
AAD ANNUAL MEETING
AEDV
highlights
SAN DIEGO
8-12 MARZO
#AEDVENAAD2024
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ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

Fotodermatosis y fotobiología

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

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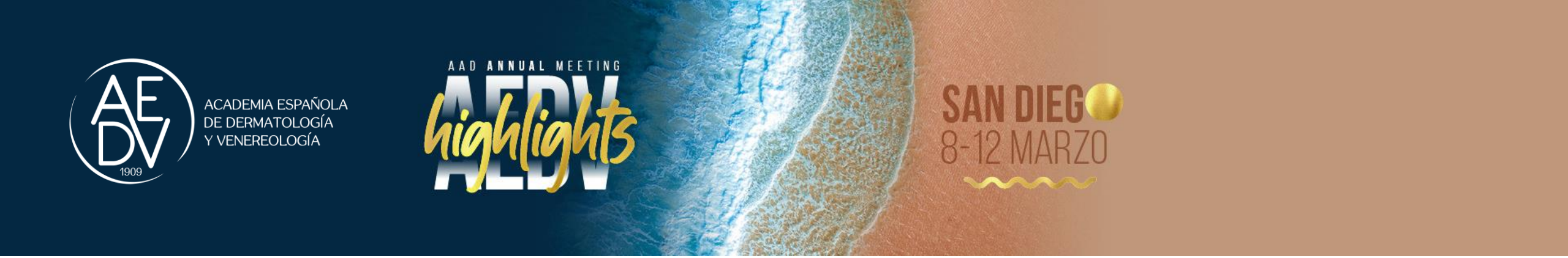


NO TENGO CONFLICTOS DE INTERÉS

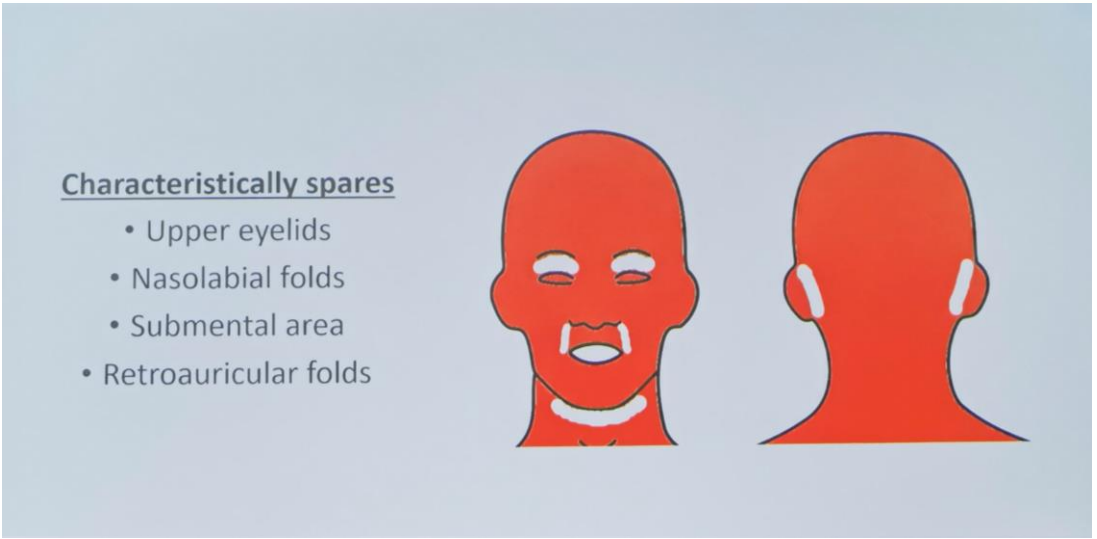
Introducción

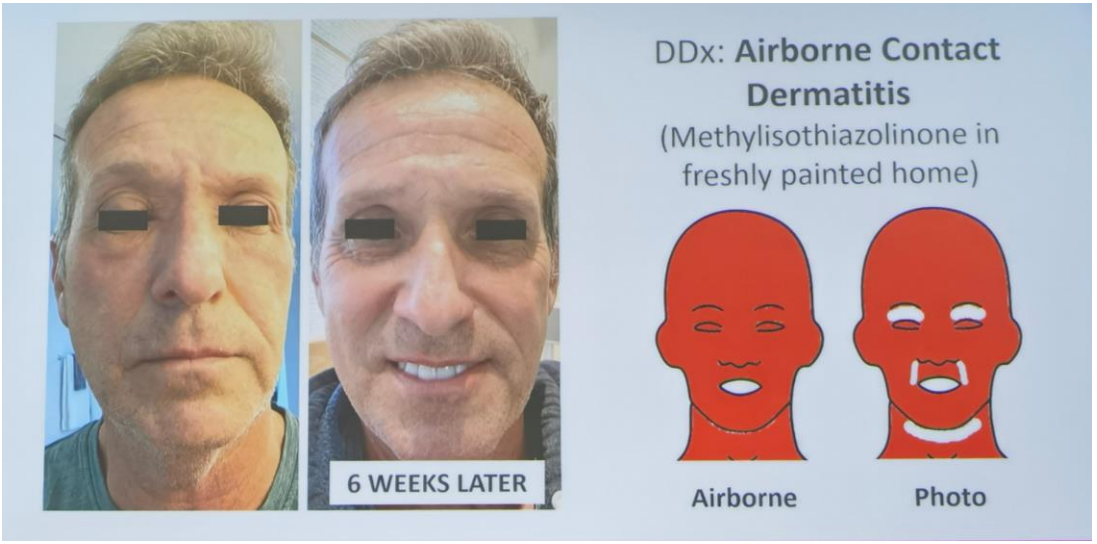
3 sesiones y 22 pósteres en total.

- Fotodermatitis de contacto y condiciones relacionadas
  - Claves para el diagnóstico diferencial
  - Recomendaciones sobre fotopatch-testing
  - Fotodermatosis idiopáticas
  - Peculiaridades en piel negra
- Terapia fotodinámica, fototerapia y fotoprotección
  - Novedades
  - Mitos y controversias sobre fotoprotección
  - “Fotoprotección personalizada”

Fun in the sun: photocontact dermatitis and related conditions – Brandon Adler y Vincent DeLeo

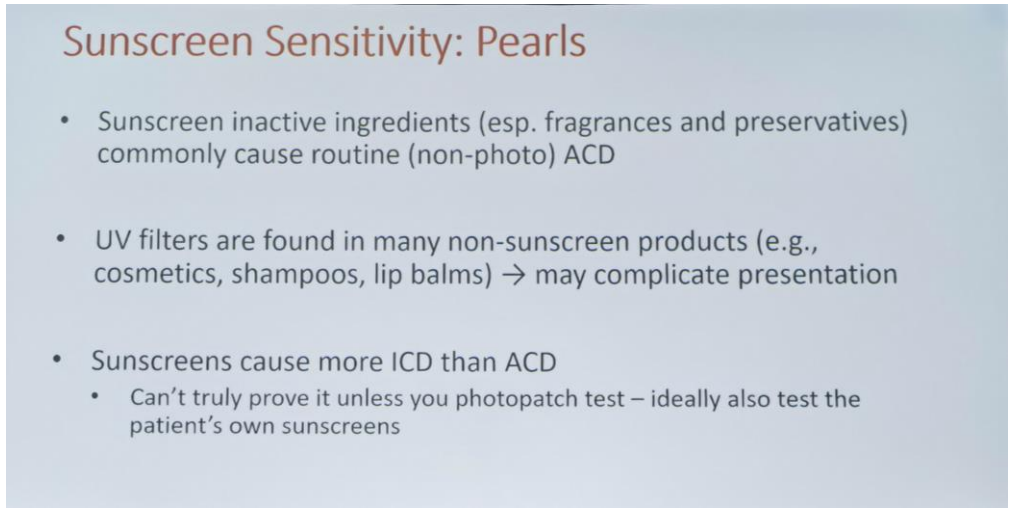
- Fotosensibilidad: 2 motivos. Respuesta anómala por absorción de cromóforos endógenos vs respuesta esperada por sustancias fotosensibilizantes conocidas.
- Causas tan variadas que requiere una anamnesis y exploración exhaustivas. Tiempo y concentración en piel dependiente: preguntar por fármacos hasta el primer episodio y **no solo los nuevos**.
- Patrón clínico áreas fotoexpuestas. IMPORTANTE áreas respetadas para diagnóstico diferencial con dermatitis de contacto aerotransportada (holofacial) vs erupción polimorfa lumínica (respeta cara).

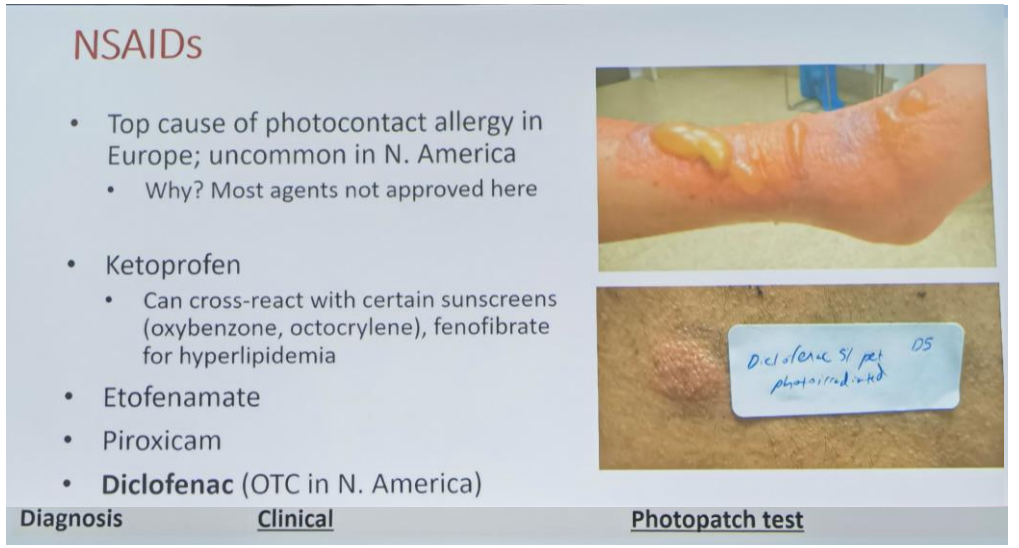




Fun in the sun: photocontact dermatitis and related conditions – Brandon Adler y Vincent DeLeo

- Diagnóstico diferencial: fotosensibles vs no fotosensibles
- Casi siempre **diagnóstico clínico.** Biopsia en casos muy concretos, no suele ser específica. Importancia del fotoparche.
- *Photodrug reactions*: más frecuente daño tisular directo que fotoalergia. Fármacos responsables. No estudios complementarios.
- Fotodermatitis de contacto: tóxica vs alérgica. Ambos por UVA. Causas tóxica: fitocumarinas, psoralenos. Causas alérgica: cambios con los años. Actual: fotoprotectores orgánicos (dx/d DAC a excipientes) y AINES tópicos (causa + frec en Europa).





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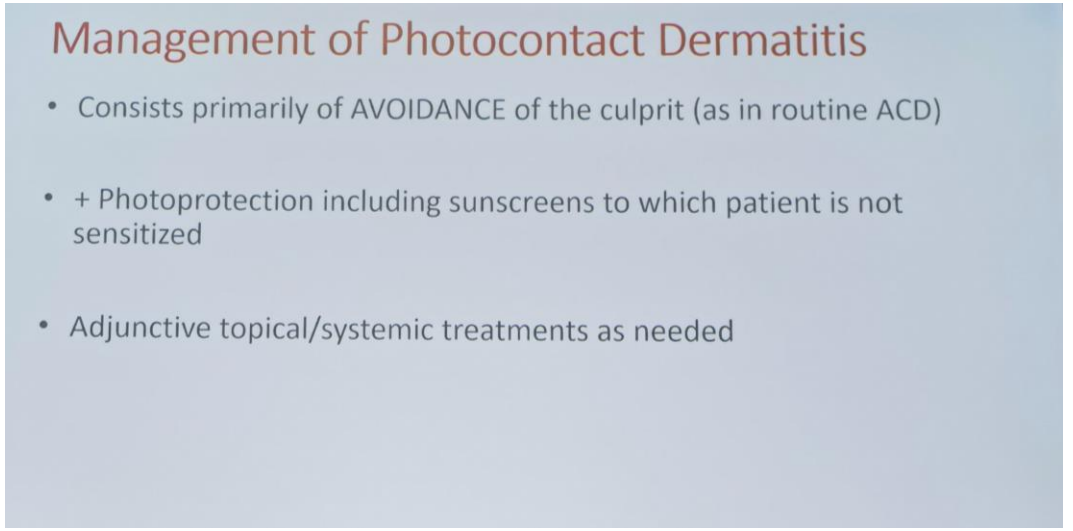
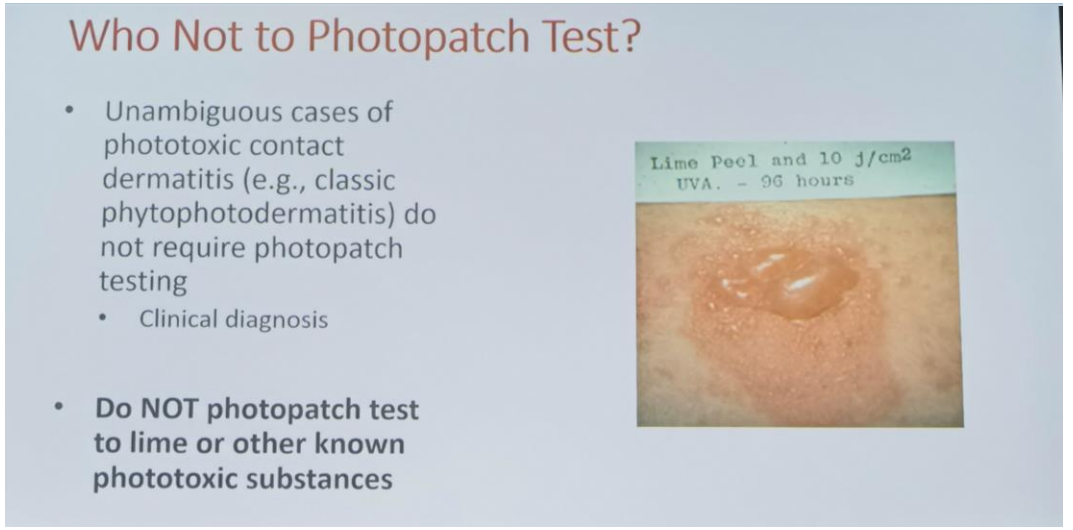
- FOTOPARCHE: disponible en pocos lugares. Menos alérgenos que la batería estándar (≈40). Se pueden solicitar a la industria. Protocolo.
- Dosis mínima eritematógena: FUNDAMENTAL. Proceso fotosensible subyacente. Normal en EPL y alterado en dermatitis actínica crónica, prúrigo actínico y dermatitis atópica fotoagravada.
- Parches aplicados por duplicado. Se irradia solo uno de ellos. En USA aplican UVA 10J/cm2. En Europa 5J/cm2 (consideran insuficiente, falsos negativos).
- Lectura final: 3 escenarios. **¿A quién sí/no?**
- Manejo: evitación, sustitución y tto brote.

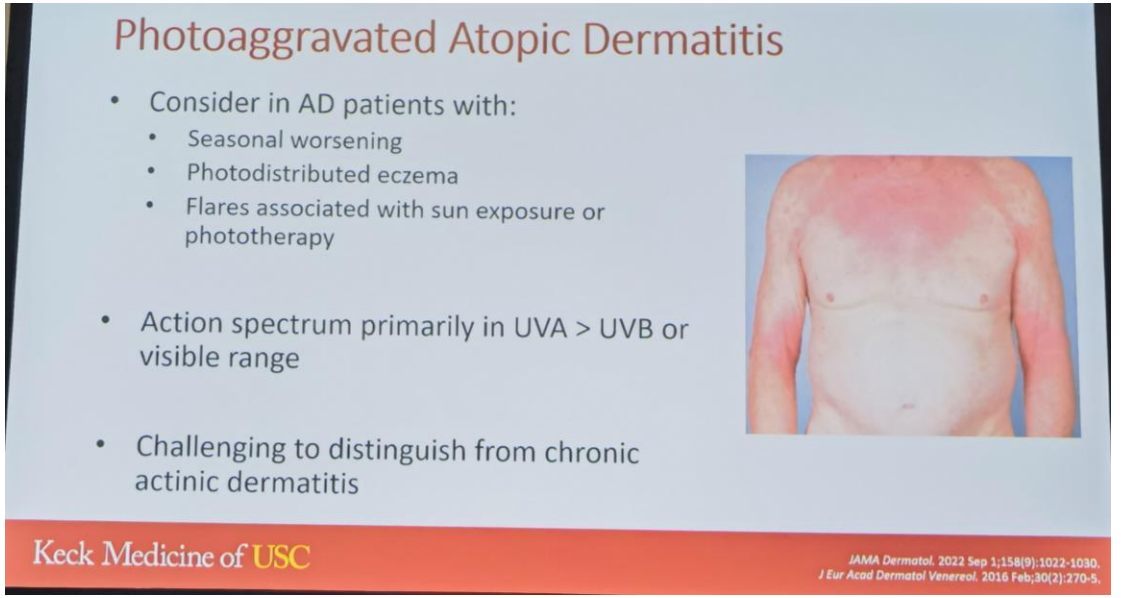




Photodermatol Photoimmunol Photomed. 2022; 38(3):288-291.

Fun in the sun: photocontact dermatitis and related conditions – Brandon Adler y Vincent DeLeo

- Dermatitis atópica fotoagravada: reto diagnóstico dx/d dermatitis actínica crónica
- Fotodermatosis idiopáticas: EPL, dermatitis actínica crónica y prúrigo actínico.



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PMLE: Treatment

- Broad spectrum sunscreen and physical protection
- Prophylactic photohardening before first intense sun of the year (most commonly NBUVB)
- Medications
  - Topical steroids
  - Hydroxychloroquine
  - Oral steroids for severe flares, or stero
- *Polypodium leucotomos* extract
- Prognosis: some patients improve o

PMLE: Clinical Features

- F>M, onset 2nd-3rd decades, **all skin types**
- Classic onset: springtime or vacation
  - Usually starts within hours of sun

(“hardening”)

al hands, arms, neck, V chest > face

onally burning

PMLE: Clinical Features

- Morphologies: polymorphous betwee for each person (usually)
  - Papular/urticarial
  - **Darker skin types – pinpoint papular**
  - Large papules or plaques
  - Vesicular / bullous
  - Eczematous
  - Edematous
  - Erythema multiforme-like
- Variant: juvenile spring eruption (helices in kids)

PMLE: Treatment

- Oral photoprotection with *Polypodium leucotomos* extract
- OTC supplement – Central/South American fern
- Rich in polyphenol antioxidants
- Non-randomized studies: may prevent or reduce symptoms of PMLE
- Negligible side effects

Keck Medicine of USC

J Clin Aesthet Dermatol. 2021 Feb;14(2):50-60.

ated +ANA without systemic symptoms; does

- Histology: non-specific and depends on clinical morphology (perivascular lymphocytic, dermal edema, spongiosis)
- Phototesting: normal minimal erythema dose (MED) responses
  - Photoprovocation testing (repeated UV doses over days) can reproduce lesions, confirm dx

Fun in the sun: photocontact dermatitis and related conditions – Brandon Adler y Vincent DeLeo

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Chronic Actinic Dermatitis (CAD)

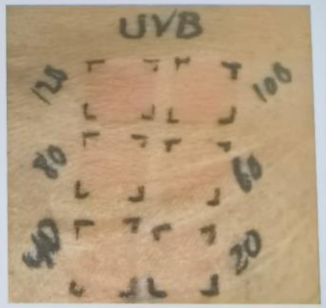
- AKA actinic reticuloid, persistent light reactivity
- Action spectrum: UVB, UVA, visible
- Etiology (proposed): type IV hypersensitivity reaction to photoinduced antigen in skin

CAD: Clinical Features

- **Chronic and persistent year-round symptoms**
  - **Affected individual may not associate with sun exposure**
- Severe cases can involve photoprotected body sites
- Morphologies
  - Eczematous
  - Lichenified
  - Infiltrated or lymphoma-like plaques, leonine facies
  - Rarely, erythrodermic
- Pruritic

CAD: Diagnosis

- Histology
  - Spongiotic dermatitis
  - Acanthosis
  - Lymphohistiocytic infiltrate
  - May mimic CTCL
- Phototesting: abnormal MEDs (UVA, UVB, and/or visible)
- Photopatch test important to rule out concomitant (photo)allergic contact dermatitis



CAD: Treatment

- **Education:** year-round symptoms → still need strict photoprotection
- Broad spectrum sunscreen, physical protection
- UV blocking window films
- Medications
  - Topical steroids/calcineurin inhibitors
  - Severe disease: systemic steroids, steroid-sparing agents, **dupilumab**
- Phototherapy
- Allergen avoidance if concomitant allergic contact dermatitis
- Prognosis: variable, ~20% resolution over 10 years

Keck Medicine of USC

Photodermatol Photoimmunol Photomed. 2020 Sep;36(5):388-400.
Arch Dermatol. 2000 Oct;136(10):1215-20.

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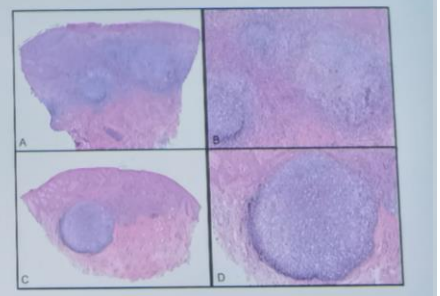
Actinic Prurigo: Diagnosis

- Histology nonspecific except **lip biopsy showing follicular cheilitis is characteristic** (pathognomonic?)
- Phototesting: reduced MED to UVA/UVB
- Photopatch testing to rule out photocontact allergy
- HLA typing



Actinic Prurigo: Treatment

- Broad spectrum sunscreen and physical protection
- UV blocking window films
- Medications
  - Topical steroids/calcineurin inhibitors
  - Severe disease: systemic steroids (brief courses), steroid-sparing agents, **thalidomide** (caution teratogenicity)
  - Case reports: successful use of **dupilumab**
- Phototherapy
- Prognosis: often resolves by adolescence, but can persist

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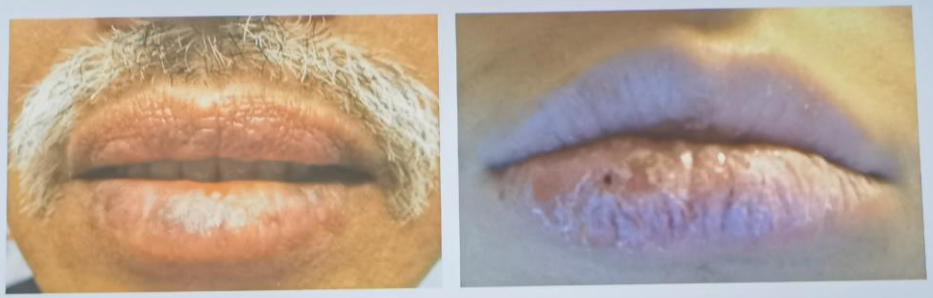
Pediatr Dermatol. 2020 Nov;37(6):1176-1178.

Actinic Prurigo Cheilitis



Lower lip predominance
*May present with isolated cheilitis

Actinic Prurigo: Clinical Morphologies

- Papules
- Plaques
- Nodules (prurigo-like)
- Lichenification
- Hemorrhagic crusting
- Pitted scars

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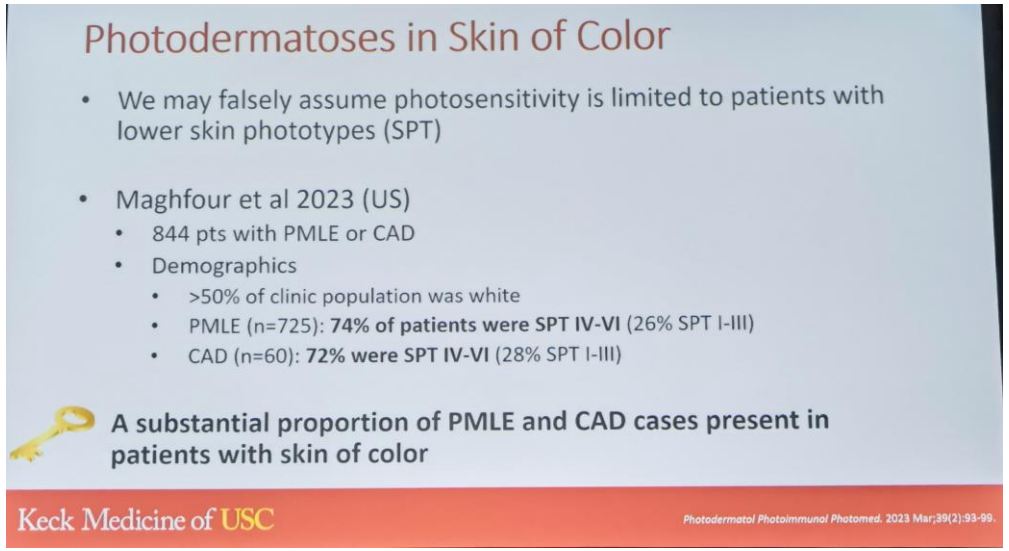
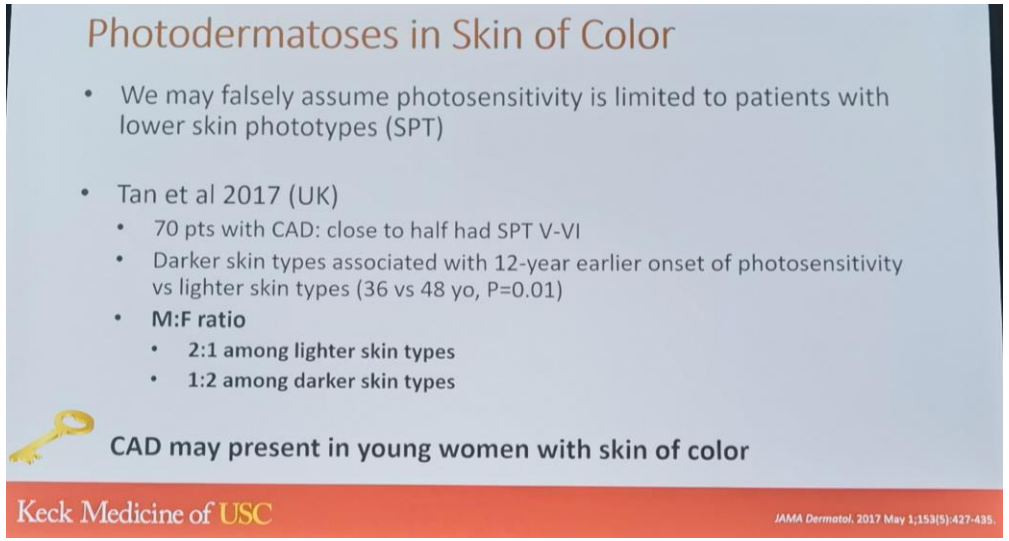
- Fotodermatosis en piel negra: falsa creencia estas patologías solo a pieles blancas.
- Serie de casos (Maghfour, 2023): 844 pacientes con EPL o dermatitis actínica crónica. Fototipo IV-VI 74% con EPL y 72% DAC.
- Serie de casos UK (Tan, 2017): 70 pacientes DAC, ≈50% V-VI. Más frecuente en mujeres y desarrollo 12 años antes que la media en pacientes con fototipos oscuros.
- Mensaje: considerar dermatitis actínica crónica en mujeres jóvenes con piel negra entre otros posibles diagnósticos.





Terapia fotodinámica (Cleveland University)

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- Revisión de TFP modificada con luz azul o roja (cortos periodos de incubación) vs convencional (3-4 h de incubación): resultados de eficacia equivalentes y reducción significativa del dolor.
- Hipótesis de mecanismo de acción a través de reclutamientos de células inmunes frente a muerte celular inducida por la TFD convencional.
- Limitaciones: bajo tamaño muestral luz roja (actualmente la más empleada en nuestro medio) y tiempos de seguimiento.

Review of Modified "Painless" Photodynamic Therapy, Why it Works, and Future Directions

Jessica Johnson, BS [1], Edward Maytin, MD, PhD [1,2]

[1] Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, U.S.A.
[2] Departments of Dermatology and Biomedical Engineering, Cleveland Clinic, Cleveland, OH, U.S.A.

Disclosures & Commercial Support: NIH Grant P01 CA084203; IIT grant from Biofrontera Inc.

Cleveland Clinic Lerner College of Medicine | School of Medicine Case Western Reserve University | Cleveland Clinic

Background

PDT uses a photosensitizing drug, 5-aminovelunic acid (ALA) or methyl aminolevulinate (MAL), and an artificial light source to target neoplastic lesions in an entire skin field. The photosensitizing drug can be activated via blue (405nm) or red (633nm) light. The downside of most current PDT treatment protocols (conventional PDT; c-PDT), are the photosensitizer's long incubation times (~3-4 hours) and the stinging pain. However, recent studies suggest that shorter incubation times during PDT (modified PDT; m-PDT) can reduce pain and have similar efficacy. These m-PDT protocols have been utilized with both blue light and red light. Herein we review the various studies utilizing m-PDT and provide mechanistic explanation for the similar efficacy to c-PDT.

Methods

We completed a review of the current literature in late 2023 and found 5 human studies utilizing m-PDT protocols with blue light illumination and 2 human studies utilizing m-PDT protocols with red light illumination, alongside one clinical trial utilizing red light illumination that is underway. We report the pain ratings and efficacy in reducing AK lesions for these studies. All studies utilized ALA as the photosensitizing agent, except where specified.

Modified Photodynamic Blue Light Therapy

Author	Study Type	Incubation Length	Illumination Length	Pain (0 – 10)*	Efficacy
Kaw[1]	Split-face design (n = 23)	• m-PDT: 15 min • c-PDT: 60 min	• m-PDT: 30, 45, 60 min • c-PDT: 1000 sec	Average pain scores: • m-PDT: 0.52 • c-PDT: 3.57	% reduction in AK's at 3 months for face, scalp**: • m-PDT: 57.7%, 43.8% • c-PDT: 59.1%, 41.9%
Pariser[2]	Randomized clinical trial (n = 235)	1, 2, or 3 hr	16 min and 40 sec (10 J/cm^2)	• % with moderate/severe stinging/burning • 1 hour - 63.8% • 2 hour - 79.2% • 3 hour - 78.7%	Lesion clearance at 12 weeks: • 1 hour - 71.4% • 2 hour - 73.6% • 3 hour - 78.6%
Gandy[3]	Case study (n = 1); PDT at initial visit and 1 month	0 min	33 min and 20 sec	m-PDT: 0	Face and scalp showed near clearance at 4 month follow up***
Martin[4]	Split face design (n = 3)	15 min	60 min	Average pain scores: • m-PDT: 0 • c-PDT: 7	% reduction in AK's at >8 weeks: • m-PDT: 52% reduction • c-PDT: 44% reduction
Anvery[5]	Randomized clinical trial (n=28)	• m-PDT: 0 min • c-PDT: 1 hr	• m-PDT: 34 min • c-PDT: 17 min	Average pain scores: m-PDT: 0.74 c-PDT: 2.73	% reduction in AK's at 8 weeks: • m-PDT: 49.5% • c-PDT: 34.9%

*Unless otherwise specified
**No statistically significant difference in efficacy between c-PDT and m-PDT of any group (30, 45, or 60 min incubation)
***Efficacy data not provided

Modified Photodynamic Red Light Therapy

Author	Study Type	Incubation Length	Illumination Length	Pain (0 – 10)	Efficacy
Li[6]	Split-face (n = 14), 3 PDT treatments at 2 week intervals	• m-PDT: 30 min • c-PDT: 3 hr	• m-PDT: 120 min, 288 J/cm^2 • c-PDT: 60 min, 144 J/cm^2	Range of pain scores: • m-PDT: 0 – 2* • c-PDT: all above 4	Lesion clearance at 1 month, post 3 treatments: • m-PDT: 91.6% • c-PDT: 89%
Mordon[7]	Split face design (n = 46); PDT session at initial visit and at 3 months, utilizing MAL	• m-PDT: 30 min • c-PDT: 3 hr	• m-PDT: 2.5 hours w/reduced light dose of 12 J/cm^2 • c-PDT: 7-10 min, 37 J/cm^2	Pain scores (mean, SD)** • m-PDT: 0.3, 0.6 • c-PDT: 7.4, 2.3	Lesion clearance at 3, 6 months**: m-PDT: 79.3%, 94.2% c-PDT: 80.7%, 94.9%
Maytin[8]	Randomized clinical trial underway (n=30)***	Group (incubation, illumination): • A: 10 min, 20 min • B: 20 min, 10 min • C: 1 hr, 10 min		Range of pain scores: • A/B: 0 – 2 • C: 2 – 8	Data not yet available

*Pain during m-PDT was significantly lower than for c-PDT
**m-PDT was statistically non-inferior to c-PDT and pain score was significantly lower for m-PDT compared to c-PDT
***Clinical trial is underway so all data presented are preliminary

Potential Mechanism of m-PDT

Previously, the hypothesis had been that extensive incubation times for the photosensitizing medication, and the associated pain, were necessary for AK lesion clearance. Studies listed here suggest this is not the case. Recent mice studies have found that instead of generating reactive oxygen species and inducing cell death as in c-PDT, the m-PDT protocol appears to work through immune cell recruitment.[9] These immune cells appear by 24 hours post treatment and persist for 1-2 weeks. Thus, the immune response, which is triggered by m-PDT, could largely be responsible for the reduction in AK lesions rather than the traditionally assumed apoptotic pathways.

Future Directions

Future studies in human AK lesions are needed to further define the mechanisms of m-PDT. Regardless, the studies highlighted above suggest that m-PDT protocols are efficacious in reducing AK lesions, when compared to c-PDT, and provide a major improvement in tolerability for patients.

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How to deliver phototherapy in 2024 – Sunil Kalia, University of British Columbia

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Evaluating adherence with phototherapy

- 851 patients with *psoriasis*
- 106 patients with *vitiligo*
- *Adherence rates:* (20 psoriasis, 60 vitiligo sessions)
  - Psoriasis: 47%
  - Vitiligo: 61%
- *Age* and *distance* from clinic most important variables for adherence

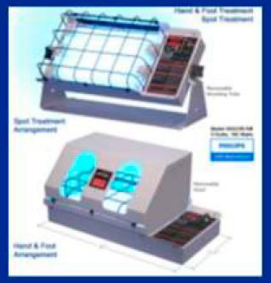
Kalia et al, JAAD 2014

Type of home phototherapy devices

- 3D panel

- Single Panel

- Localized



Low risk of skin cancer with UV phototherapy – recent studies

Psoriasis – NB-UVB therapy =22,891 pt
- *Lin et al, PPP 2019*

Vitiligo – NB-UVB meta-analysis, n=110,038 pt
- *Wu et al, Clin Exp Derm 2021*

Uremic pruritus – UVB therapy, n=10,805 pt
- *Ko et al, Acta DV 2021*

Eczema – NB or BB-UVB or UVA, n=925 pt
- *Ahad et al, JAAD 2022*

Meta-analysis (n=71,479 patients)
- Overall risk of skin cancer =0.99 (95%: 0.75-1.32)

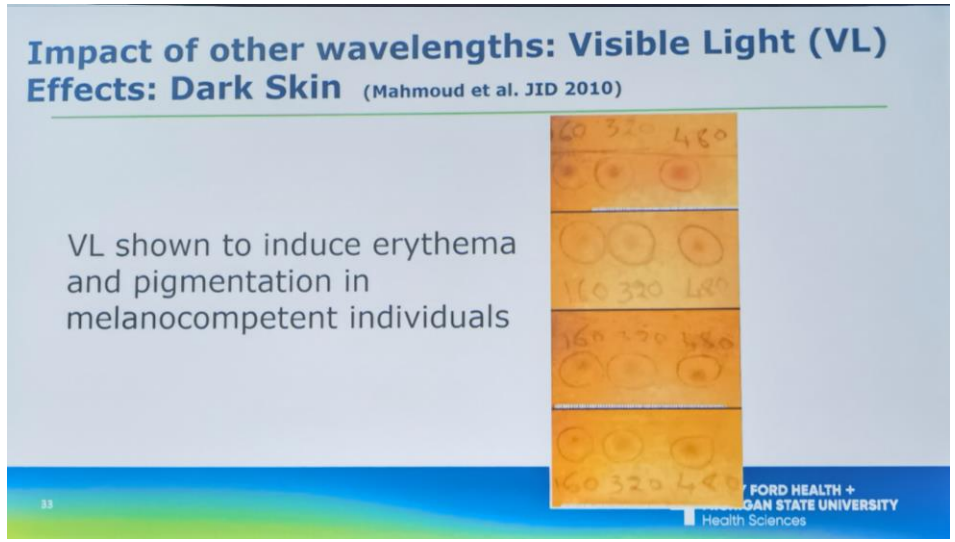
Summary– Phototherapy in 2024

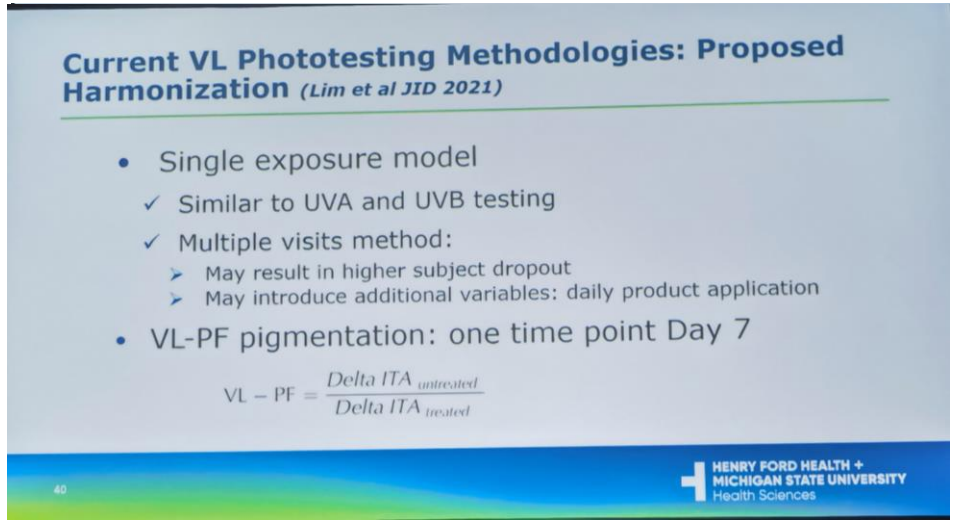
- *Home* phototherapy is equally efficacious and safe
- *Type of devices* for home phototherapy
- *Skin cancer risk is not increased* with UVB therapy

UBC Dermatology

FOTOPROTECCIÓN

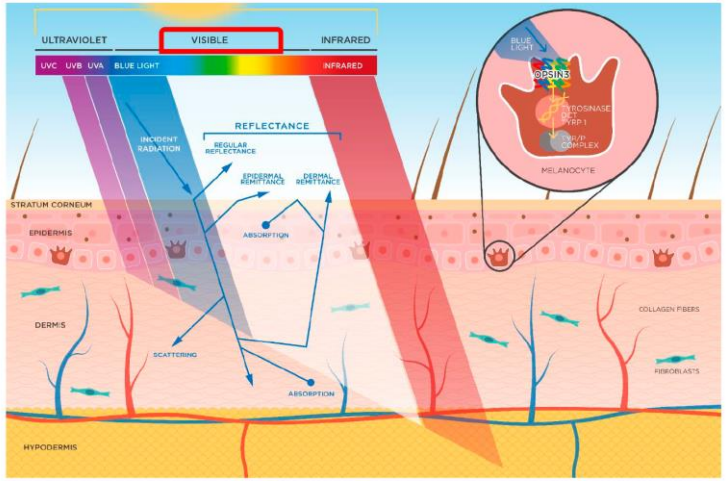
- Fotoprotectores son considerados MEDICAMENTOS en USA. En Europa se consideran cosméticos.
- Consideración de medicamento = riguroso control sanitario. Solo 9 utilizados en USA. Prioridad eficacia y seguridad.
- **SPF ≥ 30** (UVB, UVAII, más superficiales, generan eritema, estudios in vivo, medida objetiva del fototipo). Entre SPF 15 y 30 se reduce 50% UV absorbido.
- **Amplio espectro** (UVB+UVA), UVAI efectos no visibles a corto plazo (fotoenvejecimiento, pigmentación), estudios in vitro, *critical wavelenght*. Misma CW no implica igual fotoprotección frente a UVAI, NUEVO criterio propuesto: ratio UVAI/UV ≥ 0,7.
- **LUZ VISIBLE**: no cubierta en fotoprotectores habituales. Induce hiperpigmentación en fototipos oscuros, efecto sinérgico UVAI, en desarrollo nuevos métodos de evaluación.





FOTOPROTECCIÓN – LUZ VISIBLE

- Luz azul, principal responsable de la pigmentación. Interactúa con Opsina-3 induciendo una actividad aumentada de la tirosinasa.
- Estimula la pigmentación de manera aislada en pieles oscuras, y en sinergia con la UVAI en pieles claras.
- Protección frente a luz visible: fotoprotectores “tintados” (óxido de hierro), antioxidantes y agentes orales (*Polypodium leucotomos*). Limitaciones: tinte mancha y pocos estudios.



Lim, HW, Kohli, I, Granger, C, ….. Krutmann, J, Passeron, T. J Invest Dermatol, 2021 Nov;141:2569

Protection against VL and Longwave UVA1

- Tinted sunscreens
- New filters
- Antioxidants
- Oral agents

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Topical Antioxidants and VL+UVA1

(Lyons, AB, … Ruvolo, E, Lim, HW, Hamzavi, IH. Photochem Photobiol 2022 Mar;98(2):455)

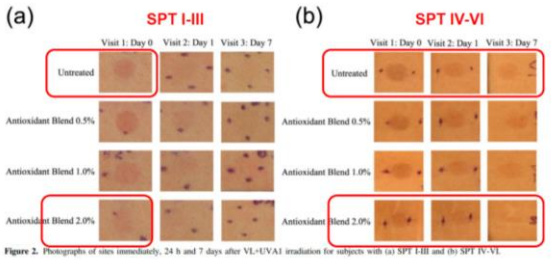

Figure 2. Photographs of sites immediately, 24 h and 7 days after VL+UVA1 irradiation for subjects with (a) SPT I-III and (b) SPT IV-VI.

AO (2%), vs control:

- SPT I-III: decreased erythema
- SPT IV-VI: decreased IPD, PPD and delayed tanning

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VL: Blue light and Opsin-3

(Duteil, L, … Passeron, T. Pigment Cell Melanoma Res 2014; 822. Nice, France. Regazzetti, C,… Passeron, T. J Invest Dermatol 2018; 138:171. Nice, Frace)

- Action spectrum: blue light
- Opsin-3 is the key sensor in melanocytes
- Blue light + Opsin-3:
  - Formation of tyrosinase/tyrosinase-related protein complex
  - Mainly formed in melanocytes from dark-skinned individuals
  - Induces a sustained tyrosinase activity

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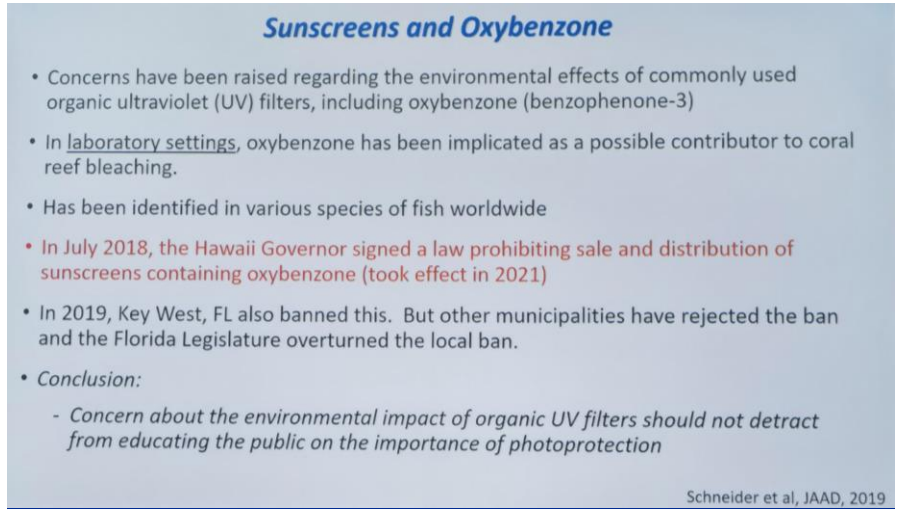
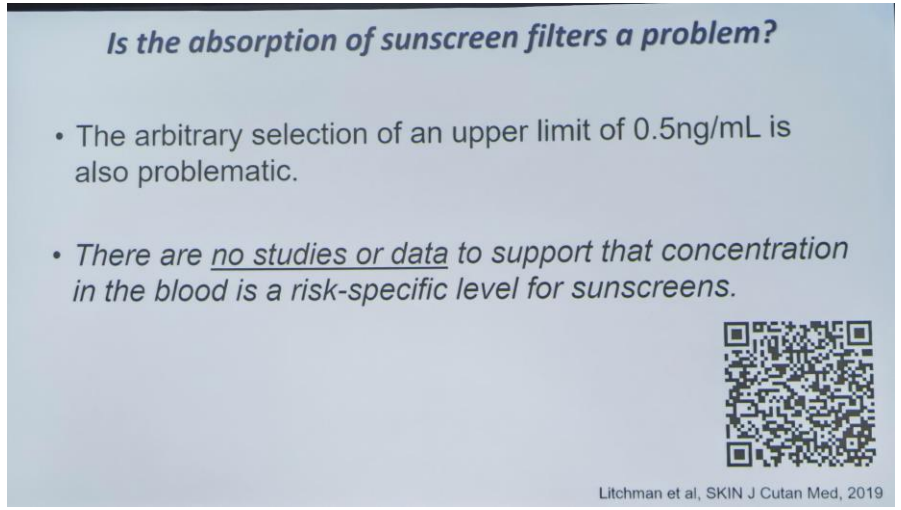
Mitos y controversias sobre fotoprotección

- No es necesario recomendar aplicación 30 minutos antes. Todos los fotoprotectores comercializados actúan desde su aplicación.
- Solo reaplicar cada 2-3 horas si se transpira mucho o se moja.
- Es incorrecto llamar a los fotoprotectores físicos o químicos por su interacción con la radiación, los "físicos" reflejan y absorben luz UV. Más correcto decir: orgánico vs mineral o soluble vs insoluble.
- Se ha demostrado absorción de algunos fotoprotectores, pero ningún estudio ha demostrado efectos perjudiciales hasta la fecha (aumenta el cáncer no usarlos).
- No se ha demostrado impacto medioambiental en las condiciones habituales de uso de los fotoprotectores.





Fotoprotección personalizada

Fitzpatrick phototype	Description	Individual Typology Angle (ITA)	Skin color (ITA classification)	UVB protection (SPF)	UVA protection (UVA-PF)	High energy visible light protection (VL-PF)
I	Always burns, never tans	ITA° >55°	Very light	SPF50+	UVA-PF +++ (>1/3 labelled SPF)	
II	Burns easily, sometimes tans	41° <ITA° <55°	Light			
III	Sometimes burns, always tans	28° <ITA° <41°	Intermediate			
IV	Rarely burns, tans easily	10° <ITA° <28°	Tan			
V	Rarely burns tans easily; moderately pigmented	-30° <ITA° <10°	Brown			
VI	Rarely burns, tans promptly and intensely; highly pigmented	ITA° <-30°	Dark	SPF30+	UVA-PF +++ (> 2/3 labelled SPF)	VL-PF+++

Figure 1 Spectral absorption profiles of sunscreens suitable for different skin phototypes. This figure represents the absorption profile of sunscreen recommended for healthy individuals with different skin phototypes for the preventation of skin cancers and photoaging. The latitude of where the individual lives should also be taken in consideration. Individuals with skin conditions (such as photodermatoses or pigmentary disorders) should follow the specific recommendations described in Table 1. ITA individual typology angle, SPF sun protection factor, UVA-PF ultraviolet A, VL visible light, PF protection factor.

J Eur Acad Dermatol Venereol. 2021 Jul; 35(7): 1460–1469

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La Academia Española de Dermatología y Venereología expresa su agradecimiento al patrocinador UCB, por su especial apoyo y contribución con la actividad formativa Highlights 2024.

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