats pre-procedure (to reduce vasovagal risk, unless under General Anesthesia).
- **Mark lesion pre-anesthesia** to guide biopsy, especially if nail is avulsed.

5. Anesthesia Techniques:

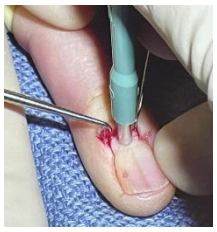
- **Always perform a block**, even under general.
- Choose between:
    - **True digital block** (base of finger/toe).
    - **Distal digital block** (most common).
    - **Wing block**.
- Use **ropivacaine** or **lidocaine w/epi** (limit volume to 3 mL to avoid ischemia).
- Emphasize difference between **pressure vs pain** during procedures.

6. Tourniquet Options: bloodless field

- Sterile glove roll-down (DIY).
- **Penrose drain** (distal to proximal, then clamp).
- **T-Ring Tourniquet**: Preferred; uniform pressure but expensive.

7. Common Procedures:

A. Punch Biopsy:



- For narrow lesions (<3 mm).
- Option to punch through soft nail or after partial nail avulsion.

B. Partial Proximal Nail Avulsion:

- Cut across plate near proximal fold, lift with hemostat.
- Enables better access to matrix or bed.

C. Nail Matrix Shave Excision:

- Preferred for lesions >3 mm wide.
- Steps:
    1. Avulse nail proximally.
    2. Score lesion.
    3. Shave in **parallel** to plate.
    4. Trim nail edge to avoid spicules.
    5. Return plate segment, **suture skin to nail** (e.g., 5-0 Vicryl Rapide).
- No sutures needed in the matrix defect itself

8. Specimen Handling:

- Nail specimens are **tiny**: Map them!
- Use **biopsy cassette** to prevent tissue loss.
- Place the entire cassette in formalin.

9. Tourniquet Removal:

"Most important part of your day."

- **Physicians should do it**, not a nurse or trainee.
- Rule: Always remove it before bandaging.

10. Bandaging Tips:

- **Longitudinal, not circumferential**, to avoid excessive pressure.
- Add splints, boots, or slings for active children.

11. Post-op Care:

- Add anesthetic at end of procedure for extended pain relief.
- **Ibuprofen preferred**, opioid only for extensive procedures.
- Leave initial dressing for 2–3 days, then daily changes.
- First post-op visit: 2–4 weeks.

12. Special Pediatric Considerations:

- Toddlers: finger-sucking risk.
- Teens: sports/play compliance.
- Be creative with protective barriers.

13. When *Not* to Operate:

- Know when to manage conservatively.
- Example: **Granulation tissue** post-trauma (treated with topical steroids, not surgery).

Take-Home Messages:

1. **Biopsy if needed** or refer—don't ignore abnormal nails.
2. **Know your anatomy**.
3. Use **nail matrix shave** for wide lesions.
4. **Always remove the tourniquet** yourself.
5. **Bandage longitudinally**.
6. Patience: Nail healing is slow.
7. Build strong **surgical referral networks**.
8. **You can do this.**

References:

- Rigopoulos D, Larios G, Gregoriou S, Alevizos A. Acute and chronic paronychia. Am Fam Physician. 2008 Feb 1;77(3):339-46
- Serour F, et al. EMLA cream prior to digital nerve block for ingrown nail surgery does not reduce pain at injection of anesthetic solution. Acta Anaesthesiol Scand. 2002 Feb;46(2):203-6.
- Haneke E. Nail surgery. Clin Dermatol. 2013 Sep-Oct;31(5):516-25
- Park HS, et al. A novel nerve block technique for nail surgery. Pediatr Dermatol. 2024 Jan-Feb;41(1):177-179
- Jellinek N. Nail matrix biopsy of longitudinal melanonychia: diagnostic algorithm including the matrix shave biopsy. J Am Acad Dermatol. 2007 May;56(5):803-10
- Richert B, et al. Tangential excision of pigmented nail matrix lesions responsible for longitudinal melanonychia: evaluation of the technique on a series of 30 patients. J Am Acad Dermatol. 2013 Jul;69(1):96-104

Childhood onychomycosis

Speaker: Robert Silverman (USA)

Epidemiology

- **True prevalence is low**:
    - **Culture-positive onychomycosis** in children: <1% worldwide.
    - **Clinical prevalence** up to 8%, with only ~38% being culture positive.
- **More common** in:
    - Warmer climates
    - Older children
    - Pediatric dermatology clinics (selection bias)
- **Increased prevalence associated with**:
    - Down syndrome
    - HIV
    - Prior nail trauma
    - Primary antibody deficiencies (e.g., CVID, XLA)
    - Hyper-IgE syndromes
    - Certain genetic skin diseases (e.g. pityriasis rubra pilaris

Risk Factors

- IL-17 inhibitors → ↑ Candida infections
- Moccasin-type tinea pedis
- Nail trauma (e.g., crushed toenails)

Clinical Variants

- Similar to adults:
  - Distal lateral subungual onychomycosis (DLSO) 
  - Proximal subungual onychomycosis (PSO) 
  - Superficial white onychomycosis (SWO) 
  - Total dystrophic onychomycosis 
- **Endonyx Onychomycosis**: 
  - No inflammation, no onycholysis, no subungual hyperkeratosis
  - Milky white discoloration, primarily fingernails
  - Often misdiagnosed (e.g., as alopecia areata, psoriasis)
  - Caused by endothrix dermatophytes (commonly *T. soudanense*)

Differential Diagnosis

- Psoriasis
- Lichen planus
- Alopecia areata
- Trauma
- Nail dystrophies

Diagnosis

- **Specimen collection tip**: Use a small curette — works better than scraping.
- **Diagnostic tools**:

  Dermoscopy clues:

    - Onychomycosis → frond-like distal edges
    - Helps differentiate from psoriasis or trauma

  - **KOH prep**: Low sensitivity, but quick and bedside
  - **Staining** → ↑ sensitivity
  - **PAS stain** on histology
  - **PCR**: High sensitivity, $$$ expensive in the U.S.
  - **Confocal microscopy**: Non-invasive, still experimental
  - **AI image analysis**: In development
  - **Culture**: Gold standard (especially to identify non-dermatophyte molds)

Treatment

Topical:

- **Preferred if**:
  - Disease is limited to distal nail
  - Matrix not involved
- More effective in children than adults
- Expensive options in U.S. (e.g., efinaconazole, tavaborole)
- Don't forget to treat **coexisting tinea elsewhere**

Systemic:

- Required for matrix or full nail involvement
- **Terbinafine**:
  - "Crush between two spoons"
  - Mix with sweet food (e.g., honey, syrup)

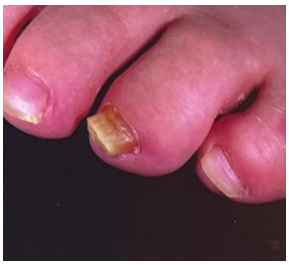
    - Avoid acidic foods (↓ drug efficacy)
- **Dermatophytoma** (biofilm-like mass in nail):
    - Linear or round, difficult to treat
    - Often requires combination therapy
    - Nail curetting/splitting may help penetration of topical agents

Organisms

- Similar to adults:
    - *Trichophyton rubrum* (most common)
    - *T. tonsurans*, *T. mentagrophytes*
    - **Candida**: More common in infants and fingernails
    - ↑ Reports of non-dermatophyte molds (e.g., *Scopulariopsis*, *Fusarium*, etc.)

Special Considerations

- **Fingernail-only disease** in infants → consider *Candida*
- Nail of the **fourth toenail** can be an isolated site of onychomycosis



    - Differential diagnosis:
        - Subungueal tumors, psoriasis, pachyonychia congenita,
- **Always perform a full skin exam**:
    - Example: Onychomycosis + scalp scaling → coexisting tinea capitis

Take-Home Pearls

1. **Clinical variants** of onychomycosis in children mirror adults but always verify with proper diagnostics.
2. **Endonyx** is often underrecognized—think of it in subtle cases.
3. **Always treat other coexisting fungal infections.**
4. **Dermoscopy** can help differentiate fungal nail disease from mimickers.
5. **Topicals are great** for early disease and in kids—less systemic exposure.
6. **Use systemic therapy** for matrix involvement or dermatophytoma.
7. **Candida is more common in babies and fingernails.**
8. **Culture everything**, especially in unusual cases or if topicals fail.

References:

- Vestergaard-Jensen S, et al. Systematic review of the prevalence of onychomycosis in children. Pediatr Dermatol. 2022 Nov;39(6):855-865
- Gupta AK, et al. Pediatric dermatophyte onychomycosis: a review. Int J Dermatol 2025;64:465-472
- Solís-Arias MP, et al. Onychomycosis in children. A review. Int J Dermatol. 2017 Feb;56(2):123-130
- Tosti A, et al. Endonyx onychomycosis: a new modality of nail invasion by dermatophytes, Acta Derm Venereol 1999; 79(1): 52-3
- Jakhar, D et al. Dendritic pattern: Unique onychoscopic feature in endonyx. JAAD 2019;8(4):e89 - e90
- Lateur N, et al. Two Hundred Ninety-Six Cases of Onychomycosis in Children and Teenagers: A 10-Year Laboratory Survey. Pediatric Dermatology 2003; 20(5): 385-388

Longitudinal melanonychia in children

Speaker: Judith Dominguez Cherit (Mexico)

Background

Longitudinal melanonychia (LM) in pediatric patients is a diagnostic challenge. While well-studied in adults, limited data is available in children. The condition may be caused by either melanocytic activation (racial/ethnic or functional) or proliferation (e.g., nevi, melanoma).

Comparison: Adults vs. Children

Feature	Adults	Children
Ethnic melanonychia	Common, especially in darker skin types	Rare, even in darker skin types
Melanoma risk	LM may be an early sign	Extremely rare
Diagnostic criteria	Well-established	Often unreliable when applied to children
Histology appearance	Predictive	May mimic melanoma, even when benign

Histological Findings & Diagnostic Limitations

- **Normal adult melanocyte count**: up to 15/mm^2
- Early **melanoma in adults**: >35 melanocytes/mm^2
- In **children**: melanocyte density in nail matrix remains **undefined**
- Histopathological features in children may show hyperplasia, hyperchromasia, and architectural disorder, but still represent benign nevi.

Typical Pediatric LM Patterns

- Pigmented bands of varying width and color
- Hutchinson's or pseudo-Hutchinson's sign often present
- Involvement of the nail fold and hyponychium
- Dermoscopy may show irregular lines, brushed patterns, or milky white streaks

Immunohistochemistry Tools

BRAFV600E, HMB-45, and PNL2 staining may assist in differentiating between benign and malignant melanocytic lesions. Negative BRAFV600E findings are typically associated with benign nevi.

Management Recommendations

- **Clinical follow-up** is the first-line approach, especially in children **<10 years**

- **Parental counseling** is essential due to frequent concern about melanoma
- **Biopsy** should be reserved for **progressive or highly suspicious cases**
- **Wide local excision** or aggressive treatment should be **avoided** unless strongly justified

Key Takeaways

- **Melanoma** is exceptionally **rare** in pediatric LM
- **Histological** features in children can be alarmingly atypical but **often benign**
- **Adult** criteria are **not applicable** to pediatric cases
- Clinical **observation** and patient-family **communication** are critical in management

References:

- Martin,B. Histopatología de la uña. Actas Dermo-Sifiliográficas. 2013; 104 (7): 564- 578
- Tsai SY, et al. Melanoma-like features in pediatric longitudinal melanonychia: A systematic review and meta-analysis. Pediatr Dermatol. 2024 Jul-Aug;41(4):613-620
- Dominguez-Cherit J, et al. Subungual spitz nevus in a Hispanic infant. Dermatol Surg. 2008 Nov;34(11):1571-3
- Ani O, et al. Clinical and Histopathological Investigation of Pediatric Melanonychia: A Single-Center Retrospective Case Series. Ann Plast Surg. 2024 Apr 1;92(4S Suppl 2):S87-S90
- Koga H, et al. Long-term Follow-up of Longitudinal Melanonychia in Children and Adolescents Using an Objective Discrimination Index. Acta Derm Venereol. 2016 Jun 15;96(5):716-7.
- Ríos-Viñuela E, et al. Subungual Melanocytic Lesions in Pediatric Patients. Actas Dermosifiliogr. 2022 Apr;113(4):388-400

Trachyonychia in pediatric patients

Speaker: Maria Sol Dia (Argentina)

Definition & Epidemiology

- **Trachyonychia** ("rough nails") derives from *trachys* (rough) and affects the nail surface.
- Can affect **1 to all 20 nails**, with variable severity per nail.

- Not a distinct disease but rather the **clinical manifestation of inflammation** involving the nail matrix.
- Predominantly a **pediatric condition**, typically presenting between **ages 3 to 12**.
- **More frequent in males** in children; **female predominance** in adult-onset cases.

Etiology & Associations

Two clinical contexts:

- **Idiopathic trachyonychia** (most common in isolated nail cases)
- **Associated trachyonychia** (linked to dermatological or systemic diseases)

Dermatologic associations:

- Alopecia areata (most common)
- Lichen planus
- Psoriasis
- Atopic dermatitis
- Vitiligo
- Ichthyosis vulgaris
- Incontinentia pigmenti
- Ectodermal dysplasia
- Congenital trachyonychia

Systemic associations:

- Down syndrome
- Sarcoidosis
- Immunodeficiency syndromes

Clinical Subtypes

Subtype	Description
Opaque Trachyonychia 	Most common and severe. Nails appear **rough**, **thin**, with **longitudinal ridging**, and **loss of shine**.
Shiny Trachyonychia 	Intermittent inflammation with **glassy appearance**, **light reflection**, and **fine ridging**.

Common findings in both types:

- **Cuticular hyperkeratosis**
- **Nail pitting**
- **Onychoschizia** (splitting)
- **Onychorrhexis** (longitudinal ridging)

Evaluation & Diagnosis

Clinical Approach:

- **History:** family and personal history of skin, nail, or autoimmune disorders
- **Physical exam:** inspect **nails**, **hair**, **skin**, **oral mucosa**

Tools:

- **Dermoscopy (onychoscopy):** enhances diagnosis, avoids unnecessary biopsies
- **Mycological tests** (to rule out onychomycosis)

Biopsy:

- **Not routinely indicated** due to risk of scarring and infection
- Reserved for **severe**, **recalcitrant**, or **ambiguous cases**

Management & Treatment

Approach	Indication
Observation	Most pediatric cases resolve spontaneously within 6 years
Topical treatments	Cosmetic concern or associated dermatoses
Intralesional corticosteroids	Refractory localized disease (painful, may be distressing)
Systemic therapy	Severe or associated with psoriasis, alopecia areata, etc.

Common topical agents:

- Calcipotriol
- Topical corticosteroids
- Tacrolimus

Systemic agents in severe/associated cases:

- Methotrexate
- Cyclosporine
- Acitretin (rarely)

Clinical Cases

⇨ Case 1:

5-year-old boy with progressive nail roughness, previously treated with various topicals without improvement.

- No underlying dermatoses
- Final diagnosis: **Idiopathic trachyonychia**
- Treatment: Calcipotriol and corticosteroids for 10 months — **no improvement**
- **Spontaneous resolution** noted two years later

⇨ Case 2:

4-year-old girl with a history of **atopic dermatitis**

- Nail roughness, cuticular hyperkeratosis, and pitting
- Treated with **calcipotriol + topical corticosteroids**
- **Marked improvement** within 4 months

Key Takeaways

- Trachyonychia is **usually idiopathic** and **self-limited** in children
- Always evaluate for **associated skin or systemic conditions**
- **Treatment is often not necessary**; reassurance and follow-up are key
- **Biopsies are discouraged** unless diagnosis is uncertain
- **Set expectations early** — cosmetic recovery can take **months to years**

References:

- Chernoff KA, et al. Nail disorders: Kids are not just little people. Clin Dermatol. 2016 Nov-Dec;34(6):736-741.
- Gordon KA, et al. Trachyonychia: a comprehensive review. Indian J Dermatol Venereol Leprol. 2011 Nov-Dec;77(6):640-5
- Haber JS, et al. Trachyonychia: Review and Update on Clinical Aspects, Histology, and Therapy. Skin Appendage Disord. 2017 Jan;2(3-4):109-115
- Lim S, et al. Dermoscopic Evaluation of Inflammatory Nail Disorders and Their Mimics. Acta Dermato-Venereologica. 2021; 101(9), adv00548
- Starace M, et al. Trachyonychia: a retrospective study of 122 patients in a period of 30 years. J Eur Acad Dermatol Venereol. 2020 Apr;34(4):880-884.

- Pradhan S, et al. Trachyonychia in Children: A Comprehensive Review with Recent Updates. Indian Journal of Paediatric Dermatology:2024: 25(2):88-93

Congenital/Inherited nail deformities

Speaker: Lourdes Navarro Campoamor (Spain)

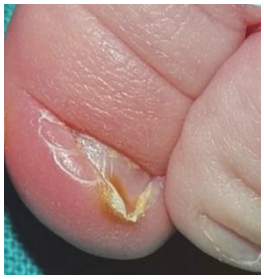
Key Concepts Presented

Diagnostic Importance of Nails in Children

- Nail abnormalities can be **early diagnostic clues**.
- Nails may be the **first or only sign** of certain systemic or congenital diseases.
- Close **clinical observation** is key, particularly in subtle or underdiagnosed conditions.

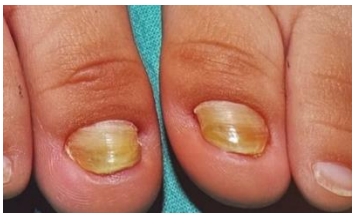
Congenital Nail Abnormalities

Congenital hypertrophy of the lateral nail fold



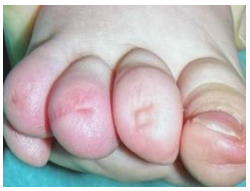
- Involves abnormal interaction between the nail plate and surrounding soft tissues.
- Often asymptomatic but may present with distal inflammation and excessive nail growth.
- Nails typically show a trapezoidal shape.

Congenital malalignment of the toenail



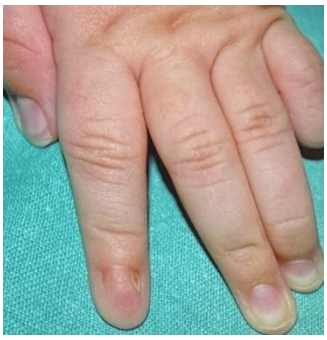
- Defined by lateral dislocation of the nail plate due to improper alignment.
- Clinical features include trapezoidal nail plate, transverse grooves, chromonychia (brown, white, green), and onycholysis.
- Pathogenesis is unclear, but spontaneous realignment occurs in about 50% of cases.

Congenital anonychia



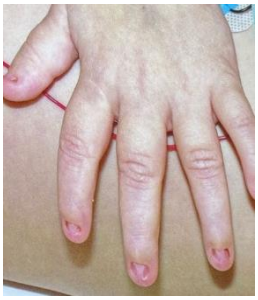
- Partial (Gene mutation of WNT pathway) or total absence of nails
- Non-Syndromic
  Syndromic: Nail patella Sme, Cooks Sme, Hypohidrotic ectodermal dysplasia

Iso-Kikuchi Syndrome



- A rare congenital nail dystrophy usually affects one or both index fingers.
- Most frequently presents as micronychia, with variable nail morphology.
- Pathogenesis:
  - Drugs during pregnancy
  - Ischemic events
  - Mesodermal malformations
  - Variants Wnt pathway

Genetic/Syndromic Nail Disorders

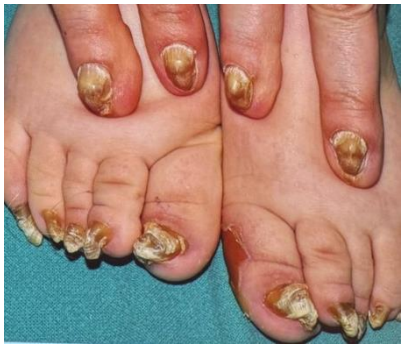


Nail-Patella Syndrome

- **Inheritance**: Autosomal dominant/De novo variants 12%
- **Gene Involvement**: LMX1B gene
- **Classic Tetrad:**
  - Pattelar and elbow dysplasia
  - Posterior iliac horns
  - Nail dysplasia (95%): bilateral symmetrical, ulnar side, triangular lunula, swan necking, micronychia, anonychia
  - Others:
    - ≈ Renal involvement
    - ≈ Eyes (glaucoma, microcornea, congenital cataract)
- **Clinical Recommendations**:

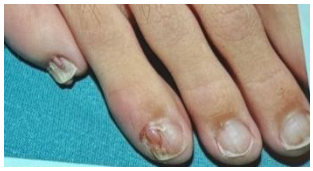
        - Clinical + radiographic exam
        - Anual Screening for renal disease and glaucoma

Pachyonychia Congenita



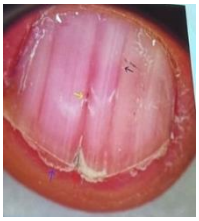
- **Inheritance**: Autosomal dominant/De novo variants 30%
- **Gene Involvement**: KRT6/16/17
- **Classic Triad:**
    - Focal palmoplantar keratoderma
    - Hypertrophic nail dystrophy
    - Plantar pain
- **Treatment:**
    - Conservative: Topical (Urea 40% - Salicylic or Lactic Acid)
    - Systemic retinoids, analgesic, botulinum toxin A, mTOR/EGFR inhibitors, Statins,

Tuberous Sclerosis Complex



- **Ungual fibromas (Koenen tumors) – 15-50%**
    - Major diagnostic criterion
    - Toenails, longitudinal nail grooves

Darier Disease



- **Nail changes (95%)**
    - Longitudinal red/white streaks, distal wedge-shaped subungual keratosis, V shaped notch

Important Diagnostic Notes

Melanonychia & Fibromas

- **Ungual fibromas** are frequently observed (50–52% of cases in some cohorts)

- **Melanonychia** (brown/black discoloration) may or may not be associated with fibromas
- **Asymptomatic melanonychia** should not be ignored, particularly in pediatrics

Summary Table: Common Nail Findings in Pediatric Disorders

Finding	Possible Associated Conditions
Triangular lúnula	Nail Patella Syndrome
Micronychia	Iso-Kikuchi, Nail Patella Syndrome
Anonychia/ Micronychia index fingers	Iso-Kikuchi
Thickened toenails	Pachyonychia congenita
Periungual fibromas	Tuberous sclerosis complex
Longitudinal red/white streaks, distal wedge-shaped subungual keratosis, V shaped notch	Darier disease

Closing Remarks from Speaker

- Many nail disorders in pediatrics are **underdiagnosed**.
- Nails can reflect **early developmental abnormalities** or **systemic conditions**.
- Clinical suspicion and knowledge of these entities aid in **early diagnosis and management**.

References:

- Peña-López S, et al. Iso-Kikuchi syndrome with Y-shaped bifurcation of the distal phalanx of the index fingers. J Dtsch Dermatol Ges. 2020 Oct;18(10):1173-1174
- Tognetti L, et al. A novel mutation in LMX1B gene in a newborn with nail-patella syndrome: Clinical and dermoscopic findings. Pediatr Dermatol. 2020 Nov;37(6):1205-1206
- Curtis KL, et al. Pachyonychia congenita: Spectrum of cutaneous disease. J Am Acad Dermatol. 2024 Nov;91(5):1021-1025

Shared decision-making in pediatric dermatology

Speaker: Kelly Cordoro (USA)

- Definition & Core Idea:
  - A collaborative care model involving clinicians, patients, and in pediatrics, caregivers.
  - Integrates medical evidence with patient and family preferences.
  - Especially useful for complex or preference-sensitive conditions (e.g., psoriasis, alopecia areata, vitiligo).
- Importance:
  - Improves patient knowledge, satisfaction, and treatment adherence.
  - Recognized as a measure of high-quality care

Shared Decision-Making vs Other Models

- Paternalistic: Doctor decides, patient complies.
- Informed: Doctor informs, patient decides.
- Shared: Iterative, two-way; both doctor and patient contribute.

When to Use It

- Best suited for conditions with:
  - Multiple viable options.
  - High emotional/psychosocial burden.
  - Uncertain outcomes or complex management (e.g., visible diseases).
- Less relevant when one clear, low-risk, high-reward treatment is obvious.

Unique Pediatric Aspects

- Minors lack full autonomy — decisions involve caregivers.
- Considerations include:

    - Cultural factors.
    - Caregiver anxiety or overprotection.
    - Patient's developmental stage and maturity.
- Empowering children fosters autonomy and prepares them for transition to adult care.

Adolescents: Special Considerations

- Their **brain development** influences decision-making (risk-seeking, impulsivity, peer influence).
- Capacity to decide varies greatly — some 14-year-olds are more mature than 18-year-olds.
- **Visible conditions** (e.g., acne, alopecia) carry strong psychosocial burdens that may prompt impulsive choices.

Clinician Challenges

- Knowing **when** to initiate a shared decision process.
- Effective **communication** across cultures and literacy levels.
- Checking personal **biases** and judgment.
- Managing **time constraints** in busy clinics.

Key Steps in the Process

1. **Share** clear, jargon-free information. Use plain language and "teach-back" techniques to assess understanding.
2. **Solicit** the family's goals, beliefs, fears, and logistical realities (e.g., travel, access, cost).
3. **Invite** collaboration: "There are many reasonable options — let's find what fits best for you."
4. **Check back** often. Allow time for reflection. Normalize the idea that decisions may change.

Tips & Insights

- Always **include the patient**
- Start visits by **addressing the child** first — give them a voice.

- Avoid rushing; patients should feel safe to **reflect, ask questions, and even change their mind**.
- Be aware of **industry influence** — newer ≠ always better.
- Frame options thoughtfully but remain aware of **clinician biases**.

Final Takeaway

- Shared decision-making leads to:
    - Better patient outcomes.
    - Improved communication and trust.
    - More personalized, patient-centered care.
- **Under-treatment** of pediatric patients is common — shared decision-making helps strike the right balance between avoiding overtreatment and addressing unmet needs, especially for visible, high-impact conditions.

Pediatric photodermatoses

Speaker: Henry W. Lim (USA)

Understanding Photodermatoses

Photodermatoses are skin disorders caused or aggravated by sunlight. Categories:

1. Immunologically mediated photodermatoses
2. Drug and chemical-induced photodermatoses
3. Genodermatoses with photosensitivity
4. Photo-aggravated dermatoses

Focus on:

- **Immunologically mediated photodermatoses**
- **Cutaneous porphyrias (under drug/chemical-induced)**

1. Polymorphous Light Eruption (PMLE)

- **Prevalence:** Most common idiopathic photodermatosis; affects 10–15% of healthy individuals.

- **Demographics:** Occurs in both children and adults; more commonly in teenagers.

Clinical Features:

- Papular eruptions (sometimes vesicular)
    - Appearing hours to a day after sun exposure.
    - Typically resolves within days.
- In dark-skinned individuals presents as small papules resembling goosebumps.

Variants:

- **Juvenile Spring Eruption:** Rare; vesicular eruption localized to ears after early spring sun exposure — often misdiagnosed.

Diagnosis:

- Primarily clinical (history and morphology).
- Phototesting is often normal.

Pathophysiology:

- **Immune activation** and skin lesions post-UV exposure.

Management:

- **Photoprotection:** Sunscreen, sun avoidance, protective clothing.
- **Phototherapy (narrowband UVB):** For resistant cases — induces hardening.
- **Short-course prednisone:** In severe, acute flares.

2. Actinic Prurigo

- **Demographics:** Frequently familial, associated with Amerindian ancestry, especially in Latin America.
- **Onset:** Childhood or adolescence.
- **Clinical Signs:**
    - Papular eruptions on sun-exposed areas, cheilitis, conjunctivitis, and photophobia.
- **Differentiators: Eyelid dermatitis and chronic lip** involvement are hallmark features.

- **Triggers:** High-altitude or intense sun exposure.

Treatment:

- Strict photoprotection.
- Topical/oral corticosteroids during flares.
- Thalidomide (effective but limited by availability and teratogenicity).
- Dupilumab and UVB hardening — under exploration.

3. Hydroa Vacciniforme (HV) & HV-like Lymphoproliferative Disease

	Classical Hydroa Vacciniforme (HV)	HV-like Lymphoproliferative Disease
Frequency	Rare	Severe variant
Age of Onset	Childhood	Childhood or adolescence
Skin Lesions	Papulovesicular eruptions healing with vacciniform scars	Lesions on sun-exposed and non-exposed areas
Systemic Symptoms	Absent	Facial edema, fever, lymphadenopathy
Association with EBV	Strong	Present
Photosensitivity	May show UVA sensitivity on phototesting	Not specifically reported
Prognosis	Variable, treatment is challenging	Risk of progression to lymphoma
Main Treatment	Photoprotection	Onco-hematological management

4. Solar Urticaria

- **Onset:** Can begin in childhood.
- **Trigger Spectrum:** UVB, UVA, visible light.
- **Rapid Onset:** Wheals within minutes of sun exposure.

- **Phototesting:** May be negative — lesions can resolve within 30–60 minutes.

Clinical Tip:
Always evaluate patients **immediately** post-exposure/testing — waiting 24 hours can miss the diagnosis.

Treatment:

- **First-line:** Photoprotection, antihistamines.
- **Biologic: Omalizumab** – highly effective; used seasonally in some centers.
- Safe for use in children under pediatric guidance.

5. Erythropoietic Protoporphyria (EPP) & X-linked Protoporphyria (XLP)

Pathophysiology:

- **EPP:** Ferrochelatase deficiency → buildup of protoporphyrin IX.
- **XLP:** Gain-of-function mutation in ALAS2 → excess precursor production.
- **Result:** Phototoxic reactions due to accumulated protoporphyrin.

Clinical Clues:

- **Subtle scarring:** Fine lines on the bridge of the nose or knuckles.
- **Severe phototoxic episodes:** Purpura and pain on sun exposure.

Recent Advances in EPP/XLP Treatment

1. **Afamelanotide**
    - **Mechanism:** α-MSH analogue that boosts melanin production.
    - **Delivery:** Subcutaneous every 2 months.
    - **Outcome:** Increases sun tolerance, improves quality of life.
    - **Status:** FDA and EMA approved.
2. **Dersimelagon**
    - **Mechanism:** Oral selective MC1R agonist.
    - **Advantages:** Easier to administer than implants.

- **Clinical trials ongoing** in patients aged 12+.
- **Preliminary Results:** Promising sun tolerance improvement after 7–8 weeks.

3. **Bitopertin**
   - **Mechanism:** Oral glycine transporter-1 inhibitor — limits substrate for heme synthesis.
   - **Status:** Ongoing trials in pediatric patients (12+).

Rationale: Blocks porphyrin accumulation upstream in the pathway.

Table: Pediatric Photodermatoses Overview

Condition / Type	Typical Age of Onset	Clinical Morphology	Diagnosis	Treatment / Management	Key Points
Polymorphous Light Eruption (PMLE)	Children, adolescents (more common in teens)	Papules, vesicles; morphology varies with skin phototype	Clinical (based on history and morphology); phototesting often normal	Photoprotection, topical corticosteroids, narrowband UVB, oral prednisone (for flares)	Delayed onset post-sun exposure; improves with progressive sun exposure ("hardening")
Actinic Prurigo	Childhood	Cheilitis, conjunctivitis, lichenified papules on sun-exposed skin	Clinical evaluation	Photoprotection, topical/oral corticosteroids, thalidomide, UVB, dupilumab (experimental)	Latin America; intense sun exposure
Classic Hydroa Vacciniforme (HV)	Children	Papules, vesicles, crusting; vacciniform scarring	Clinical, EBV association possible	Photoprotection, symptomatic care	Permanent scarring; severe phototoxic response
HV-like Lymphoproliferative Disease	Children and adolescents	HV-like lesions on both sun-exposed and	Clinical + biopsy + hematologic	Oncology referral, close monitoring	May progress to lymphoma (~10%); high mortality

Condition / Type	Typical Age of Onset	Clinical Morphology	Diagnosis	Treatment / Management	Key Points
		non-exposed skin; facial edema, fever, lymphadenopathy			(~40%); more severe in Latin America
Solar Urticaria	Children, adolescents, adults	Wheals in sun-exposed areas; rapid onset (minutes)	Clinical + immediate post-exposure evaluation	Antihistamines, omalizumab, photoprotection	Triggered even by visible light; resolves quickly but recurs with re-exposure
Erythropoietic Protoporphyria (EPP / XLP)	Early childhood	Pain, burning, erythema shortly after sun exposure; chronic changes on knuckles and face	Elevated protoporphyrin IX levels; genetic testing	Afamelanotide (implant), Derzimegalone (oral), glycine transporter inhibitors (in trials), photoprotection	Major therapeutic advances; improves quality of life significantly

Final Thoughts

- Pediatric photodermatoses, though relatively uncommon, can significantly affect **quality of life.**
- Advances in understanding pathophysiology — particularly **immunologic and genetic** mechanisms — are opening new doors in diagnostics and therapy.
- For conditions like EPP and solar urticaria, targeted treatments such as **Afamelanotide and Omalizumab** are making real-world impacts.

References:

- Choi D, et al. Evaluation of patients with photodermatoses. Dermatol Clin. 2014 Jul;32(3):267-75
- Gruber-Wackernagel A, et al. Polymorphous light eruption: clinic aspects and pathogenesis. Dermatol Clin. 2014; 32(3): 315-334
- Dawe RS, et al. Prolonged benefit following ultraviolet A phototherapy for solar urticaria. BJD. 1997; 137(1):144–148
- Balwani M, et al. Dersimelagon en protoporfirias eritropoyéticas. NEJM. 2023;388:1376 – 1385

Congenital melanocytic naevi

Speckled lentiginous nevus as a subtype of congenital nevus

Speaker: Jean Bologna (USA)

Terminology & Historical Perspective

Term Used	Notes
Speckled Lentiginous Nevus (SLN)	Preferred by some clinicians; emphasizes clinical pattern.
Nevus Spilus	More commonly used in literature (PubMed ratio 2:1); literally means “stained spot.”
Other terms	Excessive terminology noted; need for standardization emphasized.

Morphology & Clinical Course

Feature	Description
Size	Typically 3–4 cm in diameter
Base	Café-au-lait macule-like background
Overlay	Lentigines, junctional nevi, compound nevi
Evolution	More "dots" appear with age; may initially be subtle at birth
Distribution Patterns	May follow **Blaschko's lines** or **block-like** patterns; not always checkerboard

Evolution of SLN

- Lesions can be **macular** or **papular** (discouraged to describe them using analogies like "starry map"  or "polka dots" ).
- Lesions often evolve, becoming more prominent in childhood or adolescence.

- Some lesions may exhibit regional darkening or the development of new pigmented areas, occasionally concerning enough to warrant biopsy.
- SLN is viewed as a **"garden of melanocytes"**, capable of generating a broad spectrum of melanocytic proliferations:
    - Spitz nevi
    - Blue nevi
    - Congenital melanocytic nevi (CMN)
    - Melanoma
- SLN lesions can exhibit **hypertrichosis** or regression over time.
- Some lesions demonstrate **satellite nevi**.

Syndromic and Clinical Associations

Syndrome/Entity	Association with SLN
PPK (Phacomatosis pigmentokeratotica)	Papular SLN
PPV (Phacomatosis pigmentovascularis)	Macular SLN
Neurocutaneous melanocytosis	Can occur in patients with medium-sized CMN arising within SLN
Rhabdomyosarcoma	Reported in a patient with Spitz nevi within SLN (rare)
Noonan syndrome (RASopathies)	Mentioned as having overlapping features

SLN: Congenital vs. Acquired Debate

Argument	Evidence
Congenital lesion	Lesions follow embryological patterns (e.g., Blaschko's lines); hybrid presentations support this. Evidence supports **congenital origin**

Argument	Evidence
Apparent "acquisition"	Hypopigmented base may be subtle at birth; speckling appears later, leading to misclassification

Clinical Implications for Pediatric Dermatology

- SLN is relatively **common**, with most presenting as small café-au-lait macules with lentigines or nevi.
- **Atypical presentations** (larger lesions, papular morphology, multiple superimposed nevi).
- **Melanoma risk**, though low, is **real** and merits long-term monitoring:
    - Clinical features to monitor: lesion size, number/type of naevi, sun exposure, presence of atypical features
    - Histological evaluation and **biopsy** warranted for concerning features

Conclusion

- SLN is best conceptualized as a **congenital melanocytic disorder** with a spectrum of clinical behavior.
- Requires **vigilant clinical follow-up**
- Pediatric dermatologists should be **prepared to identify**, **monitor**, and **educate** families about the potential risks and need for follow-up.

References:

- Happle R. Speckled lentiginous naevus: which of the two disorders do you mean? Clin Exp Dermatol. 2009;34(2):133-5
- Torchia D, et al. Papular nevus spilus syndrome: old and new aspects of a mosaic RASopathy. Eur J Dermatol. 2019 Feb 1;29(1):2-5
- Torchia D. On the patterns of distribution of segmental nevi of melanocytic origin. Indian J Dermatol. 2012 Sep;57(5):414-5
- Sarin KY, et al. Activación de la mutación *HRAS* en nevos de Spitz agminados que surgen en un nevo de Spitz. JAMA Dermatol. 2013;149(9):1077–1081.
- Nemeth K, et al. Mosaic pathogenic HRAS variant in a patient with nevus spilus with agminated Spitz nevi and parametrial-uterine rhabdomyosarcoma. Br J Dermatol. 2018;178(3):804-806
- Kinsler VA. Multiple Congenital Melanocytic Nevi and Neurocutaneous Melanosis Are Caused by Postzygotic Mutations in Codon 61 of NRAS. JID.2013;133, 2229–2236

- Kinsler VA, et al. Next-generation sequencing of nevus spilus-type congenital melanocytic nevus: exquisite genotype-phenotype correlation in mosaic RASopathies. J Invest Dermatol. 2014;134(10):2658-2660
- Berna R, et al. Significant improvement of a nevus spilus-type congenital melanocytic nevus with oral selumetinib. Pediatr Dermatol. 2024;41(5):936-937

General aspects of congenital naevi

Speaker: Aniza Giacaman Contreras (Spain)

Dermoscopic Evaluation of Congenital Melanocytic Nevi (CMN)

- Congenital melanocytic nevi (CMN) present variably in pediatric patients.
- While most are benign, some may mimic melanoma, leading to unnecessary biopsies.
- Dermoscopy enhances diagnostic accuracy by helping clinicians identify key features and patterns based on the lesion's location.

Dermoscopic Structures in CMN

Structure	Description
Dots	Small pinpoint areas of pigmentation.
Globules	Larger than dots, may vary in shape; correspond to melanocytic nests.
Lines	Can form distinct dermoscopic patterns such as networks or branches.
Pigmented Network	Reflects melanin in keratinocytes at the dermoepidermal junction.
Cobblestone Pattern	Globules clustered in a mosaic-like pattern, commonly seen in CMN.
Target Structures	Globules within a network with central dots; may suggest melanocyte apoptosis.
Blue/Gray Dots	Indicate melanocyte apoptosis or dermal involvement.

Structure	Description
Vessels	Presence may vary by lesion evolution; can include coarse vessels.
Hypertrichosis	Often associated with congenital nevi, increasing with age.

Dermoscopic Pattern by Body Location

Location	Common Patterns
Head	Homogeneous pattern
Trunk	Predominantly globular pattern
Extremities	Reticular or mixed globular-reticular pattern
Palms/soles	Parallel ridge or furrow patterns, “peas-in-a-pod” appearance

Case Highlights and Pattern Variability

Classic Globular Pattern

- Frequently seen in neonates.
- Peripheral globules with denser clusters centrally.
- May raise concern due to clinical appearance but usually benign.
- Over time: Increase in lesion size, surface hair growth, and cobblestone arrangement.

Mixed Network and Globules

- Presence of both fine pigment network and globules.
- Hypopigmented halo around terminal hairs may be observed.
- Papular areas can appear within otherwise flat lesions.

Changes Over Time

- Others **increase** in size or develop **new surface features**
- **Regression** or **spontaneous lightening** is common and usually benign.

Special Locations

Acral Areas (Palms, Soles)

- Patterns include:
  - Parallel furrow or ridge pattern.
  - “Peas-in-a-pod” pattern.
  - Homogeneous light brown pigmentation.
  - Regression without intervention.

Nail Matrix Involvement

- Findings:
  - Longitudinal melanonychia at birth.
  - Homogeneous brown/black pattern.
  - May show pseudo-Hutchinson sign and fibrillar pigmentation.
- Management:
  - No immediate biopsy unless alarming changes are present.
  - Longitudinal monitoring is recommended in pediatric patients.

Nodular Components in CMN

Scenario	Clinical Course
Nodules stable over years	Often benign if no suspicious dermoscopic features are present.
Cobblestone globules without atypia	Favor benign course; continued monitoring recommended.
Nodules with blue coloration	May raise concern; histology may still be benign.
Rapidly growing nodules in short time	Biopsy warranted to rule out malignancy (e.g., atypical Spitz tumor).

Melanoma Considerations in Pediatrics

- Rare, but possible within CMN.

- May lack classic melanoma dermoscopic criteria.
- **"Pink is the new black"**: Subtle vascular features (e.g., hemorrhagic bands) should raise suspicion.
- Any concern mandates prompt excision.

Key Takeaways

- **Follow-Up Strategy**: Safe if lesion has **benign dermoscopic signs** and no suspicion for melanoma.
- **Excision**: Should not be delayed if melanoma is suspected.
- **Cosmetic Outcome**: Predicting long-term appearance is unreliable; families should be counseled cautiously.
- **Clinical Relevance**:
    - Most lesions are benign but require pattern recognition and longitudinal observation.

Final Notes

- CMN lesions **can be dynamic**, showing growth, fading, or evolution over time.
- **Dermoscopy** is critical in guiding monitoring vs. intervention decisions.
- Accurate assessment **minimizes** unnecessary **biopsies** and **anxiety**.

References:

- Kittler H, et al. Revised version of pattern analysis. In book: An Atlas of Dermoscopy, 2nd Edition (pp.138-146).
- Marghoob. Congenital melanocytic nevi. Dermatologic Clinics. 2002;20(4): 607 – 616
- Stefanaki C, et al. Clinical and dermoscopic characteristics of congenital melanocytic naevi. JEADV. 2018; 32:10: 1674-1680
- Haliasos EC, et al. Dermoscopy for the pediatric dermatologist part III: dermoscopy of melanocytic lesions. Pediatr Dermatol. 2013 May-Jun;30(3):281-93
- Chuah SY, et al. Dermoscopic features of congenital acral melanocytic naevi in children: a prospective comparative and follow-up study. Br J Dermatol. 2015;172(1):88-93

- Cotton CH, et al. Evolution of congenital melanocytic nevi toward benignity: A case series. Pediatr Dermatol. 2019;36(2):227-231
- Cordoro KM, et al. Pediatric melanoma: results of a large cohort study and proposal for modified ABCD detection criteria for children. J Am Acad Dermatol. 2013;68(6):913-25
- Carrera C, et al. Clinical and dermoscopic characterization of pediatric and adolescent melanomas: Multicenter study of 52 cases. J Am Acad Dermatol. 2018;78(2):278-288

Small and medium sized congenital melanocytic naevi: evidence-based management guidelines

Speaker: Julia Schaeffer (USA)

Definitions & Classifications

Term	Definition
Congenital melanocytic nevus (CMN)	Present at birth or within the first few weeks of life
Size-based classification	Based on projected adult size: small (<1.5 cm), medium (1.5–20 cm), large (>20 cm), giant (>40 cm)
Targeted CMN / Congenital-like nevi	Lesions appearing within the first 2–3 years; histologically and molecularly similar to true congenital nevi

- **Prevalence**:
  - Small/medium CMN: 1–6% of newborns
  - Giant CMN: ~1 in 20,000–500,000 live births
- **Growth patterns**: Lesions enlarge 2x on the head and 3x on the trunk/extremities as the child grows
- **Medium-sized nevi**: Often perceived as large by families, but carry **lower risk** than giant nevi

Natural History

- **Common Evolution:**
    - Thickening and textural changes (e.g., nodularity, rugosity)
    - Fading or lightening over time, especially in scalp or acral regions
    - Regression seen in Halo nevi or poliosis-associated lesions

Dermoscopic & Clinical Features

- **Typical patterns**: Globular pattern predominates, especially on scalp and trunk.
- **Morphological characteristics:**
    - Irregular/geographic borders
    - Color heterogeneity
    - Papules, rugosity, nodules

Common Dermoscopic Patterns by Location

Scalp	⇨ Fading more likely, particularly in the first 1–4 years
Trunk	⇨ Globular or reticular patterns common
Acral	⇨ Parallel, fibrillar, or "peas in a pod" patterns
Nails	⇨ Distal fibrillar pattern and longitudinal melanonychia noted

- **Microscopically**: Congenital and congenital-like nevi share molecular features (e.g., NRAS mutations)

Dermoscopic Features

Feature	Interpretation
Globular pattern	Typical of CMN; benign feature
Reticular/blue-gray globules	Seen in deeper melanocyte proliferation; not always concerning

Feature	Interpretation
Target globules	Globules within network; associated with melanocytic activity
Fibrillar brush pattern (nails)	Common in children; benign
Vascular features	Can appear over time; not always suggestive of melanoma

Melanoma Risk in Small/Medium CMN

Risk Estimate	Evidence
< 0.5–1% lifetime risk	Systematic reviews & cohort data (e.g., 15-year risk: ~0.007%)
Melanoma onset	Typically post-pubertal; rare in early childhood

- Families often **overestimate** cancer risk (60% report high concern pre-consultation)
- Education significantly reduces anxiety (post-consultation concern dropped to 7%)

Management Strategies

Clinical Monitoring

- **Preferred approach** for most small/medium CMN
- Emphasize **focal change** over global lesion changes
- Regular photography and dermoscopy to assess evolution

Indications for Excision

Indication	Reason
Cosmetic/psychosocial	Most common modern indication, especially facial lesions

Indication	Reason
Functional concerns	Lesions near joints, eyelids, etc.
Changes suggestive of malignancy	Focal color, texture, or vascular changes
Parental anxiety	When psychological impact is high and persistent

Excision Techniques

- **Staged excision** and **full-thickness skin grafts** for facial nevi
- **Risks**: Permanent scarring, surgical morbidity

Laser Therapy

- May lighten pigmentation but **does not eliminate nevus cells**
- Often followed by recurrence

Topical therapies

- Experimental; kinase inhibitors under investigation

Timing of Excision:

  - Ideally before age 4–5 for facial lesions to minimize long-term psychosocial impact.
  - Delay removal if lesion is not bothersome or if scar would be more disfiguring.

Special Considerations

Lesion Type	Management Note
Halo Nevi	Benign
Nodular components	Require thorough history and monitoring
Scalp lesions	Tends to fade
Acral/Nail lesions	Recognize benign dermoscopic patterns

- No intervention needed unless atypical features present
- Avoid premature biopsy
- Biopsy only if concerned

Final Thoughts

- **Prophylactic excision is not routinely recommended** for small/medium CMN. **Melanoma** risk is **extremely low.**
- Small and medium CMN are **common**, mostly **benign**, and often **regress or lighten**
- **Shared decision-making is essential**: balance clinical risk, cosmetic impact, and family values
- Watch for **focal, evolving changes**, not just overall nevus appearance

References:

- Kanada KN, et al. A prospective study of cutaneous findings in newborns in the United States: correlation with race, ethnicity, and gestational status using updated classification and nomenclature. J Pediatr. 2012;161(2):240-245
- Pastore LM, et al. Congenital melanocytic nevi and risk of melanoma. Clin Dermatol. 2024 18:S0738-081X(24)00173-1.
- Stinco G, et al. Absence of clinical and dermoscopic differences between congenital and noncongenital melanocytic naevi in a cohort of 2-year-old children. Br J Dermatol. 2011;165(6):1303-7.
- Scope A, et al. Dermoscopic patterns of naevi in fifth grade children of the Framingham school system. Br J Dermatol. 2008;158(5):1041-9
- Pham F, et al. Dermatoscopic and clinical features of congenital or congenital-type nail matrix nevi: A multicenter prospective cohort study by the International Dermoscopy Society. JAAD. 2022;87(3):551-558

Dermoscopy for naevus monitoring: a practical approach

Speaker: Fatima Giusti (Argentina)

Introduction

The speaker presented their experience with digital dermoscopy in pediatric dermatology, emphasizing the need for well-defined clinical indications. The

presentation was based on a retrospective study conducted at a tertiary hospital with expertise in both digital dermoscopy and pediatric care.

Background

- While handheld dermoscopy is routinely used in evaluating congenital melanocytic nevi (CMN), the role of digital dermoscopy in children remains underdefined.
- The study was motivated by a high volume of pediatric referrals for digital dermoscopy and aimed to:
    - Analyze clinical profiles of referred patients.
    - Correlate findings with existing literature.
    - Propose practical, evidence-based indications for digital dermoscopy in children.

Study Design

- System: PhotoFinder
- Inclusion criteria: Patients ≤16 years.
- Data collected:
    - Age, sex, Fitzpatrick skin type.
    - Follow-up frequency.
    - Personal/family history of skin cancer.
    - Reason for digital dermoscopy.
    - Predominant dermoscopic pattern.
    - Excision and histopathology (if performed).
- Sample:
    - 92 patients initially identified.
    - 20 excluded due to incomplete data.
    - Final cohort: 72 pediatric patients.

Key Findings

Demographics & Skin Type

- Sex: 54% male, 46% female.
- Mean age: 9 years (range 1–16).
- Fitzpatrick Type III: Present in ~70%.

Follow-up & Usage

- Single session: Most common.
- ≥2 follow-ups: 31%, suggesting limited use of serial monitoring.

Risk Factors & Clinical Syndromes

- Family history of skin cancer: ~50%.
    - Melanoma: ~25% of patients.
- Syndromes identified:
    - Atypical mole syndrome: 44%.
    - Familial atypical mole syndrome: 5.5%.
    - Personal history of melanoma: 9.6%.

Notably, the prevalence of atypical mole syndrome was significantly higher than in published pediatric cohorts, suggesting potential benefit from structured digital follow-up.

Dermoscopic Patterns

- Globular pattern: Most common (as expected in children).
- Mixed/multiple patterns: Frequently observed, correlating with high prevalence of atypical mole syndrome.

Indications for Digital Dermoscopy

- >50% of cases: Referral for nevus (nevi) monitoring.
- Other indications:
    - Multiple nevi.
    - Medium CMN.
    - Special locations.
    - Giant CMN.

Excision & Histopathology

- No excision required: 74% of cases.
- Diagnosed conditions:
    - Melanoma.
    - Dysplastic nevi.

Findings support the role of **digital dermoscopy** in **avoiding unnecessary surgery** while still identifying clinically significant lesions.

Nevus Count

- >50 nevi: One-third of patients.

Genetic Conditions

- Example: One patient with Noonan syndrome developed melanoma during follow-up.

Proposed Indications for Digital Dermoscopy in Pediatric Patients

- >60 melanocytic nevi (from puberty onward)
- >50 nevi + red hair or MC1R mutation (from puberty onward)
- >40 nevi + family history of melanoma (1st/2nd degree relatives)
- Atypical mole síndrome
- Medium congenital melanocytic nevi (CMN)
- Giant CMN with satellitosis
- Known high-risk genetic mutations for melanoma
- Genodermatoses with melanoma risk
- Congenital or acquired immunosuppression

Conclusions

- This is the first study to propose specific clinical indications for digital dermoscopy in pediatric patients, grounded in structured, real-world data.
- Further research is necessary to validate and refine these proposed guidelines

References:

- NCCN Guidelines Version 2.2025. Melanoma: cutaneous

Updates on the risk of melanoma and neurocutaneous melanosis in giant congenital melanocytic naevi

Speaker: Elena Hawryluk (USA)

Introduction

- **Melanoma risk**s primary parental concern.
- **Neurocutaneous melanosis** — identification of high-risk patients for early CNS imaging and prognosis discussion.
- **Nevus evolution and management options** — including visual impact, potential morbidity of excision, and realistic treatment expectations.

Melanoma Risk by CMN Size

Size Category	Lifetime Melanoma Risk
Small/Medium CMN	<1% Risk mostly post-puberty
Large CMN	~2%
Giant CMN with satellites	6–15% Highest risk group

- Risk stratification is based on **projected adult size**, with enlargement factors used to classify early measurements.

- Melanoma may arise in the **skin, CNS, or visceral organs**, and cutaneous presentations often involve **rapid evolution**.
- Biopsy is recommended when significant changes are observed or when uncertainty persists after short-interval follow-up.

Neurocutaneous Melanosis (NCM)

Definition & Risk:

- **Neurocutaneous melanocytosis**, involves **melanocytes in the meninges**.
- Often **asymptomatic** but associated with an **increased melanoma risk** when CNS involvement is present.

Imaging Strategy:

- **MRI before 6 months of age** recommended in high-risk patients.
  - Benefits: better visualization before myelination.
  - Imaging done **without contrast**.
- **Key paper**: Kinsler et al. showed:
  - **21%** of high-risk patients (≥2 CMN) had significant MRI findings.

Who Should Be Screened with MRI?

Criteria (vary across guidelines)
>3 cm CMN or ≥25 CMN
>1 CMN regardless of size
Giant CMN, multiple medium CMN
≥4 CMN associated with abnormal CNS findings (Mass General cohort)

MRI screening guidelines remain **non-standardized** and are resource-dependent across regions. Shared decision-making with parents is critical.

Case: Symptom-Directed Imaging

- **Patient**: 10-year-old boy with small/medium CMN; previously asymptomatic.
- **Symptoms**: Headache, vomiting, esotropia, papilledema.
- **MRI Findings**:
    - Hemorrhagic frontal-temporal lesions.
    - Leptomeningeal dissemination.
- **Diagnosis**: **Melanoma** involving the dura and brain.
- **Genetic findings**: Mutations in **NRAS, MAP2K1, CDK2A**.

Key Takeaways

- **Melanoma Risk Timing**:
    - The greatest risk for patients with **giant CMN** is during **adulthood**.
- **MRI Screening**:
    - Varies by institution and guideline.
    - Should be individualized through **shared decision-making**.
- **Imaging recommendations**:
    - **Symptom-directed imaging** is advised in older children.
    - **Early MRI** (before 3-6 months) is preferable for prognostication in high-risk neonates.
- **Monitoring strategy**:
    - **Biopsy evolving lesions**.
    - Consider short-term follow-up for uncertain changes.

References:

- Waelchli R, et al. Classification of neurological abnormalities in children with congenital melanocytic naevus syndrome identifies magnetic resonance imaging as the best predictor of clinical outcome. Br J Dermatol. 2015;173(3):739-50
- Jahnke MN, et al. Care of Congenital Melanocytic Nevi in Newborns and Infants: Review and Management Recommendations. Pediatrics. 2021;148(6):e2021051536

- Neale H, et al. Central nervous system magnetic resonance imaging abnormalities and neurologic outcomes in pediatric patients with congenital nevi: A 10-year multi-institutional retrospective study. JAAD. 2022; 87 (5): 1060-1068.
- Kinsler VA, et al. Melanoma in congenital melanocytic naevi. Br J Dermatol. 2017;176(5):1131-1143.

Update on the genetics of congenital melanocytes naevi

Speaker: Veronica Kinsler (United Kingdom)

This presentation provided an in-depth review of the genetic mechanisms underlying congenital melanocytic nevi (CMN), focusing on mosaic mutations, especially *NRAS*, *BRAF*, and *BRAF* fusion genes—and their clinical significance. The talk also explored the emerging role of targeted therapy, particularly MEK inhibitors, in treating patients with problematic CMN phenotypes.

Understanding Mosaicism in CMN

- **CMN as a mosaic disorder**: Caused by postzygotic somatic mutations during embryogenesis. These mutations occur in a single progenitor cell and are propagated in its descendants, resulting in segmental or patchy phenotypes.
- **Proof of mosaicism**:
    - Identical mutations must be found in multiple affected tissues (e.g., skin, CNS) from the same patient.
    - Recurrence in multiple patients with similar phenotypes strengthens causality.

Established Genetic Drivers in CMN

Gene	Prevalence	Mutation Type	Clinical Features
NRAS	Most common	Missense mutations	Found in skin, CNS, and tumors; consistent across tissues

Gene	Prevalence	Mutation Type	Clinical Features
BRAF	Less common	Missense mutations	Often associated with numerous soft dermal nodules
BRAF fusions	Newly recognized subgroup	Gene fusion (varied partners)	Often associated with multinodular, treatment-resistant CMN

- Each patient typically carries **one specific mutation** (e.g., a specific *NRAS* variant), confirmed across multiple tissue types, supporting clonality.
- *MC1R* (red hair gene) was investigated but **not implicated** as a primary driver in CMN.

Clinical and Phenotypic Correlations

- Initially, it was believed that genetic subtype did **not significantly affect clinical outcomes**, including neurological involvement or melanoma risk.
- More recent data suggest:
    - **BRAF missense mutations** are more frequently associated with **numerous soft, benign nodules**.
    - **BRAF fusions** are strongly associated with **severe multinodular CMN**, often difficult to treat surgically or topically.

Discovery of BRAF Fusions in CMN

- Retrospective RNA sequencing of archived tissue in *NRAS*-negative CMN cases revealed **BRAF fusions** in multiple patients.
- Key features:
    - Fusion of **BRAF kinase domain** to a variety of other genes (fusion partners differed between patients).
    - Clonality confirmed in multiple samples from the same patient.

- Detection methods included RNA sequencing and FISH (fluorescent in situ hybridization).

Clinical Features of BRAF Fusion–Positive CMN

Key Characteristics

- Multinodular growth, often extensive
- Poor response to conventional treatments
- Frequently associated with **severe itch**
- Mild female predominance (2:1)
- Histopathology may show "atypical sites"

Therapeutic Response to MEK Inhibition

- **Trametinib** (MEK inhibitor) was trialed in patients with *BRAF fusion*–positive CMN.
  - Significant **reduction in lesion thickness**, **improvement in pruritus**, and **decreased lesion activity**.
  - **Rapid onset of symptom control**, especially for **itch**.
  - Doses were tapered over time with **minimal side effects** when administered intermittently (e.g., every third day).
- In vitro studies showed:
  - BRAF fusion–positive cells did **not** overexpress *BRAF*.
  - However, **high pathway activation** (likely due to dimerization or altered signaling) was observed.
  - Trametinib suppressed this hyperactivation effectively.

Representative Case

- Published patient with *BRAF* fusion and extensive multinodular CMN:
  - Demonstrated marked clinical improvement following **trametinib treatment**.

- While **naevi were not eradicated**, significant **clinical and symptomatic benefits** were observed.
- Notable for **immediate itch relief** and improved lesion appearance.

Key Takeaways

- **Known genetic drivers of CMN**:
  - *NRAS* (most common)
  - *BRAF* (missense or fusion)
  - *KRAS*, *ALK*, and *RAF1* (rare)
- **Clinical variability** exists within each genotype, but:
  - *BRAF fusions* are most commonly associated with **severe multinodular disease**.
- **Genotyping is recommended** in cases of:
  - Melanoma
  - Extensive or treatment-resistant nodular CMN
- **Trametinib** is currently a promising off-label therapy for *BRAF fusion*–positive CMN, especially when surgical approaches are limited.

References:

- Kinsler VA, et al. Multiple congenital melanocytic nevi and neurocutaneous melanosis are caused by postzygotic mutations in codon 61 of NRAS. J Invest Dermatol. 2013;133(9):2229-36
- Papp T, et al. Mutational analysis of the N-ras, p53, p16INK4a, CDK4, and MC1R genes in human congenital melanocytic naevi. J Med Genet. 1999;36(8):610-4
- Pollock PM, et al. High frequency of BRAF mutations in nevi. Nat Genet. 2003;33(1):19-20
- Bauer J, et al. Congenital melanocytic nevi frequently harbor NRAS mutations but no BRAF mutations. J Invest Dermatol. 2007;127(1):179-82.
- Dessars B. Genotypic and Gene Expression Studies in Congenital Melanocytic Nevi: Insight into Initial Steps of Melanotumorigenesis. Journal of Investigative Dermatology. 2009; 129 (1):139-147

- Phadke PA, et al. Proliferative nodules arising within congenital melanocytic nevi: a histologic, immunohistochemical, and molecular analyses of 43 cases. Am J Surg Pathol. 2011;35(5):656-69
- Polubothu S, et al. Does the gene matter? Genotype-phenotype and genotype-outcome associations in congenital melanocytic naevi. Br J Dermatol. 2020;182(2):434-443
- Martin SB, et al. Mosaic BRAF Fusions Are a Recurrent Cause of Congenital Melanocytic Nevi Targetable by MAPK Pathway Inhibition. J Invest Dermatol. 2024;144(3):593-600.e7
- Mir A, et al. Giant Congenital Melanocytic Nevus Treated With Trametinib. Pediatrics. 2019;143(3):e20182469

Acne and rosacea

Rosacea and perioral dermatitis in children

Speaker: Marius Rademaker (New Zealand)

Key Clinical Challenges

- **Significant diagnostic overlap** exists between rosacea, perioral dermatitis, acne, seborrheic dermatitis (SD), and even atopic dermatitis (AD).
- Pediatric presentation often defies clear classification; **diagnosis** may evolve with **time** and **repeated observation**.
- There's a **lack of robust evidence**: no pediatric RCTs, no head-to-head trials, and guidelines are mostly based on expert opinion or extrapolated from adult data.

Diagnostic Pearls

	Rosacea	Perioral Dermatitis (POD)
Common Presentation	Facial erythema, flushing, papules/pustules	Papules around mouth, nose, and eyes
Flushing	Nearly universal	Usually absent
Ocular Involvement	Common (Blepharitis, conjunctivitis)	Not typical
Comedones	Absent	

	Rosacea	Perioral Dermatitis (POD)
Demodicosis	Possible	
Symptoms Description	Burning or stinging	Painful itch
Worsened by topical corticosteroids	Yes	

Common Pediatric Presentation Pitfalls

- Red cheeks can be **misinterpreted** as irritation or eczema.
- Atypical presentations often need **repeated assessment over time** to reach an accurate diagnosis.
- Phototype impacts diagnostic clarity—rosacea often harder to detect in **skin of color**.

Demographics & Epidemiology

- Equal prevalence in boys' and girls' pre-puberty. Post-pubertal rosacea is more common in girls.
- Mean age of onset: 4–5 years (literature), though often seen in older children in clinical practice.

Treatment Framework

General Principles

- Identify and attempt to eliminate **triggers** (UV, heat, stress, skincare products).
- Educate families on **"null therapy"** and simplify skincare.
- Reinforce this repeatedly; patients often resume topical products prematurely.

Topical Therapies

- First-line options:
    - **Metronidazole** (younger children)

    - **Azelaic acid** (older children)
- **Other options (less preferred):**
    - Topical ivermectin (if available)
    - Permethrin (less commonly used)
    - Calcineurin inhibitors (caution: can also exacerbate)
- Use **low-potency corticosteroids** very cautiously—only if not initial cause.
- Avoid cosmetic products in young children.

<u>Systemic Therapies</u>

Antibiotics: Use with Caution

- **Disliked** due to microbiome disruption.
- Avoid **azithromycin** unless absolutely necessary; it's too valuable systemically.
- **Doxycycline (40–50 mg/day)** for limited duration (3 months); 12+ years.

Isotretinoin (off-label)

- **Preferred oral agent** in severe/refractory cases.
- **Ultra-low dosing:**
    - 0.1 mg/kg/day target
    - **Example:**
        - 15 kg → 5 mg every 3rd day
        - 25 kg → every other day
        - 40 kg → daily

Oral Ivermectin

- Used off-label; role evolving, particularly for demodicosis-associated cases.

Resume:

Systemic treatment	Recommended dosage	Treatment duration
doxycycline	40-100 mg/day	No longer than 3 months
isotretinoin (low-dose)	5-10 mg/day	Long term, may be intermittent
hydroxychloroquine**	200 mg/day	Long term
dapsone**	50-100 mg/day	Long term
ivermectin**	0.2mg/kg single dose	Single course
prednisone/prednisolone**	40-50 mg for 1 week, 20-25 mg for 2 weeks, 10-12.5 mg for 3 weeks, 5 mg for 4 weeks	Single course

**: limited evidence

Microbiome Considerations

- Overuse of antibiotics may **drive *C. acnes (cutibacterium)*** into biofilm-forming, resistant forms.
- Disruption of skin flora likely contributes to **relapse-prone inflammation** in rosacea/POD.

Take-Home Points

1. **Diagnostic fluidity is necessary**—rosacea, perioral dermatitis, SD, acne often overlap.
2. In **children**, flushing, blepharitis, and papules without comedones lean toward rosacea.
3. POD typically lacks flushing and involves painful itch; often corticosteroid related.
4. Most therapies are **off-label** and guided by **clinical experience**, not trials.
5. **Antibiotics should be minimized** due to microbiome risks.
6. **Isotretinoin (very low dose)** can be highly effective for resistant cases.
7. Don't hesitate to **revise your diagnosis** as clinical patterns evolve over time.

References:

- Geng R, et al. Efficacy of treatments for rosacea in the pediatric population: A systematic review. JEADV. 2024. 3 (1): 17-48
- Rademaker M, et al. Pharmaceutical Management of Rosacea—An Australian/New Zealand Medical Dermatology Consensus Narrative, Dermatologic Therapy. 2024, 9678447.
- Rademaker M, Chapter 26. Perioral Dermatitis. In book: Harper's Textbook of Pediatric Dermatology, Fourth Edition.

Acneiform eruptions in kids

Speaker: Irene Lara Corrales (Canada)

Key Definitions

- **Acneiform Eruptions**: Papules and pustules resembling acne but lacking comedones (blackheads/whiteheads). Typically folliculocentric, with sudden onset and often symmetric distribution.
- **Common Locations**: Face, upper trunk, shoulders, and arms.
- **Etiologies in Pediatrics**:
    - **Drug-induced (most common)**: Steroids, EGFR inhibitors, MEK inhibitors, JAK inhibitors.
    - **Infection-related**: *Pityrosporum* (Malassezia) folliculitis, Gram-negative (hot tub) folliculitis.

Drug-Induced Acneiform Reactions

1. Steroid-Induced

- Occurs after prolonged systemic or topical corticosteroid use.
- Treatment depends on whether steroids can be discontinued.
- Management: Topicals but stopping the steroid may be necessary for resolution.

2. Targeted Therapies (e.g., EGFR & MEK inhibitors)

- Up to 100% of patients develop acneiform eruptions.
- Often severe and quality-of-life-impacting.
- Lesions can vary by age:
    - Teens: Face involvement.
    - Younger children: Trunk and other areas.
- Etiology is likely multifactorial (host genetics, inflammation, C. acnes interaction).

3. JAK Inhibitor-Induced (JAK-ny)

- ~4x higher risk of acneiform rash than placebo.
- Even higher in dermatologic patients or those with prior acne.

- Mechanism is unclear but possibly involves paradoxical immune/microbiome effects.
- JAK1/3 may be targets for acne treatment, yet inhibition may cause eruptions.

Management of Drug-Induced Acneiform Reactions

- **Prevention is key**:
  - If **preexisting** acne: **Proactive** treatment, potentially systemic (doxycycline, isotretinoin).
  - If **no acne**: **Preventative** strategies (e.g., bleach baths, antiseptics in young children).
- **Treatment Approach**:
  - Grade severity using CTCAE (Common Terminology Criteria for Adverse Events).
  - Combine acne therapy with **topical corticosteroids** to control inflammation.
  - Moisturization and sun protection are essential.
  - Swab if secondary infection suspected.

Infectious Acneiform Reactions

1. Pityrosporum (Malassezia) Folliculitis

- Very pruritic, **monomorphic papules**.
- Distribution: Chest, back, scalp, hairline, neck.
- Risk factors: **Heat, humidity, immunosuppression, antibiotics**.
- Diagnosis: Clinical + KOH scraping or culture.
- Treatment: Topical or systemic antifungals (itraconazole, ketoconazole).

2. Gram-Negative (Hot Tub) Folliculitis

- Caused by *Pseudomonas* after **exposure to under-chlorinated warm water**.
- Appears within hours to days; often spares face/soles/palms.

- More common in occluded areas (groin, axilla).
- Self-limited (7–14 days), but may require:
    - Topical antibiotics.
    - Vinegar compresses (1:9 dilution).
    - Systemic antibiotics if severe/systemic symptoms are present.

Differentiating Acneiform Reactions

Feature	Acne	Acneiform Eruption
Comedones	*Present*	*Absent*
Onset	*Gradual*	*Sudden, within days–weeks*
Distribution	*Variable*	*Symmetric, folliculocentric*
Triggers	*Endogenous*	*Drug or infectious exposure*

Summary Points

- Acneiform eruptions are common in children, particularly due to modern systemic therapies.
- Proper diagnosis requires recognizing the absence of comedones and identifying relevant history.
- Management should be **proactive**, **preventative**, and tailored based on the cause.

References:

- Boull CL, et al. Cutaneous reactions in children treated with MEK inhibitors, BRAF inhibitors, or combination therapy: A multicenter study. J Am Acad Dermatol. 2021;84(6):1554-1561
- Satoh TK, et al. IL-36γ drives skin toxicity induced by EGFR/MEK inhibition and commensal Cutibacterium acnes. J Clin Invest. 2020 2;130(3):1417-1430.
- Martinez J, et al. Janus Kinase Inhibitors and Adverse Events of Acne: A Systematic Review and Meta-Analysis. JAMA Dermatol. 2023;159(12):1339-1345
- Awad SM, et al. Activation of Janus kinase signaling pathway in acne lesions. Dermatol Ther. 2021;34(1):e14563
- Martínez-Ortega J, et al. Malassezia Folliculitis: Pathogenesis and Diagnostic Challenges. Cureus.2024;16(11): e73429

The microbiome in acne

Speaker: Maria Lertora (Argentina)

Key Concepts & Evidence

1. Traditional Acne Pathogenesis Expanded

- Classical model: **Sebum overproduction, inflammation, follicular hyperkeratinization**, and **C. acnes colonization**.
- Updated understanding: Less about overgrowth of *C. acnes*, more about **loss of microbial diversity**—especially dominance of **C. acnes phylotype IA1**.

2. Microbiome Diversity in Healthy vs. Acne Skin

- Healthy skin: Balanced presence of multiple *C. acnes* ribotypes (1, 2, 3, 6).
- Acne skin: Overrepresentation of ribotypes (4, 5, 8, 10) and phylotype IA1.
- Virulent strains produce **porphyrins, CAMP factors, biofilms**, and enzymes (e.g., hyaluronidase).

3. Microbial Interactions

- *S. epidermidis* can **suppress *C. acnes*-induced inflammation**.
- Dysbiotic *C. acnes* reduces *S. epidermidis* by altering pH (via propionic acid), promoting inflammatory dominance.

4. External Influences on the Microbiome

- **Puberty**: Hormonal changes (↑ androgens, IGF-1) → more sebum + altered alpha/beta microbial diversity.
- **Diet**: High glycemic index, dairy.
- **Overcleansing & harsh products** → barrier disruption.
- **Antibiotic use & stress** → decreased microbiota resilience.

Gut-Skin Axis

- Bidirectional communication via **immune, endocrine, and nervous systems**.

- Gut dysbiosis and **"leaky gut"** increase systemic inflammation and worsen acne.
- Supports interest in **oral probiotics** as adjunctive therapy.

Commonly Studied Probiotic Strains:

- *Lactobacillus rhamnosus*
- *Lactobacillus acidophilus*
- *Bifidobacterium spp.*

Therapeutic Implications

1. Oral Probiotics

- Shown to **reduce systemic inflammation**, **modulate gut flora**, and **improve acne symptoms**.
- Especially useful in **relapsing or treatment-resistant cases**.

2. Biome-Friendly Topical Care

- **pH-balanced cleansers** support commensal flora.
- **Ceramide-rich moisturizers** strengthen the skin barrier and have mild antimicrobial properties.
- Avoid over-stripping or irritating routines.

3. Personalized Acne Management

- Treatment plans should account for **individual microbial profiles** and **bio-individuality**.
- Goal: **Restore balance**, not eliminate bacteria.

Key Takeaways

- Acne is increasingly seen as a **dysbiosis-driven condition**.
- Modulating the microbiome—both skin and gut—is a **valuable therapeutic strategy**.
- **Prevention of imbalance** > eradication of flora.
- Skincare should be **supportive**, not disruptive.

- Future acne management may rely more heavily on **personalized, microbiome-guided protocols**

References:

- Podwojniak A, et al. Acne and the cutaneous microbiome: A systematic review of mechanisms and implications for treatments. J Eur Acad Dermatol Venereol. 2025;39(4):793-805
- Dreno B, et al. Acne microbiome: From phyla to phylotypes. J Eur Acad Dermatol Venereol. 2024;38(4):657-664
- De Pessemier B, et al. Gut-Skin Axis: Current Knowledge of the Interrelationship between Microbial Dysbiosis and Skin Conditions. Microorganisms. 2021 11;9(2):353.
- Kreouzi M, et al. Skin Microbiota: Mediator of Interactions Between Metabolic Disorders and Cutaneous Health and Disease. Microorganisms. 2025};13(1):161.

Neonatal, infantile and mild-childhood acne

Speaker: Agnes Schwieger (Switzerland)

Introduction

Hormonal Background: Acne is often an external manifestation of hormonal shifts, primarily associated with two developmental pathways:

- *HPA (hypothalamic-pituitary-adrenal) axis*
- *HPG (hypothalamic-pituitary-gonadal) axis*

Of these, adrenal androgens—specifically the activation of the HPA axis—are thought to play a more prominent role in early-onset acne. This activation begins around age six and is known as *adrenarche*. It leads to increased production of **DHEAS**, a weak androgen that can be converted into more potent forms, promoting sebaceous gland growth and sebum production. This hormonal activity contributes to acne, body odor, and the development of pubic hair.

Early and Atypical Presentations:

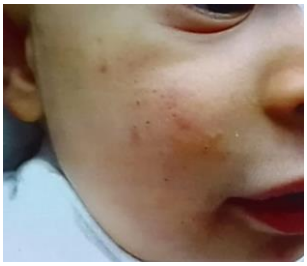
- **Adrenarche** typically manifests physically around age 11 in girls and 12 in boys.
- **Premature pubarche** is defined as signs of puberty (e.g., acne, body odor, pubic hair) before age **7–8 in girls** and before **9 in boys**.

Clinical Focus: The lecture centers on **infantile acne** (starting after 8 weeks of age) and **mid-childhood acne** (ages 1–7), noting that neonatal acne is rare

and often misdiagnosed (commonly confused with neonatal cephalic pustulosis).

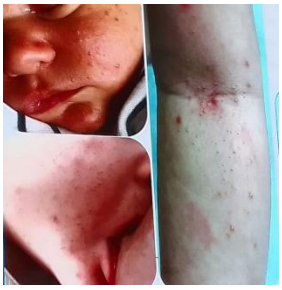
Key Case Highlights:

1. **Case 1 – 3-Month-Old Boy with Comedones**



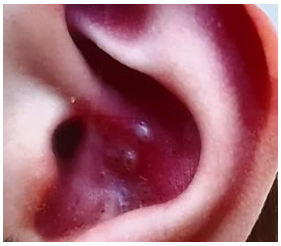
   - Classic **infantile acne**: mid-cheek comedones, no virilization.
   - Managed with topical retinoids and benzoyl peroxide.
   - Infantile acne can persist for up to two years and may result in scarring.

2. **Case 2 – 6-Month-Old Boy with Extensive Lesions:**



   - Widespread comedones (face, arms, back).
   - The workup revealed hormone levels consistent with mini puberty.
   - Treated with oral isotretinoin for one year with good results.

3. **Case 3 – 5-Year-Old Boy with Comedones in the Ear:**



   - Mild acne with signs of early pubarche (body odor, greasy hair).
   - Diagnosed with **late-onset congenital adrenal hyperplasia** after ACTH stimulation test.
   - No ongoing treatment needed, but diagnosis important for future management.

4. **Case 4 – 20-Month-Old Boy with Inflammatory Nodules and Comedones:**

   - Initially treated as IFAG (idiopathic facial aseptic granuloma).
   - Careful review showed classic **acne** with comedones.
   - Treated with oral isotretinoin and short-course steroids.

Clinical Pearls:

- **Workup**: Careful history, physical exam, and selective hormone testing are essential in childhood acne to rule out endocrine abnormalities.
- **Treatment**: Aligns with adolescent protocols, though all treatments are technically off-label for these ages. Most children tolerate topical treatments well, with oral isotretinoin reserved for severe cases.

Comedones – Papules	Azelaic acid, topical retinoids + BP
Pustules	+ topical ATB/ oral ATB (erythromycin)
Nodules - Pseudocysts	oral ATB, oral retinoid (0,3-0,5 mg/k/d) +/- steroid

- **Avoiding Scarring**: Early, appropriate treatment is crucial to prevent long-term skin damage.

Conclusion:

Childhood acne, especially in the infantile and mid-childhood periods, warrants thoughtful evaluation. While **most cases are benign and hormonally driven**, it's important to **rule out systemic or endocrine disorders**. With appropriate management, including topical and systemic treatments when needed, these children can achieve excellent outcomes without long-term consequences.

References:

- Rosenfield RL. Normal and Premature Adrenarche. Endocr Rev. 2021;42(6):783-814
- Shope C, et al. Pathologic acne in pre-pubertal children: A case series and review on when to refer to pediatric endocrinology. Pediatric Dermatology. 2023; 40 (1): 5-10
- Schachner LA, et al. The Many Faces of Pediatric Acne: A Practical Algorithm for Treatment, Maintenance Therapy, and Skincare Recommendations for Pediatric Acne Patients. J Drugs Dermatol. 2023;22(6):539-545.
- Eichenfield LF, et al. Evidence-based recommendations for the diagnosis and treatment of pediatric acne. Pediatrics. 2013;131 Suppl 3:S163-86
- Maroñas-Jiménez L, et al. Pediatric Acne: Clinical Patterns and Pearls. Dermatol Clin. 2016;34(2):195-202

Hormonal considerations in acne: when to workup

Speaker: Karen Chernoff (USA)

Overview

Acne in females may serve as an isolated dermatologic condition or as a potential clinical marker of **hyperandrogenism**—a state of androgen excess due to ovarian, adrenal, or peripheral sources. Dermatologists play a key role in recognizing clinical signs of hormonal imbalances and initiating appropriate evaluations or referrals.

Pathophysiology of Hyperandrogenism

Hyperandrogenism results from increased androgen production or peripheral conversion. The **pituitary gland** stimulates the ovaries and adrenal glands, leading to **testosterone production**, which is converted to **dihydrotestosterone (DHT)** by **5-alpha-reductase**, resulting in clinical manifestations such as acne.

Primary Causes in Adolescents

- **Polycystic Ovarian Syndrome (PCOS):**
    - Most common cause of persistent hyperandrogenism.
    - Characterized by elevated **LH** and **insulin**, reduced **sex hormone-binding globulin (SHBG)**, and increased **free testosterone**.
    - Diagnosis in adolescents is complex due to overlap with normal puberty; diagnosis should be made cautiously in the first **two years post-menarche**, requiring **longitudinal follow-up**.
- **Non-classic Congenital Adrenal Hyperplasia (NCCAH):**
    - Often underrecognized.
    - Caused by **partial 21-hydroxylase deficiency**.
    - Presents with elevated **androstenedione** and **testosterone**.
    - Management includes **ACTH suppression** for fertility and symptom control.
- **Androgen-Secreting Tumors:**
    - Rare but important to rule out, particularly in cases with virilization.

Clinical Clues for Hormonal Acne

- **Abrupt onset** or **severe acne**
- **Prepubertal or postmenopausal** onset
- **Refractory cases** (e.g., isotretinoin failure)
- **Lower face/jawline** distribution
- **Signs of hyperandrogenism**: hirsutism, androgenetic alopecia, irregular menses
- **Signs of virilization** (red flags): voice deepening, clitoromegaly, muscle mass increase, etc.

Menstrual Irregularity Definitions

- **Primary amenorrhea:** No menses by age 15 or >3 years after thelarche.
- **Secondary amenorrhea:** ≥90 days without menstruation after prior regular cycles.
- **Oligomenorrhea:** Based on time since menarche:
  - <1 year: >60-day cycles are normal.
  - 1–3 years: normal cycle length is 21–45 days.
  - 3 years: normal cycle length is 21–35 days.

Laboratory Evaluation

<u>Core Screening Tests</u>
Total & Free Testosterone (if available via **LC-MS/MS**)

- **DHEAS:** Marker of adrenal source.
- **17-Hydroxyprogesterone (17-OHP):** Screens for NCCAH. Should be drawn **early morning** during **the follicular phase** if possible.

<u>Additional Labs:</u>

- **LH & FSH:** Elevated LH:FSH ratio may indicate PCOS.
- **Androstenedione (A4):** Weak androgen correlates with disease severity.
- **Prolactin:** Rule out hyperprolactinemia (e.g., from medications, hypothyroidism).

- **TSH:** Hypothyroidism lowers SHBG, falsely elevating free testosterone.
- **Beta-HCG:** If amenorrhea or pregnancy is suspected.

Interpretation Framework

- **Regular menses with hyperandrogenism**: Rule out **tumors** and NCCAH.
- **Irregular menses**: Broader panel to assess **PCOS** or other endocrine abnormalities.
- **Severe elevations** in testosterone or DHEAS should raise suspicion for neoplasm.

Timing & Special Considerations

- **Timing of labs**: Ideally **early morning** due to diurnal variation in hormone levels.
- **Menstrual cycle phase**: Preferably **follicular phase**, but immediate testing is acceptable for screening.
- **Oral contraceptive pills (OCPs)**: Hormonal labs are unreliable on OCPs except for TSH, prolactin, and beta-HCG. Testing should be done **before initiation** or **after discontinuation** (1–3 months).

Role of Imaging

- **Transvaginal ultrasound**: Required for PCOS diagnosis in adults.
    - **Not recommended in adolescents**, as many show polycystic morphology during normal puberty.

Referral Considerations

- **Refer to Endocrinology or Gynecology** if:

- Clinical signs of **virilization**
- **Severely elevated hormone levels**
- **Tumor suspicion**
- Need for longitudinal hormonal management

Summary Take-Home Points

- Consider hormonal evaluation in **female adolescents** with acne and **signs of hyperandrogenism**.
- Evaluate **testosterone**, DHEAS, 17-OHP, and LH/FSH as primary labs.
- Add TSH, **prolactin**, and HCG if irregular menses are present.
- **Avoid testing** while on **hormonal therapies**.
- Work in collaboration with **Endocrinology/Gynecology** when needed.

References:

- Sardana K, et al. An updated clinico-investigative approach to diagnosis of cutaneous hyperandrogenism in relation to adult female acne, female pattern alopecia & hirsutism a primer for dermatologists. Expert Rev Endocrinol Metab. 2024;19(2):111-128
- Yoost J, et al. Screening and treatment of hyperandrogenic conditions in adolescents. Health of woman. 2019;9(145): 72–75

Hot topics in acne: What's new?

Speaker: Andrea Zaenglein (USA)

1. Benzoyl Peroxide in Acne Treatment

- **2024 American Academy of Dermatology Acne Guidelines**: The guidelines strongly recommend the use of benzoyl peroxide for acne treatment based on moderate evidence, specifically to prevent the development of antibiotic resistance.
- **Mechanism of Action**:
    - Benzoyl peroxide is converted into benzoic acid upon application, releasing free radical oxygen species that oxidize bacterial proteins, making it an effective bactericidal agent against *C. acne*.
    - It also works on comedones by reducing free fatty acids on the skin surface.
    - When used in conjunction with antibiotics, benzoyl peroxide prevents the development of resistance to the antibiotics.
- **Formulations and Use**:

    - Benzoyl peroxide is available in various formulations, including washes (ideal for trunk) and leave-on products (suitable for face).
    - Lower concentrations, typically 4-5%, are less irritating and are commonly used.
    - Patients should be cautioned about the potential for bleaching towels and clothing, as benzoyl peroxide can discolor fabrics.
    - Benzoyl peroxide is frequently used in combination with antibiotics, and it can be applied alongside topical or systemic antibiotics as part of the treatment regimen.
- Compatibility with Retinoids:
    - Historically, it was believed that benzoyl peroxide should not be used with tretinoin, but this is no longer the case for most retinoid formulations.
    - Newer micro-sized formulations of tretinoin allow it to be used alongside benzoyl peroxide, making it more convenient for patients.
    - There are also now fixed combination products that combine both tretinoin and benzoyl peroxide, which can simplify treatment regimens for patients.
- Benzene Controversy:
    - A report by an independent testing company raised concerns about the **presence of benzene in certain benzoyl peroxide products**. They exposed the products to high temperatures (50°C for 25–30 days and 70°C for 18 hours) and found elevated levels of benzene.
    - Benzene is classified as a **known carcinogen** by both the International Agency for Research on Cancer and the U.S. EPA. Exposure to benzene has been associated with **blood cancers like leukemia.**
    - However, **further investigations by the FDA found that over 90% of the benzoyl peroxide products tested had undetectable or extremely low levels of benzene**. Only six products were found to have elevated levels, and these were voluntarily recalled by the manufacturers.
    - Recommendations:

- Keep benzoyl peroxide products at **room temperature or below**, as excessive heat can potentially lead to benzene contamination.
- Although some dermatologists recommend refrigerating benzoyl peroxide, this is generally not recommended as it can make the product less convenient for daily use.
- Ensure that patients are aware of the **expiration dates** of their products and replace them if expired.

2. Isotretinoin and Sexual Dysfunction

- Global Concerns:
  - Although isotretinoin has not been widely associated with sexual dysfunction in the U.S., it has become a topic of concern in other countries like Canada and the UK. In fact, in April 2023, Great Britain recommended additional oversight for patients under 18 starting isotretinoin treatment and emphasized more consistent monitoring of psychiatric and sexual health.
- Global Adverse Events Report:
  - Only accounted for 54 of the 300 cases of sexual dysfunction reported across 37 countries.
    This represents a small percentage of the global isotretinoin use.
- FDA and Database Studies:
  - The FDA pharmacovigilance database reported 181 cases of erectile dysfunction linked to isotretinoin, though the quality of evidence was deemed low, and the mechanisms behind these reports were unclear.
  - A study was performed comparing patients treated with isotretinoin, tetracycline, and no systemic acne medication. It found **no significant differences in rates of erectile dysfunction, sexual dysfunction, or decreased libido** across these groups, suggesting isotretinoin may not be a significant risk factor for these side effects.
- Systematic Review of the Literature:
  - A systematic review of peer-reviewed studies on isotretinoin and sexual dysfunction concluded that the quality of the evidence

was low. There were no randomized controlled trials, and most data came from case reports, small cohort studies, or observational studies.

    - The review found that 54% of patients reported a **neutral or beneficial effect of isotretinoin on sexual function**, though there was no standardized definition of sexual dysfunction, which made the data difficult to interpret.

- **Recommendations**:
    - Dermatologists are encouraged to **counsel patients about the potential risk of sexual side effects** with isotretinoin and to monitor for these effects during follow-up visits

References:

- Garate D, et al. Benzoyl peroxide for acne treatment is not associated with an increased risk of malignancy: A retrospective cohort study. J Am Acad Dermatol. 2024 Nov;91(5):966-968.
- Chan R, et al. No association of benzoyl peroxide use with acute myeloid leukemia and hematologic malignancies in a multi-center retrospective study. J Am Acad Dermatol. 2024 Dec;91(6):1234-1236
- Healy D, et al. . Enduring sexual dysfunction after treatment with antidepressants, 5 alfa reductase inhibitors and isotretinoin: 300 cases. International Journal of Risk & Safety in Medicine. 2018;29(3-4):125-134
- Hogan C, et al. One hundred and twenty cases of enduring sexual dysfunction following treatment. Int J Risk Saf Med. 2014;26(2):109-16
- Tan E, et al. Exploring the association between isotretinoin and sexual dysfunction: a comprehensive scoping review. Clin Exp Dermatol. 2024 Oct 24;49(11):1396-1404.

Current trends and practices leading to skin problems in pediatric dermatology

Speaker: Pearl Kwong (USA)

"THE GOOD, THE BAD, AND THE UGLY: SOCIAL MEDIA'S IMPACT ON PEDIATRIC DERMATOLOGY"

Positive Aspects of Social Media in Dermatology

- Integral and **growing part of modern society**, especially post-COVID.
- Aids **information dissemination**, increasing awareness of diseases and treatments.

- Facilitates **patient engagement** and requests for newer therapies (e.g., biologics).
- Contributed to the rise of **telemedicine**, improving access, especially in rural areas.
- Raised awareness of **mental health** connections with skin conditions.

Examples of Positive Use:

- National Eczema Association, SPD, National Alopecia Areata Foundation as reputable resources.
- Disease-specific Facebook groups (e.g., HS) offering psychological support.
- Dermatology residents using Instagram for education.

Negative Aspects / Risks

- **Misinformation** due to lack of fact-checking.
- Heavy presence of **non-dermatologists and influencers** promoting unverified products.
- **Patient hesitancy** to accept medical advice due to online "research."
- **Celebrity influences** contributing to myths and dangerous practices.
- Platforms (Facebook, Instagram, TikTok, Snapchat) promote **unregulated trends**:
    - **TikTok**: Viral challenges (e.g., sunburn challenges), home remedies.
    - **Snapchat**: Filters encouraging cosmetic procedures and "Snapchat dysmorphia."
    - **Instagram**: Heavy focus on aesthetics and cosmetic marketing.
    - **Twitter/X**: Mixed scientific and non-scientific content.

Clinical Consequences and Patient Cases

Case/Trend	Description
Foot peel complication	15-year-old used a trendy foot mask post-injury → developed painful “blue” pus drainage.
Do-it-yourself filler	Attempted self-injection based on online tutorial.
Tea tree oil misuse	Use in prepubertal boys → gynecomastia.
Topical steroid misuse	Pregnant woman applied clobetasol for acne, worsening her condition.
Portal abuse	Patients send photos via EMR portal expecting remote diagnosis (e.g., no visible scale or swelling, yet labeled as such by patient).
Life coach over medical care	Delay in treating infected ulcerated hemangioma due to parental reliance on unqualified life coach.
Failed acne treatment	Long-time patient sought online acne treatments, worsened before returning.
Molluscum home remedy	Application of unknown topical remedy caused extreme hyperpigmentation and skin damage.
Snail mucin trend	Popular product among teens despite lack of robust evidence.

Common Buzzwords and Misconceptions

- "Fungal acne", "Topical steroid withdrawal syndrome", "Glass skin", "Beef tallow", "Skin flooding/lugging", "Skin cycling", "Dopamine beauty", "Retinol sandwiching", "Castor oil for lashes".
- "Yuka" and "Skin Bliss" apps used by patients to validate (or reject) prescribed treatments.
- Rise of "Dermorexia" – obsession with skincare routines, often beginning as early as age 10.

    - Extensive routines, iPad-based product lists during appointments, filter dependence, and increased anxiety regarding minor imperfections.
    - **"Sephora kids"** culture replacing more age-appropriate behaviors.

Implications for Dermatologists

- Dermatologists must **engage in patient discussions** beyond medical management, including debunking misinformation.
- Requires **time-consuming education** and empathetic redirection during consultations.
- Physicians are now **expected to "defend" evidence-based treatments** to skeptical patients.
- Need for **ongoing education** in social media trends to remain relevant.

Conclusions

- Social media's presence in dermatology is **permanent and growing**.
- While it offers opportunities for engagement and education, it also presents significant challenges in **misinformation**, **patient hesitancy**, and **altered expectations**.
- Pediatric dermatologists are urged to:
    - Stay informed on evolving trends and patient language.
    - Use **scientific evidence** to guide care and patient discussions.
    - Refer patients to **verified educational platforms**.
    - Consider professional participation in social media to serve as **credible influencers**.

A new era of treatment for naevi and other mosaic disorders

Speaker: Veronica Kinsler (United Kingdom)

Current Approach to Mosaic Disorders

- Traditional management remains centered around:
  - Surgical excision
  - Laser therapies
  - Immunoregulatory treatments
- Increasing attention is being paid to **repurposing oncologic drugs** and **developing targeted molecular therapies**.
- Genetic diagnosis now plays a pivotal role in guiding disease-specific management, although therapeutic implications are still limited for many conditions.

Drug Repurposing: Challenges and Limitations

- Mosaic disorders frequently harbor mutations in oncogenes (e.g., *KRAS*, *NRAS*), similar to those seen in cancer.
- However, therapeutic responses in mosaic conditions often diverge from those observed in malignancies.

Study Example – Arteriovenous Malformations (AVMs):

- KRAS mutations introduced into endothelial cells to mimic mosaicism.
- Comparative drug screening using:
  - Public oncologic datasets (e.g., TCGA, CCLE, DepMap)
  - Custom in vitro mosaic models

Findings:

- In cancer cell lines: MEK inhibitors were consistently top hits
- In the mosaic model: Only 2/21 MEK inhibitors showed significant effect; other hits included statins.
- Conclusion: **Pathway dependency differs** in mosaic versus malignant cells — cancer tends to rely on a dominant signaling pathway, whereas

mosaic disorders activate multiple downstream pathways, reducing sensitivity to targeted inhibitors.

Role of Calcium Signaling in Vascular Malformations

- Investigated mechanisms in **Sturge-Weber syndrome**, driven by *GNAQ* mutations.
- Clinical imaging (e.g., skull radiographs) showed **tramlining calcification** in affected vessels.
- In vitro models of mutated endothelial cells demonstrated:
  - **Increased baseline intracellular calcium signaling**
  - **Exaggerated response** upon ligand stimulation
- Highlighted the importance of exploring noncanonical pathways such as calcium signaling in vascular anomalies.

Emergence of siRNA Therapy

- Prof. Kinsler introduced **small interfering RNA (siRNA)** as a promising therapeutic strategy for mosaic disorders.
- siRNA mimics the body's innate viral defense by inducing degradation of targeted RNA transcripts.
- Mechanism:
  - Synthetic double-stranded RNA introduced into cells.
  - Triggers RNA-induced silencing complex (RISC) to degrade specific mRNA.
  - High specificity achievable with 20-base sequences, analogous to strong passwords in security systems.

Application in Congenital Melanocytic Nevi (CMN)

- CMN is primarily caused by **somatic activating mutations in *NRAS*** (commonly Q61K).
- Previous treatment attempts using **MEK inhibitors (e.g., trametinib)** showed:

    - Some efficacies in *NRAS*-driven melanoma.
    - **No significant reduction** in nevi size, even with long-term administration.
- These observations prompted the shift toward **mutation-specific RNA silencing**.

siRNA Strategy:

- Designed siRNAs targeting *NRAS Q61K* mutation.
- Goal: Selectively silence the mutant transcript while sparing the wild-type allele.
- In vitro experiments demonstrated:
    - Effective silencing of mutant *NRAS*.
    - **Induction of apoptosis** in mutant cells (e.g., upregulation of ARL6IP1).
    - Effects visible within 48 hours of treatment.

In Vivo Model – siRNA Delivery and Efficacy

- Used transgenic mouse model expressing human *NRAS Q61K* specifically in skin.
- siRNA formulated in **lipid nanoparticles** and applied topically.
- Demonstrated:
    - Selective silencing of the mutant allele.
    - Preservation of the wild-type gene.
- Confirmed safety and tolerability of topical application.

Advances in Delivery – Microneedle Patches

- siRNA delivery remains a key challenge due to RNA instability and degradation.
- Collaborated with researchers in Wales to develop **microneedle patches**:
    - Patches composed of biocompatible material.

- Contain lipid nanoparticle-encapsulated siRNA.
- Enable painless, topical delivery — especially suitable for pediatric patients.
- Patches can be self-applied and allow for sustained delivery.

Potential for Broad Application

- Untreateable mosaic disorders are becoming more treatable.
- Success of repurposing of drugs between cancer and mosaic disorders is not necessarily predictable.
- siRNA sequences can be readily designed for various pathogenic mosaic mutations (*NRAS, HRAS, KRAS*, etc.).
- Genetic thearpies are showing promise in pre-clinical studies.

References:

- Michailidis F, et al. High-throughput drug screening in a cellular model of KRAS-driven arteriovenous malformations. JID. 2025; In Press, Journal Pre-proof.
- Zecchin D, et al. GNAQ/GNA11 Mosaicism Causes Aberrant Calcium Signaling Susceptible to Targeted Therapeutics. J Invest Dermatol. 2024 Apr;144(4):811-819.e4.
- Knöpfel N, et al. GNAQ/GNA11 Mosaicism Is Associated with Abnormal Serum Calcium Indices and Microvascular Neurocalcification. JID. 2024; 144 (4):820-832.e9
- Pawlikowski JS, et al. Acute Inhibition of MEK Suppresses Congenital Melanocytic Nevus Syndrome in a Murine Model Driven by Activated NRAS and Wnt Signaling. J Invest Dermatol. 2015 Aug;135(8):2093-2101.
- Bryant D, et al. RNA Therapy for Oncogenic NRAS-Driven Nevi Induces Apoptosis. J Invest Dermatol. 2025 Jan;145(1):122-134.e11

Mosaic disorders

Mosaic rock’n’rhoa-pathies

Speaker: Pierre Vabres (France)

Overview

The presentation addressed a newly defined group of mosaic disorders characterized not only by **clinical features** but also by their **underlying molecular causes**. These disorders, previously described using various clinical terms (e.g., hypomelanosis of Ito, pigmentary mosaicism), are now

increasingly classified based on genetic alterations and signaling pathway involvement.

Main Genetic Pathways Identified

1. **mTOR Pathway (PI3K-AKT-mTOR)**
2. **RhoA-ROCK Pathway**
3. **GNA13 and Related Gα Protein Pathways**

1. mTOR-related Hypomelanosis of Ito

- **Clinical phenotype:**
  - Depigmentation along Blaschko's lines
  - Associated with megalencephaly, epilepsy, or intellectual disability
- **Genetic findings:**
  - Somatic variants in **mTOR**, found exclusively in affected skin (not blood)
- **Skin pathology findings:**
  - ↓ Melanocytes
  - ↓ Melanosomes
  - Defective melanosome maturation
- **Functional insights:**
  - Similar pigmentary alterations seen in tuberous sclerosis complex
  - mTOR inhibitors (e.g., **rapamycin**) showed no neurological benefit in this cohort
- **Related phenotypes with overlapping macrocephaly:**

Gene	Syndrome/Phenotype	Features
AKT3	MPPH syndrome	Hemimegalencephaly, PMG

Gene	Syndrome/Phenotype	Features
PTEN	Cowden/hamartoma syndromes	Macrocephaly
PIK3CA	MCAP syndrome	Capillary malformations, overgrowth
PIK3R2	MPPH syndrome	White matter anomalies

2. RhoA-related Mosaic Syndrome

- Clinical phenotype:
  - Linear depigmentation (fine lines, visible under Wood lamp)
  - Facial asymmetry
  - Acral anomalies (broad or short digits)
  - Dental anomalies
  - Ocular anomalies (severe myopia, retinal issues)
  - White matter abnormalities on MRI (asymptomatic)
- Genetic findings:
  - Identical somatic **RhoA** variant in affected skin
  - Not detected in blood or parental DNA
- Functional studies:
  - ↓ Stress fibers in NIH3T3 cells
  - Small, round cell morphology
  - ↓ Phosphorylation of downstream effectors (MYPT, MLC2)
  - Suggests **dominant-negative** or **loss-of-function** RhoA effect

3. GNA13-related Mosaic Syndrome

- Clinical phenotype (overlapping with RhoA):
  - Spindle-shaped or flag-like depigmentation
  - Facial asymmetry

    - Acral anomalies
    - Eyelash anomalies
    - Gastrointestinal anomalies
    - Delayed wound healing (up to 9 months in one case)
- **Genetic findings:**
    - Recurrent **GNA13 p.R200K** somatic variant found in four patients
    - Variant not detected in blood
    - Variant site is homologous to known activating mutations in **GNAQ/GNA11** associated with vascular malformations (e.g., port-wine stains, Sturge-Weber)
- **Functional studies:**
    - Transfected melanoma cells exhibited:
        - ↑ F-actin content
        - ↑ Circularity
        - ↓ Cell perimeter
    - Suggests altered cytoskeletal dynamics and impaired dendrite formation in melanocytes
    - ↓ Melanosome number in affected melanocytes

Unifying Concepts

- The disorders share the involvement of GTPase signaling families:
    - **RAS**, **RhoA**, and now **Gα subunits (e.g., GNA13)**
- Suggests an expanding group of **mosaic neuroectodermal syndromes** involving actin cytoskeletal regulation, pigmentation, and neurodevelopmental outcomes.

Conclusion: Novel somatic variants in **mTOR, RhoA, and GNA13** highlight the importance of exome sequencing in skin tissue and contribute to reclassifying these disorders within genetically defined entities.

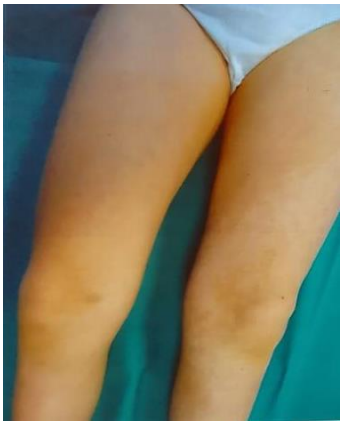
References:

- Mirzaa GM, et al. Association of MTOR Mutations With Developmental Brain Disorders, Including Megalencephaly, Focal Cortical Dysplasia, and Pigmentary Mosaicism. JAMA Neurol. 2016 Jul 1;73(7):836-845
- Carmignac V, et al. Clinical spectrum of MTOR-related hypomelanosis of Ito with neurodevelopmental abnormalities. Genet Med. 2021 Aug;23(8):1484-1491
- Wataya-Kaneda M, et al. Clinical and Histologic Analysis of the Efficacy of Topical Rapamycin Therapy Against Hypomelanotic Macules in Tuberous Sclerosis Complex. JAMA Dermatol. 2015 Jul;151(7):722-30.
- Lee JH, et al. De novo somatic mutations in components of the PI3K-AKT3-mTOR pathway cause hemimegalencephaly. Nat Genet. 2012 Jun 24;44(8):941-5
- Vabres P, et al. Postzygotic inactivating mutations of RHOA cause a mosaic neuroectodermal syndrome. Nat Genet. 2019 Oct;51(10):1438-1441
- El Masri, R, et al. A postzygotic GNA13 variant upregulates the RHOA/ROCK pathway and alters melanocyte function in a mosaic skin hypopigmentation syndrome. Nat Commun.2025; 16, 1751

Intriguing skin mosaic phenotypes and their molecular insights

Speaker: Gianluca Tadini (Italy)

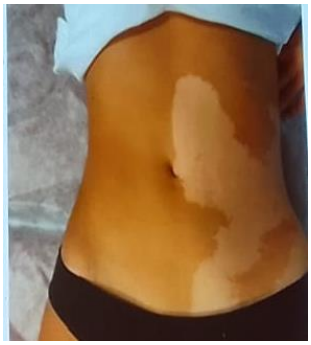
Case 1: mTOR Mosaicism Without Neurological Involvement



- **Patient:** 9-year-old female
- **Findings:**
  - Hypopigmented streaks from infancy
  - Progressive asymmetric overgrowth (left lower limb)
  - Thigh circumference: Left > Right by 2 cm
  - Limb length discrepancy: 1.5 cm
  - Mosaic pattern not classically linear; interrupted streaks across trunk and limbs
- **Imaging:** No medullary or neurological abnormalities
- **Genetic Analysis:**
  - Recurrent mosaic mutation in **mTOR**

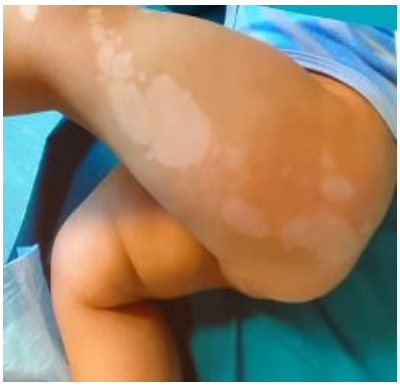
    - Mutation detected only in skin
- **Notable Points:**
    - Atypical presentation without megalencephaly or epilepsy
    - Demonstrates how phenotypic expression of mosaic mutations depends on tissue-specific distribution and mutation load

Case 2: Overgrowth Syndrome with Vascular Malformation and PIK3R1 Mutation



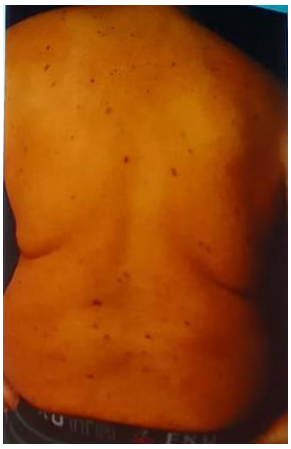
- **Patient:** 15-year-old female
- **History:**
    - Hyperpigmented checkerboard pattern at birth
    - Vascular malformation surgically removed (no prior histology)
    - Progressive soft tissue overgrowth in buttock/thigh region (muscular/adipose infiltration)
    - Previous liposuction
    - Low-grade oncocytic renal tumor (favorable evolution)
    - Thigh circumference asymmetry: Left > Right by 3 cm
    - Small congenital melanocytic nevus on left knee
- **Genetic Analysis:**
    - **PIK3CA**, **PTEN**, **mTOR**: Negative
    - Pathogenic variant found in **PIK3R1** (novel)
    - Detected in both affected tissue and blood (10% VAF)
- **Significance:**
    - First reported case of **PIK3R1**-associated pigmentation anomaly
    - Highlights the need to expand testing beyond common PI3K-AKT-mTOR genes when phenotype suggests mosaic overgrowth

Case 3: Extensive PENS with Mosaic Distribution



- **Patient:** Pediatric male
- **Clinical Features:**
  - Extensive epidermal nevi with hyperkeratotic papules
  - Mosaic distribution involving trunk and extremities
  - Histology: Classic findings of **PENS** (papular epidermal nevus with "skyline" basal cell architecture)
- **Genetics:**
  - Mutation in **EGFR** (epidermal growth factor receptor) recently described in similar patients
  - Suggests genetic heterogeneity within PENS
  - Further gene studies ongoing

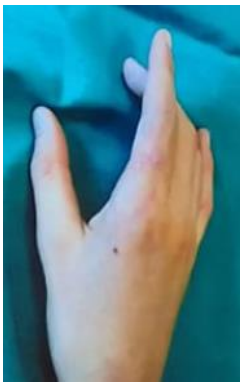
Case 4: Mosaic Eccrine Gland Hypoplasia with Seasonal Hyperpigmentation



- **Patient:** Adolescent male
- **Findings:**
  - Delayed onset of hyperkeratotic pigmented streaks, exacerbated by heat/sunlight
  - Symmetrical lesions on arms, legs, and lower back
  - Winter: Lesions poorly visible; Summer: Checkered hyperpigmentation apparent
- **Histopathology:**
  - Area 1 (normal): Well-formed eccrine glands
  - Area 2 (lesional): Rudimentary eccrine glands
- **Genetic Analysis:**
  - **HRAS** mutation present in 3% of affected tissue

- **Interpretation:**
    - First documented case of **mosaic ectodermal dysplasia** involving sweat gland hypoplasia
    - Mutation likely occurred in a progenitor stem cell, leading to dual ectodermal defects (sweat gland + pigmentation)

Case 5: Isolated Calcifying Acanthoma Misdiagnosed as Common Wart



- **Patient:** 14-year-old male
- **Clinical History:**
    - Asymptomatic hyperkeratotic nodule with wart-like appearance
    - No other malformations or systemic findings
- **Histology:**
    - Marked acanthosis
    - Basophilic calcified foci within dermis
- **Diagnosis:**
    - **Calcifying acanthoma** (benign, possibly mosaic)
- **Genetics:**
    - No mutations detected in **GNAS**
    - Whole exome sequencing pending to clarify etiology
- **Significance:**
    - Likely represents a new entity of mosaic benign cutaneous tumor with calcification
    - Rare or underrecognized in pediatric dermatology

Concluding Remarks

- These case reports underline the diagnostic challenges and clinical variability of **mosaic disorders with pigmentary and overgrowth components.**

- **Molecular diagnostics** beyond standard panels (e.g., PIK3CA, PTEN) are essential in **atypical** presentations.
- Emphasis was placed on:
    - Tissue-specific mutational burden
    - Need for functional and histopathological correlation
    - Expanding genotype-phenotype correlations for rare mosaic syndromes

References:

- Handoko M, et al. Undiagnosed Diseases Network; Lee BH, Bacino CA, Chao HT. Recurrent mosaic MTOR c.5930C > T (p.Thr1977Ile) variant causing megalencephaly, asymmetric polymicrogyria, and cutaneous pigmentary mosaicism: Case report and review of the literature. Am J Med Genet A. 2019 Mar;179(3):475-479

Segmental hyperpigmentation: new genes beyond GNAs and their clinical impact

Speaker: Nicole Knoepfel (Switzerland)

Introduction

- The focus was on **segmental macular hyperpigmentation (SMH)**
- These pigmentary patterns typically affect the **trunk**, but can also involve **limbs, face, and neck**.

Clinical Patterns of Segmental Pigmentation

- Grouped under shared melanocytic origin:
    - **Checkerboard pattern**
    - **Block or flap-like distribution**
    - **Broadband or root-like lesions**
- Often show **midline cut-off** but can sometimes **cross midline**.
- Rationale: Likely all derive from a **common melanocyte precursor**.

Background & Terminology Challenges

- **Limited knowledge** exists on SMH despite frequent observation.

- Terminological inconsistency (e.g., segmental pigmentation disorder, pigmentary mosaicism) has impaired clinical understanding.

Diagnostic Dilemmas

- Common parental concerns:
    - Is this **Neurofibromatosis Type 1 (NF1)**?
    - Could it be linked to **future medical issues**?
- Clinical challenge: **Which patients need further investigation**?
- Only well-known associated disorder:
    - **McCune-Albright syndrome**, caused by **mosaic GNAS variants**

McCune-Albright Syndrome

- **GNAS activating mosaic mutations**
- Features:
    - Hyperpigmented patches (broad bands)
    - Jagged "**coast of Maine**" borders
    - Present at **birth**
    - May precede endocrine, bone, or neurological symptoms
- Typically diagnosed by **non-dermatologists**

Study Design: Genetics of Segmental Pigmentation

- Prospective cohort:

Methodology:

- Clinical evaluation, growth monitoring
- Punch biopsy from affected skin + blood sample
- **Targeted NGS panel** used for 40 patients
- 5 patients had **prior negative GNAS hotspot testing**

Challenges in Mutation Detection

- Pigmented lesions contain **very few melanocytes** relative to whole skin.
- Requires **high-sensitivity sequencing** to detect low-frequency mosaic variants.

Key Genetic Findings

Gene	# of Patients	Clinical Notes	Allele Load	Blood
GNAS	3	One case developed hyperthyroidism at age 12	Very low	Negative
NRAS	2	Fair-skinned child with subtle pigmentation, one with nevi	Low	Negative
PTPN11	1	Patchy pigmentation, no nevi, pinkish tone	N/A	Negative
BRAF	1	Segmental pigmentation with nevi	N/A	Negative
Chromosomal Mosaicism	1	Epilepsy due to carnitine deficiency, 5q gain in skin	N/A	Negative

Clinical Correlations & Insights

- **GNAS mosaicism**:
  - May present with **non-classical features**
  - **Low allele load** can cause **false negatives**—repeat testing advised
  - Early diagnosis allows for **anticipation of systemic involvement**
- **Other novel findings**:
  - NRAS, BRAF, PTPN11: Known genes in melanocytic or vascular disorders now implicated in SMH

- **Chromosomal mosaicism** (5q gain): Highlights potential non-monogenic origins

Extracutaneous Findings in the Cohort

- **Neurological symptoms**: 16%
  - Epilepsy (1)
  - ADHD (2), autism (2), speech delay (2), dyspraxia (1), dyslexia (1 patient)
  - All MRIs normal (5 performed)
- **Ophthalmological problems**: 3 patients (no periorbital involvement)

Clinical Implications

- SMH can result from **varied genetic etiologies**, not only GNAS.
- Early molecular diagnosis allows:
  - Tailored **clinical surveillance**
  - Informed **genetic counseling** (mosaic variants may be **germline-transmissible**)
- **Negative NGS** does not rule out mosaicism—some cases may require **array CGH** or advanced sequencing.

Neurocutaneous diseases

Tuberous sclerosis, common and uncommon presentations

Speaker: Aniza Giacaman Contreras (Spain)

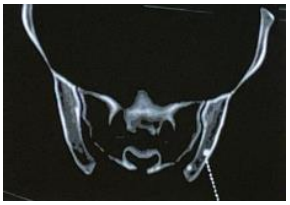
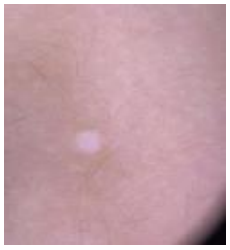
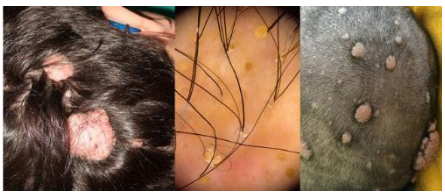
Overview

- **Tuberous sclerosis complex (TSC)** is an **autosomal dominant neurocutaneous syndrome**.
- Caused by mutations in **TSC1** or **TSC2**, leading to **mTOR pathway disinhibition** and resulting in uncontrolled cell growth and multiple hamartomas.

- Manifestations are **age-dependent**, often not congenital, and may vary significantly, even among family members.
- Mutisystemic involvement: SNC (cortical dysplasias subependymal nodules, subependymal giant cell astrocytoma); Kidneys (Multiple Cysts, angiomyolipomas); Eyes (Retinal hamartomas); Heart (Rhabdomyoma); Lungs (Lymphangioleiomyomatosis)
- Diagnosis is based on **clinical and genetic criteria**.

Cutaneous Manifestations

Lesion	Features	Clinical Notes
Hypomelanotic macules	Oval, ash-leaf, polygonal, confetti	Often first sign; requires differentiation from vitiligo, nevus anemicus/acromicus
Poliosis	White hair patch	Rare but diagnostic
Facial angiofibromas	Pink-red papules on central face, sparing upper lip	May resemble acne or rosacea; dermoscopy may show **Demodex tails** in rosacea
Fibrocephalic plaque	Yellowish to brown plaques, scalp or forehead	May be congenital or arise in early infancy
Oral fibromas & dental pits	Papules on gums and enamel pitting	Mandates dental referral
Peri-/subungual fibromas	Skin-colored or pink papules; nail groove formation	More common on feet; may also appear post-trauma in healthy individuals
Shagreen patch	Connective tissue hamartoma with "orange peel" texture	Usually on lumbosacral area
UNCOMMON PRESENTATION OF TSC		

Lesion	Features	Clinical Notes
Sclerotic bone lesions 	Detected radiologically	Important differential: osteoblastic metastases
Red comets 	Corkscrew-shaped periungual vessels with whitish halo	Seen in adult women with TSC
White epidermal nevi (WEN) 	Early-life white hyperkeratotic papules	May precede hypomelanotic macules; potential early marker of TSC
Folliculocystic and collagen hamartoma 	Congenital scalp tumor; comedo-like openings with tufted hairs	Histology: follicular cysts, collagen bundles, and ruptured follicles

Therapeutic Approaches

- Facial angiofibromas:
    - Photoprotection
    - Topical mTOR inhibitors (e.g., sirolimus)
    - Laser therapy
- Case examples show long-term efficacy and safety of sirolimus and eventual transition to **everolimus** for renal angiomyolipomas.

Clinical Insights

- Early recognition of **uncommon presentations** (e.g., WEN, red comets) can facilitate earlier diagnosis.
- **Multidisciplinary follow-up** is essential due to multi-organ involvement.
- Always conduct **full-body examination**, including nails, oral cavity, and scalp.
- Awareness of **age-related progression** helps avoid misdiagnosis or delay in recognition.

Key Takeaway

TSC exhibits a **broad phenotypic spectrum**, and while many signs are cutaneous, several are subtle or underrecognized. Early detection, thorough examination, and multidisciplinary care are essential for effective management.

References:

- Monich A, et al. Tuberous Sclerosis Complex and the kidneys: what nephrologists need to know. Braz. J. Nephrol. (J. Bras. Nefrol.) 2024, 46(3):e20240013
- Schwartz RA, et al. Tuberous sclerosis complex: advances in diagnosis, genetics, and management. J Am Acad Dermatol. 2007 Aug;57(2):189-202
- Northrup H, et al. Updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations. Pediatr Neurol. 2021 Oct;123:50-66.
- Aldrich CS, et al. Acral lesions in tuberous sclerosis complex: insights into pathogenesis. J Am Acad Dermatol. 2010 Aug;63(2):244-51
- Elam AL, et al. White epidermal nevi at birth in a patient with tuberous sclerosis. Pediatr Dermatol. 2014 May-Jun;31(3):360-2.
- Giacaman A, et al. Multiple Folliculocystic and Collagen Hamartomas in a Patient with Tuberous Sclerosis Complex. Actas Dermosifiliogr. 2022 Nov-Dec;113(10):985-987.

Vascular anomalies with CNS involvement, what we need to know?

Speaker: Maria Rosa Cordisco (USA)

Vascular Anomalies Overview

- **Vascular anomalies** are categorized into:

1. **Vascular tumors**
2. **Vascular malformations**
3. **Intermediary entities** (anomalies with undetermined behavior)

1. Capillary Malformations (CM)

- **Nevus Simplex**:
  - V-shaped, feathered borders, blanchable
  - No workup required, fades with time
- **Port-Wine Stain**:
  - Red, well-demarcated borders
  - 15% risk of Sturge-Weber Syndrome (SWS) if facial involvement (forehead/upper lip)

➔ Syndromes Associated with Capillary Malformations

Syndrome	Key Features	Imaging Findings	Treatment Considerations
MCAP Syndrome	Capillary malformation on upper lip/philtrum, megalencephaly, digital anomalies	Polymicrogyria, corpus callosum anomalies, Chiari I	Early neurologic referral, genetic counseling
Sturge-Weber Syndrome (SWS)	Facial CM (bilateral V-shaped), leptomeningeal angiomatosis, ocular involvement (glaucoma)	MRI with contrast, eye exams, follow-up imaging for seizures	Early MRI (repeat if negative at <8 weeks), ophthalmologic follow-up
GNA11 Mutation	Extensive, reticulated CM, CNS involvement, less aggressive than SWS	MRI brain, less severe neurological involvement	Treat seizures, monitor for glaucoma

Management of Sturge-Weber Syndrome

- Early imaging:
    - MRI with contrast (if <8 weeks old, may need repeat scans)
    - Imaging technique: Feed-and-wrap
- Ophthalmologic evaluation: Monitor for glaucoma, even in adulthood
- Seizure management: Treat early for better outcomes

➔ Multifocal Capillary Malformations

- CM-AVM Syndrome (Capillary Malformation-Arteriovenous Malformation):
    - Genetic mutations: RASA1 (60%), EPHB4 (20%)
    - Key features: Orange-brown CM, telangiectasias, "Bier spots"
    - Neuroimaging: MRI brain, spine, head & neck to evaluate AVMs
    - Associated risks: CNS AVMs, need for surgical interventions
- MIC-CAP Syndrome (Microcephaly-Capillary Malformation):
    - Autosomal recessive inheritance
    - Key features: Congenital microcephaly, reduced sulcation on brain MRI, developmental delay
    - Genetic testing for diagnosis

2. Arteriovenous Malformations (AVMs)

- Pathophysiology: Direct arterial-venous connections without capillary bed
- Diagnosis: MRI/MRA or angiography

Key Features	Occurrence	Treatment
AVMs in CNS	90% in CNS	Surgery, embolization
CAMS (Cerebrofacial Arteriovenous Metameric Syndrome)	Unilateral, metameric distribution	Neurosurgical embolization

3. Hemangiomas with CNS Involvement

Type	CNS Risk	Key Associations
Multifocal hemangiomas	Rare CNS lesions (may be asymptomatic)	Screen for visceral involvement
Segmental hemangiomas	Risk of PHACE Syndrome	Requires CNS imaging

PHACE Syndrome

- P: Posterior fossa brain malformations
- H: Hemangioma (large facial, segmental)
- A: Arterial anomalies (including dysplasia or absence)
- C: Cardiac anomalies (coarctation)
- E: Eye abnormalities

Imaging: MRI head/neck/chest; echocardiogram
Monitoring: Early MRI for stroke risk, less frequent imaging after first year

Final Remarks

- **Vascular anomalies with CNS involvement** require a high degree of suspicion and a multidisciplinary approach.
- **Genotype-phenotype correlations** help guide clinical workup and treatment.
- **Regular follow-up** with neurology, ophthalmology, and radiology is essential for early diagnosis and intervention.

References:

- ISSVA Classification for Vascular Anomalies. 2025
- Hausman-Kedem M, et al. Long-term clinical and radiological trajectories of craniocervical vasculopathy in children with PHACE syndrome. Dev Med Child Neurol. 2024 Oct;66(10):1348-1360
- Metry D, et al. PHACE Syndrome Research Conference. Consensus Statement on Diagnostic Criteria for PHACE Syndrome. Pediatrics. 2009 Nov;124(5):1447-56

- Haggstrom AN, et al. Patterns of infantile hemangiomas: new clues to hemangioma pathogenesis and embryonic facial development. Pediatrics. 2006 Mar;117(3):698-703.
- Amyere M, et al. Germline Loss-of-Function Mutations in EPHB4 Cause a Second Form of Capillary Malformation-Arteriovenous Malformation (CM-AVM2) Deregulating RAS-MAPK Signaling. Circulation. 2017 Sep 12;136(11):1037-1048
- Zallmann M, et al. Screening for Sturge-Weber syndrome: A state-of-the-art review. Pediatr Dermatol. 2018 Jan;35(1):30-42

Exploring pigmentary mosaicism, what is new?

Speaker: Maria Teresa Garcia Romero (Mexico)

Key Points:

1. **Introduction to Mosaicism**:
    - Mosaicism is a biological concept occurring in nature, affecting flowers, plants, animals, and humans, leading to various patterns in color and texture. Humans are mosaics to a certain extent.
    - **Alfred Blaschko** first explored skin mosaicism, describing patterns in 1900. His work was rediscovered in the 1970s, sparking renewed interest in the subject.
2. **Pigmentary Mosaicism**:
    - Heterogeneous group of pigmentation disorders marked by the presence of **hypo-** and **hyperpigmented macules** following mosaic patterns.
    - The **melanocyte number** in pigmentary mosaicism remains **normal**
    - Historically called terms like "hypermelanosis of Ito," "pigmentary nibbles," and others, these terms are now grouped under the broader concept of **pigmentary mosaicism**.
3. **Key Patterns of Cutaneous Mosaicism**:
    - **Blaschko's Lines**: Narrow, broad, and block-like patterns.
    - **Lateralization**: A pattern often observed in unilateral lesions.
    - **Sash-like** and **large patches** are also common manifestations.
    - **Timing of Mutation**: The time at which mutations occur plays a significant role in the pattern and extent of the disease.

4. Pathophysiology:
    - Mosaicism can be **genomic** (with multiple genetically distinct cell populations) or **epigenetic** (functional changes in gene expression, such as the random inactivation of one X chromosome in females).
    - **Gene Expression**: New research suggests that migration patterns of melanocyte precursors via **ventral pathways** and **dorsolateral pathways** contribute to pigmentary mosaicism.
5. Extra-Cutaneous Manifestations:
    - Approximately **56%** of patients with pigmentary mosaicism have extra-cutaneous manifestations, including **neurological** (developmental delays, seizures), **musculoskeletal**, **ocular**, and **dysmorphic features**.
    - The **Montreal group** observed that children with more **localized** pigmentary patterns had a **lower rate of systemic involvement**, while those with **generalized** involvement were **more likely** to have multi-systemic abnormalities.
6. Genetic Insights:
    - Many patients with pigmentary mosaicism exhibit **chromosomal aberrations** (e.g., **polychromic anomalies, rings, deletions**, or **translocations**).
    - Mutations in **mTor** and **RHO** genes have been identified in certain forms of pigmentary mosaicism, which are involved in melanocyte regulation and pigmentation.
    - **Hypomelanosis of Ito**: Associated with chromosomal aberrations and mosaic mutations in genes related to skin pigmentation.
7. Genetic Testing and Diagnosis:
    - **Genetic Testing** is important in patients with **generalized involvement** or **extra-cutaneous manifestations**. Though it does not always impact treatment directly, it may provide insight into the diagnosis and help guide management.
    - Techniques such as **next-generation sequencing** and **microdissection of tissue** from affected sites allow for better detection of mosaic genetic variants.

8. Management Approach:
    - **Multidisciplinary approach**: dermatologists, pediatric specialists, genetic counselors, and psychosocial support.
    - **Genetic counseling**, especially in cases involving mutations in the gonads, as they may transmit the disease to offspring.
    - **Physical exam**: Essential for identifying affected areas, differentiating from other conditions, and directing to appropriate specialists.
9. Challenges:
    - **Differential Diagnosis**: Biopsy can help differentiate between other skin conditions but is not always necessary unless specific conditions need to be excluded.
    - Early identification and monitoring of extra-cutaneous symptoms can improve outcomes, as these symptoms may affect quality of life.

Table: Types of Pigmentary Mosaicism and Associated Patterns

Pattern Type	Description	Associated Manifestations
Blaschko's Lines	Narrow or broad lines following a linear distribution	Found in both **melanocytic** and **non-melanocytic** mosaicism
Block-like Patterns	Well-defined, localized patches	Associated with **neurocutaneous disorders** and systemic involvement
Lateralization	Unilateral involvement, often localized	**Mosaic** may manifest only on one side of the body
Sash-like Patterns	Diagonal stripes across the body	Typically associated with **segmental mosaicism**
Large Patches	Larger, well-circumscribed areas	Seen in conditions like **hypomelanosis of Ito**

Conclusion:

- ≈ Pigmentary mosaicism shows patterned skin pigmentation due to genomic and **epigenetic** changes.
- ≈ May involve systemic abnormalities.
- ≈ Genetic advances aid in identifying chromosomal/gene mutations.
- ≈ Ongoing monitoring and **genetic counseling** are advised.
- ≈ Multidisciplinary care and genetic testing are key in complex cases.

References:

- Kromann AB, et al. Pigmentary mosaicism: a review of original literature and recommendations for future handling. Orphanet J Rare Dis. 2018 Mar 5;13(1):39
- Schaffer JV. Pigmentary mosaicism. Clinics in Dermatology. 2022 Jul-Aug;40(4):322-338.
- Belzile E, et al. Patterned cutaneous hypopigmentation phenotype characterization: A retrospective study in 106 children. Pediatric Dermatology. 2019; 36(6):869-875
- Salas-Labadía C, et al. Genetic and clinical characterization of 73 Pigmentary Mosaicism patients: revealing the genetic basis of clinical manifestations. Orphanet J Rare Dis. 2019 Nov 15;14(1):259.

Rasophathies, mosaicism and the brain, how are these linked?

Speaker: Camila Downey (Chile)

Clinical and Genetic Correlations

Embryological & Pathogenic Link:

- Skin, brain, and eye share **ectodermal origin**, explaining overlapping manifestations.
- **RASopathies**: Genetic syndromes due to mutations in the **RAS-MAPK pathway**, impacting:
    - Cell proliferation
    - Differentiation
    - Senescence

Types and Severity of RASopathies:

RASopathy Type	Extent of Cell Involvement	Examples	Notes
Germline (all cells affected)	Systemic	Noonan Sme, NF1	Requires mild/moderate dysregulation to allow survival
Mosaic (tissue-specific)	One/few tissues	Shimmelpenning	Severity depends on mutation timing and affected cells

- Early embryogenesis mutation → Multilineage involvement (e.g., skin, CNS, eye)
- Late embryogenesis/postnatal mutation → Limited/localized tissue involvement

Genetic Mutations & Dermatologic Lesions:

Mutation Associated Lesions

K-RAS	Nevus sebaceous, capillary malformations, AVMs
H-RAS	Keratinocytic epidermal nevi, Spitz nevi
N-RAS	Congenital melanocytic nevi
B-RAF	Spitz nevi, congenital melanocytic nevi

Clinical Syndromes ("True RASopathies") with Mosaic Presentation:

Specific dermatologic and extracutaneous findings:

Syndrome	Mutation	Key Features
Shimmelpenning (Linear Nevus Sebaceous Syndrome)	K-RAS	Linear nevus sebaceous, coloboma, PDA, cerebral malformations
Keratinocytic Epidermal Nevus Syndrome		Widespread keratinocytic nevi, lymphatic malformation, cardiac anomalies

Syndrome	Mutation	Key Features
Oculoectodermal Syndrome		Aplasia cutis, eyelid tags, dermoids, neurodevelopmental delay, cardiac anomalies
Encephalocraniocutaneous Lipomatosis		Alopecia, orbital tags, CNS lipomas, seizures, ocular defects
Phacomatosis Pigmentokeratotica	H-RAS	Sebaceous + melanocytic nevi, scoliosis, rhabdomyosarcoma, epilepsy
Cutaneous Skeletal Hypophosphatemia Syndrome		Epidermal nevi, rickets, bone demineralization, eye/CNS involvement

Genotype-Phenotype Correlations:

- BRAF and NRAS:
    - Less frequent but **more likely to involve multiple extracutaneous organs**
    - Associated with **giant congenital melanocytic nevi**
- KRAS:
    - More severe phenotypes; neonatal death reported
    - Found in 49% of epidermal nevi with systemic involvement
    - Strongly associated with ophthalmologic tumors, MRI brain abnormalities
- HRAS:
    - Milder phenotype
    - Associated with hypophosphatemia syndromes
    - 86% of keratinocytic epidermal nevi cases

Clinical Work-Up Recommendations:

Evaluate for systemic involvement when:

- Lesions are **extensive**, involve **head/neck**, or **≥2 body regions**

Suggested assessments:

- **Medical history**: Growth, puberty, neurodevelopment, bone pain
- **Physical exam**: Cardiac, ocular, auditory findings
- **Imaging/labs** (depending on case): MRI, abdominal ultrasound, phosphate levels

Research Insight:

- Mouse model: Introduction of **K-RAS mutation** (as seen in linear nevus sebaceous syndrome) led to **neurologic features**, reversed upon suppression of the mutated protein.
- Suggests potential for **targeted molecular therapies**.

Key Takeaways:

- **Cutaneous distribution is an early clinical marker** for systemic RASopathies.
- **Extensive or head/neck lesions** warrant further systemic evaluation.
- **40% of sebaceous nevus syndromes** are due to RASopathies; others may involve **PIK3CA** or **FGFR** mutations.
- **KRAS mutations** correlate with more severe multisystem involvement than **HRAS**.
- **Multidisciplinary approach** is essential for diagnosis, management, and surveillance

References:

- Zenker M. Clinical overview on RASopathies. Am J Med Genet C Semin Med Genet. 2022 Dec;190(4):414-424
- Sánchez-Espino LF, et al. Single dominant lesion in capillary malformation-arteriovenous malformation (CM-AVM) RASA1 syndrome. Pediatric Dermatology. 2024; 41 (5): 861-865.
- Morren M, et al. Mosaic RASopathies concept: different skin lesions, same systemic manifestations? Journal of Medical Genetics 2024;61:411-419.

- Torchia D, et al. Phacomatosis spilosebacea: A new name for a distinctive binary genodermatosis. Journal of the American Academy of Dermatology. 2023;89 (4):764 - 773

Novel treatments for neurocutaneous disorders

Speaker: Irene Lara Corrales (Canada)

Evolving Molecular Understanding and Targeted Therapeutics

1. Congenital Melanocytic Nevus (CMN)

- **Risk Factors for Neurocutaneous Melanocytosis:**
  - Giant/large CMN
  - Multiple satellite lesions
  - Posterior axial location
- **Genetic Landscape:**
  - CMNs are **mosaic single-gene disorders**.
  - ~75% have defined mutations (mostly *NRAS*).
  - ~25% unclassified—recently, **gene fusions** identified in some of these.
- **Clinical Impact of Gene Fusions:**
  - Strong pathway hyperactivation—greater than NRAS variants.
  - Associated with more **pruritic**, **nodular**, and **proliferative lesions**.
- **Treatment Insight:**
  - **Trametinib** (MEK inhibitor):
    - ↓ bulk, erythema, and pruritus.
    - In vitro/in vivo studies confirm dose-responsive suppression of proliferation in *NRAS* and *BRAF* fusion-positive lines.
  - **PIK3CA Pathway Involvement:**
    - Preliminary data suggests **PIK3CA inhibitors** may reduce CMN melanocytes.
    - Clinical relevance under investigation; safety profile pending.

2. Tuberous Sclerosis Complex (TSC)

- **Pathogenesis:** Mutations affecting the **mTOR** pathway.
- **Therapeutic Advances:**
  - **Everolimus (oral mTOR inhibitor):**
    - Used for renal manifestations.
    - Limited and variable response in facial angiofibromas—often requiring **adjunctive topical therapy**.
  - **EGFR Pathway as Target:**
    - Histological overexpression in SEGA, cortical tubers, and dysplasia.
    - **Afatinib** (EGFR inhibitor) combined with everolimus showed ↓ tumor proliferation.
  - **Preventive Sirolimus in Infants:**
    - Pilot study in 5 infants <6 months old.
    - ↓ seizure incidence and normal cognitive development in most cases.
    - Laid groundwork for a **Phase II clinical trial**.
  - **Prenatal Therapy:**
    - Prenatal **sirolimus** use in fetal cardiac rhabdomyomas showed ↓ tumor size and improved cardiac function.
    - Outcomes encouraging, but **long-term neurodevelopmental impact** unclear.
  - **Future Prospects:**
    - **CRISPR gene editing** under investigation.
  - **Topical Timolol:**
    - Small study suggested possible improvement in erythema and size of angiofibromas.

3. Neurofibromatosis Type 1 (NF1)

- **Key Clinical Challenge:** Plexiform neurofibromas – benign histologically but often disfiguring, painful, and impairing function.

- Therapeutic Advances:
    - Selumetinib (MEK inhibitor):
        - FDA-approved for children ≥2 years with inoperable symptomatic plexiform neurofibromas.
        - Significant **tumor shrinkage** and **clinical improvement** (pain, disfigurement).
        - Real-world data supports long-term efficacy and safety.
    - Trametinib:
        - Approved for NF1-associated low- and high-grade gliomas (alone or with dabrafenib).
    - Cutaneous Neurofibromas:
        - Ongoing trials exploring Selumetinib for this indication.
        - Early results: limited objective reduction, variable adherence.

Summary Table – Targeted Therapies in Neurocutaneous Disorders

Disorder	Genetic Pathway	Targeted Therapy	Outcome/Notes
CMN (NRAS/BRAF fusion)	MAPK	Trametinib	↓ lesion bulk, pruritus, erythema
CMN (PIK3CA-related)	PI3K-AKT-mTOR	PIK3CA inhibitors	↓ melanocyte density (early evidence)
Tuberous Sclerosis	mTOR	Everolimus / Sirolimus	↓ renal tumors; variable angiofibroma response
	EGFR	Afatinib + Everolimus	↓ SEGA and cortical lesions (preclinical)
	–	Prenatal Sirolimus	↓ fetal rhabdomyomas (case reports)

Disorder	Genetic Pathway	Targeted Therapy	Outcome/Notes
Neurofibromatosis Type 1	RAS-MAPK	Selumetinib	↓ inoperable plexiforms, improved QoL
		Trametinib (gliomas)	FDA-approved for brain tumors

Key Takeaways

- **Molecular diagnostics** are guiding **precision therapy** in neurocutaneous syndromes.
- MEK and mTOR inhibitors are reshaping the management of **CMN**, **TSC**, and **NF1**.
- **Selumetinib** has shown durable responses in **plexiform neurofibromas** and is under evaluation for **cutaneous neurofibromas**.
- **Prenatal and preventive therapies** are emerging, though long-term safety remains to be fully elucidated.
- **Interdisciplinary** management and ongoing research are key to optimal outcomes.

References:

- Schaffer JV. Update on melanocytic nevi in children. Clin Dermatol. 2015 May-Jun;33(3):368-86
- Martin SB, et al. Mosaic BRAF Fusions Are a Recurrent Cause of Congenital Melanocytic Nevi Targetable by MAPK Pathway Inhibition. J Invest Dermatol. 2024 Mar;144(3):593-600.e7
- Molho-Pessach V, et al. Giant congenital melanocytic naevus with a novel CUX1-BRAF fusion mutation treated with trametinib. Br J Dermatol. 2022 Dec;187(6):1052-1054
- Imataka G, et al. The Therapeutic Potential of Oral Everolimus for Facial Angiofibromas in Pediatric Tuberous Sclerosis Complex: A Case-Based Analysis of Efficacy. Diseases. 2024 Dec 20;12(12):334
- Schachenhofer J, et al. Targeting the EGFR pathway: An alternative strategy for the treatment of tuberous sclerosis complex? Neuropathol Appl Neurobiol. 2024 Apr;50(2):e12974.
- Racioppi G, et al. Prenatal mTOR Inhibitors in Tuberous Sclerosis Complex: Current Insights and Future Directions. J Clin Med. 2024 Oct 23;13(21):6335

- Dombi E, et al. Activity of Selumetinib in Neurofibromatosis Type 1-Related Plexiform Neurofibromas. N Engl J Med. 2016 Dec 29;375(26):2550-2560

Phototherapy and photoprotection

Is there a role for phototherapy in 2025?

Speaker: Maria Agustina Acosta (Uruguay)

Phototherapy in Pediatric Dermatology

General Role & Indications

- Phototherapy remains a **valuable treatment option** for pediatric dermatologic conditions, despite the emergence of **biologic and systemic agents**.
- Particularly useful due to its **minimal systemic side effects** and **non-invasive nature**.
- Common pediatric indications:
  - **Atopic dermatitis**
  - **Psoriasis**
  - **Vitiligo**
  - **Cutaneous T-cell lymphoma (early stages)**
  - **Pityriasis lichenoides chronica**
  - Occasionally: granuloma annulare, morphea, lichen planus

Phototherapy Modalities

Modality	Comments
Narrowband UVB (NB-UVB)	Most commonly used in children
PUVA (Psoralen + UVA)	Rare in pediatrics due to safety concerns
Targeted phototherapy	Used for localized lesions
Home-based UVB	An emerging alternative with careful supervision

Pediatric Considerations

- **Age**: Often feasible from age 5–6, depending on cooperation and parental support.
- **Scheduling**: One of the **major limitations** due to school conflicts and multiple weekly visits.
- **Monitoring**: Skin type, lesion distribution, disease chronicity, and overall tolerance must guide treatment.
- **Adverse effects**: Generally minimal—transient erythema, dryness, and rare phototoxicity.

Home Phototherapy

- **NB-UVB home units** are a potential option to improve adherence and reduce logistical burden.
- Useful for localized diseases requires thorough training and parental involvement.
- Not yet standard of care in all regions due to **device access and cost**.

Phototherapy vs Biologics

- **Biologics**: More targeted, effective, and faster in some conditions (e.g., psoriasis, atopic dermatitis).
- **Phototherapy**: Non-invasive, avoids lab monitoring and injections, especially suitable for younger children.
- **Current challenge**: Balancing effectiveness with practicality—**time commitment and accessibility** remain key barriers.

Key Takeaways

- Phototherapy remains a **relevant, effective, and safe** option in pediatric dermatology.
- Particularly appropriate when biologics are not feasible or desired.
- Should be considered in a **personalized approach** based on disease severity, family logistics, and patient age.

- A **multidisciplinary and flexible model** is crucial to integrate phototherapy effectively in pediatric care.

References:

- Crall CS, et al. Phototherapy in children: Considerations and indications. Clin Dermatol. 2016 Sep-Oct;34(5):633-9.
- Wollenberg A, et al. European guideline (EuroGuiDerm) on atopic eczema - part II: non-systemic treatments and treatment recommendations for special AE patient populations. J Eur Acad Dermatol Venereol. 2022 Nov;36(11):1904-1926.
- Slimani Y, et al. Phototherapy in children: Epidemiology, clinical profile, and outcome. Photodermatol Photoimmunol Photomed. 2021 May;37(3):224-225.
- Magdaleno-Tapial J, et al. Comparison of Phototherapy in Pediatric and Adult Patients. Actas Dermosifiliogr (Engl Ed). 2020 Jan 2;111(1):41-46

Special considerations for phototherapy in pediatric patients

Speaker: Matias Maskin (Argentina)

Introduction: Pediatric Dermatology and Challenges with Medications

- **Pediatric dermatology** faces **delays** in treatment approvals, as medications are usually **approved for adults first**.
- **Off-label use of adult-approved medications is common** due to a lack of pediatric-specific trials and evidence.

Phototherapy vs. Systemic Medications: Understanding the Debate

- **Phototherapy** is often seen as a **safer alternative** than **systemic medications** for children, for parents, because it's non-invasive, doesn't involve injections, and appears to have fewer side effects.
- The **long-term risks** of phototherapy are still debated, with **older studies** suggesting risks such as skin cancer or photo-itching. More **recent studies** on pediatric dermatology and phototherapy are lacking.
- **Off-label usage of medications** remains high in pediatric dermatology due to the lack of pediatric-specific research.

Types of Phototherapy: UVB vs. UVA

- **UVB (Ultraviolet B)** is used more frequently in pediatric dermatology.

    - **Benefits of UVB**: Easier to administer, does not require pre-treatment medications, accessible for younger children (as long as they stay still).
- **UVA (Ultraviolet A)** is less commonly used in Argentina
    - **Drawbacks of UVA**: Requires pre-treatment medications, and the equipment for UVA isn't as widely available as UVB.

Phototherapy Risks and Concerns

- **Short-term risks of phototherapy** include **edema**, **blistering**, and **photo-aging**.
- **Long-term risks** include concerns about **photocarcinogenesis** (skin cancer) due to prolonged exposure to UV radiation. **20 years of follow-up studies** show some risk of **skin cancer**, although it is still debated, especially in children.

Phototherapy in Pediatric Dermatology: Conditions Treated

1. Psoriasis

*Phototherapy is now generally used as a **second-line therapy** or in combination with **biologics** for severe cases.*

    - Phototherapy is very effective in **mild to moderate psoriasis**.
    - **Combination therapy** (phototherapy + new medications) is recommended for **severe cases**.
    - **Guttate psoriasis** is particularly responsive to phototherapy.
    - **Long-term effectiveness**: Phototherapy doesn't offer long-lasting remission, especially when used as **monotherapy**.
    - **Biologic therapies** like **IL-17** or **IL-23 inhibitors** are more effective for severe cases, but **phototherapy remains useful for mild cases**.

2. Atopic Dermatitis.

*Phototherapy is recommended for **moderate cases**, but **systemic biologics** are preferred for **severe atopic dermatitis***

    - **Phototherapy** may be used in **combination therapy** with **topical treatments** or biologics for **flare-ups**.

- Phototherapy's role in **atopic dermatitis** is diminishing as new **biologic treatments** are more effective.

3. **Mycosis Fungoides**

*Phototherapy remains a viable option for **early-stage** cases*

- **Combining phototherapy with other treatments** (e.g., methotrexate, interferon) may be effective.
- **Monotherapy with phototherapy** works well in **plaque mycosis fungoides**, while **follicular trophic mycosis fungoides** may need more intensive treatments.

4. **Vitiligo**

- Phototherapy is a common treatment option for **vitiligo**.
- There are no **FDA-approved treatments** for pediatric vitiligo, making phototherapy a viable option in these cases.

Comparing Phototherapy with Systemic Medications

- **Effectiveness**:
  - Biologics are **more effective** for conditions like **psoriasis** and **atopic dermatitis**, especially in severe cases, compared to phototherapy.
- **Safety**:
  - Biologics, such as **IL-17** and **IL-23 inhibitors**, are **highly effective** and generally considered **safe** despite being immunosuppressive.
  - **Phototherapy** is perceived as a safer option because it is non-invasive, but biologics have fewer long-term side effects compared to phototherapy.
- **Cost**:
  - Phototherapy can be more **cost-effective** compared to biologics, especially in countries where biologics may not be easily accessible or affordable.
  - **Biosimilars**, such as **adalimumab**, have become cheaper, and this reduces the gap in cost between biologics and phototherapy.

Key Takeaways

- **Access to phototherapy** remains an issue in some regions, such as **Argentina**, where the cost of **office-based phototherapy** can be prohibitive for many families.
- **Phototherapy is most useful for mild to moderate cases**, such as **guttate psoriasis**, **vitiligo**, and **early-stage mycosis fungoides**.
- **Phototherapy is still a valuable tool** for managing certain conditions, but its role is diminishing in favor of **biologic therapies** that are more effective for severe cases.
- **Biologic treatments** have proven to be **highly effective** and **safe** for pediatric patients with severe **psoriasis** and **atopic dermatitis**, often rendering phototherapy unnecessary for these cases.
- **Combination therapies** (e.g., biologics + phototherapy) may be the future approach for managing **chronic dermatologic conditions**.

Audience Q&A: Insights from Clinical Practice

- **Maintenance Therapy**:
    - Some dermatologists prefer to **taper** phototherapy slowly in patients, for up to a year or more in some cases, especially with conditions like **mycosis fungoides**, to prevent flare-ups.

Conclusion

The role of **phototherapy** in pediatric dermatology is evolving. While it remains an essential treatment option for **mild to moderate conditions**, newer **biologic therapies** are increasingly becoming the go-to treatments for more severe conditions. Moving forward, phototherapy will likely be incorporated more into **combination therapies**, making it a valuable tool but no longer a first-line treatment in most cases.

References:

- Petkova V, et al. Off-Label Prescribing in Pediatric Population-Literature Review for 2012-2022. Pharmaceutics. 2023 Nov 21;15(12):2652
- Al-Gawahiri M, et al. Investigation of the applicability of adult definitions of disease severity for psoriasis in a pediatric cohort: A prospective registry study. J Am Acad Dermatol. 2025 Feb 14:S0190-9622(25)00262-2.
- Torres AE, et al. Role of phototherapy in the era of biologics. J Am Acad Dermatol. 2021 Feb;84(2):479-485

- Ponte P, et al. Efficacy of narrowband UVB vs. PUVA in patients with early-stage mycosis fungoides. J Eur Acad Dermatol Venereol. 2010 Jun;24(6):716-21
- Garza-Mayers AC, et al. Narrowband ultraviolet B phototherapy in pediatric vitiligo: A retrospective study. J Am Acad Dermatol. 2023 Jul;89(1):135-136

Do children need photoprotection?

Speaker: Henry W. LIM (USA)

Pediatric Photoprotection – Summary

Composition and Effects of Sunlight

- Sunlight reaching the Earth's surface consists of:
  - **UV radiation (~2%)**
  - **Visible light (~50%)**
  - **Infrared radiation (remaining portion)**
- **Photobiological effects:**
  - **UVB**: Erythema, photocarcinogenesis (especially in lighter skin)
  - **UVA1**: Tanning, photoaging, carcinogenesis
  - **Visible light**: Induces erythema in all skin types and persistent pigmentation in darker skin, minimal/no pigmentation in **lighter skin**

Intrinsic Skin Protection

Darker skin:	**Lighter skin**:
More and larger melanosomes, individually dispersed	Smaller melanosomes, grouped in keratinocytes
Intrinsic SPF ~13	Intrinsic SPF ~3

Pediatric Photoprotection: Evidence & Behavior

Family & Cultural Influence

- Children mirror **parents' sun-protective behaviors**
- Hispanic and Black children less likely to practice sun protection

- Lighter-skinned children more at risk; photoprotection highly needed
- Adolescents show **declining adherence** to photoprotection

Clinical Correlations

- Childhood **sunburns** linked to:
    - Increased number of **nevi**
    - **Freckles**
    - Elevated **melanoma risk**

Controversies

- **Percutaneous absorption** of chemical filters: detected in bloodstream, significance unknown
- Concerns over **endocrine disruption**
- Environmental impact: **coral reef bleaching**, **ocean pollution**
- Increasing awareness and questions from parents
- **Only mineral (inorganic) filters** (zinc oxide, titanium dioxide) classified as **"safe and effective"** by the FDA

Pediatric Sunscreen Recommendations

Age-Specific Advice

- **<6 months**:
    - Avoid direct sunlight
    - Emphasize **shade**, **clothing**, and **hats**
- **<2 years**:
    - Prefer **mineral sunscreens** for exposed areas
    - Limit chemical sunscreen due to systemic absorption

Practical Challenges

- Mineral sunscreens may leave **white cast**
- Aesthetic concerns in **darker-skinned children**
- Adjustments required based on **skin tone** and **acceptability**

Personalized Photoprotection Strategy

Skin Tone–Specific Recommendations

Skin Type	SPF Recommendation	UVA Protection	Visible Light Protection
Type I–III (Light)	≥ SPF 50	Moderate	Not critical
Type IV–VI (Dark)	≥ SPF 30	Higher preferred	Important (pigmentation risk)

- **No standardized method** exists yet to measure **visible light protection** in sunscreens
- **International consensus** efforts underway to develop a harmonized testing standard

Total Photoprotection Package

Sunscreen on exposed areas (SPF and spectrum tailored to skin type)
+

- **Shade**
- **Wide-brimmed hats** (preferable to baseball caps)
- **Long-sleeved, tightly woven clothing**
- **Sunglasses**

Emerging Adjunctive Options

- Under study:
  - **Polypodium leucotomos extract**
  - **Nicotinamide**
  - **Antioxidants**
- Currently **limited data**; not yet standard

Final Takeaways

- **All children**, regardless of skin tone, require photoprotection
- **Darker-skinned children** have lower but **not zero** risk
- Education must be:
    - **Family-centered**
    - **Realistic**
    - Tailored to **individual needs and skin tone**
- Sun exposure has **benefits**; protection should be **sensible**, not prohibitive

References:

- Mahmoud BH, et al. Impact of long-wavelength UVA and visible light on melanocompetent skin. J Invest Dermatol. 2010 Aug;130(8):2092-7.
- Kohli I, et al. Synergistic effects of long-wavelength ultraviolet A1 and visible light on pigmentation and erythema. Br J Dermatol. 2018 May;178(5):1173-1180
- Pantelic MN, et al. Ultraviolet filters in the United States and European Union: A review of safety and implications for the future of US sunscreens. J Am Acad Dermatol. 2023 Mar;88(3):632-646.
- Shetty NP, et al. Personalized photoprotection: Commentary on "Adjusting best practices in the treatment of melasma with a focus on patients with skin of color". J Am Acad Dermatol. 2023 Sep;89(3):635-636.
- de Troya-Martín M, et al. Personalized Photoprotection: Expert Consensus and Recommendations From a Delphi Study Among Dermatologists. Photodermatology, Photoimmunology & Photomedicine, 2025; 41:e70001

Phototherapy in pediatric photodermatoses

Speaker: Antonio Torrelo (Spain)

Photodermatoses in Children – Updates and Management

Overview: Phototherapy is a valuable tool in dermatology, including pediatric cases, though protocols are often adult-centered. Its application in children must be individualized, especially in rare or severe cases. The following summarizes insights into **photodermatoses** such as **Polymorphic Light Eruption (PMLE)** and **Actinic Prurigo (AP)**, with recent treatment updates.

Polymorphic Light Eruption (PMLE) in Children

- **Epidemiology:**

    - Rare in children.
    - Often mild or misdiagnosed as juvenile spring eruption.
- Pathophysiology:
    - Hypersensitivity to photoantigens.
    - Possible resistance to UV-induced immunosuppression.
    - UVA is the main part of the solar spectrum involved.
- Management:
    - Photoprotection: Broad-spectrum sunscreens, Emphasis on broad-spectrum (UV-A) sunscreen, protective clothing.

Systemic antioxidants: Safe for children (e.g., beta-carotene), less standardized in children.

    - Photohardening: Should begin one month before expected exposure. Preferred over phototherapy in younger children.
    - Phototherapy:
        - Rarely necessary in children.
        - If used, UVB is preferred over UVA (UVA contraindicated in <7 years).
        - Non-standardized protocols.
- New insights (Limited Pediatric Data):
    - Omalizumab led to complete symptom remission in an adult with longstanding PLE and chronic urticaria. Potential use in selected severe cases.
    - Tofacitinib (JAK 1-3 inhibitor): it can abrogate the effects of the predominant cytokine milieu of PLE and thus reduce the expression of aberrant inflammatory T lymphocyte expression.
    - Roflumilast 0.3% cream: A single-case report was presented of a patient with PLE who experienced resolution after treatment

Actinic Prurigo (AP)

- Epidemiology:
    - More common in Central and South American populations.

    - Genetic predisposition (HLA-related).
- Diagnosis:
    - Primarily clinical.
    - Histopathology can assist in diagnosis.

- Treatment Challenges:
    - **Topical steroids and phototherapy** are typically ineffective.
    - **Hydroxychloroquine**: Limited efficacy; mostly disappointing.
    - **Talidomide**:
        - Used in Latin America; not approved in EU/US.
        - Acts via NF-κB inhibition and T-helper modulation (likely TH1/TH17).
    - **Dupilumab**:
        - IL 4/IL 13 receptor antagonist, disrupts Th2 pathway
        - Example: 3 cases reports of pediatric pacients with severe, recalcitrant actinic prurigo who achieved rapid and sustained clearence.
    - **JAK Inhibitors (*Upadacitinib*, *Baricitinib*, *Tofacitinib*)**:
        - Inhibit pro-inflammatory cytokines (e.g., IL-4, IL-13, IL-31) via JAK-STAT pathway.
        - Example: Case series including a 9-year-old girl with rapid resolution of pruritus and inflammation following JAK inhibitor therapy.
        - Applied in isolated pediatric cases with severe inflammatory dermatoses (e.g., actinic prurigo, chronic urticaria)
        - **Considerations**: Not first-line - Require monitoring for adverse effects - May be used off-label in selected refractory pediatric cases.

Nicotinamide (Vitamin B3)

- **Use**:

- Trialed as a preventive agent for photodermatoses.
- **Mechanism**: Enhances DNA repair and reduces UV-induced immunosuppression.

- **Efficacy**:
  - Mixed outcomes in general, but a few reports show clinical attenuation in pediatric actinic prurigo.
  - Completely non-toxic and considered a safe adjunctive or preventive option.

Polypodium leucotomos supplementation

- Exerts a pleiotropic **immunomodulatory and antioxidant effect** by shifting the balance from pro- to an antiinflammatory cytokine environment. This counteracts the effects of UV-induced cellular damage characteristic of photodermatoses.

Resume:

Condition	Presentation in Children	First-line Therapy	Emerging/Alternative	Remarks
Polymorphic Light Eruption (PLE)	Rare, mild; juvenile spring eruption	UV-A protection, antioxidants	Omalizumab (adults), topical tacrolimus	Desensitization rarely used in <7 years
Actinic Prurigo (AP)	Common in Latin America; rare in Europe	Steroids (low response), avoidance	Talidomide, JAK inhibitors, nicotinamide	Associated with specific HLA types

Condition	Presentation in Children	First-line Therapy	Emerging/Alternative	Remarks
Photodermatoses (refractory)	Severe, resistant to topical therapy	Photoprotection, antioxidants	JAK inhibitors, nicotinamide	Requires individualized approach

Conclusions:

- Photodermatoses like PMLE and AP are rare but challenging in children.
- **Photoprotection remains the cornerstone** of management.
- **Phototherapy is rarely indicated** and must be carefully adapted in pediatric populations.
- Emerging biologics and small molecule therapies (e.g., dupilumab, JAK inhibitors) show promise in **severe or refractory cases**, though pediatric use is still limited and requires further study.
- Non-toxic agents like **Polypodium leucotomos** may be useful adjuncts

References:

- Sopeña AO, et al. Polymorphous light eruption treated with omalizumab. Photodermatol Photoimmunol Photomed. 2023 Jan;39(1):85-86.
- Sardana K, et al. Tofacitinib: A Treatment Option for Recalcitrant Polymorphic Light Eruption and Its Mechanistic Rationale. Dermatitis. 2024 May-Jun;35(3):246-249
- Garg KS, et al. Polymorphous Light Eruptions Treated With Roflumilast 0.3% Cream: A Case Report. J Drugs Dermatol. 2024 Aug 1;23(8):686-687
- Stump M, et al. Attenuation of actinic prurigo eruptions with Polypodium leucotomos supplementation. Pediatr Dermatol. 2022 Jan;39(1):145-146.

Sunscreens and the environment

Speaker: Fernando M. Stengel (Argentina)

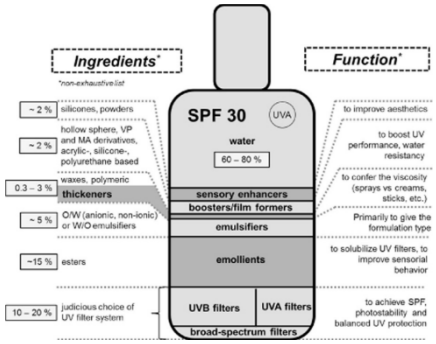
Conceptual Foundation

- Genes, organisms, and environments are interdependent in evolution — external and internal environmental factors shape living systems.

- Environmental elements, including **climate change**, act as **catalysts in evolution**, requiring **balanced, multifactorial analysis**.

Classification of Sunscreens

- **Organic (Chemical) Filters**: Soluble in formulation, absorb UV light.
- **Inorganic (Physical) Filters**: Insoluble nanoparticles (e.g., **zinc oxide, titanium dioxide**) that reflect, scatter, and absorb UV.
- **New Organic Particles**: Hybrid agents with reflective, dispersive, and absorptive properties.



Environmental Concerns of UV Filters

- **Complex Formulations**: Sunscreens often contain **20–30% UV filters**, along with other cosmetic additives.
- **High SPF** products correlate with higher concentrations of both **organic and inorganic compounds**.

Pollution Sources

- Sunscreens are part of a broader issue, with **personal care and hygiene products** contributing significantly.
    - ~30% of skincare products
    - ~50% of makeup products
    - ~75% of perfumes contain UV filters
- **Titanium dioxide (TiO_2)** found in: food (as E171), plastics, paints, water treatment, chemical warfare.

Surface Water Contamination

- **Organic UV filters** are **lipophilic** and **poorly removed** in sewage treatment, leading to persistent contamination in:
    - High population density zones
    - Recreational waters (pools, beaches)
    - Seasonal peaks (spring/summer)

- Chlorinated pools can lead to formation of **new toxic compounds** via filter-chlorine interactions.

Coral Reefs and UV Filters

- Corals live in **symbiosis with algae**. Environmental stress (temperature, pollution) causes **bleaching**.
- **Oxybenzone, octocrylene, and octinoxate** are implicated in:
    - **Larval toxicity**
    - **Oxidative DNA damage**
    - **Skeletal endocrine disruption**
    - **Bleaching and general coral toxicity** (especially in the presence of light)

Geographic Evidence

- UV filters have been detected in **remote regions**, including **Arctic waters**, suggesting global spread via currents.
    - **Bans** on oxybenzone and octinoxate have been implemented in regions such as Hawaii, Palau, U.S. Virgin Islands, Aruba

Marine Biodiversity & Bioaccumulation

- UV filters accumulate in marine organisms:
    - **Bioaccumulation**: Higher filter concentrations in organisms than in water.
    - **Biomagnification**: Increasing concentration up the food chain (fish → humans).
- In fish, oxybenzone is an **endocrine disruptor**, causing **reduced egg production** and **male feminization**.

Climate Change vs. Sunscreens

- Coral bleaching primarily driven by **sea surface temperature** (SST) increases.
    - Example: **Great Barrier Reef, 2016** — bleaching occurred due to SST > 3–4°C above baseline.

- **Jarvis Island case**: Bleaching occurred without sunscreen exposure, confirming **temperature as the main factor**.
- **Recent data (2025, *Nature*)** shows rising SST over the past two years as a consistent trigger of bleaching.

Titanium Dioxide and Zinc Oxide

- Classified as **safe and effective** by FDA.
- **Agglomerate in seawater**, precipitating to the sea floor — **lower coral interaction risk.**
- Not systemically absorbed in humans; however, **nanoform** TiO_2 is the **most produced nanomaterial globally**.

Dermatological Responsibility

- Emphasize **scientific facts** while acknowledging limitations.
- Educate patients: **benefits of sunscreen use outweigh environmental risks.**
- In children, **recommend mineral sunscreens** (TiO_2, ZnO).
- Seek **safer organic alternatives** where regulations permit (Europe, Latin America).

Key Messages

1. **Primary cause of coral bleaching**: Elevated sea water temperature
    - UV filters may contribute as a **secondary stressor.**
2. **Sunscreens are critical for skin cancer prevention**; efforts must focus on:
    - Educating about **proper use**
    - Encouraging **physical protection** (clothing, shade)
    - Promoting **behavioral change** in sun exposure habits

Table: Sunscreen Ingredients – Environmental and Human Impact

Compound	Category	Environmental Concern	Human Safety	Comment
Oxybenzone (BP-3)	Organic	Coral bleaching, endocrine disruption in fish	Potential endocrine disruptor	Banned in several regions
Octinoxate		Coral toxicity, marine pollution	Moderate absorption, hormonal data	Banned in reef-sensitive areas
Octocrylene		Marine toxicity, bioaccumulation	May accumulate in tissue	Still widely used in many countries
Titanium Dioxide	Inorganic (mineral)	Precipitates in seawater, low coral interaction	Not absorbed dermally	Considered safe; used in children
Zinc Oxide		Similar to TiO_2 – precipitates, low coral impact	Not absorbed dermally	Recommended for pediatric use
New Organic Agents	Organic hybrid	Limited data	Under investigation	Safer formulations under development

References:

- Osterwalder U, *et al.* Global state of sunscreens. Photodermatol Photoimmunol Photomed. 2014 Apr-Jun;30(2-3):62-80
- González S, *et al.* Expert Recommendations on the Evaluation of Sunscreen Efficacy and the Beneficial Role of Non-filtering Ingredients. Front Med (Lausanne). 2022 Mar 31;9:790207.
- Abdel Azim S, *et al.* Sunscreens part 1: Mechanisms and efficacy. J Am Acad Dermatol. 2025 Apr;92(4):677-686.
- Abdel Azim S, *et al.* Sunscreens part 2: Regulation and safety. J Am Acad Dermatol. 2025 Apr;92(4):689-698.
- Downs CA, *et al.* Toxicopathological Effects of the Sunscreen UV Filter, Oxybenzone (Benzophenone-3), on Coral Planulae and Cultured Primary Cells and Its Environmental Contamination in Hawaii and the U.S. Virgin Islands. Arch Environ Contam Toxicol. 2016 Feb;70(2):265-88.

- Hughes TP, *et al.* Global warming transforms coral reef assemblages. Nature. 2018: 556, 492–496
- Schneider SL, *et al.* A review of inorganic UV filters zinc oxide and titanium dioxide. Photodermatol Photoimmunol Photomed. 2019 Nov;35(6):442-446.

Report written by Dr Paola Stefano (Paediatric Dermatologist, Argentina)

SIAV (Ibero-American Society for Vascular Anomalies)

Case reports: presentation with experts

Panellists: Dr Juan Carlos Lopez Gutierrez (Spain), Dr Eulalia Baselga (Spain), Dr Isabel Colmenero (Spain), Dr María Rosa Cordisco (United States)

In this session, Dr Maria Rosa Cordisco first announced the publication of the book 'Anomalías vasculares en la infancia', in Spanish, with the participation of international experts in genetics, radiology, dermatology, pharmacology and other disciplines. She explained the importance of interdisciplinary teamwork for the diagnosis, treatment and follow-up of these anomalies. Thanks to recent advances in genetics, classifying and diagnosing the different anomalies and establishing treatment with targeted therapies has been possible in these complex patients. Dr Natalia Torres emphasised that the book is up-to-date with the latest diagnostic and therapeutic advances, as well as the latest 2025 ISSVA classification.

In turn, Dr Teplinsky, a Paediatric Radiologist and Coordinator of the Vascular Anomalies Group at Hospital de Pediatría "Prof. Dr Juan P. Garrahan" ["Prof. Dr Juan P. Garrahan" Paediatric Hospital] and of the Centro de Anomalías vasculares del Sanatorio Mater Dei [Mater Dei Sanatorium Vascular Anomalies Centre], announced the creation of the Ibero-American Society for Vascular Anomalies (SIAV). This Society was founded in September 2024, is based in Spain and includes Spanish-speaking countries. This Society's mission is to promote knowledge in the diagnosis and treatment of vascular anomalies and to foster collaboration among the different specialities and countries in Latin America, thereby contributing to improving the quality of life of patients. Another objective of this Society is to work together in the same language, in order to give correct nomenclature to vascular anomalies, create diagnosis and treatment guidelines and hold meetings to discuss

cases. He also reinforced the desire for this new Society to be linked to the parent societies the Spanish Society of Vascular Anomalies (SEAV) and ISSVA (International Society for the Study of Vascular Anomalies).

Conference 1: First case report to be discussed

Speaker: Dr Natalia Torres (Argentina)

Paediatric Dermatologist. Hospital Dr Juan P. Garrahan, Coordinator of the Vascular Anomalies Interdisciplinary Group - Hospital Dr Juan P. Garrahan - Argentina

The case of a 12-year-old girl was presented for discussion who had been seen for headache, pain and functional impotence of her arm. The patient also had macrocephaly and cognitive deficit. On dermatological examination, she had a vascular-looking, erythematous-telangiectatic lesion with evidence of venous pathways on her forearm from the first years of her life that progressed with her growth, and another lesion in her thoracic region. She had undergone two embolisations and was seeking a second opinion.

Ultrasound showed soft tissue enlargement and dilated vessels with high flow. Magnetic resonance angiography imaging also showed multiple arteriovenous shunts dependent on the subclavian, axillary and brachial arteries.

In addition, she had left ventricular dysfunction secondary to her vascular anomaly which generated volume overload, so she was administered enalapril and the decision was made to perform a new embolisation.

A skin biopsy was performed, confirming the diagnosis of an arteriovenous malformation.

She was administered thalidomide 50 mg/day and contraception was indicated. The patient continued to experience chronic pain and progressive loss of arm function.

The suspected diagnosis was PHOST syndrome (PTEN hamartoma of soft tissue) related to PTEN hamartoma tumour syndrome (PHTS), so a genetic study was requested and, in consultation with Dr Denise Adams, treatment with sirolimus was initiated. During the clinical course, the patient presented with bleeding ulcers and uncontrollable pain, so after an interdisciplinary evaluation, the decision was made to amputate her arm. The patient recovered her cardiac function. She continues to be treated with sirolimus for the chest lesion. In the end, the *PTEN* gene mutation was confirmed.

It is an underdiagnosed disease which requires early diagnosis to initiate appropriate treatment, and tumours can develop in adulthood.

Dr Juan Lopez Gutierrez suggested a registry of patients with *PTEN* mutations in order to identify different manifestations and associations in these patients.

Conference 2

Speaker: Dr Maria Laura Cossio (Chile)

Dr Cossio presented the case of a patient with the diagnosis of intracranial arteriovenous malformation with a large secondary cranial defect.

This was a newborn baby girl with congenital erythematous lesions on her scalp and convulsions at one month of age. MRI: right frontotemporal infarction with haemorrhages in the right parenchyma and cranial bone defect.

She initiated treatment with sirolimus as the scalp lesions started bleeding.

A biopsy of the scalp lesion could not be performed for genetic study, due to the associated risk of haemorrhage.

Dr Juan Carlos Lopez Gutierrez believed that MEK inhibitors such as trametinib could be indicated, biopsy of the scalp lesions could be performed if possible or perhaps a genetic blood study could be attempted.

Conference 3

Speaker: Dr Alejandro Celisv (Mexico)

A 29-year-old patient, who has had a bluish tumour on their lower lip since the age of 16 with gradual growth. At the age of 19, the patient presented with significant bleeding. The patient underwent embolisation with coil embolisation of nutrient vessels but continued to bleed and had to undergo vessel ligation. They were administered thalidomide for 1 year and remained stable. Surgery was then performed, following embolisation with resection of the tumour and reconstruction with skin flaps. The patient is currently on thalidomide and asymptomatic.

As comments, emphasis was placed on the early and combination treatment of arteriovenous malformations.

Conference 4

Speaker: Dr Irene Lara Corrales (Canada)

She presented a female patient with CM-AVM (capillary malformation associated with arteriovenous malformation).

This patient was seen at the age of 6 for asymmetric growth in a foot in which she had a capillary malformation (CM).

Genetic testing confirmed *RASA1* mutation, both in skin biopsy and in blood. Genetic studies in both parents were negative.

An MRI of the brain and spine showed a cerebral arteriovenous (AV) fistula.

The CNS fistula was embolised, with no recurrence to date.

CM-AVM is an autosomal dominant inherited RASopathy.

Approximately 18% of patients with RAS 1 mutations have AV malformations or fistulas.

Dr Baselga suggested that newly diagnosed patients and adolescents should be asked to undergo follow-up brain and spine MRI scans prior to discharge, even if they are asymptomatic.

Conference 5

Speaker: Dr Felipe Enrique Velasquez Valderrama (Peru)

He presented a one-month-old patient with a congenital, vascular-looking, erythematous-violaceous tumour on the thigh, with a central crust.

The patient was hospitalised for systemic infection. Doppler ultrasound was performed on the tumour: thickened saphenous vein, collateral branches, tumour with venous and arterial components.

Days later the tumour started bleeding. All attempts were made to stop the bleeding, but the patient died from profuse haemorrhage.

Comments from Dr Colmenero: Rapidly involuting congenital haemangiomas (RICH) can have this fatal outcome. When prominent arterial vessels are detected on ultrasound, they should be embolised early.

Laser

Coordinator: Dr Agustina Vila Echague

Co-Coordinator: Dr Mirna Erendira Toledo Bahena & Dr Héctor Cáceres Ríos

Conference 1: Light and acne: myth and reality

Speaker: Betina Pagotto (Argentina)

Introduction:

Acne is a chronic inflammatory disorder of the pilosebaceous unit, which mainly affects adolescents and may continue into adulthood. It is estimated that it affects approximately 90% of the population at some point in their lives. Its main predisposing factors include age, skin type, obesity and family history.

Prevalence is almost 100% in adolescence and decreases with age. Its impact goes beyond the skin: it is associated with impaired quality of life, depression and low self-esteem, which highlights the importance of early treatment, especially in inflammatory cases.

Pathophysiology

The pathogenesis of acne is multifactorial:

- Follicular hyperkeratinisation
- Increased sebum production
- *Cutibacterium acnes* colonisation
- Cytokine-mediated inflammation

Recently, the following new factors have been identified as being involved:

- Hormonal influences
- Neuropeptides
- Skin microbiome

Laser and pulsed light therapies

Different technologies have been used for the management of active acne and its sequelae:

- IPL (intense pulsed light)
- Photodynamic therapy (PDT)
- KTP laser, low-level laser therapy (LLLT)
- Non-ablative and ablative fractional lasers (such as CO_2 for scars)
- Q-switched and other pigment lasers for post-inflammatory sequelae

Mechanisms of action

- Reduction in the size and number of pilosebaceous units
- Destruction of *C. acnes* by producing reactive oxygen species following porphyrin activation
- Modulation of immune response: decrease in TNF-α and increase in TGF-β, thereby reducing inflammation

These therapies, especially when properly combined, can improve the inflammatory component, reduce bacterial colonisation and treat sequelae with remarkable aesthetic results.

Conference 2: Treatment of vascular anomalies: vascular lasers

Speaker: Dr Agustina Vila Echague (Salvador)

Capillary vascular malformations (CVMs or port-wine stains) are low-flow vascular malformations, present since birth, caused by genetic *GNAQ* mutation leading to progressive ectasia of the superficial cutaneous vascular plexus. They affect 0.3% of newborns.

Clinical presentation: They can present in different clinical subtypes: from flat, pale pink macules to violaceous, hypertrophic or nodular lesions. A significant percentage of these lesions are associated with Sturge-Weber syndrome, which accounts for approximately 20% of all vascular malformations. Symptoms of this syndrome may not be present at birth, but manifest progressively up to the age of 5. For this reason, performing clinical and neurological examinations is key for at least the first five years of life in patients with facial port-wine stains to confirm or rule out the presence of the syndrome.

Histologically, depending on the subtype, important differences have been observed:

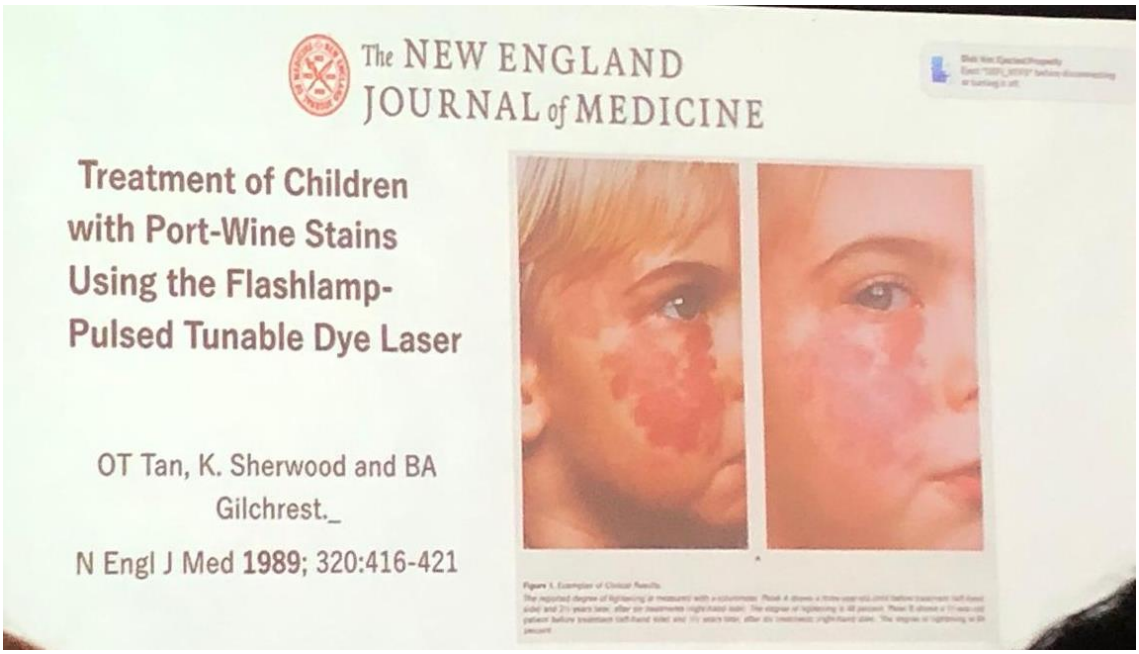
- In the paler (difficult-to-treat) lesions, vessels are dilated but few and far between in the dermis, which limits laser effectiveness due to the low concentration of oxyhaemoglobin.
- The more common violaceous lesions have denser dilated capillaries, which enables a better response to laser treatment, given their higher oxyhaemoglobin content.
- In hypertrophic lesions, not only are vessels dilated, but the dermis is also thickened. This is usually found after adolescence, although some areas such as the lips may develop hypertrophy in early stages,

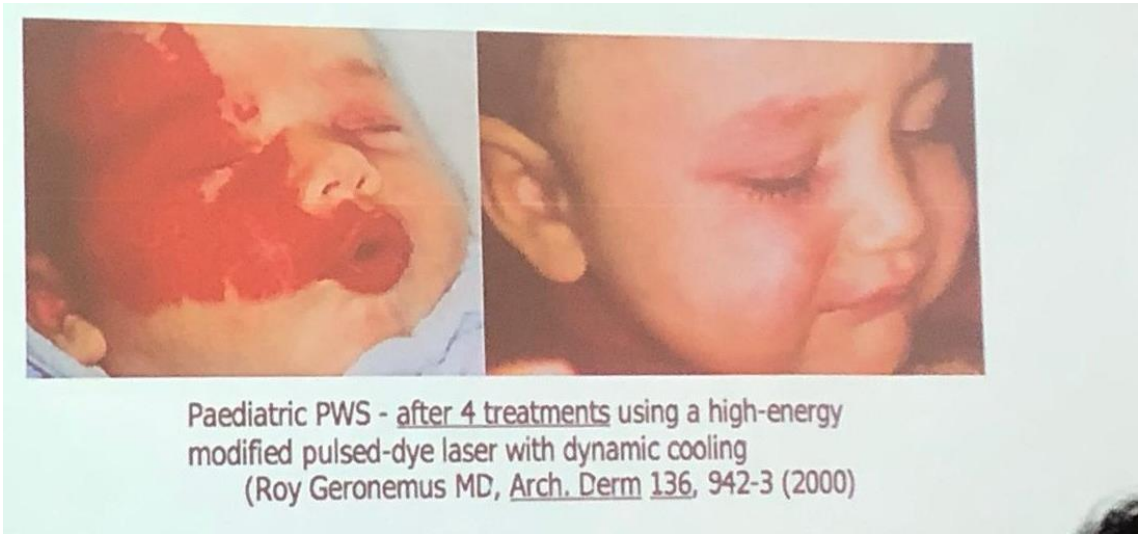
complicating treatment and in many cases requiring a combined surgical approach.

- Although rare in childhood, nodular forms are an advanced stage of capillary malformation and usually onset in adulthood.

CVMs can be treated with pulsed-dye laser (PDL, 595 nm). Initiating treatments at an early age is recommended, as vessels are more superficial and smaller.

Reference: He HY, Shi WK, Jiang JC, Gao Y, Xue XM. An exploration of optimal time and safety of 595-nm pulsed dye laser for the treatment of early superficial infantile hemangioma. Dermatol Ther. 2022 May;35(5):e15406. doi: 10.1111/dth.15406. Epub 2022 Mar 9. PMID: 35199898; PMCID: PMC9285537.





Reference: Geronemus R *et al.* High fluence modified pulsed dye laser photocoagulation with dynamic cooling of port wine stains in infancy. Arch Derm 2000; 136: 942–943

Conference 3: Laser use in paediatric vascular lesions not associated with port-wine stain

Speaker: Héctor Cáceres Ríos (Peru)

Introduction

He initially referred to infantile haemangiomas, benign tumours with endothelial proliferation. They usually onset in the first few weeks of life and grow rapidly for the first 3 months. They then remain stable in growth or grow very little until one year of age and then begin to involute and slowly decrease in size. There are precursor signs in up to 50% of cases: telangiectasias, anaemic macules or bluish spots.

There are small lesions, with no clinical repercussions, and others that are located near vital organs such as the eyes and mouth, for which treatment must be defined.

Clinically, they may be superficial in 60% of cases ("strawberry" variant), deep (bluish in colour) in 15%, or mixed in 25%.

Differentiating them from neoplastic processes such as lymphomas or rhabdomyosarcomas is essential.

As for their origin, they have been found to share the same markers as the placenta, which backs the theory of placental tissue embolisation. GLUT-1, merosin, FcYRII and Lewis Y antigen expression, among others, have been detected, confirming that haemangiomas represent vasculogenesis and angiogenesis processes, influenced by different factors.

He then listed the lasers that can be used on vascular lesions:

- Devices available:
  - Pulsed-dye laser (595 nm): uses rhodamine as a dye, most effective for capillary lesions.
  - Low-pulse KTP laser (532 nm).
  - Long- and short-pulsed Nd:YAG (1064 nm).
  - Alexandrite, diode and IPL (although, strictly speaking, the latter is not a laser).
- The laser should be chosen according to the type, depth and extent of the lesion.

He stressed the importance of initiating treatment at an early age:

- Neonatal skin is thinner and vessels are more superficial.
- Early treatment improves clinical response and reduces aesthetic sequelae.

Combination therapy: he also mentioned the possibility of combining topical and systemic laser treatments.

- Timolol, 0.7% + vascular laser
- Propranolol + PDL laser
- Sirolimus + PDL laser

Conclusion:

Current knowledge about the genetics of vascular anomalies and the availability of effective laser technologies enables a more precise and personalised approach. Early initiation of treatment improves clinical outcomes and quality of life for paediatric patients.

References:

Asilian, Ali1,2,3; Mokhtari, Fatemeh1,3; Kamali, Atefeh Sadat1,3,4,; Abtahi-Naeini, Bahareh1,3; Nilforoushzadeh, Mohammad Ali2,5; Mostafaie, Shayan3,6. Pulsed dye laser and topical timolol gel versus pulse dye laser in treatment of infantile hemangioma: A double-blind randomized controlled trial. Advanced Biomedical Research 4(1):p 257, | DOI: 10.4103/2277-9175.170682

Kavitha K. Reddy MD, Francine Blei MD, Jeremy A. Brauer MD, Milton Waner MD, Robert Anolik MD, Leonard Bernstein MD, Lori Brightman MD, Elizabeth Hale MD, Julie Karen MD, Elliot Weiss MD, Roy G. Geronemus MD Retrospective Study of the Treatment of Infantile Hemangiomas Using a Combination of Propranolol and Pulsed Dye Laser. Dermatol Surg Volume39, Issue6. June 2013.Pages 923-933.https://doi.org/10.1111/dsu.12158

Conference 4: Laser treatment of pigmented lesions

Speaker: Dr Mirna Erendira Toledo Bahena (Mexico)

Introduction:

Dr Toledo Bahena first referred to laser advances over the last 30 years that have led to the development of new therapeutic strategies for common paediatric skin conditions. She emphasised laser treatment as a non-invasive alternative to surgical options, and in many cases, it can provide better results.

In expert hands, laser therapy has been shown to be safe in both children and adults. This is very important and receiving specific training in treating paediatric patients is essential.

In the paediatric population, the scope of treatment has been extended to a variety of conditions including vascular and pigmented lesions, inflammatory diseases, scars, vitiligo and for tattoo and hair removal as well.

The laser works by emitting high-intensity monochromatic light, which is absorbed by specific structures in the skin called chromophores. This absorption generates selective thermal destruction of the target without damaging the surrounding tissue. In vascular lesions, the chromophore is haemoglobin, and in pigmented lesions, it is melanin.

Understanding the following parameters when using the laser is essential:

- Wavelength (in nanometres): defines the depth and target in the skin.
- Pulse duration: it can be in picoseconds, nanoseconds, etc.
- Thermal relaxation time: this indicates how long it takes for the tissue to dissipate heat.
- Energy (fluence): it is measured in Joules per cm^2 and must be sufficient to damage the target, but not healthy tissue.
- Spot size: the larger the spot, the deeper the light penetrates.
- Cooling system: it reduces the risk of thermal damage and enables more energy to be used.

There are several types of lasers:

- Continuous pulse laser
- Intense pulsed light (IPL)
- Pulsed-dye laser (PDL)
- Q-switched laser
- Long pulse lasers
- Lasers such as Nd:YAG, Ruby, Alexandrite
- And the latest: picosecond lasers

In pigmented lesions, the chromophore is melanin; in vascular lesions, it is haemoglobin. Light absorption varies from 250 to 1200 nm, depending on lesion depth.

Q-switched or picosecond lasers fragment the pigment so that it is eliminated by the lymphatic system. These are ideal for many of the conditions we treat in paediatric dermatology, including tattoos.

In pigmented lesions such as naevus of Ota, the gold standard is the Q-switched laser. Nd:YAG, Ruby or Alexandrite lasers are used. These act via photoacoustics, destroying the dermal pigment.

One study reported that approximately 5 Alexandrite laser sessions achieved 50% effectiveness with a low adverse event rate (between 2% and 7.9%). Dr Toledo Bahena reported that, at her hospital, they have treated 15 patients (aged 3–16 years, phototype IV) and assessed their response after several Q-switched Nd:YAG sessions.

They obtained:

- 45% with excellent response
- 13% with moderate response
- 25% with poor response

Only one patient showed residual hyperpigmentation.

The doctor showed several photographs of children treated for naevus of Ota who showed good results.

She also spoke about the excimer laser for pigmentary conditions:

Although it is not strictly a laser, excimer light (308 nm) is a very useful technology for diseases such as vitiligo. It works by inducing apoptosis in lymphocytes and keratinocytes, and stimulates melanocyte migration and melanin production.

It is a safe option that only acts on the epidermis, which is ideal for children and patients with sensitive skin.

References:

Sakio R, Ohshiro T, Sasaki K, Ohshiro T. Usefulness of picosecond pulse alexandrite laser treatment for nevus of Ota. Laser Ther. 2018 Dec 31;27(4):251–255. doi:10.5978/islsm.27_18-OR-22

Mejoría clínica de pacientes pediátricos con nevo de ota utilizando tecnología láser Q-Switched en el Hospital Infantil de México Federico Gómez. https://hdl.handle.net/20.500.14330/TES01000761986

Melanocytosis and melanocytomas

Speaker: Jean L. Bolognia (United States)

Introduction

Dr Jean L. Bolognia proposed a clinical and pathological journey along the “blue brick road”, from congenital sacral dermal melanocytosis to cellular blue naevi, with emphasis on the clinical, histological, genetic aspects and diagnostic implications of these pigmented melanocytic lesions. Entities such as acquired and congenital forms of the naevus of Ota and Ito, as well as the association with neurocutaneous syndromes, malignant potential and therapeutic management were discussed.

Main points

1. Congenital dermal melanocytosis (CDM)

- Usual location: sacral region, lower back; atypical if affecting limbs or ventral trunk
- Colouring: blue, blue-grey variation, sometimes with multiple shades in a single lesion
- Histology: melanin-laden spindle-shaped dermal melanocytes in the deep dermis
- Especially in Asians, Native Americans and people of African descent
- Disappears in >95% of cases
- Clinical classification: sacral, extensive/persistent and localised-atypical
- Association with PPV (phakomatosis pigmentovascularis) syndrome and possible lysosomal storage diseases such as Hurler syndrome (mucopolysaccharidosis I) and GM1 (gangliosidosis type 1).

2. Naevus of Ota and Ito

Naevus of Ota: also called oculodermal melanocytosis. It involves V1-V2 dermatomes, is usually unilateral and has ocular involvement (50% in mild forms, up to 100% in extensive forms).

- They predominantly affect females; onset may be in childhood or adolescence.
- Association with ocular hypertension and low but possible risk of uveal or CNS melanoma.
- Other sites that may be involved: eardrum (55%), nasal mucosa (28%), pharynx (24%) and palate (18%).

Naevus of Ito: similar, but in brachial nerve territories; no ocular involvement.

In addition, she described acquired bilateral naevus of Ota-like macules (ABNOM), also known as Hori's naevus, a benign dermal melanocytosis characterised by the appearance of blue-brown or slate grey macules on the face, especially on the cheeks, temples and forehead. It is most commonly seen in women of Asian descent after the third decade of life. ABNOM differs from naevus of Ota in that its onset occurs later and there is no involvement of the conjunctiva, mucosa and tympanic membrane.

3. Common genetic aspects

- *GNAQ* and *GNA11* mutations present in CDM, naevus of Ota, and uveal and leptomeningeal melanomas.

- Loss of BAP1 associated with unfavourable prognosis in uveal melanoma.

4. Blue naevi

"Common" and "cellular" are histological terms, not clinical ones.

- Common: frequent location on back of hands/feet and scalp. Histology with dendritic melanocytes/melanophages.
- Cellular: larger (>1 cm), proliferative, possible nodules. They may have atypia and a low but real risk of malignant transformation.
  Combined: association of compound naevus with blue naevus (greyish colour).

Histology is key to differentiating benign from malignant forms.

5. Variants and related entities

- Plaque-type blue naevus: it may mimic naevus of Ota, but without ocular involvement or V1-V2 distribution.
- Patch blue naevus: no palpable component, heterogeneous in presentation, various names in the literature.
- Naevus spilus and agminated blue naevus: there may be multiple blue naevi within a naevus spilus; low but relevant risk of melanoma.
- Rare associated neoplasms:
  - Neurocristic cutaneous hamartoma: mixture of naevus and neural crest cells.
  - Pigmented epithelioid melanocytoma: entity with multiple names, kinase fusion, low metastatic potential.

Conclusion

Congenital dermal melanocytosis and the different types of blue naevi represent a broad spectrum of melanocytic lesions with diverse clinical, genetic and prognostic implications. Detailed knowledge of its clinical presentation, anatomical distribution, histological characteristics and syndromic associations enables an accurate diagnosis to be made, cases at risk of malignancy to be identified, and appropriate follow-up to be implemented, including ophthalmological monitoring and possible CNS imaging in selected patients. Identifying *GNAQ/GNA11* mutations and BAP1 loss are key in understanding its biology and potential for malignant transformation.

References:

Cordova A. The Mongolian spot: a study of ethnic differences and a literature review. Clinical Pediatrics 1981 vol 20: 714–719

Romagnuolo M, Moltrasio C, Gasperini S, Marzano AV, Cambiaghi S. Extensive and Persistent Dermal Melanocytosis in a Male Carrier of Mucopolysaccharidosis Type IIIC (Sanfilippo Syndrome): A Case Report. Children (Basel). 2023 Dec 13;10(12):1920. doi: 10.3390/children10121920. PMID: 38136122; PMCID: PMC10742075.

Pruritus treatment in genetic skin disorders

Speaker: Dr Amy Paller (United States)

Introduction

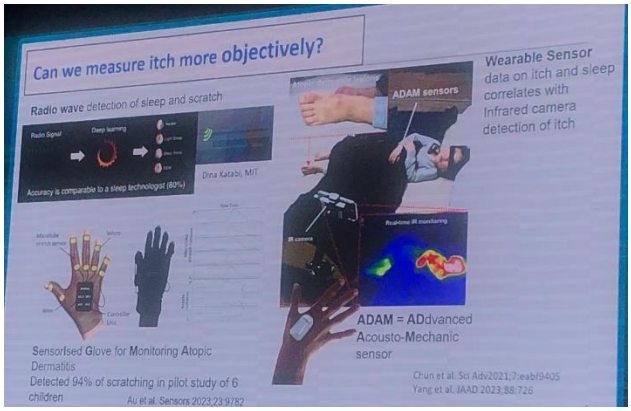
Pruritus is a common manifestation in a variety of dermatoses, but its treatment in genetic diseases such as ichthyosis (now called *epidermal differentiation disorders*) and epidermolysis bullosa (EB) represents a considerable clinical challenge.

Epidemiology and assessment of pruritus

Up to 17% of children and adolescents report chronic pruritus, and it is even more prevalent in genetic skin diseases. Scales such as the NRS (Numerical Rating Scale) or the VAS (Visual Analogue Scale) have been validated to quantify intensity, including versions adapted for parents of children who cannot self-assess. However, it highlights the need for more holistic assessments that take into account the impact on physical, mental and social health.

Objective tools for quantifying scratching

Devices such as sensorised gloves, digital sensors and portable acoustic systems (e.g. ADAM sensor) have been developed that are able to record scratching events during sleep, differentiating these from other movements.



Neurobiology of pruritus

Pruritus is transmitted by C- and A-delta nerve fibres, with endings reaching the epidermis. These neurons express key receptors such as IL-4, IL-13 and IL-31 and communicate bidirectionally with keratinocytes and immunocytes, amplifying or regulating the pruritic stimulus.

New pathogenic pathways: role of the microbiota

Methicillin-resistant *Staphylococcus aureus* (MRSA) induces pruritus in murine models by producing *V8 protease*, which activates the PAR-1 receptor on nerve fibres. This pathway, which is independent of histamine and ILs, opens up novel therapeutic opportunities with topical PAR-1 inhibitors.

Specific genetic diseases: therapeutic advances

Ichthyosis

Up to 93% of patients present with pruritus. In studies with pregabalin, a benefit on neuropathic pain was found, but with little effect on pruritus. In murine models, the use of endocannabinoid system modulators has been explored, showing promising results.

Epidermolysis bullosa (EB)

Increased substance P has been documented in the skin of patients with dystrophic EB, correlating with increased pruritus intensity. Neurokinin 1 (NK-1) receptor antagonists such as *serlopitant* have shown a tendency to reduce pruritus in pilot studies.

Cannabinoids

A recent survey reported that 45% of patients with EB use tetrahydrocannabinol/cannabidiol (THC/CBD) products, and 64% report improvement of pruritus. Cannabinoid CB1 and CB2 receptors are present in dorsal root ganglia and skin fibres, and alterations in their expression have been identified in animal models.

Current therapies: biologics and JAK inhibitors

Dupilumab

This biologic, fully human monoclonal antibody (mAb) targets the α-subunit of the interleukin 4 receptor (anti-IL-4Rα) and is approved for atopic dermatitis. It has been evaluated in an open-label study in patients with epidermolysis bullosa (n=22). At 16 weeks, a **significant reduction in mean and severe pruritus** was found, as were objective improvements in sleep using recording devices. Response was independent of baseline IgE levels.

In a subgroup with junctional epidermolysis bullosa (collagen VII deficiency), a reduction of more than 4 points on the pruritus scale was documented, with a positive impact on autonomy and quality of life. Safety was favourable, with minimal local reactions and only one case of mild conjunctivitis.

Other therapeutic objectives

IL-31R antibody (nemolizumab): with therapeutic potential, especially because of the correlation of IL-31 with pruritus in EB.

JAK inhibitors: used off-label (baricitinib, tofacitinib, etc.) with good results in reducing pruritus and lesions in EB, although their risk profile in immunocompromised patients is of concern.

Conclusion

Pruritus is multifactorial in genetic diseases, with complex neuroimmunological mechanisms. The use of objective tools, together with targeted therapies (biologics, cannabinoids, specific pathway inhibitors), opens a new paradigm in the personalised treatment of these patients. Further studies are needed to optimise safe and effective therapeutic strategies in the affected paediatric population.

Reference:

Deng L, Costa F, Blake KJ, Choi S, Chandrabalan A, Yousuf MS, Shiers S, Dubreuil D, Vega-Mendoza D, Rolland C, Deraison C, Voisin T, Bagood MD, Wesemann L, Frey AM, Palumbo JS, Wainger BJ, Gallo RL, Leyva-Castillo JM, Vergnolle N, Price TJ, Ramachandran R, Horswill AR, Chiu IM. S. aureus drives itch and scratch-induced skin damage through a V8 protease-PAR1 axis. Cell. 2023 Nov 22;186(24):5375-5393.e25. doi: 10.1016/j.cell.2023.10.019. PMID: 37995657; PMCID: PMC10669764.

Dermoscopy

Conference 1: Which naevi are important in children?

Speaker: Dr Giovanni Pellacani (Italy)

Introduction

This session addressed the most relevant criteria for the differential diagnosis of melanocytic naevi, the importance of clinical follow-up and the indications for excision. He referred mainly to melanoma, an extremely rare malignancy in the paediatric population. Its rarity, coupled with the extensive clinical and dermoscopic variability of naevi in children, poses significant diagnostic and therapeutic challenges.

Epidemiology

- Melanoma is very rare in children under 10 years of age.
- On average, it is estimated that about 1000 excisions are performed for each melanoma diagnosed in patients between 10 and 14 years of age.
- At between 10 and 20 years, the rate remains low (more than 500 cases assessed per confirmed case of melanoma).
- Despite its low incidence, it should not be underestimated given its potential seriousness.

Congenital naevus and melanoma risk

- Medium and large congenital naevi require special attention.
- The risk of malignant transformation is higher in giant naevi.
- Approximately 60% of melanomas in these patients develop before the age of 18.
- Strict follow-up should be performed from the early stages of life.

Assessment of melanocytic lesions

- Physical examination: it continues to be a fundamental tool.
- Dermoscopy:

Useful for identifying patterns suggestive of malignancy such as:

- Irregular blood cells
- Asymmetric pigment network
- Areas of regression or atypical dark spots
- Histopathology: necessary in view of any clinical suspicion or recent changes

Differential diagnosis

At school age, lesions may appear with:

- Changing morphology
- Unusual or combined patterns

Differential diagnoses include:

- Benign proliferative naevi
- Cellular blue naevi
- Spitz-like melanomas
- Complex pigmented lesions with dendritic cells

Criteria for indicating excision

Lesions with:

- Recent changes in size, shape or colour
- Atypical elements in dermoscopy
- Irregular distribution of pigmented or vascular structures
- Lack of evolutionary stability

In these cases, diagnostic excision with adequate margins is recommended.

Case report presented:

- Child with multiple pigmented eruptive lesions
- History of chemotherapy for haematological malignancy
- The abrupt onset of multiple lesions was related to immunosuppression and previous systemic treatment

Conclusions

Melanoma in childhood is rare but clinically significant.

Any medium or large congenital naevus should be carefully evaluated and monitored over time.

Physical examination and dermoscopy are essential for decision-making.

Excision with adequate margins should be indicated for any suspected clinical or dermoscopic atypia.

It is essential to avoid both under- and overestimation of pigmented lesions in children.

Reference:

Excised melanocityc lesions in children and adolescents-a 10 year survey. E Moscarella 1, I Zalaudek, L Cerroni, I Sperduti, C Catricalà, J Smolle, R Hofmann-Hellenhof, A Sgambato, G Pellacani, G Argenziano. Br J Dermatol. 2012 Aug;167(2):368-73. doi: 10.1111/j.1365-2133.2012.10952.x

Conference 2: Longitudinal melanonychia

Speaker: Dr Horacio Cabo (Argentina)

Introduction

Nail pigmentation is a common reason for dermatology consultations, and although most of the time these are benign lesions, there is a small but significant risk of subungual melanoma, even in children. This talk addressed diagnostic difficulty, dermoscopy use and key clinical criteria to differentiate between benign melanonychia and melanoma.

Main points of the talk

Pathophysiology and clinical presentation

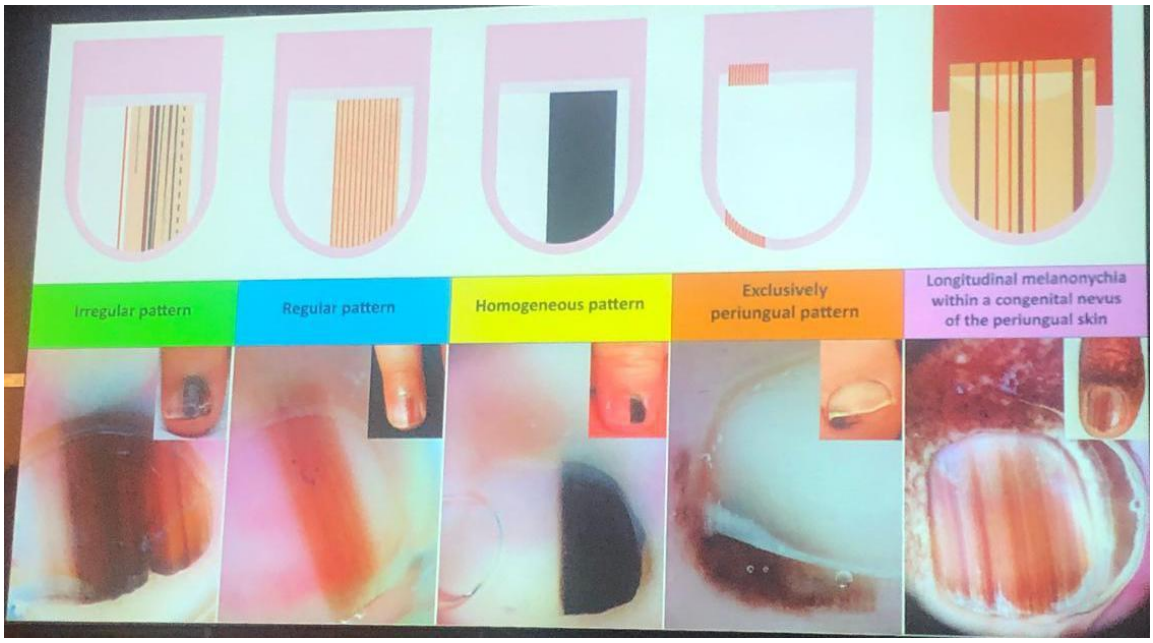
- Subungual pigmentation may be due to **melanocytic activation or proliferation**.
- It clinically manifests as a brown-to-black **longitudinal pigmented band** (striated melanonychia) extending from the nail matrix to the free edge of the nail.
- In children, many of these lesions are benign, but require follow-up.

Subungual melanoma: epidemiology and case reports

- Although rare in childhood, it **can even occur in children under 5 years of age.**
- In adults, it can be confused with trauma or chronic benign changes.

Dermoscopy: keys to diagnosis

- Dermoscopy is essential to differentiate benign lesions from melanoma:
  - **Dermoscopic warning signs**:
    - Irregular longitudinal lines (colour, thickness, spacing)
    - Band fragmentation
    - Presence of Hutchinson's sign (pigment extending to the periungual skin)
    - Multiple colours: brown, red, blue and black
- In benign lesions, the bands are usually **homogeneous, symmetrical** and **uniform in colour**.



Clinical assessment and follow-up

- Take into account:
  - Patient age
  - Number of affected nails
  - Changes over time
  - Personal/family history (trauma, genetic syndromes)
- **ABCDEF rule for nail melanoma**:
  - **A**ge
  - **B**and (band characteristics)
  - **C**hanges
  - **D**igit (affected finger, most common in thumb and first finger)
  - **E**xtension (pigment in periungual skin)
  - **F**amily history

Biopsy and treatment

- Lesions with **atypical characteristics** should be biopsied.
- In doubtful lesions, but without clear malignancy criteria: **strict clinical and photographic follow-up**.
- The importance of **early biopsies** in new lesions was stressed.

Importance of photographic documentation

- Comparing current images with previous photographs may reveal progression of the lesion.
- Example presented: 27-year-old patient with melanoma diagnosed via comparative images taken 2 years earlier.

Conclusions

- Striated melanonychia requires **careful evaluation**, especially when it appears on a single finger or has atypical characteristics.
- Dermoscopy is an essential tool to differentiate benign lesions from melanoma.
- It is essential to take into account clinical context, the evolution of the lesion and to perform biopsies when there are diagnostic doubts.
- **Serial photographic documentation** can be key to detecting subtle changes and avoiding diagnostic errors.
- Although rare, **subungual melanoma can affect children** and should not be underestimated.

Conference 3: Dermoscopy in inflammatory and infectious diseases

Speaker: Dr Virginia Gonzalez (Argentina)

Introduction

Dermoscopy is no longer a tool exclusively for evaluating pigmented lesions, but has become an essential method for the diagnosis of various **inflammatory, infectious and parasitic dermatoses**. It has been called "the dermatologist's stethoscope", and its systematic use after physical examination improves diagnostic accuracy, avoids unnecessary biopsies and facilitates therapeutic follow-up.

Key points of the talk

Fundamentals of dermoscopic analysis in inflammatory diseases

- Assessment of:
  - Scale morphology (peripheral, central, diffuse distribution)
  - Vascular pattern (vessel type and distribution)
  - Presence of specific structures associated with some dermatoses
  - Inclusion of fluorescent findings via UV dermoscopy

Highlighted clinical examples

Psoriasis

- Erythematous background with **regularly distributed punctate vessels**
- Thick, white and often peripheral scales
- Under UV light: **red coral fluorescence** due to protoporphyrin IX of the stratum corneum
- Also useful for visualising nail pitting

Eczema

- Pink background with patchy or irregularly distributed **yellow scales**
- Few punctate vessels with an irregular distribution
- **Yellow-green** fluorescence under UV light

Pityriasis rosea

- Peripheral scale in oval form (herald patch)
- Vertical vessels, fine scales
- Peripheral intense white fluorescence via keratin under UV light

Porokeratosis

- Thick peripheral scale (keratin wings) with free edge
- Central whitish or skin-coloured area
- Open linear vessels; in high phototypes, **brown or grey globules** may be seen
- Peripheral intense white fluorescence

Granulomatous diseases (e.g. sarcoidosis, granulomatous rosacea)

- Structurally amorphous orange areas
- Variably distributed vessels
- Typical **orange colour** in dermoscopy

Lichens and pruritic diseases

- Papules with prominent follicular pattern
- Linear, sometimes spiral structures
- Scattered greyish-brown globules or small vessels

Scabies

- Wavy, linear burrows with terminal scale
- "Triangle" sign (anterior part of the mite)
- With UV: green or white fluorescence of the parasite's body ("ball sign")

Pediculosis (lice)

- Nits visible as yellowish-white oval structures, attached to the hair shaft
- Empty nits appear translucent with a flattened edge
- With UV: "Christmas tree" pattern due to follicular arrangement

Molluscum contagiosum

- Yellowish-white, umbilicated papules
- Crown vessels
- Central UV fluorescence due to keratinisation

Warts (HPV)

- Mosaic or dotted pattern
- Punctate or clustered vessels
- Surrounding white scale and black areas due to capillary thrombosis
- UV useful for highlighting irregular central pattern

Colouring and fluorescence: emerging keys

- **Fluorescent red**: porphyrins in bacterial infections (e.g. *Corynebacterium*)
- **Blue**: associated with *Malassezia* spp.

- UV dermoscopy expands the colour palette and improves the visualisation of structures invisible to the naked eye

Conclusion

Dermoscopy is an invaluable diagnostic tool in general dermatology, and it should be used beyond pigmented lesions.

The use of **UV light** enables detecting fluorescent findings useful in several inflammatory and infectious pathologies.

Its appropriate use can avoid unnecessary biopsies, improve therapeutic monitoring and increase clinical precision.

Using dermoscopy in the routine evaluation of dermatoses and becoming familiar with the characteristic signs of each condition is recommended.

Conference 4: Vascular lesions

Speaker: Dr Rosario Peralta (Argentina)

Introduction

Dermoscopy is an essential tool in the non-invasive assessment of vascular skin lesions. In paediatrics, it enables better characterisation of tumours and vascular malformations, optimising the differential diagnosis in the presence of melanocytic or even malignant lesions. Recognising specific vascular patterns facilitates classifying and treating these lesions, often without the need for biopsy.

Key dermoscopic findings by condition

1. **Infantile haemangioma**

- Most common benign vascular lesion in children

- Well-defined **reddish-violet lacunae** of different sizes

- Homogeneous or mosaic pattern; no additional structures

- Clinical course: colours vary according to the depth of the vascular component

2. **Tufter angioma (“tufted haemangioma”)**

- Prominent peripheral linear vessels, often accompanied by areas of erythrosis

- Frequent structural variability: structurally specific white areas can be seen

3. Glomangioma

- Painful, bluish or blackish lesion

- Dermoscopy: **blue-violet areas**, **white-blue veil structure** and occasional rainbow pattern

- Signs of thrombosis: homogeneous black areas or "black lagoon" structures

4. Angiokeratoma

- Red, dark blue or black lacunae, sometimes with hyperkeratosis

- Presence of **whitish areas** and frequent thrombosis

- Differential diagnosis with metastatic melanoma or nodular melanoma

5. Lymphangioma (superficial lymphatic malformation)

- Yellowish-whitish or pinkish lacunae, sometimes mixed with reddish-violet lacunae

- Polymorphic pattern: mix of clear and haemorrhagic lacunae

- Under UV dermoscopy: fluorescence varies according to liquid content

6. Angiosarcoma (take into account in differential diagnosis)

- Although rare in children, it should be considered for rapidly growing vascular tumours

- Dermoscopy: homogeneous reddish areas with irregular vascular lines and ulceration areas

- Important to suspect it with atypical lesions that mimic haemangiomas

7. Capillary and venous malformations

- Capillary malformation: red, linear or serpiginous spots, depending on whether they are superficial or deep

- Venous malformation: bluish or purplish, often compressible lacunae, without specific structures

- Distribution according to vessel location (horizontal or vertical in superficial or deep dermis)

Special considerations

- **Dermoscopic vascular structures are not always specific**, so clinical context, course and location are key.
- Some lesions such as haemangiomas in the proliferative phase may mimic melanocytic lesions.
- The **rainbow pattern** should be interpreted with caution, as it can also be seen in malignant tumours.

Conclusion

- Dermoscopy is an essential tool for the diagnosis and follow-up of **paediatric vascular lesions**.
- Identification of **lacunae**, **specific vascular patterns**, and assessment of **colours and internal structures** enables differentiating between benign tumours, malformations and malignant lesions.

Properly interpreting these findings, coupled with clinical impression, prevents unnecessary procedures such as biopsies in children and improves the therapeutic approach.

Conference 5: Trichoscopy

Speaker: Dr Ramiro Cano (Argentina)

Introduction

Trichoscopy is a non-invasive tool that has revolutionised the diagnostic approach to childhood alopecia. It enables assessing the scalp and hair shafts via dermoscopy, facilitating the differential diagnosis between the different aetiologies of alopecia. This talk focused on the clinical applications of trichoscopy to differentiate the most common causes of patchy alopecia in children, mainly tinea capitis, alopecia areata and trichotillomania.

Key points

1. Three-step diagnostic approach

Step 1: Medical history and detailed physical examination to classify the alopecia as:

- Congenital or acquired
- Diffuse, focal or patchy

Step 2: Initial trichoscopic assessment to define if it is:

- Cicatricial alopecia: absence of follicular orifices, milky-white areas and fibrosis
- Non-scarring alopecia: preservation of follicular orifices

Step 3: Detailed trichoscopy to identify specific patterns and confirm the presumptive clinical diagnosis.

2. Classification and trichoscopic patterns

- Acquired non-scarring patchy alopecia (more common in children):
  - Tinea capitis
  - Alopecia areata
  - Trichotillomania

- Observed patterns
  - Hair shaft patterns:
    - Alopecia areata: vellus hairs, exclamation mark hairs, circle hairs, Pohl-Pinkus constriction, tapering hairs
    - Tinea capitis: comma hairs, corkscrew hairs, zigzag hairs, "Morse code" hairs, broken hairs, block hairs
    - Trichotillomania: tulip hairs, flame hairs, hair dust, burnt matchstick, V-sign, eye hairs
    - Note: Most of the patterns are non-specific, except for some that have a higher positive predictive value

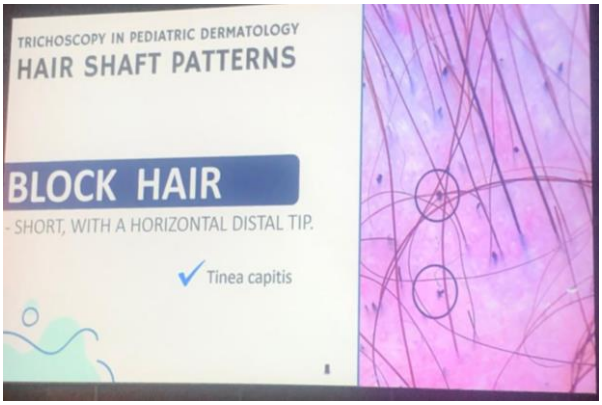
  - Follicular patterns:
    - Black dots: broken hairs at scalp level
    - Yellow dots: keratosebaceous material in dilated orifices
    - White dots:
    - Punctiform (regular): normal or in non-scarring alopecia
    - Fibrous (irregular): indicative of cicatricial alopecia

- Peripapillary and interfollicular patterns:

3. Trichoscopic findings most useful in differential diagnosis

▪ Tinea capitis:	Corkscrew, zigzag, block, Morse code-type hairs
▪ Alopecia areata	Exclamation mark hairs, vellus hairs, circle hairs, constrictions
▪ Trichotillomania:	Hair dust, V-sign, flame hairs, occasional haemorrhages

- Common but non-specific findings: black dots, broken hairs, comma hairs
- Some findings are shared by two conditions:
- e.g. eye hair (trichotillomania and tinea), tulip hair (trichotillomania and areata), zigzag hair (tinea and areata)



Conclusion

Trichoscopy is a useful and accessible technique for the diagnosis and follow-up of childhood alopecia, especially in the outpatient setting. Although many findings are shared by different conditions, some patterns have a high specific diagnostic value. A structured approach, based on medical history, physical examination and targeted trichoscopy, enables:

- Making a more accurate diagnosis
- Avoiding unnecessary studies
- Guiding treatment and assessing therapeutic response

It is essential for paediatric dermatologists to become familiar with the key trichoscopic patterns to optimise the treatment of these conditions.

Conference 6: Clinical-dermoscopic cases

Speaker: Dr Gabriel Salerni (Argentina)

Introduction

The speaker presented a selection of case reports observed in the paediatric population, with the aim of highlighting relevant clinical and dermoscopic patterns in the differential diagnosis of nodular and pigmented lesions. The topics ranged from benign and self-limiting entities such as idiopathic facial aseptic granuloma, to more serious pathologies such as childhood melanoma.

Relevant cases and findings

- **Idiopathic facial aseptic granuloma**

Patient: 9-year-old girl with a 3-week history of a 2 cm erythematous nodule on her cheek, with no history of trauma or sting.

- Dermoscopy: erythematous background with peripheral unbranched vessels.
- Histology: lymphohistiocytic inflammation, central granulomas with multinucleated foreign body-type giant cells.
- Negative cultures. Confirmed diagnosis: **idiopathic facial aseptic granuloma**, a benign self-limiting entity initially described as "pyodermite froide du visage".

Reference:

Errichetti E et al. Dermoscopy of idiopathic facial aseptic granuloma (IFAG): an observational controlled study Int Dermatol 2025 Feb; 64(2):422-424

- **Pigmented Spitz naevi**

Cases in children and adolescents, typically as red or pigmented nodules on the face or extremities.

- Dermoscopy: clinical course of starburst pattern, bright white structures or pseudo-reticular pattern.

- It was emphasised that symmetric, flat and pigmented lesions in children under 12 years of age can be clinically followed up. However, **nodular, hypochromic or atypical lesions should be excised**.

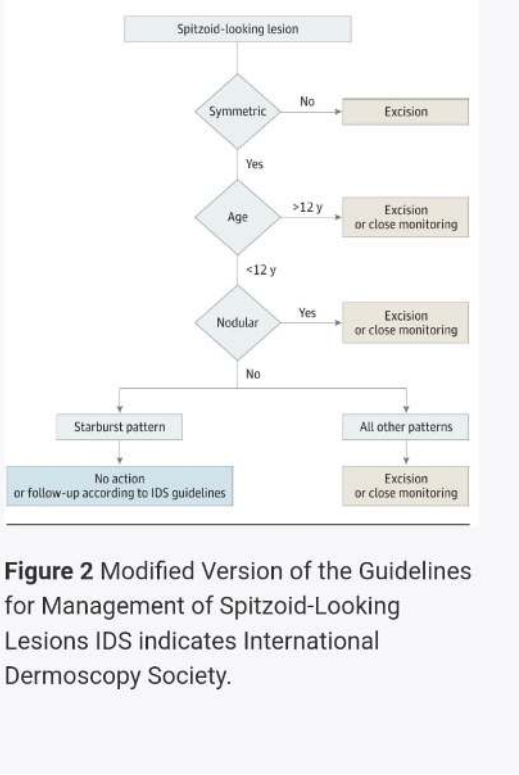


Figure 2 Modified Version of the Guidelines for Management of Spitzoid-Looking Lesions IDS indicates International Dermoscopy Society.

Reference:

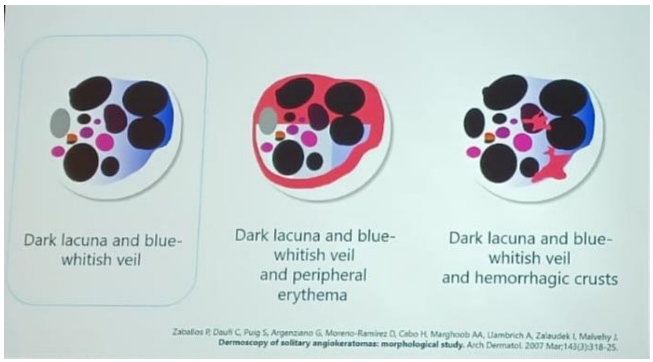
Lallas A, Apalla Z, Papageorgiou C, Evangelou G, Ioannides D, Argenziano G. Management of Flat Pigmented Spitz and Reed Nevi in Children. JAMA Dermatol. 2018 Nov 1;154(11):1353-1354. doi: 10.1001/jamadermatol.2018.3013.

Kerner M, Jaimes N, Scope A, Marghoob AA. Spitz nevi: a bridge between dermoscopic morphology and histopathology. Dermatol Clin. 2013 Apr;31(2):327-35. doi: 10.1016/j.det.2012.12.009. Epub 2013 Jan 30. PMID: 23557659.

- **Solitary angiokeratoma**

16-year-old adolescent with a bleeding violaceous lesion on the knee

- Dermoscopy: purple-red lacunae, blue-whitish veil, haemorrhagic crusts
- Diagnosis confirmed after surgical excision



Reference

Zaballos P, Daufí C, Puig S, Argenziano G, Moreno-Ramírez D, Cabo H, Marghoob AA, Llambrich A, Zalaudek I, Malvehy J. Dermoscopy of solitary angiokeratomas: a morphological study. Arch Dermatol. 2007 Mar;143(3):318-25. doi: 10.1001/archderm.143.3.318. PMID: 17372096.

- **Childhood melanoma**

Unusual case in a 12-year-old boy with a 3-month history of polymorphic leg lesion.

- Dermoscopy: asymmetric structure with multiple colours (light and dark brown, red, white), crystalline structures.
- Histology: **0.4 mm thick melanoma**. Confirmed by two dermatopathologists.

The classification was reviewed:

- **Childhood melanoma (<11 years):** typically spitzoid-type
- **Adolescent melanoma (11–19 years):** most commonly conventional type

The use of the **modified ABCD** was discussed:

- A: *Amelanotic*
- B: *Bulge*
- C: *Colour not variegated*
- D: *De novo*

- **Atypical congenital melanocytic naevus**

Two cases in 4-year-old children

- Lesions present since birth, no relevant changes according to parents

- One case was followed up because of its symmetry and flat appearance; excision was decided upon in the other case because of the presence of a nodular component, resulting in a **benign proliferative nodule**.

Conclusion

- Nodular and pigmented lesions in childhood should be carefully evaluated, combining clinical and dermoscopic criteria and clinical course.
- Idiopathic facial aseptic granuloma is a benign, self-limiting entity. Recognising it is important in order to avoid unnecessary treatment.
- Spitz naevi can be clinically followed up in selected settings, although treatment should be tailored to the clinical profile and level of family anxiety.
- Melanoma is rare in childhood, but may present with atypical clinical and dermoscopic characteristics and should be suspected in recent polymorphic growths.
- Experience and multidisciplinary team discussion are fundamental for the diagnostic/therapeutic approach in paediatric dermatology.

Molluscum contagiosum in paediatrics: is treatment always necessary?

Speakers: Dr Bruno Ferrari (Argentina), Dr Carla Torres Zegarra (United States)

1. Introduction

- *Molluscum contagiosum* (MC) is a common childhood viral infection caused by a poxvirus that affects the skin and occasionally the mucosa.

- It presents as umbilicated papules which are usually asymptomatic and are located anywhere on the body.

- It is a self-limiting and benign disease in immunocompetent patients.

2. Natural clinical course

- CM usually resolves spontaneously within **6 to 12 months**, although it can last up to **18 or even 30 months.**

- During its course, local inflammation with signs of eczema ("beginning of the end" phenomenon) may develop, which usually precedes lesion resolution.

- The "scars" they usually leave are not permanent.

3. Rationale for watchful waiting

- In most cases **no active treatment is required**.

- Available therapies (e.g. cryotherapy, imiquimod, curettage, intralesional injections) can be painful, cause anxiety and scarring and require multiple medical visits.

- There is no conclusive evidence that treatment significantly accelerates resolution compared to watchful waiting.

- Cochrane Review 2017: no clear superiority found between treatments, nor against watchful waiting.

- Studies highlight that many treatments have **limited efficacy (30–40%)**, and are associated with recurrences.

4. Psychosocial and financial aspects

- Painful procedures generate anxiety in children and an aversion to future medical visits

- Multiple treatment sessions place an **emotional and financial burden** on families

5. Contagion and preventive measures

- CM is **mildly contagious**, with an estimated intrafamilial transmission rate of 30–40%.

- Restricting children from their activities (e.g. school, swimming) is not recommended

- Basic hygiene measures are advised: avoid scratching, cover inflamed lesions, do not share personal hygiene items

6. Exceptions where treatment may be necessary

- Immunocompromised patients

- Extensive or recalcitrant infections

- Facial or genital involvement with aesthetic or functional impact

- Lesions with severe secondary eczema

7. Conclusion

- *Molluscum contagiosum* is a **self-limiting viral infection** in most healthy children.

- Active treatment **is not always necessary** and risks may outweigh benefits.

- **Watchful waiting** should be considered as the first line of treatment in healthy patients.

- Informing parents and carers about the natural course of the disease and avoiding unnecessary treatment are essential.

Reference: van der Wouden JC, van der Sande R, Kruithof EJ, Sollie A, van Suijlekom-Smit LW, Koning S. Interventions for cutaneous molluscum contagiosum. Cochrane Database Syst Rev. 2017 May 17;5(5):CD004767. doi: 10.1002/14651858.CD004767.pub4. PMID: 28513067; PMCID: PMC6481355.

Paediatric dermatological procedures

Speaker: Dr Maria Gnarra Buethe (United States)

Introduction:

The focus was on pain management, anxiety and the overall paediatric patient experience during minor dermatological procedures:

Distress during procedures in paediatric dermatology represents a major clinical challenge, both for patients and their families. This talk presented a multidisciplinary approach to reduce pain, anxiety and improve children's experience through pre-, trans- and post-procedure interventions.

1. Pre-procedure preparation:

Initiating patient and carer orientation prior to the day of the procedure is recommended. Including a Child Life specialist, if available, improves understanding and reduces anxiety. The process can also be carried out in the procedure room, while consents are being reviewed.

2. Surgical setting organisation:

Preparing the material out of children's field of vision and having everything ready for an efficient procedure (<30 seconds for punch biopsies) are key to reducing distress.

3. Patient positioning:

Different techniques of comfortable immobilisation, adapted to the age of the patient, were described:

Infants: Burrito wrap with sheets

Older children: Ergonomic positions on the carer's lap, allowing access to different anatomical areas as needed

4. Distraction techniques:

Active distraction (e.g. video games) has been shown to be more effective than mild sedation (midazolam) and passive distraction (e.g. cartoons) in reducing both pain and anxiety. Prior familiarisation with the applications and their suitability for the procedure site (hands free if limbs are involved) is recommended.

5. Additional distraction tools:

Sensory toys and virtual reality (VR) were mentioned. Although VR and noise-cancelling headphones offer similar benefits, both have shown efficacy in reducing perioperative anxiety.

6. Validation and positive reinforcement:

Language should focus on reinforcing the child's courage and avoiding negative associations ("it was painful"). Emphasis was placed on the use of distractor questions and emotionally validating statements.

7. Pain management:

Newborns: Skin-to-skin contact, breastfeeding and sucrose solution decrease signs of pain (facial grimace, heart rate).

Topical anaesthetics:

- EMLA® (lidocaine/prilocaine): requires occlusion and 60 minutes for effect
- LMX® (liposomal lidocaine): faster acting (30 minutes), no need for occlusion

Caution with methaemoglobinemia in infants

Topical anaesthesia enhancement: Greater efficacy has been documented if applied after cryotherapy, due to the change in the epidermal barrier.

8. Infiltration anaesthesia:

Use small needles.

Warm lidocaine is less painful than cold lidocaine.

Buffered lidocaine (with sodium bicarbonate) decreases infiltration pain with no clear evidence of loss of potency or stability.

Injection technique: start in the deep dermis and advance superficially.

9. Complementary methods:

Local cooling: ice, ethyl chloride

Vibration (gating theory): the device should be placed proximal to the surgical site and between the surgical site and the brain.

Playful cryotherapy on the scalp: use of frozen water balloons for analgesia prior to infiltration

10. Sedation and general anaesthesia:

Nitrous oxide: commonly used in paediatric dentistry, effective as mild sedation, with need for monitoring for risk of hypoxaemia

General anaesthesia: parents should be informed about the FDA warning in children under 3 years of age for prolonged (>3 h) or repetitive procedures, such as laser treatments for capillary malformations.

Conclusion:

Encourage a relaxed and calm environment to relieve the patient's anxiety.

Apply topical anaesthetics whenever appropriate to reduce discomfort.

Inject anaesthetic slowly, starting at deeper levels for better tolerance.

Using distraction techniques, mobile phone apps, music, conversation or interaction with the carer can be effective.

Therapeutic advances in genodermatoses

Speaker: John Mc Grath (United Kingdom)

Introduction

Genodermatoses represent a large group of inherited skin diseases, many of which have high morbidity and require complex diagnostic and therapeutic approaches. More than 8,000 Mendelian diseases are currently recognised, with more than 1,000 presenting with cutaneous manifestations. This talk provided a critical update on advances in molecular diagnostics and emerging therapeutic strategies, particularly focusing on epidermolysis bullosa (EB) and related conditions.

- Molecular diagnostics has transformed clinical management.
- Access to next-generation sequencing (NGS) enables causal mutations to be more precisely identified.

Example: Cobalamin J disease: autosomal recessive disease of vitamin B12 metabolism leading to progressive hyperpigmentation, which can be

successfully treated with vitamin B12. The diagnosis was made with NGS which identified the ABCD4 gene. These untreated patients are at increased risk of stroke starting in their 20s.

Reference: Takeichi T, Hsu CK, Yang HS, Chen HY, Wong TW, Tsai WL, Chao SC, Lee JY, Akiyama M, Simpson MA, McGrath JA. Progressive hyperpigmentation in a Taiwanese child due to an inborn error of vitamin B12 metabolism (cblJ). Br J Dermatol. 2015 Apr;172(4):1111-5. doi: 10.1111/bjd.13413. Epub 2015 Feb 27. PMID: 25234635.

He also referred to the therapeutic complexity of epidermolysis bullosa due to its aetiopathogenesis. Dystrophic EB has a mutation in the type VII collagen gene with deficient formation of anchoring fibrils. In addition to structural damage, there is a significant systemic inflammatory involvement, driven by TGF-β, which promotes fibrosis and squamous carcinoma.

Current and emerging therapies

Curative:

- Topical gene therapy (Vyjuvek®): inactivated herpes simplex type 1 vector to introduce the collagen VII gene directly into wounds. Promising results, but high cost (approximately USD 20 M) and limited application.
- Reverse mosaicism: technique applied in Japan
- Therapy with recombinant proteins, stem cells or genetically modified fibroblasts

Symptomatic/anti-inflammatory:

- Filsuvez® (Oleogel S10): birch bark extract: improves inflammatory symptoms
- IV allogeneic mesenchymal stem cells: UK clinical trials show improvement
- Systemic gentamicin: treatment for nonsense variants (15% of dystrophic EB cases)
- Biologics and JAK inhibitors: promising but costly approach
- Repositioned (low-cost) therapies:
  - Methotrexate: useful for pruritus and inflammation
  - Statins and diluted calcitriol: improved healing
  - Losartan: inhibits TGF-β, reduces fibrosis and improves quality of life
  - Sodium valproate: potential epigenetic anti-fibrotic inhibitor

Challenges and access

- There is a critical gap between research and patient access.

- Effective therapies must be affordable and tailored to a patient's needs.
- The aim is often not to cure, but to provide symptomatic control and improve quality of life.

Conclusion

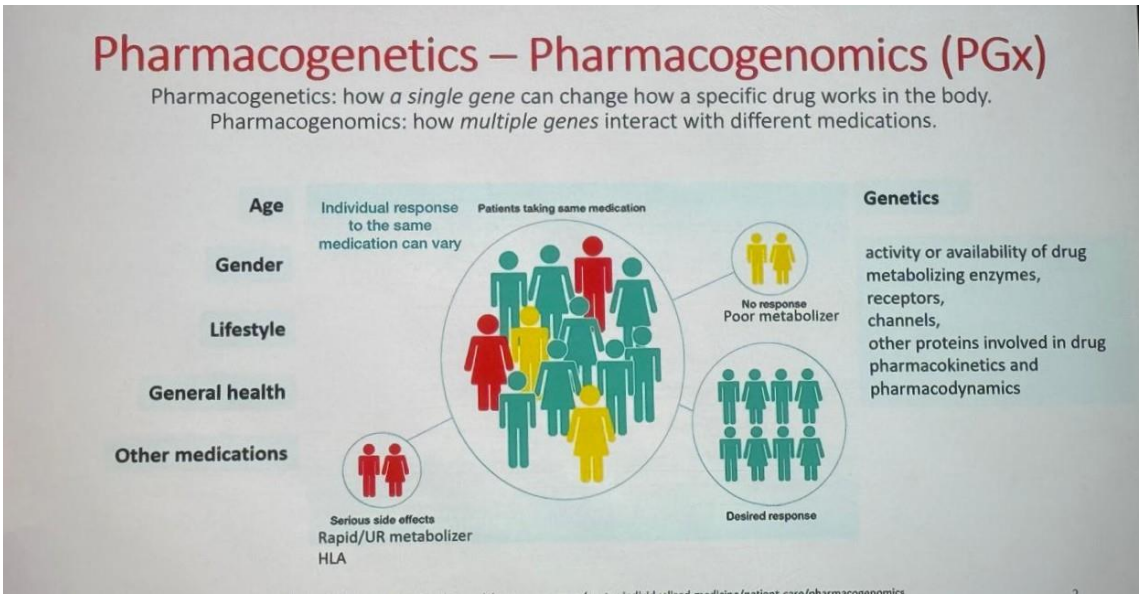
The approach to genodermatoses, and especially to EB, has shifted from a purely symptomatic approach to an era of precision medicine and targeted therapies. Molecular identification of genetic mutations has been key to establishing targeted therapies, some of them curative. However, accessibility, cost, and customisation of treatment are still major barriers. A holistic approach is required, combining primary treatment, inflammatory control and symptomatic care, all focused on the patient's priorities.

Pharmacogenetics

Speaker: Dr Cristina Has (Germany)

Introduction

Pharmacogenetics (PGx) and pharmacogenomics (PG) are rapidly evolving disciplines that study how individual genetic variability influences drug response. While pharmacogenetics focuses on the influence of individual genes, pharmacogenomics considers several genetic interactions. These areas have enabled progress towards personalised medicine, with greater therapeutic efficacy and lower risk of adverse effects, including severe cutaneous reactions (SCARs) such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).



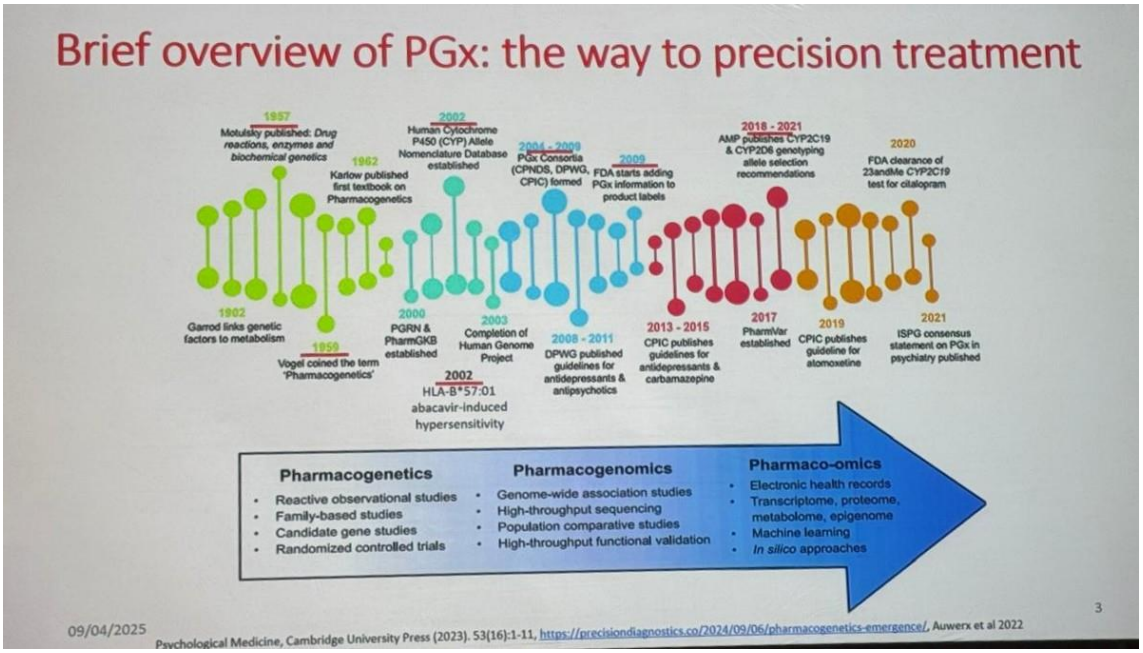
Reference: Kabbani et al. Pharmacogenomics in Practice: A Review and Implementation Guide. Frontiers in Pharmacology, 18 de mayo de 2023. DOI: 10.3389/fphar.2023.1189976

Key points of the talk

History and evolution

The term “pharmacogenetics” was coined in 1959.

Milestones: discovery of cytochrome P450 enzymes that control the metabolism of most drugs and HLA genes associated with hypersensitivity reactions.



Major events in the emergence of pharmacogenomics in psychiatry. AMP, Association of Molecular Pathology; CPIC, Clinical Pharmacogenetics Implementation Consortium; CPNDS, Canadian Pharmacogenomics Network for Drug Safety; DPWG, Dutch Pharmacogenetics Working Group; FDA, Food and Drug Administration; ISPG, International Society of Psychiatric Genetics; PGRN, Pharmacogenomics Global Research Network; PGx, pharmacogenomic; PharmGKB, Pharmacogenomics Knowledge Base; PharmVar, Pharmacogene Variation Consortium.

Methodological advances

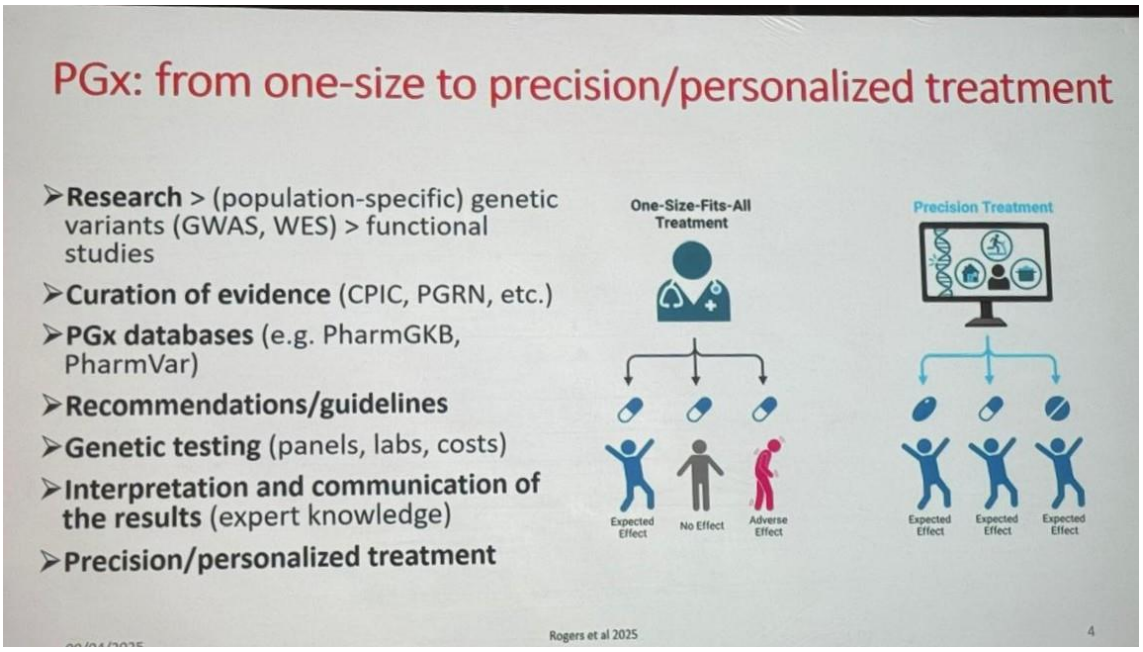
Studies: observational, familial, candidate genes, clinical trials

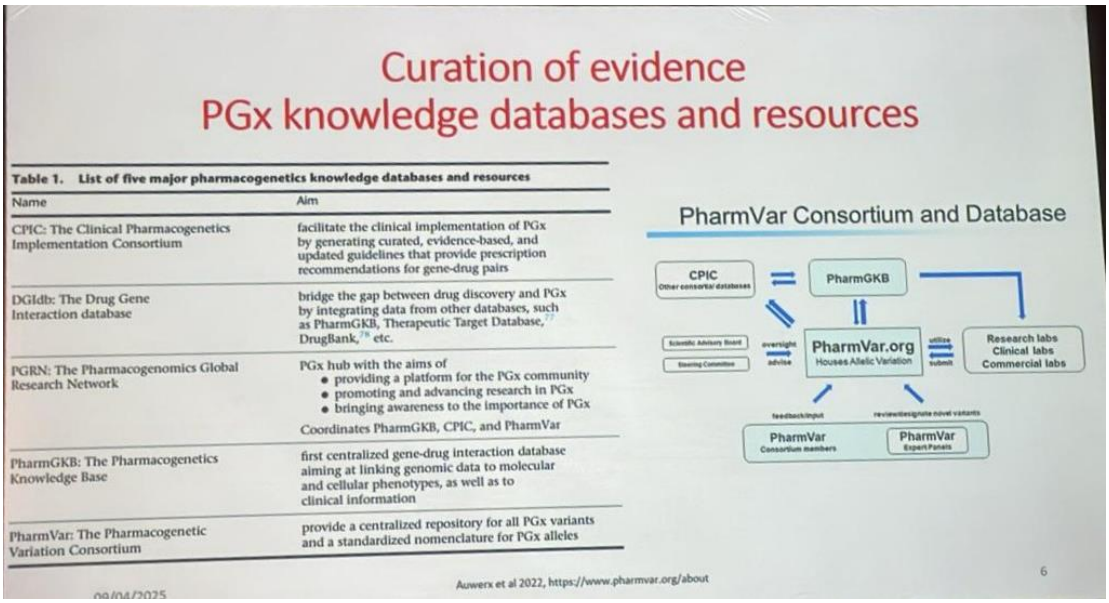
Modern techniques: genome-wide association study (GWAS), high throughput sequencing (HTS), multi-omics technologies (genomics, transcriptomics, proteomics, metabolomics, etc.), artificial intelligence.

From research to clinical practice

Requires: basic research → validation → databases →clinical guidelines → implementation.

International consortia such as CPIC® (Clinical Pharmacogenetics Implementation Consortium) or PharmGKB® generate evidence-based guidelines (for example) that are available to all.





Reference: Auwerx, Chiara et al.From pharmacogenetics to pharmaco-omics: Milestones and future directions. Human Genetics and Genomics Advances, Volume 3, Issue 2, 100100

Pharmacogenetic tests

Models:

Point-of-care model: a gene or several genes and specific drugs are tested before treatment or when the patient does not respond to treatment or has experienced adverse reactions

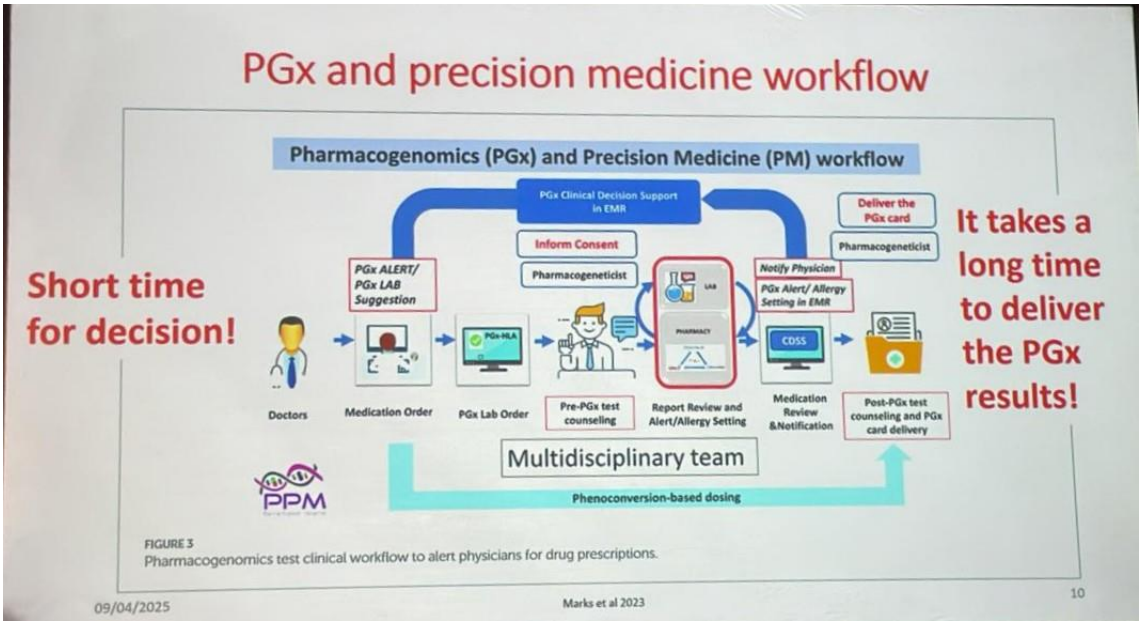
Pre-emptive: preventive model where a broad genetic profile is studied, regardless of the patient's medical history

Methods: candidate gene panels, exome or whole genome

Clinical applications

Real-time customised prescription requires a complex workflow: informed consent, extraction, interpretation and treatment adjustment

Specialists needed: pharmacogeneticists and multidisciplinary teams



Reference:

Marks et al. Updates in SJS/TEN: collaboration, innovation, and community. Front. Med., 10 October 2023.Sec. Dermatology.Volume 10
2023 https://doi.org/10.3389/fmed.2023.1213889

Barriers

Lack of generalised medical knowledge

Costs, sustainability, integration with clinical systems

Population variability in risk alleles

Dermatology applications

Drugs with genetic implications

e.g. Azathioprine: inherited thiopurine methyltransferase (TPMT) deficiency can lead to severe toxicity; genetic testing is useful, but does not detect all cases → close clinical monitoring is required.

Severe cutaneous adverse reactions (SCARs)

Examples: SJS/TEN

High mortality (up to 50% in adults)

Associated with >80% with drugs such as: Allopurinol, aromatic anticonvulsants, sulphonamide antibiotics, NSAIDs, antiretrovirals

Pathophysiological mechanism

Type IV immune reaction mediated by cytotoxic T lymphocytes.

Risk factors: HLA alleles, impaired drug metabolism (e.g. CYP2C9), viral infections, drug-drug interactions

Population variability

HLA risk alleles vary according to ethnicity (e.g. HLA-B*15:02 in Asians for carbamazepine, HLA-B*57:01 in Europeans for abacavir).

No universal approach → requires local adaptation

Case reports and studies

Example of a patient with major depression treated unsuccessfully with multiple drugs → improvement after PGx test

Paediatric studies (Toronto): up to 80% with actionable variants after genomic sequencing

Actual implementation

Successful trials in psychiatry, oncology, cardiology

Reimbursement in some European countries, but still limited clinical use

Conclusion:

Pharmacogenetics enables more effective and safer personalised medicine.

Effective clinical implementation requires continuing medical education, technological resources, scientific validation and adaptation to population genetic variability.

In dermatology, SCARs represent a critical application with a high clinical/prophylactic impact.

The future of personalised medicine includes preventive tests integrated into electronic medical records, with personalised risk lists for each patient.

References:

Cohn I, Manshaei R, Liston E, et al. Assessment of the Implementation of Pharmacogenomic Testing in a Pediatric Tertiary Care Setting. JAMA Network Open, 2021;4(5):e2110446 DOI: 10.1001/jamanetworkopen.2021.10446Europe PMC+3

Barker, C.I.S., Groeneweg, G., Maitland-van der Zee, A.H., Rieder, M.J., Hawcutt, D.B., Hubbard, T.J., Swen, J.J., & Carleton, B.C. (2021). Pharmacogenomic testing in paediatrics: Clinical implementation strategies. British Journal of Clinical Pharmacology, 88(10), 4297–4310

Hidradenitis suppurativa

Conference 1: Introduction, epidemiology and symptoms

Speaker: Dr Maria Cecilia Rivitti Machado (Brazil)

Introduction

Hidradenitis suppurativa (HS) is a chronic, recurrent inflammatory disease of the hair follicle, not of the sweat glands as previously thought. It typically presents with nodules, abscesses and tunnels (fistulous tracts), mainly in intertriginous areas. Despite its significant clinical and psychosocial burden, it continues to be underdiagnosed. This is especially true in the paediatric and adolescent population, where its incidence seems to be increasing.

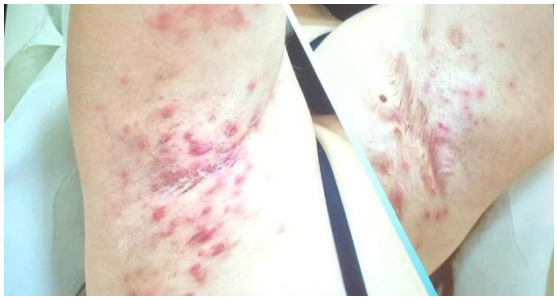
Key points of the presentation

- Definition and clinical characteristics

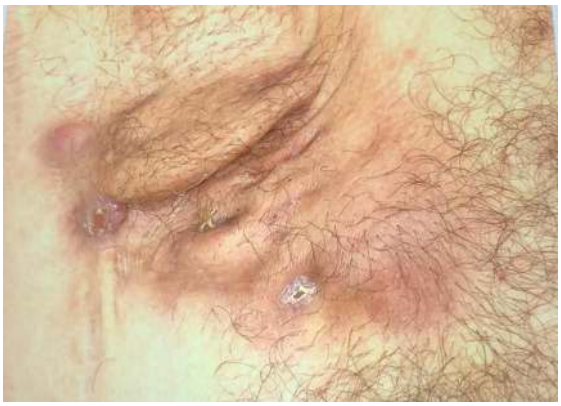
Chronic, progressive inflammatory disease of the hair follicle

It is characterised by the presence of painful inflammatory nodules, abscesses and tunnels in typical locations such as the armpits, groin, buttocks and breast region.

Lesions recur ≥2–3 times in a six-month period.



Double comedones and nodules in both armpits



Retractable scars and armpit tunnels

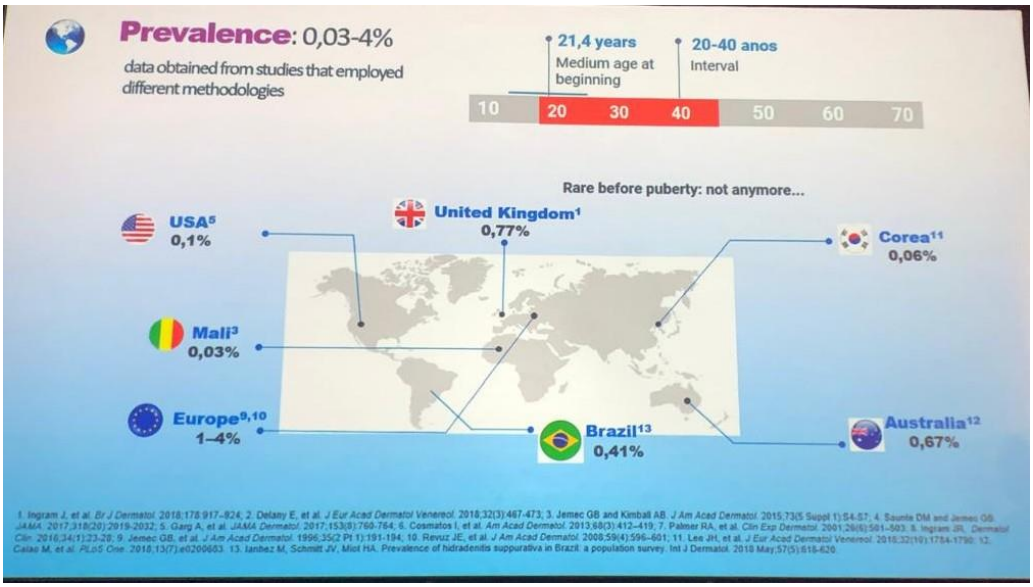
- Epidemiology and affected groups

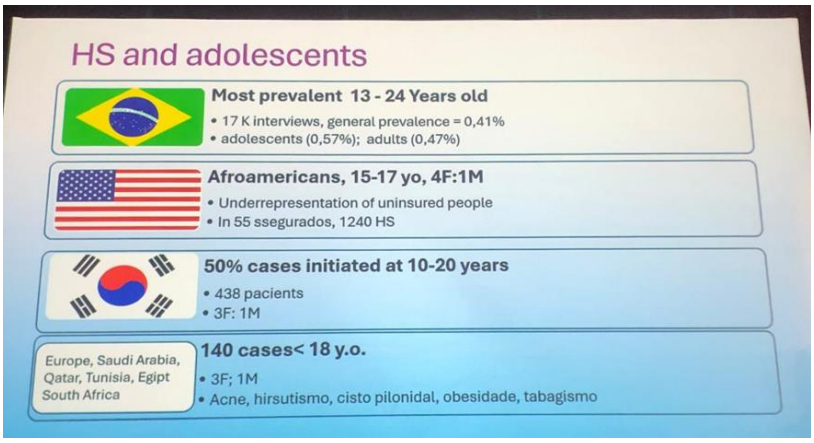
It is not a rare disease, although its prevalence varies according to the region and population studied.

Higher prevalence in adolescents and young adults (10–40 years).

High incidence in adolescents of African descent in the USA and in populations in Brazil and Korea.

An increase in severe cases has been found in the paediatric population.





- Diagnostic delay

Diagnosis often delayed (>12 years), despite family history in one third of cases.

Patients often see multiple doctors before the correct diagnosis is made.

- Clinical diagnosis

Presence of firm, inflamed nodules (<1 cm), often difficult to recognise in early stages.

Painful fluctuating abscesses, sometimes mistaken for boils.

Tunnels (dermal or subcutaneous fistulas) which may be numerous, draining or dry, with multiple orifices.

Residual lesions: atrophic scars and double comedones

Typical anatomical distribution: armpits, groin, gluteal region, breast region.

- Differential diagnosis

It is important to differentiate HS from superficial folliculitis: the latter does not leave atrophic scars or characteristic comedones.

In advanced cases, it may coexist with dissecting cellulitis of the scalp.

- Course and progression

HS is a progressive disease: over time, lesions spread and tissue damage accumulates.

Pain is a cardinal feature, along with occasional pruritus.

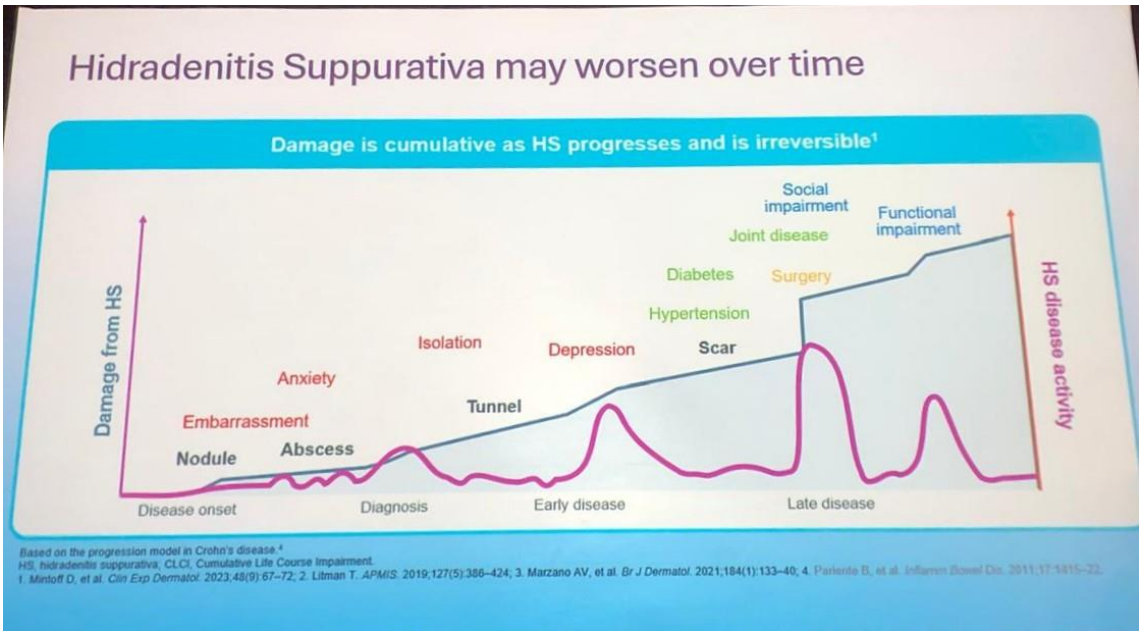
Progression has been documented in two thirds of patients at four-year follow-up.

The impact is not only physical; it significantly affects quality of life, productivity and interpersonal relationships.

Importance of early diagnosis

There is a “window of opportunity” where early diagnosis and treatment can limit progressive damage.

Skin ultrasound can be a useful tool to improve diagnostic accuracy.



Conclusion

Hidradenitis suppurativa is a severe, under-diagnosed follicular inflammatory disease that can begin in adolescence and progress rapidly if not recognised early. Clinical diagnosis should take into account lesion morphology, lesion distribution and recurrence. Given its cumulative physical and psychosocial

impact, increasing medical awareness is essential, particularly in the field of paediatric dermatology, as is ensuring appropriate follow-up and treatment from an early stage.

Conference 2: Pathogenesis

Speaker: Dr Virginia Ruth Lopez Gamboa (Argentina)

Introduction

Hidradenitis suppurativa (HS) is a chronic, recurrent and progressive inflammatory disease of the hair follicle, with an auto-inflammatory basis and a significant physical and psychosocial impact. Understanding its pathogenesis is essential to improve diagnostic and therapeutic strategies, especially in early forms of the disease, including the paediatric population.

Fundamental aspects of the pathogenesis of HS

HS is not an infection. It is not due to lack of hygiene and is not determined by race.

It is a **complex, systemic**, autoinflammatory **disorder** with **immune dysregulation** and **altered stem cell fate.**

Main theories of pathogenesis

1. **Genetic theory**

- **Complex inheritance**, with involvement in 50–70% of cases (mostly women)

- Some mutations detected:

- **Gamma-secretase** genes (NOTCH pathway)

- Polymorphisms in **TNF**, **IL-1** and **IL-6** receptors

- **SOX9**, a transcription factor in hair follicle stem cells, is key:

    - It regulates cell fate: hair vs hyperkeratotic epithelium
    - Its overexpression favours tunnel formation and inflammation

2. **Immunocellular theory**

- It involves cells such as:

- Dendritic cells, Th1 and Th17 lymphocytes, neutrophils and plasma cells

- Excessive secretion of pro-inflammatory cytokines

- Involvement of **fibroblasts and keratinocytes** in chronic phases: fibrosis and aberrant scarring

- These mechanisms are the targets of currently approved biological therapies

3. **Hormonal theory**

- **Incomplete X chromosome inactivation** in females has been proposed as a cause of immune dysfunction.

- Androgen-regulated **SOX9** is altered in this context.

- Adiposity increases the conversion of androgens to oestrogens, modulating inflammation.

- This explains the use of drugs such as **spironolactone**, **finasteride** or **metformin** in some cases.

Triggering and progression factors

- **Skin and intestinal dysbiosis**: disrupts local immunity
- **Nutrition**: some pro-inflammatory foods can exacerbate the disease
- **Tobacco**: exacerbates keratinisation and scarring; it should be avoided
- **Stress**: cortisol pathway as an inflammatory modulator
- **Mechanical factors**: friction, perspiration, depilation
- **Obesity**: adipocytes secrete pro-inflammatory cytokines

Chronification of the disease

The traditional model suggests that the **follicular plug** initiates the process.

Current evidence suggests that **dermal inflammation** precedes plugging, creating a **vicious circle**.

The process includes: inflammation → plugging → rupture → more inflammation → tunnelling and scarring.

Conclusion

HS is a multifactorial disease, with interrelated genetic, immunological and hormonal mechanisms.

Early identification of mild forms, especially in the paediatric population, can prevent progression and permanent sequelae.

SOX9 emerges as a central molecule in pathogenesis.

It is essential to personalise the therapeutic approach, taking into account triggering factors and the clinical stage.

The **primary triggering mechanism** is still unknown and further clinical and translational research is needed.

Conference 3: Use of skin ultrasound in the diagnosis and treatment of hidradenitis suppurativa (HS)

Speaker: Dr Ximena Wortsman (Chile)

Introduction

Hidradenitis suppurativa is a chronic, devastating and underdiagnosed inflammatory disease involving hair follicles in intertriginous areas. Historically, it was considered to be a disease of the apocrine glands, but recent evidence has shown that its origin is related to follicular disruption. Skin ultrasound has emerged as a key diagnostic tool for early disease detection, disease activity assessment, treatment guidance and surgical planning.

Key points of the talk

1. Advantages of high-frequency skin ultrasound

It enables viewing skin layers, hair follicles, glands and fistulous tracts in detail.

It has better axial spatial resolution than CT or MRI scans for skin structures.

It detects abnormalities that are not clinically visible, enabling earlier diagnosis.

2. New findings in the pathophysiology of HS

The disease originates in the hair follicles, not in the apocrine glands.

Follicular rupture contributes to the formation of fluid collections and inflammatory tunnels.

Fragments of keratin and hair shafts have been found to be retained within these tunnels, which is associated with increased severity.

3. Ultrasound protocol and diagnostic criteria

There are standardised protocols for different anatomical regions.

Ultrasound criteria include: cystic structures, fluid collections, fistulous tracts and changes in echogenicity.

The ultrasound classification has been updated to include sub-stages (3A and 3D) and number of affected regions.

4. Value of ultrasound as a staging tool and biomarker

Useful for accurate determination of the degree of active inflammation.

It enables differentiating HS from its simulators (such as abscesses or recurrent folliculitis).

In more than 80% of cases in adults (and 90% in children), the use of ultrasound changed therapeutic behaviour.

5. Monitoring and evaluation of treatment response

It enables changes in echogenicity, tunnel collapse and decreased vascularity with Doppler to be assessed after treatment.

Useful for monitoring the effectiveness of biological treatments, antibiotics and photodynamic therapy.

6. Surgical planning and guided procedures

Improved delineation of surgical margins, which may reduce recurrences.

It guides intralesional corticosteroid injections, ensuring accuracy and avoiding adverse effects.

7. International validation of the use of ultrasound in HS

Recent Chilean guidelines and international consensuses validate the use of ultrasound as part of the diagnostic and therapeutic algorithm for HS.

More than 95% agreement was achieved on the items evaluated (diagnostic criteria, staging, monitoring, guided procedures and usefulness in research).

Conclusion

High-frequency skin ultrasound is a **validated, reproducible and highly effective** tool for diagnosis, staging, therapeutic monitoring and procedural planning in patients with hidradenitis suppurativa. Its use should be established as a **standard of care**, especially due to its ability to detect disease at early stages, guide clinical decision-making and optimise multidisciplinary treatment.

Conference 4: Impact of HS

Speaker: Dr Jacek Szepietowski (Poland)

Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease characterised by painful, recurrent and debilitating lesions mainly affecting the intertriginous areas. Although its clinical presentation is well known, the subjective and psychosocial burden associated with the disease is often underestimated. This talk addressed the emotional, social and psychological consequences of HS, especially in paediatric and adolescent populations, highlighting the need for an interdisciplinary approach to improve patient quality of life.

Key points

- **Subjective symptoms and pain:**

HS manifests with visible skin lesions as well as with subjective symptoms such as severe pain.

Pain correlates directly with clinical severity according to the Hurley and IHS4 scales.

More than 80% of patients report significant pain.

- **Psychosocial burden:**

Patients perceive HS to be a “miserable”, “unbearable” disease that destroys physical and emotional well-being.

It has a profound impact on quality of life, affecting physical and mental health, social life and self-esteem.

- **Assessment instruments:**

There are multiple validated tools for assessing quality of life in HS, although many are validated only in the adult population.

Quality of life decreases proportionally with the number of areas affected and the seriousness of the clinical stage.

- **Specifics in adolescents:**

In a small number of studies in adolescents with HS, a higher prevalence of anxiety, depression and alexithymia (difficulty identifying and expressing emotions) has been observed.

Problems of passive self-destructiveness, demotivation, and problematic substance use have also been identified.

- Stigmatisation:

HS causes marked social stigma, comparable to other visible dermatoses such as atopic dermatitis or alopecia.

This stigma affects social integration, interpersonal relationships and self-perception.

- Sexuality and relationships:

HS has a significant impact on sexuality, especially in adolescents who are just beginning their sex lives.

High levels of sex life dissatisfaction and difficulties in establishing intimate relationships have been reported.

- Life satisfaction and doctor-patient relationship:

There is a strong correlation between low life satisfaction, anxiety, depression and perception of disease management.

A good doctor-patient relationship based on trust can significantly improve therapeutic outcomes.

- Therapeutic recommendations:

The need for effective and personalised treatments was emphasised.

An interdisciplinary approach was recommended, including dermatologists, rheumatologists, psychologists and psychiatrists.

Psychological support is key to improving adjustment to the disease and quality of life.

Conclusion

HS is much more than a skin disease; it represents a major physical, emotional and social burden. Patients need to be heard not only regarding their clinical symptoms, but also regarding their personal experiences. Comprehensive care should contemplate clinical management, psychosocial support and improving self-esteem and functioning. As doctors, our role must go beyond dermatological treatment and encompass a holistic view that accompanies patients from suffering to stabilisation and well-being.

Conference 5: Medical treatment

Speaker: Dr Renata Magalhaes (Brazil)

Introduction

Hidroadenitis suppurativa (HS) is a chronic, debilitating inflammatory disease. Its manifestation in the paediatric population represents a diagnostic and therapeutic challenge. Although it has traditionally been considered to be a young adult disease, early onset cases are increasingly recognised, even before the age of 12 years. This highlights the need for specific and timely therapeutic approaches in this age group.

Main points of the talk

- Epidemiology and clinical characteristics

In a centre of excellence with more than 200 HS patients, 15% reported symptoms before the age of 12 years, and another 15% between the ages of 12 and 18 years.

The disease in adolescents tends to have a more aggressive course with a significant impact on quality of life.

Case reports showed childhood onset with severe progression, including one that progressed from mild lesions to severe disease in seven years.

- Diagnosis and associated comorbidities
  - Common comorbidities include:
  - Obesity
  - Arthritis (including juvenile arthritis)
  - Diabetes
  - Anxiety and depression
  - Autoimmune and inflammatory diseases (psoriasis, lupus, inflammatory bowel disease)

Identifying these associated conditions enables more comprehensive and earlier intervention.

- Importance of early diagnosis

Early diagnosis and treatment are essential to modify the course of the disease.

Delaying the initiation of biologic treatments can significantly decrease the response rate.

An Italian study showed that a delay of more than 10 years is associated with double the risk of treatment failure.

Therapeutic options in the paediatric population

- Topical treatment

Useful in early stages or mild disease

Options: topical clindamycin, resorcinol (although not officially approved), zinc supplementation (empirical use)

- Systemic antibiotics:

First-line treatment for moderate-to-severe cases

They include cephalexin, doxycycline (from age 8), clindamycin and rifampicin (with caution).

- Oral retinoids

Mainly considered in cases with coexisting severe acne

Isotretinoin is useful, although with variable results; acitretin may be considered in specific cases.

- Hormone therapy

Limited evidence, but may be considered in cases with signs of hyperandrogenism or insulin resistance

Biologics

They represent the most evidence-based option for patients aged ≥12 years.

Main agents used:

- Adalimumab: approved from the age of 12
- Secukinumab: approved from age 6 for psoriasis; use in HS extrapolated
- Ixekizumab: under study and some guidelines include it as an option
- Ustekinumab: option in cases with associated inflammatory bowel disease

Surgical procedures

Surgery may be considered in selected patients, ideally after stabilisation with medical treatment.

Example: 15-year-old patient with right axillary involvement managed with biologics followed by surgical excision with good results.

Other therapeutic methods

Laser and light therapies (CO_2 laser, Nd:YAG) may be useful as an adjunct.

Essential multidisciplinary management: dermatology, rheumatology, psychology, nutrition.

Conclusion

The treatment of hidradenitis suppurativa in the paediatric population represents a unique window of opportunity to modify the course of the disease and improve long-term prognosis. Early recognition, comprehensive management of comorbidities, and timely initiation of effective therapies, including biologics, are fundamental pillars of the current approach. While there are still limitations in the evidence, especially in children under 12 years of age, new guidelines are starting to include specific recommendations for this age group. This marks important progress in treatment personalisation.

Conference 6: Surgical treatment of hidradenitis suppurativa: an opportunity in the paediatric and adolescent population

Speaker: Dr Mario Chaves Cirujano (Brazil)

Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory disease of the pilosebaceous unit, which is often underdiagnosed, delaying appropriate treatment. In children and adolescents, the delay in surgery compromises prognosis and perpetuates progression to more severe forms. This talk addressed the importance of timely surgical intervention, the therapeutic options available, and the role of complementary technologies in optimising outcomes.

Key points of the surgical approach in HS

- **Early surgery and personalised planning:**

Surgery should be considered early, even in adolescents, to prevent progression to advanced stages (Hurley III).

The decision to perform surgery should be based on the extent, location and severity of HS and the patient's comorbidities.

Not interfering with their school calendar is essential in children and adolescents.

- **Surgical objectives:**

Removal of inflammatory masses, keratotic debris and chronic granulation tissue

Control of the infection and reduction of the risk of recurrence

- **Surgical techniques available:**

Incision and drainage of abscesses

Deroofing and unroofing (tunnel roofing and unroofing techniques)

Wide excision with 1–2 cm lateral margins and flap or graft coverage

Primary closure where possible, especially in localised lesions

- **Common complications:**

Haemorrhage, infection, hypertrophic scarring, retraction, dehiscence and recurrence

- **Assistive technologies:**

CO_2 laser: useful for chronic lesion ablation or excision with minimal thermal injury and better visualisation Promotes secondary intention healing.

Negative pressure (vacuum): indicated for high-risk surgical incisions; reduces the risk of infection and dehiscence

Paediatric clinical examples:

Cases in adolescents with axillary, inguinal and perineal lesions treated with wide excision and reconstruction with V-Y flaps or primary closure

Satisfactory functional and aesthetic postoperative results

Conclusion

Surgery is a fundamental tool in the treatment of hidradenitis suppurativa, especially in young patients. Early surgery can slow disease progression, reduce inflammatory burden and improve quality of life. Adopting a multidisciplinary approach is key, taking into account the mental health, psychological support and social context of paediatric patients. The use of technologies such as CO_2 laser and negative pressure therapy optimises surgical outcomes and minimises complications. Early, well-planned and personalised surgical treatment can radically transform the prognosis of HS patients.

New topical treatments

Coordinator: Dr Catherine C. McCuaig (Canada)

Co-Coordinator: Dr Ana María Saénz (Venezuela) & Dr Josaine Sanjinés (Bolivia)

Conference 1: New topical treatments for warts and molluscum contagiosum

Speaker: Dr Josaine Sanjinés (Bolivia)

Introduction

The pathophysiology, epidemiology, clinical manifestations and current treatment options for molluscum contagiosum and warts caused by human papillomavirus (HPV) were reviewed. Both conditions are common cutaneous viral infections in the paediatric population. Although they are usually self-limiting infections, their treatment can be challenging, especially in multiple, symptomatic or localised cases in visible areas.

Molluscum contagiosum

- **Aetiology and transmission**:

Caused by a human-specific poxvirus

It is transmitted by direct contact with infected skin, auto-inoculation or fomites.

Waterborne transmission has not been proven, although it has been associated with activities such as swimming ("water wart").

- **Epidemiology**:

Prevalence in US children: approximately 62%

More common between the ages of 0 and 16 years

- **Clinical symptoms**:

Incubation period: 2 weeks to 6 months

Pearly, skin-coloured, umbilicate lesions measuring 1 to 10 mm

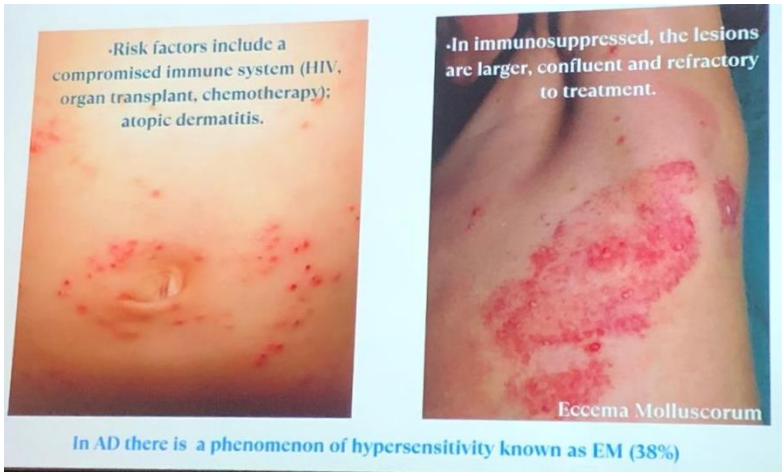
Koebner phenomenon in trauma areas

In atopic dermatitis, hypersensitivity and extensive dissemination may be found.

- **Risk factors**:

Immunosuppression: HIV, transplants, chemotherapy (more extensive and refractory lesions)

Atopic dermatitis



- **Treatment**:

Watchful waiting in non-symptomatic or sparse lesions

The sign of perilesional inflammation may indicate imminent resolution.

- **Therapeutic options**:
  - Destructive methods: cryotherapy, curettage, trichloroacetic acid (20–35%)
  - Topical agents:
    - Potassium hydroxide, 10%: strong alkaline with keratolytic action
    - Cantharidin (0.7–0.9%): vesicant that causes superficial blistering without scarring
    - Imiquimod (5%): immunomodulator, used little due to local adverse effects
    - Benzoyl peroxide (1%): applied 2 times/day for 20 days
    - Natural extracts: little scientific evidence
- **Berdazimer sodium, 10%**: most recent FDA-approved treatment (from age 2 years)
- **The "coup d'état" method**: puncture and evacuation of the contents, with prior topical anaesthesia

References:

Keam SJ. Berdazimer Topical Gel, 10.3%: First Approval. Drugs. 2024 Mar;84(3):363-368. doi: 10.1007/s40265-024-02012-9. PMID: 38409574.

Paller AS, Green LJ, Silverberg N, Stripling S, Cartwright M, Enloe C, Wells N, Kowalewski EK, Maeda-Chubachi T. Berdazimer gel for molluscum contagiosum in patients with atopic dermatitis. Pediatr Dermatol. 2024 May-Jun;41(3):438-444. doi: 10.1111/pde.15575. Epub 2024 Feb 27. PMID: 38413239.

Viral warts (HPV)

- **Clinical types**:

Common warts: hyperkeratotic lesions on the face and extremities

Plantar warts: smooth surface with dark spots (thrombosed capillaries)

Condylomata acuminata: in the genital and perianal region

Oral warts: on the lips, gums, palate or tongue

- **Treatment**:
  - Generally asymptomatic; they do not always require intervention
  - Conventional methods:
    - Salicylic acid, trichloroacetic acid
    - Cryotherapy
    - Immunomodulatory agents: vitamin D, acetate
- **Immunotherapy** (especially for recalcitrant warts):
  - Agents such as BCG, candida,
  - Tuberculin, HPV vaccine
  - Green tea polyphenols: activate innate immunity and cell apoptosis
  - DNCB, DPCP, PPD: synthetic agents that cause a local inflammatory reaction
- Painful or traumatic treatments should be avoided in young children

Conclusion

Both molluscum contagiosum and viral warts are common, benign, self-limiting infections in childhood. The choice of therapy must be personalised, taking into account the patient's age, wart location, symptoms, number of lesions and immune status. There are multiple approved options, but watchful waiting is also valid in many cases. Communication with parents and appropriate follow-up are key to successful and safe treatment.

Conference 2: Newly approved medications for atopic dermatitis and psoriasis

Speaker: Dr Catherine C. McCuaig (Canada)

Introduction

In recent years, the topical treatment of inflammatory skin diseases such as atopic dermatitis and psoriasis has evolved considerably. New molecules with innovative mechanisms of action have been approved, notably phosphodiesterase-4 (PDE-4) inhibitors, Janus kinase inhibitors (JAKi) and aryl hydrocarbon receptor (AHR) agonists. These therapies promise to significantly improve clinical management, particularly in the paediatric population. However, their high cost and limited availability continue to be major barriers.

Highlights

1. PDE-4 inhibitors

- **Apremilast:** Approved since 2013, but with limited clinical effectiveness in real practice (comparable to hydrocortisone 1%)
- **Roflumilast:**

- Greater potency and affinity for the epidermis
- Formulations:
  - 0.3% in adults
  - 0.15% for children aged 6–12 years
  - 0.05% for children aged 2–5 years
- Daily use, well tolerated in intertriginous areas
- Symptomatic improvement in 2 weeks; clearance in 4 weeks
- Adverse events: local burning (rare), headache, nausea and diarrhoea (very rare)
- Maintenance effect: twice-weekly use can prolong remission up to 281 days

- **Difamilast (Asia):**
  - Used in children from 3 months of age
  - Systemic absorption possible; not recommended in pregnant women or on abraded skin
  - Under study as potential prophylaxis for food allergy

2. Topical JAK inhibitors

- **Mechanism:** They block multiple cytokine pathways; rapid relief of pruritus (within 24 hours)

- **Ruxolitinib:**

- Approved for atopic dermatitis and vitiligo in individuals over 12 years of age
- Effective: 71% improvement vs triamcinolone and placebo
- Safety: no bone marrow suppression in maximum-use studies

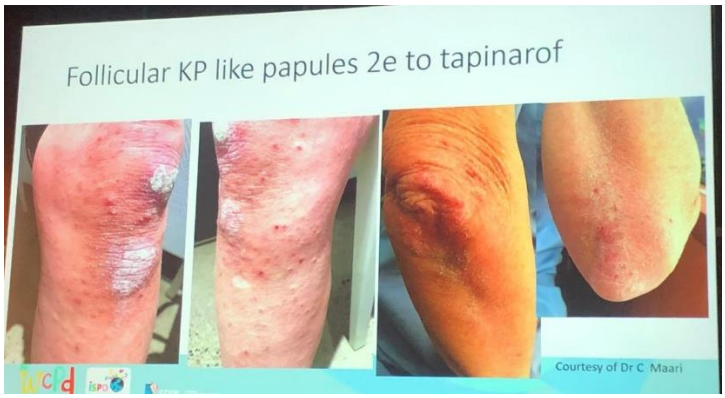
- **Delgocitinib:**
  - Used from 6 months of age in Japan
  - Assessed in hand eczema and paediatric linear morphea

- **Tofacitinib and other JAK inhibitors:** under study for various types of dermatosis

Adverse events: local irritation (<1%), some follicular KP-like reactions

3. Aryl hydrocarbon receptor (AHR) activators

- **Tapinarof:**
  - They improve the skin barrier and reduce inflammation.
  - Remarkable results in psoriasis:
    - Complete clearance at 12 weeks
    - Maintenance of remission up to 24 weeks post-treatment
  - Approved for children over 2 years of age
  - Adverse effects: contact dermatitis and follicular reactions in up to 10%



4. Clinical and comparative considerations

- **Meta-analysis:**
  - Most effective therapies: topical corticosteroids, tacrolimus, ruxolitinib and delgocitinib
  - Short studies (28 days), with limited data on AHR activators

- **Drug vehicle:**
  - Ointments more effective and less irritating than creams
  - **Therapeutic combinations:** little formal evidence, although frequently used in clinical practice
  - **Cost:** main barrier to access, for example, tapinarof and roflumilast cost over USD 1000.

Conclusion

New topical therapies offer valuable and effective alternatives for the treatment of atopic dermatitis and psoriasis, including in the paediatric age group.

- **PDE-4 inhibitors:** Effective and well tolerated, ideal for maintenance use, although slower acting
- **JAK inhibitors:** High effectiveness, fast acting, potential for multiple inflammatory dermatoses; restricted by age and body area
- **AHR agonists:** Promising due to their ability to achieve prolonged remissions after treatment

Current challenges: lack of head-to-head comparative studies, limited evidence on treatment combinations and high cost. The future looks bright with innovative molecules that could redefine the topical treatment of chronic inflammatory diseases in paediatric dermatology.

Conference 3: Topical treatment for epidermolysis bullosa

Speaker: Dr Ana María Saénz (Venezuela)

Introduction

Epidermolysis bullosa (EB) is a group of rare genetic diseases characterised by extreme fragility of the skin, causing blistering and sores with minimal trauma. Treating this pathology is a major challenge, especially in resource-limited countries, as it requires a multidisciplinary approach. During the Paediatric Dermatology Congress, new developments in innovative topical

treatments were presented, from gene therapies to accessible natural solutions.

Highlights of the talk

- **Importance of diagnosis and a holistic approach**
  - EB is usually initially diagnosed by dermatologists following referral from general paediatricians
  - The diagnosis carries a great emotional burden and requires comprehensive support for patients and their families.
  - The need for multidisciplinary teams to properly treat the disease was emphasised.
- **Limitations of advanced therapies**
  - Gene, protein and cell therapies still face difficulties of sustained effectiveness and high costs.
  - Example: gene-corrected keratinocyte autografts have shown ulcerative recurrences after a few years, showing that optimisation is still required.

- **First approved topical gene therapy: Vyjuvek®**
  - Developed by Crystal Biotech, FDA approved for dystrophic EB from 6 months of age
  - It uses an inactivated herpes simplex type 1 vector to introduce the type VII collagen gene directly into wounds.
  - Benefits observed:
    - Epithelialisation of chronic wounds
    - Reduction of pain during healing
  - Limitations:
    - Very high cost: approx. USD 331,000 per patient/year
    - Inaccessibility for many Latin American countries

- **Promising natural alternative: birch bark extract:** Oleogel-S10 **(Filsuvez®)**
  - Multicentre study by the Colombian group led by Dr Mauricio Torres.
  - Outcomes:
    - Decreased inflammation after 5 days
    - Rapid onset of epithelialisation
    - High patient and family satisfaction
  - Greater affordability compared to gene therapies

- **Other emerging research**
  - Use of eye drops to improve ocular complications in EB, as presented in a Chilean pilot study

- The relevance of treating not only skin lesions but also extracutaneous abnormalities such as ocular ones was mentioned, given the shared involvement of type VII collagen.

Conclusion

Topical treatment in EB has progressed significantly, offering new hope, especially with the approval of the first in vivo gene therapy. However, most of these therapies are inaccessible to many regions due to their high cost. Alternatives such as birch bark extract are an effective and feasible option in resource-limited contexts. Continuing to promote research, international collaboration and comprehensive patient support is essential in order to achieve a more equitable and effective approach to this complex disease.

Conference 4: Hidradenitis suppurativa and acne

Speaker: Dr Irene Lara Corrales (Canada)

Introduction

This talk addressed topical treatments approved over the last five years for the management of **acne vulgaris** and **hidradenitis suppurativa (HS)**. These pathologies share similar pathophysiological mechanisms—mainly **follicular occlusion and secondary inflammation**—which justifies their joint analysis. While multiple systemic therapies are available, optimising topical options is key, especially for patients with mild disease or as part of combination or maintenance strategies.

Topical therapeutic novelties in acne (last 5 years)

- **Minocycline topical foam, 4%** (FDA: Amzeeq®, 2019)

It has been shown not to generate significant systemic exposure, unlike its oral formulation.

Two phase III trials confirmed its **efficacy in reducing inflammatory and non-inflammatory lesions**, with good tolerability and safety after 52 weeks.

Included in new treatment guidelines with high recommendation and moderate level of certainty

- **Clascoterone cream, 1%** (FDA: Winlevi®)

First topical anti-androgen approved for acne; it inhibits dihydrotestosterone (DHT) action at the level of androgen receptors in sebaceous glands.

Studies in adolescents and adults have shown efficacy and a favourable safety profile, although its use may be limited by its high cost.

Conditional recommendation with high level of evidence in the new guidelines

- **Benzoyl peroxide + tretinoin, 0.1% microencapsulated** (FDA: **Twyneo®**)

Topical combination that improves the tolerability of benzoyl peroxide

Effective for moderate-to-severe acne, comparable or superior to other combinations

Strong recommendation with moderate certainty in guidelines

- **Triple topical combination: clindamycin + benzoyl peroxide + adapalene (FDA: Cabtreo®)**

First three-in-one topical therapy approved for acne

Studies in adults and adolescents have shown superiority over vehicles and dual combinations, with good tolerability.

Not yet included in the guidelines due to its recent approval

Emerging topical options for hidradenitis suppurativa (HS)

There are currently **no approved topical treatments specifically for HS**, but trials are ongoing:

- **Topical roflumilast** (PDE-4 inhibitor): promising preliminary results in open-label and controlled trials
- **Tapinarof** (AHR agonist): with potential effect on skin barrier restoration; under study for HS
- **Innovative formulations with new vehicles and delivery systems** targeting the hair follicle are also under investigation

American guidelines for the medical treatment of HS, including specific recommendations for the paediatric population, have recently been published.

- They contain **20 recommendations**, 5 of which are oriented towards topical therapies, many based on consensus due to the lack of robust evidence.

Conclusion

In acne, the development of **new topical formulations** has expanded the therapeutic arsenal with more specific, effective and safer products.

Although **cost and adherence** continue to be clinical challenges, these advances enable **personalised treatment stratification**.

For **hidradenitis suppurativa**, there is still a shortage of topical therapies with solid evidence, although current studies are promising.

Staying up-to-date with future approvals and the results of ongoing clinical trials is essential.

Conference 5: Vitiligo and alopecia areata: when to use topical vs systemic treatment

Speaker: Dr Felipe Enrique Valderrama (Peru)

Introduction

Alopecia areata and vitiligo are chronic autoimmune inflammatory diseases that commonly affect the paediatric population. Although clinically different, they share common pathogenic mechanisms and similar therapeutic challenges. This presentation addressed the most relevant topical therapeutic options in children, with emphasis on JAK inhibitors as a promising new alternative.

Alopecia areata in children

- General aspects

Autoimmune disease with genetic predisposition

It can have a mild, moderate or severe course (totalis, universalis, diffuse).

Clinical diagnosis supplemented by trichoscopy: black dots, exclamation mark hairs, broken hairs

Severity assessment using the SALT score.

- Topical treatments

Topical and intralesional corticosteroids: first line, safe in children

Prostaglandin analogues: (bimatoprost, latanoprost) for scalp and eyelashes, although with limited evidence

Topical JAK inhibitors (tofacitinib, ruxolitinib): emerging option when steroids fail

Topical minoxidil: useful adjuvant

Other methods:

In extensive cases (>50%): systemic therapy with corticosteroids or immunomodulators (methotrexate among others)

- Highlighted case report

10-year-old girl with extensive alopecia areata, refractory to steroids and methotrexate

Successful treatment with tofacitinib 5 mg twice daily: 60–70% improvement in SALT score within a few months

Vitiligo in children

- Specific clinical aspects

Increased frequency of segmental vitiligo

High association with atopy and family history of autoimmune diseases

Classification: segmental, non-segmental, mixed or unclassified

- Pathogenesis

Multiple mechanisms: genetic predisposition, autoimmunity, oxidative stress and neurogenic theories

Convergent theory: unification of hypotheses explaining the loss of melanocyte viability

- Topical treatments

Indicated when <10% of the body surface area is affected

Topical corticosteroids: mometasone or fluocinolone used intermittently to minimise local adverse effects

Calcineurin inhibitors: tacrolimus or pimecrolimus, especially on the face and sensitive areas

Topical JAK inhibitors: FDA-approved ruxolitinib cream (paediatric use still under study)

- Highlighted case report

Paediatric patient with vitiligo on her upper lip, treated with topical ruxolitinib and phototherapy, with 80% repigmentation in 2 months

- Other methods

In widespread cases: Narrowband UVB phototherapy: most commonly used method

Surgery (suction blister epidermal grafts): option for refractory areas (lips, face)

Conclusion

Both alopecia areata and vitiligo share pathogenic mechanisms such as autoimmunity and oxidative stress.

The choice of treatment should be based on clinical assessment and severity.

Topical corticosteroids and calcineurin inhibitors continue to be mainstays of initial treatment.

Topical JAK inhibitors, such as tofacitinib and ruxolitinib, have shown to be promising alternatives due to their efficacy and safety profile in paediatrics.

Combination treatment with phototherapy can enhance therapeutic results.

Conference 6: Toxicity of topical treatments

Speaker: Dr Fernanda Bellodi Schmidt (United States)

Introduction

Although topical treatments are generally considered safe, especially in paediatrics, their inappropriate use can have serious consequences. This talk aimed to highlight the acute toxicity risks associated with topical medicinal products frequently used in paediatric dermatology. Through real case reports, it was shown how factors such as age, skin barrier status, dose and application form can contribute to significant systemic adverse events.

Physiological aspects of paediatric skin

Children's skin is significantly different from adult skin:

Immature stratum corneum until 2 to 5 years of age

Thinner epidermis and lower lipid content

Higher body surface/weight ratio

These characteristics favour increased percutaneous absorption and risk of toxicity.

1. Topical anaesthetics (lidocaine/prilocaine – EMLA®, lidocaine – LMX®)

- Systemic toxicity: convulsions, methaemoglobinaemia, cardiotoxicity
- Case reports:
  - Excessive application of EMLA® + occlusion → generalised convulsions
- Recommendations for use:
  - Contraindicated in neonates
  - Restricted use according to age, weight and exposure time
  - Give preference to 5 g tubes to limit doses
  - Important to inform carers on safe application, especially if applied at home

2. Alcohols and antiseptics

- Products such as methylated spirit, isopropyl alcohol and methanol can cause systemic toxicity in infants.
- Symptoms: weakness, metabolic acidosis, neurological compromise
- Case reports: prolonged use in umbilical cord care → severe poisoning, hospitalisation
- Caution: avoid using potentially toxic antiseptics in newborns or on large areas

3. Hydrogen peroxide

- Despite being sold over the counter, it can cause serious adverse effects.
- Fatal case: infant with severe atopic dermatitis treated with repeated applications on large areas → death from intestinal haemorrhages (possible chemical colitis)
- Warning: Avoid use on children under 2 years of age and do not apply to large areas or on broken skin.

4. DEET (diethyl-meta-toluamide, topical insecticide)

- Used as an insect repellent
- Neurological toxicity: encephalopathy; convulsions; in severe cases, death
- Greater risk in dermal exposure versus inhalation or ingestion
- Recommendations:
  - Use concentrations <30%.

- Do not apply to children under 2 months of age.
- Do not use under clothing, on irritated skin or on large areas.
- Wash skin at the end of exposure.

5. Salicylic acid

- Used to treat warts or other dermatoses
- **Case report**: child with 50% topical application for 3 days → metabolic acidosis, respiratory distress, hospitalisation
- **Danger**: high concentration + repeated use on occluded skin → systemic poisoning

Conclusion

- Although perceived as safe, topical treatments in paediatrics can cause significant systemic toxicity if used inappropriately.
- **Risk factors**:
  - Early age
  - Impaired skin barrier
  - Excessive use or use on large areas
  - Application under occlusion or at home without medical supervision
- **Key recommendations:**
  - Inform carers regarding dosage, duration and safe application.
  - Prescribe presentations that limit overuse.
  - Watch for early signs of toxicity.
  - Ensure safe storage and disposal to avoid accidental exposure.

What's new?

Conference: What's new in paediatric dermatology: recent clinical findings

Speaker: Dr Lisa Weibel (Switzerland)

Introduction

During this presentation, recent advances were shared in paediatric dermatology focusing exclusively on clinical observations, excluding therapeutic and genetic aspects. The talk was based on a selection of ten scientific publications highlighting new clinical entities, unusual phenotypic

patterns and relevant associations with diagnostic implications. The most important findings are described below.

1- Segmental corymbiform congenital melanocytic naevi

- Atypical pattern with multiple small congenital melanocytic naevi with a segmental distribution.
- A variant in NRAS was identified in most cases, without neurological involvement.
- Its origin in Schwann cell precursors with a postzygotic mutation has been suggested.

2- Orthostatic vascular syndrome in children

a. Urticarial lesions with erythrocyanosis alternating with anaemic macules when a patient stays in an orthostatic position for some minutes

b. A Canadian study reported 42 cases; predominance in girls, frequently associated with ADHD (50% of cases) and dysautonomia symptoms (60%) such as intolerance to orthostatic position. Cases have also been described in infants.

c. Beta-blockers and antihistamines did not show good response. Its course is benign; spontaneous resolution in most cases in 3 to 4 years

3- Voriconazole phototoxicity with xeroderma pigmentosum phenotype

a. Cases in immunocompromised patients, including children with Down's syndrome treated with voriconazole.

b. Voriconazole can cause phototoxicity, but has also been linked to a high risk of aggressive squamous cell carcinoma and even melanoma in both children and adults.

c. Patient skin phenotype is remarkably similar to that seen in individuals with xeroderma pigmentosum (XP).

d. It was shown that the drug does not directly modify the expression of genes involved in DNA repair (as in XP), but reduces repair by altering chromatin density, which prevents the repair system from accessing damaged DNA.

e. This adverse voriconazole effect can be reversed by the concomitant administration of histone deacetylase inhibitors, such as valproic acid, ribostatin, etc.

References:

AK Haylett, S Felton, DW Denning, LE Rhodes.Voriconazole-induced photosensitivity: photobiological assessment of a case series of 12 patients British Journal of Dermatology, 2013

Alberdi Soto, M., Aguado Gil, L., Pretel Irazabal, M., Bonaut Iriarte, B., Irarrázabal Armendariz, I., Lera Imbuluzqueta, J. M., ... Ivars, M. (2014). Accelerated photoaging induced by voriconazole treated with Q-switched Nd:YAG laser: Case report and review of the literature. Journal of Cosmetic and Laser Therapy, 16(6), 314–316. https://doi.org/10.3109/14764172.2014.957215

Miller DD, Cowen EW, Nguyen JC, McCalmont TH, Fox LP. Melanoma Associated With Long-term Voriconazole Therapy: A New Manifestation of Chronic Photosensitivity. Arch Dermatol. 2010;146(3):300–304. Doi:10.1001/archdermatol.2009.362DD Arch Dermatol 2010

CowenEW, Nguyen JC, Miller DD, et al.Chronic phototoxicity and aggressive squamous cell carcinoma of the skin in children and adults during treatment with voriconazole. J Am Acad Dermatol 2010;62:31–7.

4- How many lesions are too many? Clinical thresholds for genetic assessment.

a. When present in large numbers, we know that some skin lesions may be associated with underlying diseases. However, for many of these lesions, the numerical threshold that should alert us is not well defined.

Suggestions for suspecting systemic diseases based on the number of lesions:

- ≥5 haemangiomas → rule out hepatic haemangiomas
- ≥4 capillary malformations → suspect CM-AVM syndrome
- ≥6 hypopigmented macules → consider tuberous sclerosis
- ≥3 facial angiofibromas or 2 or more periungual angiofibromas → assess for tuberous sclerosis
- ≥6 pilomatrixomas → suspect myotonic dystrophy
- ≥1 juvenile xanthogranuloma → controversy on the need for systemic study; some authors suggest eye and abdominal studies with a single lesion

5- MiTES (Mid-facial Toddler Excoriation Syndrome)

a. Self-inflicted ulcers in the centrofacial region in children under 1 year of age, with symmetrical excoriations in an “X” pattern

b. Self-limiting course (approximately 5 years), leaving atrophic scars. Differentiate from congenital insensitivity to pain (CIP), in which touch, pressure and temperature are normal, but no pain is perceived.

c. Both associated with variants in the PRDM12 gene; they differ in the expansion of polyalanine repetitions in this gene

6- Transient infantile lingual leukoplakia

a. Non-removable whitish plaque on the dorsal tongue, sparing the tip of the tongue

b. Not associated with *Candida* or systemic pathologies

c. Spontaneous resolution on initiation of solids

Reference:

Lam JM, Schwieger-Briel A, Nguyen T, Torrelo A. Transient infantile lingual leukoplakia: An underrecognized cause of white tongues in infancy. Pediatr Dermatol. 2024 May-Jun;41(3):476-479. doi: 10.1111/pde.15576. Epub 2024 Feb 27. PMID: 38413200.

7- Verrucous epidermal naevus in Blaschko pattern related to PTEN

a. Patient with linear verrucous naevus, macrocephaly, developmental delay (cortical dysplasia on MRI) and cataracts. Biopsy showed a sebaceous naevus but the genetic study enabled diagnosing a germline variant in the PTEN gene.

b. Diagnosis: PTEN hamartomatous syndrome, presenting as mosaicism. The naevus may be called linear PTEN naevus or also linear Cowden naevus. The main characteristic of this naevus is that it is very verrucous and papillomatous and has a hyperkeratotic component.

Keep in mind that a linear verrucous epidermal naevus associated with macrocephaly may have a PTEN mutation, and should therefore be monitored and followed up with oncological surveillance protocols.

8- Epidermolytic epidermal naevus: biopsy or no biopsy?

a. Low risk of transmission of epidermolytic ichthyosis in parents with extensive naevi

b. Genetic counselling is very complicated in this context because the risk of transmission varies enormously, from 0% if no gonadal cells are affected, to 50% if all gonadal cells are affected in one of the parents.

It is also difficult because the current techniques to investigate gonadal involvement are either not feasible (e.g. in women) or do not reliably determine the degree of gonadal involvement.

c. Biopsy is recommended in extensive lesions to assess risk and consider genetic counselling.

9- Segmental stiff skin syndrome

a. Skin hardening since childhood, with hypertrichosis and joint involvement (joint pain or restriction of movement, due to involvement of underlying fasciae and joints)

b. Clinical differential diagnosis with localised scleroderma (has adnexal atrophy) and connective naevus

c. Diagnosis requires clinical/histological findings and imaging studies.

10- How to take the best scabies sample: under Wood's light

Traditionally, in polarised dermoscopy, the characteristic sign of scabies is the "delta sign", representing the anterior parts of the *Sarcoptes scabiei* mite (head and forelegs). However, this method does not always enable visualising the mite's entire body.

With the addition of UV dermoscopy (using 365 nm light), the authors found that the mite's entire body emits a bright fluorescence, appearing as an oval or spherical structure. This finding has been dubbed the "ball sign". This technique improves mite visualisation by eliminating interferences such as skin scales, thereby enabling the parasite to be more clearly identified.

Reference:

Aslan Yürekli. A new sign with UV dermoscope in the diagnosis of scabies: Ball sign. Skin Res Technol. 2023;29:e13336

Conclusion

These recent clinical findings underline the importance of close dermatological observation, especially in paediatrics. Several of the patterns described have important diagnostic, prognostic and genetic implications and should be considered in daily clinical practice. When necessary, the

clinical approach should be complemented with histological and molecular studies to achieve an accurate diagnosis and guide the appropriate follow-up of these patients.

Conference: New developments in therapeutics

Speaker: Lawrence Eichenfield (United States)

Therapeutic update in paediatric dermatology: recent advances in atopic dermatitis, psoriasis and alopecia areata

Introduction

In recent years, remarkable progress has been made in the development and approval of dermatological treatments in the paediatric population, especially for chronic and inflammatory diseases such as atopic dermatitis, psoriasis and alopecia areata. This presentation reviewed recent findings from multicentre clinical trials and extension studies that have expanded the therapeutic arsenal for these patients, highlighting both topical and systemic treatments and their clinical impact beyond skin management.

Atopic dermatitis (AD)

Non-steroidal topical treatments:

- Tapinarof: aryl hydrocarbon receptor agonist, approved in the US from age 2. Anti-inflammatory, antioxidant and epithelial regenerating effect. Promising results in maintenance studies, with relapse an average of 75 days after clearance.

- Roflumilast: PDE-4 inhibitor approved as a 0.15% cream from the age of 6 years. More modest efficacy, but with excellent tolerability and effective proactive use (281 days on average without recurrence).

- Topical ruxolitinib: JAK inhibitor approved from age 12 years; similar results in children aged 2–12 years. High efficacy compared to topical corticosteroids, although with restrictions on the percentage of treatable body surface area.

Systemic treatments:

- Dupilumab: widespread clinical use (>1 million patients). Emerging data show:

- Reduction in the development of allergic comorbidities (asthma, rhinitis)
- Growth benefits in children aged 6–11 years with severe AD

- Trelokinumab and lebrikizumab: approved from the age of 12. They show good, sustained efficacy with the possibility of spacing doses in maintenance treatment.
- Abrocitinib and upadacitinib: oral JAK inhibitors with a growing safety database
- Nemolizumab: anti-IL-31 antibody approved in some countries from the age of 12 years, targeting severe pruritus

Paediatric psoriasis

- Deucravacitinib (oral): TYK2 inhibitor approved from the age of 6 years
- Icotralimod: oral anti-IL-23 peptide. Recent data in adolescents show:
  - PASI90: 89% at 24 weeks
  - IGA 0/1:86.4%
  - Excellent safety profile. Possible oral alternative to injectable biologics.

Alopecia areata

- For localised forms (<25%): increasing use of topical minoxidil, 5%, with multiple studies supporting its efficacy in paediatrics
- Low-dose oral minoxidil: under study in adolescents and young children (international Delphi consensus ongoing)
- Contemplate rare adverse effects: facial hypertrichosis, headaches, oedema and, very rarely, pericardial effusion
- Complex cases, such as alopecia in genetic syndromes, have also shown response to minoxidil

Conclusion

Paediatric dermatology is undergoing a therapeutic transformation, with significant clinical advances driven by international collaborations. New non-steroidal topical agents and targeted systemic therapies have improved both skin management of diseases such as AD and psoriasis, as well as systemic comorbidities and quality of life. The importance of continuing education for

paediatricians and healthcare professionals on the up-to-date treatment of these pathologies was highlighted.

Conference: What's new in the microbiome

Speaker: Dr Brigitte Dréno (France)

Introduction

This presentation addressed advances in the understanding of the skin microbiome and its key role in skin homoeostasis and in inflammatory, infectious and neoplastic diseases. The speaker highlighted the dynamic balance between commensal and pathogenic bacteria, the influence of the skin microenvironment on bacterial virulence, and advances in bacteriotherapy as an emerging therapeutic approach.

Key points

- Early colonisation: The skin is sterile in utero and is colonised by micro-organisms within minutes of birth. The microbiome includes bacteria, viruses and fungi.
- Resident vs transient microbiome:
  - Commensal bacteria: *Cutibacterium acnes*, *Staphylococcus epidermidis*
  - Pathogenic bacteria: *Staphylococcus aureus*, etc.
- Factors modifying the microbiome:
  - Tallow (quantity and quality)
  - pH, humidity, salinity, lipid content
  - Specific anatomical area
- Skin microenvironment as an ecosystem:
  - Commensal bacteria receive nutrients from the skin.
  - In turn, these commensal bacteria secrete antimicrobial peptides that protect and repair the skin.

Any chronic disturbance (such as UV damage) can cause dysbiosis, with loss of bacterial diversity and increased virulence profiles in previously commensal bacteria.

- Recent advances in acne and the microbiome
- *Cutibacterium acnes* (*C. acnes*) is a key commensal bacterium that is capable of:
  - producing protective lipids for the epidermis.
  - improving barrier function and modulating inflammation.

- In acne, the altered sebaceous environment (sebum type 1A1) promotes a virulent *C. acnes* phenotype.
  - This phenotype secretes proinflammatory cytokines (IL-6, IL-8, TNF-α, GM-CSF).
  - This behaviour is not found in healthy skin.

Bacterial extracellular microvesicles

- Bacteria such as *C. acnes* release extracellular vesicles containing proteins, nucleic acids and lipids.
  - These vesicles target keratinocytes and sebocytes.
  - They are able to directly modulate inflammation and epidermal differentiation (induction of filaggrin, cell proliferation).
- Different bacterial phenotypes (such as 1E1, 1E2) produce vesicles with different inflammatory capacity.

- Adaptive immunity:
  - The immune system can recognise commensal bacteria and promote their activity against pathogens.
  - Example: *S. epidermidis* stimulates secretion of antimicrobial peptides and promotes healing.

- Role of the microbiome in healing:
  - Influences granulation and tissue repair
  - Imbalance or dysbiosis delays healing

- Microbiome and skin cancer:
  - *S. epidermidis* produces 6-HAP (6-N-hydroxyaminopurine), a molecule that inhibits DNA polymerase and protects against melanoma and squamous cell carcinoma in murine models.
  - The microbiome can counteract UV-induced immunosuppression.

- Prophylactic and therapeutic strategies:
  - Topical application of bacteria to protect against UV and pigmentation
  - Use of probiotics and prebiotics to modulate immunity, skin barrier and inflammation

- Impact of psychological stress:
  - Increases *Streptococcus pyogenes* infections
  - Inhibits epidermal lipid synthesis and decreases antimicrobial peptides

- Microbiome and ageing:
  - Significant differences in the microbiota among people with and without photoageing
  - With age, diversity is lost and chronic low-grade inflammation increases.

- Future of bacteriotherapy:
  - Vaccines under study (phase I in acne)
  - Use of bacteriophages, topical probiotics and skin transplantation
  - Need to use strains of cutaneous origin, ensure their stability, efficacy and safety, especially in immunocompromised patients

Conclusion

The skin microbiome is a dynamic ecosystem that is essential for skin homoeostasis. Commensal bacteria are involved in the defence against pathogens and also modulate inflammation, healing and even skin cancer prevention. New therapeutic strategies—such as bacteriotherapy, the use of extracellular vesicles and modulation of the microenvironment—open up a promising field in dermatology, both as regards the prevention and treatment of inflammatory and neoplastic diseases. The key is to maintain the diversity and balance of the microbiome.

Reference:

Lee YB, Byun EJ, Kim HS. Potential Role of the Microbiome in Acne: A Comprehensive Review. J Clin Med. 2019 Jul 7;8(7):987. doi: 10.3390/jcm8070987. PMID: 31284694; PMCID: PMC6678709.

C. Cheung, C. Mias, U. Lancien, S. Corvec, V. Mengeaud, A. Khammari, H. Duplan, B. Dreno,

333 Different proinflammatory profiles of Cutibacterium acnes IA1 extracellular vesicles from healthy and acne skin: modulation by Myrtacine and Celastrol, Journal of Investigative Dermatology,Volume 144, Issue 12, Supplement,2024,Page S285

Cros MP, Mir-Pedrol J, Toloza L, et al. New insights into the role of Cutibacterium acnes-derived extracellular vesicles in inflammatory skin disorders. Sci Rep. 2023;13:16058. doi:10.1038/s41598-023-43354-w

Jin C, Lagoudas GK, Zhao C, Bullman S, Bhutkar A, Hu B, et al. Commensal microbiota promote lung cancer development via γδ T cells. Cell. 2019;176(5):998–1013.e16. doi:10.1016/j.cell.2018.12.040.

Conference: What's new in vascular conditions

Speaker: Dr Ilona Frieden (United States)

Introduction

- The talk addressed recent advances in the diagnosis and treatment of vascular anomalies, especially in relation to the new ISSVA classification, targeted therapies and recent findings in infantile haemangiomas.
- Emphasis was placed on providing practical tools for dermatologists who, although not part of multidisciplinary teams, treat patients with vascular birthmarks.
- Key references and recent open access publications that are useful for clinical practice were shared.

Most relevant points

ISSVA Classification Update (2024)

- The new version of the classification for vascular anomalies was published (available online and in press in the *Journal of Vascular Anomalies*).
- The classification is considered a "living document" that will be updated over time.
- It includes an annotated glossary to unify terminology.
- It highlights the subdivision of capillary malformations into seven subtypes, with relevant clinical implications.

Capillary malformations - Subtypes highlighted

- Naevus simplex: common in neonates, self-limited, located on the midface and occipital region
  "Port-wine" capillary malformation: well demarcated, saturated, often on the face, may have a reticulated component
- Reticulate capillary malformations: extensive, fine, not always associated with macrocephaly
- Geographic capillary malformation: linked to PIK3CA or PIK3R1 mutations; well-defined pattern and frequently associated with lymphatic components
- Capillary malformations with faster flow (CM-AVM): associated with CM-AVM syndrome. They fill instantly when pressed. Their clinical identification is key to deciding on neurological or genetic studies.

Clinical significance of the classification

- Determines indication for studies (MRI, genetic studies) and therapeutic approaches (laser, topical and systemic treatment).
- Management guidelines available from European groups (VASCERN-VASCA Pathways), with algorithms accessible online.

Reference: https://vascern.eu/group/vascular-anomalies/clinical-decision-support-tool-vasca/vasca-patient-pathways/

Targeted therapies and repurposed medicinal products

- Vascular abnormalities often involve RAS/MAPK and PI3K/AKT/mTOR pathways
- Alexandra Borst's featured publication: provides a practical treatment decision tree, with colour coding (green: no treatment; red: systemic therapy)
- Sirolimus: effective systemic therapy, well known; useful in low-flow malformations
- Alpelisib: alternative to sirolimus treatment failures; useful even without confirmed PIK3 mutation Caution in prepuberals due to possible growth arrest

Reference: Borst A. Targeted medical therapies for vascular anomalies. Hematology Am Soc Hematol Educ Program. 2024 Dec 6;2024(1):709-717. doi: 10.1182/hematology.2024000599. PMID: 39644074; PMCID: PMC11665586.

Infantile haemangiomas and prematurity

- Retrospective study of 830 patients: preterm infants have a higher incidence of haemangiomas with "stepped" borders (risk factor for scarring sequelae).

Reference:

Bradley, Flora *et al.* A retrospective multicenter cohort study of differences in clinical characteristics of Infantile Hemangiomas in preterm and term infants: Prematurity increases risk of permanent cutaneous sequelae. JAAD 2025, Volume 92, Issue 3, Pages 546-553. doi: 10.1016/j.jaad.2024.09.066

- Greater thickness was also found in superficial haemangiomas in preterm infants.
- Preterm infants received beta-blocker treatment more frequently.
- Questions arise about the efficacy and safety of these treatments in large preterm infants.

Failure of beta-blocker treatment

- Multicentre study of 25 cases: most were focal lesions with deep component

- Options for treatment failure: change beta-blocker, consider sirolimus (little evidence), laser or surgery
- Ongoing studies on the use of statins as an alternative based on the molecular mechanisms of the active enantiomer of propranolol.

Conclusion

- The new ISSVA classification significantly improves the way we identify and manage vascular malformations, especially capillary malformations.
- The value of targeted therapies, such as sirolimus and alpelisib, was reaffirmed, although adverse effects need to be carefully monitored.
- The phenotype of haemangiomas in premature infants may require differentiated care and a differentiated therapeutic approach.
- Promising advances in basic and clinical research assure more targeted and effective treatments.