BIODERMA
CONGRESS **REPORTS**

Bioderma Congress Reports DST 2024

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CPC: DERMPATH

Speakers: Dr. Siri, Dr. Suthep Jirasutha, Dr. Manasmon Chairatchaneeboon, Dr. Poonawis Asudtikoonaseth, Dr. Jade Wititsuwannaku and Dr. Anakaporn Tiyawatanaroj
Report written by Dr. Chanika Kulapatrapa

Interesting cases with uncommon drug reaction topic

Dr. Siri (from Chiang mai University Hospital, Chiang mai, Thailand)

Case 1:

A rash developed in the groin area 5 days following chemotherapy treatment. Histological examination revealed changes in the skin cells, including clouding and irregular shapes of the keratinocytes, their apoptosis, widespread necrosis of the upper epidermidis, degenerative changes in the basal layer of the epidermidis, swelling in the dermis, and eccrine squamous syringometaplasia. The condition was diagnosed as malignant intertrigo, a type of toxic skin reaction to chemotherapy, often occurring in areas with dense sweat glands such as palms, soles, and skin folds, or under taped areas. The approach to management is primarily focused on palliative treatment.

Case 2:

Case 2 involves a 62-year-old male with a known history of refractory relapsed acute myeloid leukemia (AML) positive for FLT3-ITD mutation, who developed a skin rash on day 18 following treatment with *gilteritinib*. He presented with erythematous lesions affecting the hands, right arms, both feet, and trunk.
Histological examination revealed findings consistent with eccrine squamous hyperplasia, accompanied by neutrophils within the eccrine glands and formation of intraductal abscesses. The diagnosis was established as neutrophilic eccrine hidradenitis, a condition typically manifesting around 10 days following the initiation of chemotherapy, with a predilection for the trunk over the extremities and face.

Case 3:

A 30-year-old male exhibited a skin rash 17 days post-chemotherapy with *mitoxantrone*, *etoposide*, and *cytarabine*. The biopsy showed inflammation primarily in the deeper dermis, subcutaneous fat with necrotic collagen surrounded by inflammatory cells and histiocytes. The presence of necrotic collagen 'floating' in inflamed tissue, a finding termed the "floating sign," was notable. The inflammatory response was CD68 positive and myeloperoxidase (MPO) negative, indicating the presence of macrophages and the absence of neutrophil involvement, respectively. Dermal mucin is typically scant to absent, with vasculitis usually absent. The diagnosis typically points to interstitial granulomatous dermatitis, most commonly associated with autoimmune pathology. Predominantly, lesions manifest on the lower extremities rather than the trunk and upper extremities. Approximately 75% of cases exhibit lesions in multiple locations.

Interesting case n°1

Dr. Suthep Jirasuthat (from Ramathibodi Hospital, Bangkok, Thailand)

A 69-year-old man has been experiencing a slowly enlarging, asymptomatic mass on his right palm for the past year, without any other symptoms or history of injury. The initial clinical assessment suggested the possibility of squamous cell carcinoma developing from palmar warts. Histology examination revealed abnormal, variously shaped cells, including atypical polygonal and spindle-shaped cells, as well as large, oddly shaped giant cells. The connective tissue matrix displayed numerous capillary blood vessels and areas of bone formation, while the epidermidis exhibited growth of thin strands of consistent, poroid cells. A significant portion of the tumor cells tested positive for **vimentin**, an indicator of mesenchymal origin. While considering other possibilities such as Atypical fibroxanthoma, Dermatofibroma with monster cells, and Malignant epidermal tumors, the final diagnosis was undifferentiated pleomorphic sarcoma with an associated ESFA (eccrine syringofibroadenoma)

Interesting case n°2

Dr. Manasmon Chairatchaneeboon (from Siriraj Hospital, Bangkok, Thailand)
The speaker addressed the diagnostic challenges encountered in identifying a red plaque on the face in a 58-year-old female. The patient presented with erythematous indurated plaques on the right cheek intermittently over a three-year period, which recently progressed to a thicker consistency within four months. Notably, no lymphadenopathy was evident, and the patient was otherwise in good health.
Histological examination revealed a dense infiltrate of atypical lymphocytes in the dermis, adipose tissue, and surrounding hair follicles, termed folliculotrophism. Immunohistochemical analysis demonstrated a strong positive for CD3, partial positivity for CD30, and negativity for CD4, with negative TCRGR staining. The potential differentials encompassed pseudolymphoma, mycosis fungoides, CD30+ anaplastic large cell lymphoma, lupus panniculitis, and plasma cell gamma delta T cell lymphoma (PCGDTCL). The most probable diagnoses were identified as mycosis fungoides and primary cutaneous gamma delta T cell lymphoma, necessitating clinicopathological correlation for confirmation.
Ultimately, the diagnosis in this instance was established as mycosis fungoides with a gamma delta T cell phenotype. The speaker implemented low-dose electron beam therapy, resulting in an excellent response without any adverse effects. Delta TCR staining proved instrumental in confirming the diagnosis, yielding positive results.
Regarding future trends in cutaneous T cell lymphoma (CTCL) with a gamma delta phenotype, targeted therapies such as those targeting the JAK-STAT pathway are emerging as promising treatment modalities. Key takeaways underscore the challenging nature of CTCL, the importance of recognizing that existing PCGDTCL classification may not encompass the entire spectrum of gamma delta lymphoproliferative disorders, and the necessity for reassessing the classification of gamma delta T cell diseases within cutaneous lymphomas and lymphoproliferative disorders.

Interesting case n°3

Dr. Poonawis Asudtikoonaseth (from Institute of Dermatology, Ministry of Public Health, Bangkok, Thailand)
This case describes a 58-year-old woman presenting as unwell, with a history of hyperthyroidism and progressive purplish-brown nodules appearing on her buttocks and thighs, some of which are hemorrhagic. A CT scan revealed several enhancing lesions affecting soft tissues in the pelvic region, spleen, and lungs.
Skin biopsy findings indicated nodular infiltration in the dermis, with large aggregates in the upper dermis, accompanied by hemorrhage within the lesions. Overlying epidermal hyperplasia was noted, with a normal deep dermis. The presence of large, atypical epithelioid-like cells with atypical nuclei, luminal formation with red blood cells, and cytoplasmic vacuolarization was observed.
Differential diagnoses considered included malignant melanoma, malignant epithelial carcinoma, and angiosarcoma/hemangioendothelioma. Further investigation, including negative melan A staining but positive AE1 AE3 and CD31 staining, suggested a vascular origin. Histological indications leaned towards angiosarcoma. While angiosarcoma commonly manifests in areas such as the head and neck or in irradiated skin post-therapy for breast cancer, or in cases of long-standing lymphedema, the atypical presentation on the buttocks prompted a clinicopathological diagnosis of epithelioid angiosarcoma.

Interesting case n°4

Dr. Jade Wititsuwannakul (from Chulalongkorn University Hospital, Bangkok, Thailand)

The case involved a patient presenting with facial swelling characterized by non-pitting edema, ultimately diagnosed as solid facial edema. Histopathological examination revealed lesions similar to rosacea. There were notable perivascular and perifollicular lymphohistiocytic infiltrates, with a significant presence of mast cells, but no mucin was found in the dermis. The clinicopathologic diagnosis confirmed Mobihan's disease, a condition typically associated with persistent erythema and a history of acne and rosacea. A crucial histological indicator for this diagnosis, besides the rosacea-like lesions, is the infiltration of mast cells. Treatment options for Mobihan's disease include an extended course of *isotretinoin*, *ketotifen*, or *doxycycline*.

Interesting case n°5

Dr. Anakaporn Tiyawatanaroj (Bangkok, Thailand)

A 61-year-old female patient presented with a decade-long history of intermittent eruptions characterized by unilateral eroded, scaly, pink patches located in the left axilla and left groin area. Both KOH and Gram stain tests returned negative results.

Histopathological examination revealed irregular epidermal hyperplasia and the presence of atypical pagetoid cells throughout the entire thickness of the epidermis. The histological diagnosis identified these atypical pagetoid cells with evidence of dermal invasion. Immunohistochemical staining was positive for AE1/AE3 and CK7, but negative for Melan-A, HMB45, CK20, and S100.

The final diagnosis was extramammary Paget's disease (EMPD) affecting the axilla and vulva. Notably, CK20 positivity is often associated with secondary EMPD, yet in this case, its absence suggested a primary form of the disease. Similarly, if the diagnosis had been melanoma, positive staining for S100, HMB45, and Melan-A would be expected, which was not observed here.

The key takeaway is that chronic dermatitis in elderly patients, particularly in regions with a high density of apocrine sweat glands, should raise suspicions for EMPD.

THE RISE AND FALL OF SKIN PIGMENTATION

Speakers: Dr. Yen-Jen Wang, Dr. Liang-Chen Lin, Dr. Cheng-Che E. Lan, Dr. Pravit Asawanonda and Dr. Sasima Eimpunth

Report written by Dr. Chanika Kulapatrapa

Activated melanocytes and senescent collagen fibers as predictors of prognosis in melasma after laser treatment: an optical biopsy based prospective cohort study.

Dr. Yen-Jen Wang (Taiwan)

The speaker highlighted the limitations of using the MASI (Melasma Area and Severity Index) score for evaluating melasma, noting its focus solely on hyperpigmentation without considering photoaging alterations. The MASI score also fails to detect subtle changes in treatment response or accurately reflect the real-time condition of melasma-affected skin. To address these shortcomings, the speaker conducted a prospective cohort study to assess the efficacy of a 755 nm Alexandrite picosecond laser equipped with a diffractive array in improving melasma through dermal remodeling.

This study involved 15 subjects with Asian skin types III and IV. Evaluations compared baseline assessments using cellular resolution full field optical coherence tomography (CRFF-OCT) at week 0 and follow-up evaluations at week 12, which occurred four weeks after the third treatment (with treatments spaced four weeks apart). The results demonstrated that the photoaging milieu was positively altered following laser treatment. This included a reduction in activated melanocytes, decreased epidermal hyperpigmentation, a repaired basement membrane with fewer melanophages, new collagen formation, and a mild increase in vascularity and inflammatory cells. Additionally, there was a decrease in large "coffetti" melanin density and an increase in small granular melanin, with the "coffetti" melanin becoming more clustered and less widespread.

While the mean MASI score significantly improved, 3 out of 15 patients showed elevated MASI scores. These patients had more activated melanocytes at baseline, indicated by more rod dendrite and starburst cell bodies, suggesting they might benefit from combined treatment with antioxidants. Despite the elevated MASI scores, post-treatment optical biopsy still showed improvements in the photoaging milieu as previously discussed. The speaker emphasized that the picosecond laser treatment led to a decrease in senescent fibroblasts and melanocyte activity, thus reducing epidermal hyperpigmentation. In conclusion, optical biopsy using CRFF-OCT offers a new avenue to surpass the limitations of invasive biopsies for in vivo studies. Despite an elevation in MASI scores in patients with baseline hyperactivated melanocytes, dermal remodeling after laser treatment can result in the improvement of hyperpigmentation.

Treating complex pigmentation with Picosecond laser: How and why?

Dr. Liang-Chen Lin, MD (Taiwan)

The speaker expressed a preference for the 755 nm picosecond laser compared to the 1064 nm variant, primarily because the 755 nm laser is less likely to damage blood vessels. He incorporates a focus lens array DLA in his treatment protocol. The approach involves treating patients and conducting a follow-up after 7 days to observe improvements, particularly in epidermal pigmentation, without inducing post-inflammatory hyperpigmentation. A subsequent follow-up is scheduled a month later to assess dermal pigmentation, maintaining the same energy level as the initial visit.
For addressing epidermal pigmentation, the protocol specifies using zoom optics/focus array with 2-3000 pulses. Dermal pigmentation treatment follows a similar pulse range but utilizes a high-frequency zoom optic, with sessions spaced one month apart, totaling 6-12 sessions. Melasma treatment involves fixed optics for 1-2 passes with a focus array of 2-3000 pulses, also scheduled monthly over 6-12 sessions. The speaker noted that functional pigmentation, such as lentigo, is more readily eliminated compared to more challenging acquired pigments like Ota and Hori's nevus, which should only be treated using a focused area DLA.
The use of low energy settings with LIOB (laser-induced optical breakdown) is advocated to create subtle damage that initiates dermal remodeling, thereby improving pigmentation. The speaker emphasizes that lower power settings are preferable to higher ones and that longer intervals between treatments are more beneficial than shorter ones. Employing a focus array is deemed safe. The overarching message is that this treatment protocol may not only address melasma but also reverse photoaging, which in turn improves pigmentation.

Treatment for vitiligo: the journey continues

Dr. Cheng-Che E. Lan (Taiwan)

The topic of vitiligo was discussed in depth. The speaker began by clarifying that vitiligo, although not contagious or life-threatening, still lacks fully satisfactory treatments. The pathogenesis of vitiligo, which involves melanocyte stress, is not completely understood. However, it was pointed out that interferon gamma plays a significant role in vitiligo's development, acting through the JAK/STAT signaling pathway.
Dr. Lan delineated three stages of vitiligo:

1. Active Vitiligo: Characterized by progressing depigmentation, requiring immune suppression or high-dose narrowband UVB treatment.
2. Stable Vitiligo: No new areas of depigmentation.
3. Repigmenting Vitiligo: Notable for follicular or perilesional repigmentation.

A targeted therapy approach involving Janus Kinase inhibitors, specifically *Tofacitinib*, aims to inhibit the interferon gamma pathway. However, for repigmentation in vitiligo, the use of JAK inhibitors may still necessitate concurrent light exposure. The clinical efficacy of 308 nm excimer laser therapy was highlighted for providing more rapid initial pigmentation, particularly beneficial for segmental vitiligo. The speaker emphasized that combining low-dose phototherapy with low-dose immunosuppression could minimize the side effects commonly associated with higher doses of phototherapy while still yielding positive results.
Additionally, Dr. Lan referenced a clinical trial that utilized 5 mg of Tofacitinib for treating severe alopecia areata, noting its efficiency and cost-effectiveness. Another study was mentioned, examining the use of a minipulse of low-dose steroids or methotrexate over three months for vitiligo treatment. This study observed

that disease activity ceased, but approximately 15% of patients required further treatment nine months after the initial cessation of therapy. It was suggested that for these relapsing patients, additional treatments such as Tofacitinib or phototherapy should be considered.

Selected cases in pigmented disorders

In an engaging session led by **Dr. Pravit Asawanonda**, a professor at Chulalongkorn University Hospital, an insightful discussion was held on the relatively uncommon presentations of mycosis fungoides (MF) in darker-skinned patients, specifically focusing on hypo/hyperpigmented mycosis fungoides. Dr. Asawanonda pointed out the diagnostic challenge of this condition, noting that it may require at least three skin biopsies to confirm a diagnosis of mycosis fungoides or Sézary syndrome. He highlighted that hypopigmented mycosis fungoides often manifests on the inner thighs or buttocks and has shown a favorable response to narrowband UVB (NbUVB) therapy, typically after approximately 21 treatments. This positive response to phototherapy can also aid in diagnosis.

The importance of early diagnosis and treatment was emphasized, as these steps lead to significantly better outcomes. The pathogenesis of hypopigmented MF is thought to be related to CD8 cells, which might induce cytotoxic activity against melanocytes. Dr. Asawanonda mentioned that hypopigmented mycosis fungoides in children generally has an excellent prognosis, with narrowband UVB therapy being the primary treatment option. However, for cases unresponsive to NbUVB, alternatives such as PUVA (psoralen plus UVA) therapy or interferon can be considered.

Dr. Asawanonda described three patterns of hypopigmented mycosis fungoides observed in China: typical presentation, resemblance to pityriasis lichenoides, and poikiloderma changes, the latter often seen in relapse cases. In contrast, hyperpigmented MF, though rarer than its hypopigmented counterpart, typically presents with parapsoriasis-like lesions marked by CD4 and tends to occur in older patients than those with hypopigmented MF. Hyperpigmented MF also has a better prognosis compared to classical MF and responds well to narrowband UVB treatment.

An important takeaway from Dr. Asawanonda's talk was the need to examine more than just one lesion to make an accurate diagnosis, considering the potential for diverse manifestations of the disease across the body. Lastly, he cautioned against misdiagnosing vitiligoid lichen sclerosus as vulvar vitiligo, stressing the importance of annual follow-ups to ensure accurate diagnosis and appropriate management of conditions that may initially present with similar clinical features.

Platelet rich plasma for pigmentation

In the concluding presentation of the skin pigmentation session, **Dr. Sasima Eimpunth** from Siriraj Hospital explored the use of platelet-rich plasma (PRP) in treating pigmentation issues, particularly melasma. Dr. Eimpunth clarified that PRP, a component derived from blood, has shown promise in improving melasma conditions through methods such as microneedling or microinjection, even after a single session. The efficacy of PRP, as emphasized by the speaker, lies in the growth factors contained within the platelets. She recounted how PRP has been utilized for an extended period across various medical fields, including surgery, dentistry, and ophthalmology.

A specific study was presented to underscore the effectiveness and safety of PRP, focusing on its application to the periorbital skin, frontal hairline, and eyebrows. This study involved 15 patients undergoing three PRP treatments at monthly intervals, followed by evaluations at 1, 3, and 6 months after the final treatment. The findings indicated noticeable improvements in melasma as early as four weeks following the initial treatment.

A critical discussion point was the identification of the specific component—either growth factor or cytokine—that contributes to pigmentation improvement. Dr. Eimpunth pointed out that the underlying mechanisms might involve the epidermal growth factor, which inhibits the activity of the tyrosinase enzyme, along with prostaglandin E2 and transforming growth factor-beta. The improvement in pigmentation was attributed to several factors: healing of the basement membrane, inhibition of melanin synthesis, and enhancement of skin volume through rejuvenation, which collectively contribute to pigmentation improvements.

Dr. Eimpunth concluded her lecture by summarizing that evidence supports the benefits of PRP in pigmentation treatment. The pivotal role of growth factors released from activated platelets was highlighted as a key to the therapeutic process.

LASER SESSIONS: BEYOND THE LIGHTS

Speakers: Prof. Woraphong Manuskiatti, Dr. Wareeporn Disphanurat, Dr. Junjira Sawasdipong and Dr. Do Young Rhee
Report written by Dr. Chanika Kulapatrapa

The application of red light in aesthetics

Prof. Woraphong Manuskiatti (Bangkok, Thailand)
This interesting topic was delivered by Pr. Woraphong Manuskiatti from Siriraj Hospital. The outline of this topic is about the 675 nm light.
The speaker's technique is used in dark skin patients with 6 months duration in Siriraj Hospital. He found that there were a lot of benefits of red light 675 nm.
Why is it interesting? The light selectively targets collagen fiber with no pain and as well as giving pigment lightening effects. It can target the collagen absorption more than melanin and with low absorption by water, proper interaction with melanin. Potential applications are skin photorejuvenation, facial wrinkles reduction, tightening skin, benign pigmented lesions. The only precaution is hypopigmentation in dark skinned patients. However, there are techniques to minimize adverse effects which are decreasing power, decreased dot density and proper epidermal cooling.
The study in Siriraj Hospital was done is these tested indications including skin tightening, melasma, atrophic acne scars, facial and lips rejuvenation and hypertrophic scar.
Using 2 modes which are:

1. Constantly moving technique (moveo mode) power 4 (decreasing energy) to induce tightening,
2. Conventional setting (static mode) power 5 for benign hyperpigmentation such as melasma with non-overlapping stamp.

For the new promising treatment of lip rejuvenation, he uses standard mode with power 8 dwell time 200 ms, spacing 1000 mcm, 1 pass. No pain, no downtime for this laser treatment.
In conclusion, the red light gives promising benefits in skin tightening, melasma, atrophic acne scar, facial rejuvenation, lip rejuvenation and hypertrophic scars.

Fractional RF: beyond scars

Dr. Wareeporn Disphanurat (Pathum Thani, Thailand)
Another popular subject was beautifully provided by Dr. Wareeporn Disphanurat from Thammasat Hospital. The scope of the topic is about fractional microneedle radiofrequency (FMRF) with the application beyond treatment of scars. She introduced that biopolar radiofrequency is delivered by microneedles. With these insulated needles, you can preserve epidermal injury.
Histologic study showed microneedle radio frequency depth affected dermal coagulation. But if the depth is less that 1 mm, epidermis can be injured. Indications are skin rejuvenation, acne scar and acne *vulgaris*.
But how does it works for acne *vulgaris*? It can decrease sebum level and excretion rate and decrease inflammatory markers, significant reduction in inflammatory acne can be seen.
A meta-analysis of fractional radio frequency treatment for acne and/or acne scars. The study compared fractional CO2 laser VS fractional microneedle RF. It found that they can both improve scar but microneedle RF showed less downtime with less duration of erythema and Post inflammatory hyperpigmentation (PIH). The study also compared diode laser and fractional microneedle RF and found that they can all showed treatment of acne and seborrhea but with less PIH and downtime with microneedle RF .
There is an ongoing study with efficacy of low dose *isotretinoin* and fractional MRF and *isotretinoin* alone in treating acne *vulgaris*. Study is not done yet but can already see better result of active acne and scarring in combined treatment.
So the conclusion is that FMRF is an effective treatment for active acne with less downtime and fewer side effects that ablative fractional laser.

Long pulsed Nd: YAG more than hair removal

Dr. Junjira Sawasdipong (Bangkok, Thailand)
This topic was given by Dr. Junjira Sawasdipong who is the staff from Dermatology institute of Thailand, Ministry of public Health. The speaker stated that there are further several conditions beside hair removal for long pulsed Nd-YAG.
Normally pulsed laser is the first line of vascular treatment; however, the depth is short compared to long pulsed Nd-YAG with longer pulse that can penetrate deeper. Thus, she typically uses long pulsed Nd-YAG with high energy for deeper feeding vessels. To avoid overheat and epidermal damage, the adequate cooling is needed to lessen side effects.
As well as knowing how to adjust pulse duration, spot size and fluence depending on size of targeted vessels. Endpoints are vasoconstriction, vasospasm and darkening of vessels targeting. Repeated treatments can be done in 8-12 weeks.
Longer pulsed duration with around 50 ms can show increased dermal collagen and improve wrinkles. Super long pulsed Nd-YAG now can be adjusted to 60 ms pulse width.
Advantages of Nd-YAG are less epidermal melanin absorption, deep penetration, completely controlled depth and fluence of the treatment.
Another indication of long pulsed Nd-YAG is palmoplantar and periungual warts. Target of the laser in this condition is hemoglobin, thermalcoagulation and destruction of warts blood vessels. By using spot size 3-7 mm, pulse duration of 15-25 ms, fluence 100-270 j/cm2 with10-20% overlap. The treatment can be repeated every 4 weeks. Remission rate is 46-100%. Recurrence rate is 0-10%
Another treatment is for onychomycosis. Fungicidal effects from the heat is the proposed mechanism, although still unclear. She uses spot 4 mm, pulsed duration of 30-35 ms, fluence 35-45J/cm2, 2 passes with 2 minutes interval for entire nail plate. Repeated treatment can be done every 1 weeks. No serious adverse reactions is seen.

3 wavelength diode lasers for skin lifting and tightening

Dr. Do Young Rhee (South Korea)

The last but not least topic was given by Dr. Do Yong Rhee from South Korea. Immediately effects can be seen within 10 minutes of treatment with nasolabial folds that are improved and with brighter skin tone.
Can all kinds of hair removal laser be used for skin lifting and tightening? The answer is no. Only with 3 wavelengths: 1064, 810, 755 nm simultaneously emit energy that seem to be more efficient in heating tissue. He uses 2 modes with stack mode that delivered static stamping technique and with super hair removal (SHR) mode with dynamic technique to all over the face. 3 waves diode laser can reduce the risks of burn compared to long pulsed Nd-YAG 1064.
This mentioned laser targets 4 important areas which are:

1. more energy on retaining ligament and
2. reticular cutis for lifting and contouring,
3. platysma auricular fascia and
4. hair follicle with a lot of connective tissue sheath contraction that may improve pore size.

CURRENT TREATMENT IN GENODERMATOSIS: WHERE ARE WE NOW?

Speakers: Dr. Vesarat Wessagowit and Dr. Chavalit Supsrisunjai
Report written by Dr. Chanika Kulapatrapa

Drug repurposing in genetic skin diseases

Dr. Vesarat Wessagowit, MD, PhD, a specialist in Genetic Skin Disease from the Institute of Dermatology, initiated the session by delving into the concept of drug repurposing, which explores existing drugs for new therapeutic uses. Highlighted examples of successfully repurposed drugs include *Sildenafil* (Viagra®), initially developed for erectile dysfunction but now also used to treat Raynaud's disease, pulmonary hypertension, and to enhance endometrial thickness in elderly pregnancy.

Thalidomide, once notorious for causing birth defects, has found redemption in treating leprosy and multiple myeloma.
Molnupiravir has been repurposed for COVID-19, while *Posaconazole* and *Ravuconazole* are now being used against Chagas disease. *Clotrimazole* and *Ketoconazole* have been adapted for anti-trypanosome therapy.
The benefits of repurposing drugs, especially for genetic diseases, are profound, including reduced clinical trial phases and the unveiling of new mechanisms of action for old medications. Discovery of new drug indications often arises from serendipity, targeted mechanisms, and extensive screening processes, including library and computational methods. An instance of serendipity includes *Minoxidil*, initially for hypertension, accidentally discovered to induce hypertrichosis and now used for androgenetic alopecia (AGA) treatment alongside 2% *Ketoconazole* and *Finasteride*.
Other noteworthy mentions include *Cetirizine*, repurposed for AGA treatment due to its eyelash lengthening properties, and GLP-1 analogues, initially diabetes medications now celebrated for their weight reduction and cardiac morbidity decrease in obese patients, as demonstrated by *Semaglutide*'s effectiveness.
Unexpected discoveries in psoriasis treatment were highlighted, such as the clearance of psoriasis following a spinal block operation, leading to the intralesional injection of *Lidocaine* as a novel treatment approach. This method has shown efficacy even beyond conventional treatments in mouse models.
Drug repositioning extends to Atopic Dermatitis, treated with asthma medication *Dupilumab* and JAK inhibitors, and CHILD syndrome, where Statins and topical cholesterol address the underlying cholesterol pathway defect. Tuberous sclerosis sees repurposing with Sirolimus, while Netherton syndrome benefits from biologicals like *Ustekinumab* and *Dupilumab*. Muckel-Wel syndrome and pansclerotic morphea find new treatments in drugs designed for rheumatoid arthritis and JAK inhibitors, respectively. Low dose *Naltrexone* and *Apremilast*, initially for other conditions, now offer relief for Hailey-Hailey disease, with aspirin being used in Muir-Torre syndrome to prevent colorectal cancer.
In summary, drug repurposing holds a promising avenue for treating rare genetic diseases with known safety profiles and significantly reduced trial costs, showcasing a strategic approach to expanding therapeutic options.

Investigational treatment for inherited epidermolysis bullosa

Dr. Chavalit Supsrisunjai delivered an insightful lecture on Epidermolysis Bullosa (EB), a group of rare diseases characterized by mechanically induced blistering of the skin. He detailed the key proteins involved in EB, including plakin, integrin, collagen, and laminin, and outlined the four main types: Epidermolysis Bullosa Simplex (EBS), Junctional EB, Dystrophic EB, and Kindler's EB. Notable genetic mutations associated with these types include a new gene mutation in KLHL24 linked to cardiomyopathy in EBS and BPAG2 mutations in non-Herlitz (benign) Junctional EB. He further explained that Laminin 332 mutations are found in Herlitz Junctional EB, while Dystrophic EB is characterized by Type VII collagen mutations, leading to deeper dermal scarring.
Dr. Supsrisunjai highlighted the various novel therapeutic approaches being explored for EB, focusing on gene therapy and gene editing, protein therapy, RNA-based therapy, and regenerative approaches involving somatic cells, mesenchymal stem cells, hematopoietic stem cells, umbilical cord stem cells, and bone marrow transplantation. He also mentioned disease-modifying approaches that include biological/cytokine targeting therapies, small molecules, and repurposed drugs, all of which are currently in preclinical and clinical development stages.
Specific advances in gene therapy were shared, such as the use of viral vectors to replace mutated genes with functional ones. He cited the first keratinocyte gene therapy used in 2006 for Junctional EB and the significant progress made by 2017, where keratinocyte gene therapy managed to repair 80% of the skin surface. Additionally, a 2022 breakthrough with gene cream, a topical gene therapy using an HSV-1 virus vector, was mentioned as showing promising results in a clinical trial for severe Dystrophic EB.
Other innovative treatments include the use of *Gentamicin* for premature termination codon readthrough, showing potential in wound healing for Dystrophic EB, and cell-based therapies using fibroblasts and stem cells to produce normal Type VII collagen. Dr. Supsrisunjai shared about a 2021 study involving intravenous mesenchymal stem cells derived from bone marrow or umbilical cord blood in children and adults with RDEB, showing encouraging outcomes.
Emerging therapies like intradermal injection of allogenic fibroblasts, bone marrow transfer, and injection of recombinant Type VII collagen were also discussed. A 2019 clinical trial using intravenous recombinant Type VII

collagen demonstrated modest improvement in wound healing, marking a hopeful advancement in the treatment of EB. This lecture underscored the dynamic and evolving landscape of therapies for EB, emphasizing the potential for significant improvements in patient care through ongoing research and development.
collagen were noted at DEJ.

AUTOIMMUNE BLISTERING DISEASES (AIBDS): PRACTICAL POINTS AND TREATMENT PEARLS

Speakers: Dr. Napatra Tovanabutra, Dr. Kumutnart Chanprapaph, Dr. Chutima Seree-aphinan and Dr. Chuda Rujitharannawong
Report written by Dr. Pichanee Chaweekulra

Clinical pearls in the diagnosis of pemphigus and pemphigoid

Assistant professor Napatra Tovanabutra - Division of Dermatology, Department of Internal Medicine, Faculty of Medicine Chiang Mai University, Chiang Mai, Thailand

The speaker discussed three instances of autoimmune bullous diseases. The initial case involved a 67-year-old Thai woman diagnosed with erythrodermic pemphigus foliaceus (PF). She exhibited generalized erythema and exfoliation that initially misdiagnosed with exfoliative dermatitis. Despite initial treatment with systemic corticosteroids, her rash worsened upon dose reduction, revealing acantholysis cells in the epidermis and eosinophils in the dermis upon repeated biopsy. Positive IgG intercellular junction in direct immunofluorescence (DIF) study confirmed the diagnosis of erythrodermic PF, a rare presentation found in 0.5-5% of erythroderma cases. Clinical features included moist, crusted lesions, and thin-walled bullae eruptions, with potential complications such as bacterial infection and kaposi's varicelliform eruption. The erythrodermic PF is refractory to treatment.

The second case involved a 56-year-old Thai man with paraneoplastic pemphigus secondary to marginal zone B-cell lymphoma. Presenting with a painful rash on the lips and skin, he exhibited erythematous patches, target lesions, and crusted lips. Initial treatment with systemic corticosteroids and *azithromycin* failed, leading to worsening erosions and crusted lesions. Diagnosis was confirmed by repeated biopsy, showing interface dermatitis with suprabasal separation. Treatment involved systemic corticosteroids and *rituximab*.

Paraneoplastic pemphigus manifested polymorphic cutaneous lesions, resembling PV, PF, bullous pemphigoid (BP), erythema multiforme-like, and toxic epidermal necrolysis-like lesions. The different histologic features in the same patient could be found in paraneoplastic pemphigus.

The third case involved a 69-year-old male with an 8-month history of pruritic bumps. The underlying diseases of the patient were diabetes mellitus, hypertension, dyslipidemia, and ischemic stroke. Despite treatment attempts with phototherapy and intralesional corticosteroids, poor response was observed. Biopsy indicated prurigo nodularis clinically, but positive IgG at the dermoepidermal junction (DEJ) in DIF study confirmed the diagnosis of DPP4-induced pemphigoid nodularis, a rare variant of BP.

Challenging cases in AIBDs and lessons learned

Associate professor Kumutnart Chanprapaph - Division of Dermatology, Ramathibodi Hospital, Mahidol University, Thailand

The speaker presented three complex cases of AIBDs. The first case involved a 35-year-old female presenting with bullae lesions for one week. A skin biopsy revealed a subepidermal blister with a predominant neutrophil and eosinophilic infiltrate. DIF study showed linear deposition of IgG/C3 at the DEJ in n-serrated pattern. Immunology labs indicated positive ANA 1:320 with a homogenous speckle pattern, while tests for anti-BP 180 and 230 were negative, as was anti-collagen VII. Immunoblotting with human dermal extract revealed circulating antibodies binding to a 200 kDa protein, leading to the diagnosis of anti-p200 pemphigoid, a rare subepidermal AIBD. This condition typically develops in a younger age group, with lesions predominantly found in cephalic and acral distributions, sometimes involving mucosal surfaces. Treatment involved high-dose *prednisolone* and *colchicine*, yielding positive results.

The second case involved a 92-year-old female presenting with tense bullae and erosions for three months, without mucosal involvement. She had type 2 diabetes mellitus treated with a DDP4 inhibitor and dementia. Skin biopsy showed subepidermal blisters with eosinophil infiltrates, and autoantibody profiles were positive for anti-BP-180. The diagnosis was DPP4-associated BP. The implicated drug was discontinued, and treatment included systemic corticosteroids and *dupilumab*.
The third case was a 13-year-old girl with severe, treatment-resistant pemphigus vulgaris (PV) despite undergoing multiple *rituximab* treatments. The ineffectiveness of treatment was attributed to the presence of anti-drug antibodies. Studies have shown that approximately 43% of patients exposed to *rituximab* develop anti-*rituximab* antibodies. The speaker also emphasized the importance of initiating rituximab therapy early in PV patients, ideally within 6-12 months after disease onset, to achieve a higher remission rate. In this case, treatment involved IVIG administered over six doses and *dupilumab*, aiming to reduce autoantibody production.
The key takeaway is that BP is mediated by both B and T cells, whereas PV is predominantly mediated by B cells. BP can be triggered by certain medications, while PV is less likely to be drug-induced. In PV, treatment strategies should focus on minimizing antibodies to effectively manage the condition.

New and accessible treatment of phemphigus and bullous pemphigoid

Dr. Chutima Seree-aphinan - Division of Dermatology, Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

This session primarily addressed advancements in the treatment of autoimmune pemphigus and pemphigoid. The initial segment of the session outlined treatment strategies for immunobullous diseases, aiming to diminish autoantibodies, reduce autoreactive immune cells, and inflammation. Classic treatments for neutralizing autoantibodies included intravenous immunoglobulin (IVIG), plasma exchange (PLEX), and immunoadsorption (IA). *Efgartigimod* alfa, a novel alternative treatment, impedes IgG recycling via FcRn, thereby promoting IgG degradation. Approved by the US-FDA in 2023 for myasthenia gravis, *efgartigimod* alfa is administered once weekly for four weeks, followed by subsequent cycles based on clinical evaluation. Phase II data indicated a 70% reduction in total and antigen-specific IgG in moderate-to-severe pemphigus, with onset of action observed 2-3 weeks post the first dose and no major safety concerns. Phase III data revealed efficacy comparable to high-dose corticosteroids in treating moderate-to-severe pemphigus, suggesting potential benefits when combined with *rituximab* for rapid reduction of antigen-specific IgG or in replacing IVIG or PLEX in specific scenarios.
Omalizumab, the second medication discussed, functions by binding to the Fc portion of free circulating IgE. There is mounting evidence suggesting its favorable efficacy in patients with immunobullous diseases who exhibit antigen-specific IgE or display signs of Th2-skewed inflammation. A previous study demonstrated the benefit of omalizumab in BP patients who tested positive for anti-BP 180 IgE. However, evidence supporting the use of *omalizumab* in pemphigus is currently limited to case reports. In these cases, indications of Th2-skewed inflammation such as pruritus, eosinophilia, comorbidities of chronic spontaneous urticaria, and occasionally elevated IgE levels were observed.
To diminish the production of autoantibodies, conventional treatments include *rituximab*, IV *cyclophosphamide*, and pulse *methylprednisolone*. These mechanisms operate by reducing the overall number of circulating B cells, thereby decreasing the rate of immunoglobulin production by B cells. Alternatively, low-dose or ultra-low dose *rituximab* and the newer generation of B-cell directed biologics such as fully human anti-CD30 antibodies (*ocrelizumab*, *obinutuzumab*), and anti-B-cell activating factor (BAFF) antibodies (*belimumab*) are emerging as alternative treatments. Some studies have reported successful B cell depletion and clinical remission with lower doses (200-500 mg/dose) of *rituximab* in pemphigus, with a reduced risk of drug-related complications. Newer generation B-cell directed biologics offer advantages over *rituximab* as they lack a chimeric component and possess slower off-rates and higher affinity. They may be utilized in certain situations such as incomplete B cell depletion after rituximab treatment, rituximab allergy, or loss of rituximab efficacy.
In regard to Bruton kinase inhibitors, *tirabrutinib* demonstrated a reduction in anti-desmoglein (anti-dsg) IgG levels without significantly affecting total IgG or CD19+ cells. Pemphigus patients treated with *tirabrutinib* at a dose of 80 mg once daily for 52 weeks achieved a remission rate of 64.3%. Conversely, *rilzabrutinib*,

administered at a dose of 400 mg twice daily for 12 weeks, resulted in a 28.4% reduction in anti-dsg IgG levels but showed a low overall complete remission rate.
Alternative treatments aimed at attenuating disease-specific inflammation include *dupilumab* and JAK inhibitors. *Dupilumab*, an IL-4/13 inhibitor, exhibited promising treatment outcomes in BP based on multiple retrospective studies, with approximately 90% of BP patients achieving disease control within 4 weeks. *Dupilumab* may also offer benefits to pemphigus patients with Th-2 skewed inflammation. Additionally, in patients with refractory pemphigoid, JAK inhibitors decreased both itch and disease progression, with an onset of action observed within 1 week.

Practical pearls in the management of other AIBDs

Assistant professor Chuda Rujitharannawong - Department of Dermatology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand

During the session, the speaker addressed the treatment approaches for various AIBDs such as mucous membrane pemphigoid (MMP), epidermolysis bullosa acquisita (EBA), bullous systemic lupus erythematosus (BSLE), and anti-p200 pemphigoid.
For MMP, initial treatment typically involves systemic corticosteroids in combination with *dapsone* or *tetracycline*. Moderate to severe cases may require second-line treatments like systemic corticosteroids with *methotrexate* (MTX), *mycophenolate mofetil* (MMF), *azathioprine* (AZA), or *cyclophosphamide*. In refractory cases, combination therapy with *rituximab* or IVIG is recommended. Studies have shown marked responses in 85.3% of MMP patients treated with rituximab, but relapse occurred in 38.7% of cases. Achieving clinical remission in MMP may take longer and require more *rituximab* cycles compared to pemphigus, particularly in patients with MMP with anti-type VII collagen reactivity.
For non-severe EBA, initial treatment options include oral *colchicine* or *dapsone*, with additional systemic corticosteroids in partial response cases. Severe EBA cases may require IVIG with systemic corticosteroids or pulse *methylprednisolone*. *Rituximab* has shown effectiveness in severe EBA cases previously resistant to other therapies.
In BSLE, dapsone is an option for patients without systemic complications, while those with systemic involvement may require corticosteroids and/or immunosuppressant therapy. Case reports have suggested efficacy with various combinations such as corticosteroids with *AZA*, *cyclophosphamide*, *hydroxychloroquine*, *MMF*, or *MTX*. *Rituximab* has been effective in refractory cases, although responses were relatively short-lived with relapse occurring after 6 months.
For anti-p200 pemphigoid, adjuvant therapy to systemic corticosteroids commonly includes *dapsone*, followed by long acting tetracyclines, *cyclosporine*, and *AZA*. Treatment with systemic corticosteroids and adjuvant therapies has shown a 90.7% complete remission rate, with 44.4% experiencing at least one relapse. However, concerns exist regarding side effects of dapsone, notably hemolytic anemia and methemoglobinemia, particularly at dosages exceeding 100 mg/day.

CPC: DERMPATH

Speakers: Dr. Siri Chiewchanvit, Dr. Manasmon Chairatchaneeboon, Dr. Poonawis Sudtikoonaseth and Dr. Anakaporn Tiyawatanaroj
Report written by Dr. Pichanee Chaweekulra

Associate professor Siri Chiewchanvit - Chiangmai University, Thailand

The speaker presented three cases of **uncommon drug reactions** in patients with **hematologic malignancies.**

Case 1: Malignant Intertrigo

Malignant intertrigo is a subtype of toxic erythema of chemotherapy. It occurs due to the excretion of chemotherapy agents through eccrine sweat glands. It mainly affects areas with high eccrine gland density, such as palms, soles, and intertriginous zones covered by tape. Histopathology reveals epidermal dysmaturation, keratinocyte apoptosis, basal layer vacuolar degeneration, and eccrine squamous

syringometaplasia. Treatment involves symptomatic management with cool compresses, analgesics, bland emollients, and topical corticosteroids.

Case 2: Gilteritinib *-induced Neutrophilic Eccrine Hidradenitis*
This condition falls within the spectrum of toxic erythema of chemotherapy. Patients present with asymptomatic or painful erythematous papules or plaques, predominantly on the trunk, occurring around 10 days after chemotherapy initiation. Histopathology shows polymorphonuclear (PMN) infiltrates surrounding and within eccrine glands, along with necrotic eccrine epithelial cells. Eccrine hidradenitis is commonly observed in acute myeloid leukemia patients receiving chemotherapy, particularly cytarabine and targeted antineoplastic agents like BRAF inhibitors, EGF receptor inhibitors, and tyrosine kinase inhibitors. Other medications implicated include *acetaminophen*, *adalimumab*, *azathioprine*, *carbamazepine*, and granulocyte colony-stimulating factor (G-CSF).

Case 3: Interstitial Granulomatous Dermatitis
Interstitial granulomatous dermatitis (IGD) is characterized by erythematous papules, plaques, or patches with annular or linear subcutaneous cords. It primarily affects the lower extremities, trunk, and upper extremities, with involvement of multiple locations in 75% of patients. Histopathology reveals dense interstitial infiltration of histiocytes arranged in a palisade fashion, often with collagen necrobiosis. The inflammatory process typically exhibits a pandermal, bottom-heavy, or band-like distribution. Floating signs are present in a significant percentage of cases. Interstitial granulomatous drug reactions are most commonly associated with calcium channel blockers, statins, and tumor necrosis factor alpha (TNF-α) inhibitors.

Assistant professor Manasmon Chairatchaneeboon - Department of Dermatology, Faculty of Medicine Siriraj hospital, Mahidol University, Thailand

The speaker presented a case of mycosis fungoides (MF) with a gamma/delta phenotype, characterized by an asymptomatic erythematous rash on the right cheek persisting intermittently for 3 years, progressing into thick plaques over the last 4 months. Histopathological examination revealed dense infiltration of small to medium-sized atypical lymphocytes in the dermis, with epidermotropism and folliculotropism. Immunohistochemical staining was positive for CD3 and CD30, and negative for CD4 and CD8. Additionally, TCR gene rearrangement was positive for gamma TCR. The differential diagnosis included primary cutaneous gamma-delta T-cell lymphoma (PCGDTCL), as MF can present with similar histological findings and immunohistochemistry. Previous studies have shown that some patients initially diagnosed with MF may progress to aggressive PCGDTCL. Serial clinical surveillance and potentially additional biopsies are recommended if gamma-delta cells exceed 25%. The patient in this case was treated with low-dose electron beam therapy, resulting in an excellent response without any side effects.
The key takeaway is that diagnosing cutaneous T-cell lymphomas (CTCLs) with a gamma-delta phenotype poses challenges. The current definition of primary cutaneous gamma-delta T-cell lymphoma (PCGDTCL) may not encompass the entire spectrum of gamma-delta lymphoproliferative disorders (LPDs), including mycosis fungoides (MF) and lymphomatoid papulosis (LyP). There may be a need to reassess the classification of gamma-delta T-cell diseases in cutaneous lymphoma and lymphoproliferative disorders.

Dr. Poonawis Sudtikoonaseth - Institute of Dermatology, Thailand

Case 1: epithelioid angiosarcoma
The speaker presented a case of epithelioid angiosarcoma, which manifested as multiple necrotic plaques on the thighs. Histological examination revealed dense infiltration of the upper dermis by epithelioid-like cells with large nuclei. Some of these cells exhibited luminal formation containing red blood cells. Epithelioid angiosarcoma is a rare variant of angiosarcoma, typically occurring in locations such as extremities, retroperitoneum, gastrointestinal tract, pelvic and genitourinary tract, and central nervous system. Unlike typical angiosarcomas, which often affect the head and neck of elderly men or develop in irradiated skin following breast cancer therapy or long-standing lymphedema, epithelioid angiosarcoma arises in the intramuscular deep soft tissues of the extremities. The 5-year survival rate for epithelioid angiosarcoma is low, with approximately 20% of patients presenting with metastases at diagnosis. Common sites of metastasis

include the lung, bone, liver, and regional lymph nodes. Treatment typically involves surgery with wide margins, adjuvant radiotherapy or chemotherapy. Some cases have shown partial responses to endothelial/vascular blockers such as paclitaxel and propranolol, when combined with radiotherapy.

Case 2: morbihan's disease

Morbihan's disease is characterized by solid, persistent erythema and firm, non-pitting swelling affecting the central and upper parts of the face. This swelling typically lacks pain or itchiness. The absence of pathognomonic clinical or histopathological features makes diagnosing Morbihan's disease challenging, often resulting in delayed diagnosis. Diagnosis relies on recognizing this distinct clinical presentation and ruling out other potential diseases. Prolonged pharmacological treatment is often required to achieve satisfactory results, and regular evaluation of the clinical response to treatment is recommended.

Dr. Anakaporn Tiyawatanaroj - Pyathai hospital, Thailand

The speaker presented a case of extramammary Paget's disease (EMPD) characterized by a skin lesion in the left axilla persisting for 1 year. Histological examination revealed atypical pagetoid cells without dermal invasion. Immunohistochemistry studies indicated positivity for Ck7, CEA, and CAM5.2, and negativity for CK20 and S100. Malignancy screening yielded negative results. Histological mimickers of Paget's disease/EMPD include squamous cell carcinoma (positive for p63), melanoma, and sebaceous carcinoma.

ILLUMINATING 2024: ADVANCEMENTS IN PHOTODERMATOLOGY

Speakers: Dr. Ploysyne Rattanakaemakorn, Dr. Chayada Chaibutr, Dr. Suteeraporn Chaowattanapanit and Dr. Kamonrat Sunantawanich
Report written by Dr. Pichanee Chaweekulra

Exploring the dermatological applications of afamelanotide

Associate professor Ploysyne Rattanakaemakorn - Division of Dermatology, Ramathibodi Hospital, Mahidol University, Thailand

This session provides information on *afamelanotide*, including its indications, contraindications, precautions, and adverse effects. *Afamelanotide* is a potent analogue of alpha-melanocyte-stimulating hormone (αMSH) that stimulates the production of eumelanin in the skin, a protective melanin for the human body. In 2019, the FDA approved SCENESSE® (*afamelanotide* 16 mg) implant every 2 months for the prevention of painful skin damage from the sun in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria (EPP). Unlike human MSH, *afamelanotide* specifically targets melanocytes and does not affect the central nervous system (CNS). Adverse effects of the medication are primarily limited to the skin, and *afamelanotide* exhibits significantly higher binding affinity to MC1R.

Indications for *afamelanotide* include EPP, vitiligo, polymorphous light eruption, solar urticaria, Hailey-Hailey disease (based on phase II open-label pilot studies), and acne vulgaris (based on phase II open-label pilot studies). Although *afamelanotide* has been associated with a 50% decrease in epidermal sunburn cells and reduction in thymine dimer formation, it is not recommended for use as a sunscreen or treatment for sunburn.

Precautions for *afamelanotide* include the potential for darkening of pre-existing nevi and ephelides due to its pharmacological effects. Regular full-body skin examinations are recommended to monitor all nevi and other skin abnormalities. *Afamelanotide* has not been associated with any documented malignancies; in fact, studies have shown inhibition of melanoma cell proliferation. Additionally, melanocyte stem cells and melanoblasts do not express the MC1 receptor and are not activated in response to UV radiation.

Light sensitivity in atopic dermatitis

Associate professor Chayada Chaibutr - Department of Dermatology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand

It is widely acknowledged that sunlight exposure or phototherapy typically improves atopic dermatitis (AD) in most patients. However, there exists a subset of AD patients in whom their condition is worsened by sunlight

exposure, known as AD with photosensitivity. While sunlight exposure is beneficial for most AD patients, it does not have a positive effect on all individuals. There have been variations in the terminology and criteria used for diagnosing light sensitivity status in AD across different phototesting centers.
In China, photosensitive AD refers to AD patients who exhibit abnormalities in phototesting outcomes, such as abnormal minimal erythema dose (MED) or minimal phototoxic dose (MPD) values, or who experience abnormal skin responses at the phototested sites (such as pruritus, pain, papules, and diffuse erythema). In Germany, photosensitive AD refers to AD patients who test positive in photoprovocation tests but have normal MEDs. In the Netherlands, photosensitive AD refers to AD patients who exhibit positive photoprovocation tests of an eczematous type. Photoaggravated AD refers to AD patients who display evidence of photoprovoked eczema of constitutional origin but do not exhibit the characteristic phototest findings of chronic actinic dermatitis.
Previous research has proposed diagnostic criteria for photosensitivity in AD. The first group is photo-exacerbated AD (PEAD), characterized by exacerbation of AD rash after UV exposure but with normal MED. The second group is photo-sensitive AD (PSAD), where patients have slightly abnormal MED. The third group is CAD, where patients have markedly abnormal or normal MED. AD coexisting with polymorphous light eruption (PLE) was found in 47% of cases.
The speaker also discussed diagnosing CAD in AD patients. Those with CAD typically develop the condition at a young age, with 36% experiencing CAD before the age of 40. Among those with early-onset CAD, there were significantly higher rates of AD (90%). There were no significant differences in the severity of abnormal monochromator phototesting between the two groups. Low UVA-MED and positive baseline series of patch testing were associated with a poor prognosis for the disease.

Phototherapy landscape in 2024: Navigating treatment options between hospital and home settings

Associate professor Suteeraporn Chaowattanapanit - Division of Dermatology, Department of Medicine, Faculty of Medicine, KhonKaen University

Phototherapy stands as a standard treatment for various skin conditions, offering mechanisms like immunomodulation, apoptosis induction, increased skin pigmentation, antipruritic, and antifibrotic effects. Among the different types, NB-UVB is widely utilized. It's generally safe with mild adverse effects and can be safely combined with other treatments like systemic medications, biologics, and small-molecule inhibitors. For patients unable to tolerate systemic medications due to various reasons, phototherapy remains the sole option. However, its time-consuming nature and inconvenience pose barriers.
Home phototherapy, introduced in the 1980s, has gained traction. A 2009 study revealed its efficacy comparable to office-based NB-UVB. The American Academy of Dermatology guidelines of Care for the management of psoriasis and psoriatic arthritis in 2010 endorsed home-based UVB phototherapy as safe and effective for managing psoriasis. Currently, the National Psoriasis Foundation recommends six home phototherapy equipment vendors including Clarify Medical, National Biological Corporation, Daavlin, Luma Therapeutics, Solarc Systems, InC, and UVBioTek Phototherapy. Home-based phototherapy offers convenience, but it comes with drawbacks like device cost, lack of reimbursement, limited staff familiarity, and the need for patient education and maintenance.
In essence, phototherapy remains a primary treatment choice for many skin conditions, and home phototherapy alleviates several care barriers. However, improvements are needed to address existing limitations.

Optimizing phototherapy for mycosis fungoides: a comprehensive review of the latest evidence

Dr. Kamonrat Sunantawanich - Institute of Dermatology, Thailand

During this session, the speaker focused on discussing the various phototherapy options available for treating MF, the importance of maintenance phototherapy, and the current recommendations for managing pediatric patients with MF.

When comparing the effectiveness of different phototherapy modalities, oral PUVA (psoralen plus ultraviolet A) has shown higher rates of complete response compared to NB-UVB (narrowband ultraviolet B), with a significantly longer disease-free interval. Systematic reviews and meta-analyses have consistently favored PUVA over NB-UVB for patients with early-stage MF, leading to a notable increase in the relapse-free interval from 14.9 to 45.1 months with PUVA therapy, without a significant difference in adverse reactions. Other phototherapy options for treating MF include UVA1, excimer light, laser therapy, and photodynamic therapy. UVA1 offers the advantage of deeper penetration without psoralen-associated toxicity and relatively low carcinogenic risk, but its availability is limited. Excimer light and laser therapy have demonstrated efficacy rates of 50-100%, particularly in treating MF palmaris et plantaris, with the added benefits of shorter treatment duration and lower carcinogenic risk. However, these modalities are associated with high costs and limited availability. Photodynamic therapy, while effective, may be less suitable for thick and adnexal lesions and may be easily interrupted in high-touch areas. Predictors of a good treatment response include the presence of patches or thin plaques, classic and poikilodermic lesions, and a lighter skin phototype. Conversely, darker skin phototypes, long-lasting disease, thick plaques, folliculotropic lesions, poikilodermic lesions, and hypopigmented lesions are associated with poorer prognoses.

Maintenance therapy involves continued exposure to either skin-directed or systemic therapy once remission has been achieved, aiming to maintain response and prevent relapse and disease progression. These maintenance treatments typically have excellent safety profiles and minimal interference with daily life. PUVA and NB-UVB are commonly used for maintenance therapy in MF. PUVA has been shown to significantly decrease the relapse rate and prolong the relapse-free interval. While NB-UVB also offers benefits, there is no direct comparison between PUVA and NB-UVB for maintenance therapy. Studies have indicated that patients with stage IA disease and those over 50 years old are less likely to experience relapse. Moreover, maintenance therapy for more than 6 months has been associated with a significantly increased relapse-free interval. However, there is no significant difference in relapse rate and disease-free interval between maintenance therapy lasting less than 12 months and more than 12 months with NB-UVB. Given the significantly reduced overall survival of stage IB and IIA compared to stage IA, a longer remission period may have a positive impact on patients' survival outcomes.

To initiate phototherapy in MF, it is typically divided into three phases: induction, consolidation, and maintenance. During the induction phase of NB-UVB, treatment usually begins with 70% of the minimum erythema dose (MED), administered 2-3 times per week, with a 20% increment per session. If there is no response after 20 treatments, the exposure may be increased by an additional 50-100 mJ/cm2. For PUVA induction, 8-MOP at a dosage of 0.4-0.6 mg/kg or 25 mg/m2, taken 2 hours before UVA exposure, or oxsoralen-ultra at a dosage of 0.5 mg/kg, taken 1-1.5 hours before UVA exposure, is typically administered. PUVA is typically administered 2-3 times weekly, with a spacing of 48 to 72 hours between sessions. The lifetime limit for PUVA is usually set at 250 sessions or 1200 J/cm2. The induction phase continues until clearance of lesions for at least 1 month. If the physician initiates retinoids after phototherapy, the phototherapy dose should be decreased to one-third to one-half and increased more slowly. During the consolidation phase, the UV dose and frequency are maintained at a constant level for 1-3 months after clinical clearance. The final phase is the maintenance phase, during which the frequency of treatment is gradually decreased until it is stopped altogether. This phase should not be less than 3 months in duration.
In the case of pediatric mycosis fungoides, there isn't a universally agreed-upon treatment protocol. However, NB-UVB therapy appears to be a safe option for children. Prior to treatment, it's advisable to conduct MED testing to minimize the risk of symptomatic erythemal episodes. On the other hand, PUVA therapy should be approached cautiously in pediatric patients due to its association with long-term skin cancer risks and an increased likelihood of cataract development.

In summary, for early-stage disease, both NB-UVB and PUVA have shown effectiveness. Oral PUVA and bath-PUVA have demonstrated longer disease-free intervals. Phototherapy can serve as a primary treatment or as an adjunctive therapy for advanced-stage disease. Short-term maintenance therapy is recommended for patients experiencing disease relapse or seeking symptom relief. However, when considering long-term phototherapy,

the benefits must be carefully weighed against the potential risks. In pediatric patients, NB-UVB is considered effective and safe for managing early-stage diseases.

CONTACT DERMATITIS

Speakers: Dr. Pailin Puangpet, Prof. Penpun Wattanakrai, Dr. Praneet Sajjachareonpong, Dr. Chotinij Lertphanichkul and Dr. Thanisorn Sukakul
Report written by Dr. Pichanee Chaweekulra

The detective's Guide to Allergic Contact Dermatitis

Dr. Pailin Puangpet - Institute of Dermatology, Thailand

Dr. Pailin's lecture provides a comprehensive guide to diagnosing allergic contact dermatitis (ACD), likened to the methodology of a detective. The process entails four key steps: elimination, perception, detection, and deduction.

Firstly, the elimination step involves ruling out non-allergic conditions before proceeding with patch testing. These include non-dermatitis dermatoses (e.g., psoriasis, tinea), endogenous dermatitis (e.g., atopic dermatitis, seborrheic dermatitis), and irritant contact dermatitis (ICD). However, it's important to acknowledge that both endogenous dermatitis and ICD may coexist with ACD, particularly in challenging cases such as difficult-to-treat atopic dermatitis case. The second step, perception, involves making a preliminary diagnosis before patch testing. If the diagnosis remains unclear, it's recommended to revisit the patient's medical history and physical examination, consider the possibility of hidden or proxy dermatitis, rule out dermatitis artefacta, or conduct further investigations such as skin biopsies.

The third step involves detecting the culprit allergen. Physicians are advised to maintain a low threshold for adding extra series of patch test allergens to enhance sensitivity. Additionally, testing with patients' own samples and reviewing results on day 7, especially for metals, steroids, *neomycin*, gold, and acrylates, can further increase sensitivity. The final step, deduction, involves assessing the relevance of exposure. After patch testing, a more precise and detailed history and examination can help determine the significance of exposure. Lastly, Dr. Pailin emphasizes that becoming an expert in patch testing requires ample clinical experience and membership in contact dermatitis societies.

Testing procedures other than patch testing

Prof. Penpun Wattanakrai - Division of Dermatology, Ramathibodi Hospital, Mahidol University, Thailand

This lecture explores alternative testing methods beyond patch testing, including closed patch test/strip patch test, open test, semi-open test, and repeated open application test (ROAT).

Often, the standard series of allergens may not suffice or may be unavailable. In such instances, additional allergens should be considered based on the patient's contact history, occupational or environmental exposures, such as topical medications, cosmetics, workplace chemicals, fabrics, shoe components, and rubber pieces. Proficiency in patch testing with the patient's own products is essential to avoid false-negative and false-positive (irritant) reactions. Physicians should carefully consider the patch testing method, including the appropriate concentration (undiluted or diluted), and the vehicle of the tested substance, referencing material safety data sheets and relevant literature. However, caution must be exercised to avoid testing with unknown substances, strong acids or alkalis, corrosive or toxic materials, and abrasive materials.

Closed patch testing with chambers can be utilized to test the patient's products. Leave-on products should be tested as is, while rinse-off products should be diluted at a ratio of 1-10%. For solid materials, testing should be conducted as is with extracts. Professor Penpun presented a case with a positive patch test for acrylates, along with a positive reaction to the ear tip and device body of an earphone. In certain cases, strip patch testing is

employed to enhance test sensitivity by repeatedly stripping the tape from the test area before patch application to facilitate allergen penetration.

The open test is recommended for evaluating unknown substances or products (e.g., paints, glues, oils, detergents, cleansing agents) or substances suspected to cause strong reactions (e.g., hair dyes, PPD). During an open test, the product is applied directly to the skin, either undiluted or diluted, on areas such as the volar forearm, back, or upper arms, without occlusion. In a semi-open test, the product is applied directly "as is" to a 2x2 cm area of skin. After drying, the area is covered with permeable acrylate tape for 2 days. Results are interpreted similarly to a standard patch test. This method is suitable for substances that may induce irritant reactions, such as shampoos, liquid soaps, cleaning products, detergents, soluble oils, solvents, and paints. The Repeated Open Application Test (ROAT) replicates real-life exposure scenarios. It is used to confirm or rule out false-negative patch test reactions and false-positive reactions from closed patch tests and contact urticaria. During the ROAT, test products sized between 2x2 cm and 5x5 cm are applied to skin areas (such as the antecubital fossa, outer aspect of the upper arm, and facial skin) for at least 2 weeks. It is advisable to conduct open and semi-open tests before closed patch tests.

Management in facial dermatitis patients when patch testing is not available

Dr. Praneet Sajjachareonpong - Institute of Dermatology, Thailand

This session focuses on the practical management of facial dermatitis when patch testing is not available. Epidermal barrier dysfunction can arise from environmental factors or irritants present in cosmetic products or procedures. In managing facial dermatitis, Dr. Praneet recommends that physicians inquire about the history of cosmetic products used by patients over the past month. Additionally, they should inquire about any history suggestive of contact dermatitis by proxy.

The speaker proposes a two-week strategy for managing facial dermatitis. During this period, patients are advised to cease using all topical cosmetics and skincare products and instead use synthetic detergent (syndets) soap. They should also discontinue any topical prescription medications containing drying or irritating ingredients, such as *tretinoin* or *benzoyl peroxide*. Furthermore, patients should eliminate sources of skin friction and undergo examination for any underlying dermatoses, such as rosacea, and treat them with appropriate medication.

If the rash improves, patients can gradually reintroduce cosmetic products over a one-week interval, starting with lipstick, followed by face powder, powder blush, low-allergenic cream, and mineral sunscreen, respectively. The key message for facial dermatitis patients is to avoid trigger factors, carefully select cosmetic products, use mild cleansers, non-perfumed and non-preservative facial creams, mineral sunscreen, conduct a provocative test before introducing new products, and apply prescribed medication only when the rash flares up.

Relevance of positive patch test reactions

Dr. Chotinij Lertphanichkul - Department of Dermatology, Faculty of Medicine, Srinakharinwirot University, Thailand

The focus of this session was on grading the relevance and assessing relevance in patch testing. A positive reaction in patch testing indicates a contact allergy to the tested allergens, but it may or may not be clinically relevant, as not all contact allergies lead to contact dermatitis. Therefore, distinguishing between contact allergy and allergic contact dermatitis is crucial, and determining clinical relevance is the most critical aspect of the patch test procedure. Patients should be questioned about their exposures at home, work, or during leisure activities. Additionally, the localization of dermatitis on physical examination provides clues about the expected allergen.

Grading of relevance are categorized in to past, current, or unknown. Past relevance occurs when a positive allergen explains previously unrelated dermatitis, but the patient is no longer exposed to it, such as nickel

causing earring dermatitis. If exposure cannot be identified, it is categorized as unknown relevance. Current relevance can be definite, probable, or possible. To establish definite relevance, the allergen must be tested and yield a positive result, along with the product the patient is exposed to. Probable relevance would apply when a positive allergen is an ingredient in a product used by the patient. Possible relevance is indicated when a positive allergen aligns with the distribution of dermatitis, correlating with exposure to product use.
In the assessment of relevance, the speaker focused on nickel, fragrance, and *isothiazolinone*. Nickel is commonly found in cosmetic tools like eyelash curlers, as well as in cosmetic products such as eye shadow, foundations, makeup bases, and powders. For instance, a patient who exhibited a positive reaction to nickel experienced improvement in eyelid dermatitis upon discontinuing the use of eye makeup containing nickel. Therefore, nickel is clinically relevant in this scenario. However, there isn't a definitive recommendation regarding the use of skincare products containing ingredients that may have high nickel content, such as oat, safflower, soy, or wheat, in individuals with nickel allergies. If a patient experiences significant discomfort from dermatitis, the doctor may advise avoiding such products.

Fragrance ranks among the top 10 allergens in the North American Contact Dermatitis Group (NADCG) patch test results from 2019-2020. It's not limited to perfumes; fragrance can also be present in various other products such as skincare, cosmetics, and hair care items. Physicians should caution patients that essential oils and plant extracts often serve as fragrances. Both natural and synthetic fragrances have the potential to trigger allergic contact dermatitis. Additionally, aroma diffusers and scented candles can also emit fragrances that may cause skin reactions.

Finally, the discussion turned to *isothiazolinone*, with the speaker specifically focusing on *benzisothiazolinone* (BIT), the latest addition to the European baseline series. Since 2017, there has been an increase in the prevalence of positive patch tests to BIT. By 2021, the positive reaction rate to BIT was nearly 5% in European countries and as high as 10% in North America. However, data from the IVDK (Information Network of Departments of Dermatology) spanning from 2002 to 2021 suggest that BIT may potentially exhibit irritant or false-positive properties. One significant challenge in assessing the relevance of BIT is the lack of information about it on product labels, as BIT is commonly used in industries, paints, and glues, where labeling is not mandatory. Household products also serve as another source of BIT, and while there are no legal restrictions on its use in most regions, European regulations mandate its labeling in detergents. It's noteworthy that BIT is prohibited in skincare products in European countries but remains permissible in the US and Canada. For take home message, relevance can only be verified if the dermatitis clears on the allergen removal and the dermatitis reappears when the allergen is reintroduced. Physician and patients should work as a team work to identify the clinical relevance. True relevance is only known weeks or months after patch testing is complete.

Product labeling dermatologist should know

Dr. Thanisorn Sukakul - Lunds University, Sweden

In Thailand, the regulation of cosmetics is under the jurisdiction of the Thai Food and Drug Administration (FDA THAI), while in the EU, the European Commission is responsible for overseeing the regulation of a wide range of consumer products, including cosmetics, with the aim of ensuring customer safety. It's important to note that regulations differ from one country to another. For instance, products manufactured in the EU and marketed in Thailand are required to comply with EU regulations, but they may not necessarily need to meet the same standards for commercial claims. These regulations are regularly updated to keep pace with evolving standards and scientific advancements. Over the next two years, there will be an additional 80 fragrances that must be declared in EU products.

Product labeling typically includes the International Nomenclature of Cosmetic Ingredients (INCI), Color Index (CI), and natural raw materials. INCI names are systematic identifiers used internationally to label cosmetic ingredients. Natural raw materials often consist of natural extract substances, many of which already have INCI names. However, these materials contain numerous chemicals, some of which are identified, while others are unidentified fractions. Ingredients on product labels are listed in descending order of concentration, with those

present in less than 1% concentration not required to be labeled. One challenge with natural raw materials is that some contain unknown chemicals, and there is limited data available on their skin toxicity and allergenicity. In terms of marketing claims, the EU has specific regulations, but other countries, such as the US, have less comprehensive guidance in this regard. Additionally, the same product produced in different countries may have different ingredient formulations.

BENEFIT BEYOND IMMUNE SYSTEM FOR ORAL RETINOIDS USE IN PSORIASIS

Updated Thai Clinical Practice Guideline for Psoriasis

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The speaker discussed the updates in the Thai Psoriasis Clinical Practice Guideline (CPG) 2022. Previously, psoriasis severity was classified as mild or moderate to severe based on criteria such as ≥10% Body Surface Area (BSA), (Psoriasis Area Severity Index) PASI ≥10, or Dermatology Life Quality Index (DLQI) ≥10. However, with the introduction of multiple biologic drugs in 2020, a new classification was proposed by the American Academy of Dermatology and the International Psoriasis Council. Moderate to severe psoriasis is now defined as >5% BSA or involvement of special areas resistant to localized therapy. In the new Thai Psoriasis CPG, moderate psoriasis encompasses involvement of 5-10% BSA or rash in special areas unresponsive to localized therapy, while severe psoriasis is characterized by BSA >10%, PASI >10, or involvement of special areas with DLQI >10.

Regarding treatment recommendations, oral conventional medications, phototherapy, and/or biologic agents are options for patients with lesions covering at least 5% BSA or those with lesions in special areas with DLQI >10. Treatment success is defined as a PASI improvement of more than 75% compared to baseline after 8-12 weeks of treatment. If PASI improvement falls between 50-75%, the patient should have a DLQI of less than 6. The CPG focuses on conventional topical treatments due to the unavailability of newer topical medications such as aryl hydrocarbon receptor modulators, phosphodiesterase-4 inhibitors, and JAK/STAT inhibitors in Thailand. Topical steroids are considered safe during pregnancy if used in quantities less than 60 g per week. In systemic treatment, baseline non-invasive blood serology tests such as fibrosis 4 index (FIB-4), nonalcoholic fatty liver disease fibrosis score (NAFLD) or steatosis-associated fibrosis estimator score (SAFE) should be conducted before initiating *methotrexate* (MTX), even in patients without risk factors for hepatotoxicity. *Acitretin*, while non-immunosuppressive and relatively safe, requires pregnancy testing due to teratogenic concerns. *Cyclosporin* (CsA) should not be used continuously for more than 2 years due to renal and hypertensive effects, and dose adjustments may be necessary if creatinine levels rise.

Biologic drugs, including IL-17 and IL-23 inhibitors (excluding *tildrakizumab*), are mentioned in the new CPG. Tuberculin skin tests or interferon gamma release assays should be conducted before initiating biologics. However, there are concerns about tuberculosis reactivation, particularly in Thailand, which has a high prevalence of tuberculosis. Biologic drugs are contraindicated in patients with certain underlying diseases, such as congestive heart failure class III-IV and multiple sclerosis or demyelinating diseases for TNF-α inhibitors, and inflammatory bowel disease for IL-17 inhibitors. IL-17 and IL-23 inhibitors are considered safer in terms of infection risk compared to TNF-α and IL12/23 inhibitors. Psoriasis patients who meet severity criteria outlined in the CPG may be eligible for reimbursement from the government if they are government officers.

Oral retinoids: monotherapy for psoriasis

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This session delves into the use of oral retinoids in the treatment of psoriasis, covering indications, contraindications, efficacy, safety, and lab monitoring. FDA-approved indications include monotherapy for pustular, palmoplantar, and erythrodermic psoriasis, as well as moderate to severe plaque-type psoriasis. Additionally, it is approved for combination therapy with phototherapy for chronic plaque psoriasis. *Acitretin*'s benefits in generalized pustular psoriasis include rapid onset of action (within weeks), with no new pustules observed within 3 days and skin remission achieved within 5-7 days. In comparison to *secukinumab*, *acitretin* demonstrates an onset of action of approximately 1 week for pustular psoriasis, whereas *secukinumab* takes around 3-4 days. For erythrodermic psoriasis, 58% of patients achieve 50-75% clearance at 4 weeks, and 85% achieve >75% clearance at 12 weeks. However, the efficacy of *acitretin* at a dosage of 25 mg/day for plaque-type psoriasis in achieving PASI-75 is 30%, which is lower than that of MTX, CsA, and phototherapy.

The expert consensus strongly supports the use of *acitretin* for patients with recent malignancy. Additionally, acitretin is preferred for patients with chronic inflammatory bowel disease, advanced heart failure, and concomitant latent or treated tuberculosis. Regarding psychiatric disease, there is insufficient evidence-based data to establish a link between *acitretin* and depression or suicidality. While only a few cases of depression and suicidality associated with *acitretin* have been reported, the European Medicines Agency (EMA) has decided to include a warning about the potential risk of depression associated with oral retinoids.

The absolute contraindications for *acitretin* include pregnancy, lactation, severe renal or hepatic dysfunction, cirrhosis, alcoholism, uncontrolled hypertriglyceridemia, poorly controlled diabetes mellitus, pancreatitis, and blood donation. Laboratory investigations, including liver function tests and lipid profiles, should be conducted at baseline and monitored every 3 months. Spine x-rays and bone density assessments should be performed annually or as needed based on symptoms. The most common side effects of *acitretin* are dry skin, mucosa, peeling of the palms and soles. Other side effects may include hypertriglyceridemia, myalgia, joint pain, and transaminitis. Chronic side effects may include extraspinal bone spurs, syndesmophytes, diffuse idiopathic skeletal hyperostosis (DISH), extraspinal tendon and ligament calcification, degenerative spondylosis, and premature closure of the epiphyseal plates in young patients. A previous study reported that 90% of psoriasis patients treated with *acitretin* experienced adverse events, with the majority being cutaneous side effects, followed by dyslipidemia and elevated liver enzymes. However, no serious adverse events were reported. The age at initial treatment with *acitretin*, duration of treatment, and average daily dose did not have a significant impact on the height and bone development of children. No patients experienced premature closure of epiphysis before or after being treated with oral acitretin at doses less than 1 mg/kg/day for periods ranging from 1 to 90 months. However, the risk of short stature was higher when *acitretin* was combined with glucocorticoid treatment compared to *acitretin* monotherapy. Therefore, if prescribing *acitretin* to children, it is important to regularly monitor their growth. In elderly patients, there is no evidence suggesting an increased risk of osteoporosis.

In summary, conventional systemics are first line therapies for psoriasis. *Acitretin* has less efficacy but cheaper than biologics. *Acitretin* monotherapy is suitable for pustular, palmoplantar psoriasis, erythrodermic psoriasis and plaque type in cancer patients. The drug survival is 8.6 months. Long term side effects of *acitretin* that should concern are psychiatric disorders and skeletal system.

Oral retinoids: combination therapy for psoriasis

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The reported co-prescribed medications with *acitretin* include topical *corticosteroids* (51%), *calcipotriene* (31%), biologics (6%), CsA (5%), MTX (5%), and *tazarotene* (2%). Combining acitretin with UVB phototherapy significantly reduces the PASI score compared to phototherapy or *acitretin* alone. In patients with suboptimal responses to initial acitretin monotherapy, reducing the acitretin dose before introducing phototherapy can

minimize erythema caused by acitretin-induced thinning of the stratum corneum. For patients who have not previously undergone ReUVL treatment, low-dose *acitretin* (0.3-0.5 mg/kg/day) should be initiated for 2 weeks before starting phototherapy. In patients with suboptimal responses to phototherapy alone, the phototherapy dose should be reduced by 50% before introducing *acitretin*. Maintenance therapy should be instituted for at least 4 weeks after clearing, using 75%-90% of the final UVL dose. Patients should be advised that the initial spreading of plaques does not imply worsening of the disease with *acitretin*-UVB, which may help promote compliance.

A previous study demonstrated that the combination of acitretin and MTX was more effective and did not significantly affect liver function in both patients and mice. Furthermore, the combination groups showed less elevation of profibrotic factors compared to the MTX alone group. Patients tolerated well the administration of acitretin (20 mg/day) and MTX (7.5 mg during the first week and then 25 mg/week) in combination at routine dosages. The incidence of hepatic fibrosis in psoriasis patients receiving MTX and acitretin was not increased compared to those receiving MTX monotherapy. Diabetes and obesity were identified as significant factors associated with hepatic fibrosis in long-term MTX-treated psoriatic patients regardless of cumulative MTX dose.

Regarding biologic treatment, acitretin appears to be an effective and safe option for use in combination with *secukinumab*. Combining *secukinumab* with low dose *acitretin* resulted in complete or almost complete skin clearance in all patients, with no adverse events or increased toxicity.

PIGMENTARY DISORDERS

Pigmentary complications from cosmetic procedure

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This session addresses pigment-related complications arising from cosmetic procedures, encompassing issues like dyspigmentation, complications from tattoo removal, and strategies to prevent complications in individuals with darker skin tones. The initial segment focuses on hypopigmentation resulting from fully ablative laser resurfacing, including temporary, mottle, relative, and delayed hypopigmentation. Temporary hypopigmentation stems from excessive thermal damage, affecting both epidermal and follicular melanocytes, compounded by the inflammatory response triggered by laser injury, which suppresses melanogenesis. Though melanocyte count remains normal, there's a reduction in tyrosinase activity, sensitive to heat. Full repigmentation occurs within two months of follow-up.

Laser toning employs subcellular selective photothermolysis, utilizing collimated flattop beams, large spot sizes, ultrashort pulse durations, low fluence, and multiple passes of Q-switched lasers (QSL). This technique induces dendrectomy, down-regulates functional melanocytes, decreases melanosome production, and reduces expression of melanogenesis-associated proteins. A systematic review and meta-analysis indicate significant improvement in MASI/mMASI scores with laser toning up to 24 weeks, though melanin index changes are sustained only up to 8 weeks. Risks include hypopigmentation or punctate leukoderma (3.9%), post-inflammatory hyperpigmentation (PIH) (1.9%), and recurrence (18.3%). Punctate leukoderma correlating with session frequency rather than spot size, fluence, or treatment interval. Mottled depigmentation results from direct phototoxicity to melanocytes and cumulative laser dose.

Rebound hyperpigmentation may arise from aggressive laser settings, particularly in darker skin types, necessitating careful management. Hypopigmented-depigmented macules should contraindicate further treatment, though management is challenging as depigmentation often persists. There are two primary treatment approaches for hypopigmented-depigmented macules: attempting to repigment the depigmented areas or lightening the surrounding normal or hyperpigmented melasma skin. The goal of treatment is to

reduce the contrast between the light and dark areas of the skin. Additionally, relative hypopigmentation, appearing as a halo following lentigo fading, may result from sublethal laser fluence.
Hyperpigmentation primarily occurs due to factors such as high fluence and inadequate cooling during treatments, and it can manifest in tanned patients. Skin type, skin thickness, sebaceous glands, and hair follicles influence IPL treatment susceptibility, with prevention strategies including minimal threshold fluences, limiting fluence and exposure duration, and covering melanocytic lesions with wet white gauze during treatment. Hyperpigmentation from PDL arises from hemosiderin deposits, typically resolving within 2-3 months. Preventive measures for PIH during hair removal laser treatments involve longer pulse durations, wavelengths, and appropriate cooling, with caution against multiple laser passes. PIH resulting from fractional resurfacing lasers is attributed to high treatment density, small treatment sites, inadequate epidermal cooling, and prolonged treatments.

Regarding tattoo removal complications, the speaker discussed cutaneous allergic reactions and paradoxical darkening. Allergic reactions post-QSL tattoo removal stem from rapid thermal expansion of pigment-containing cell fragments, while paradoxical darkening may occur in certain tattoo colors due to reduced metallic compound levels, turning irreversibly black after QSL irradiation. Treatment involves continuing QSL with pulse durations >1ms or switching to 532nm and 1064nm picosecond lasers.
In summary, the speaker advocates for using the lowest fluence possible to achieve the target endpoint, employing longer wavelengths and larger spot sizes to minimize PIH risk in patients with varying skin colors.

Myths and facts about hypopigmented mycosis fungoides

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Hypopigmented mycosis fungoides (HMF) is not as rare as perceived. Although it is very rare in Caucasian populations, but it is the common MF subtype in Thailand. The HMF predominantly affects individuals with darker skin types. It is not easy to distinguish HMF from other hypopigmented conditions. Other differential diagnoses of acquired hypopigmented macules and patches are tinea versicolor, post inflammatory hypopigmentation, progressive macular hypomelanosis, extensive pityriasis alba, and parapsoriasis. According to histologic study, HMF showed epidermotropism at epidermis with partial or total loss of epidermal melanocytes. Therefore, the absence of melanocyte cannot be used to differentiate between HMF and vitiligo. TCR gene rearrangement can be negative in HMF and positive in other inflammatory disorders.

Clinicopathological correlation is crucial
Some authors have suggested that HMF is a low-grade lymphoproliferative disorder. However, it still has a potential risk of disease progression. For treatment, HMF follows the same guideline as classic MF. HMF is incurable but rarely progresses. Aware of over diagnosis in HMF. Delayed diagnosis may be less harmful than overdiagnosis. Repeat skin biopsy after off treatment for at least 4 weeks may be considered.

Leukonychia: etiology, diagnosis, and treatment

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Leukonychia can be classified into three categories: true leukonychia, apparent leukonychia, and pseudoleukonychia. These categories are assessed based on anatomical and morphological types. True leukonychia affects the matrix and nail plate, pseudoleukonychia affects the dorsal or ventral nail plate, and apparent leukonychia affects the nail bed. True leukonychia and pseudoleukonychia lesions do not fade under pressure, whereas apparent leukonychia lesions do. Morphological assessment involves determining whether the leukonychia is partial or total, longitudinal, transverse, or punctate.

Punctate leukonychia is the most common presentation, especially in children, and must be differentiated from punctate pseudoleukonychia caused by superficial white onychomycosis. Transverse true leukonychia may

result from various factors such as Mee's lines (associated with arsenic toxicity), trauma, hematologic disorders, psoriasis, medications, hormonal changes (such as those occurring during the menstrual cycle), infections, and systemic conditions like systemic lupus erythematosus (SLE) or chronic kidney disease (CKD). Transverse apparent leukonychia can be caused by systemic conditions like hypoalbuminemia or CKD, as well as certain medications like retinoids or chemotherapy.

Longitudinal leukonychia results from focal alterations in the nail matrix leading to focal parakeratosis. Causes of longitudinal true leukonychia include conditions like Darier's disease (often accompanied by longitudinal erythronychia), Hailey-Hailey disease, tuberous sclerosis complex, and onychomatricoma. On the other hand, longitudinal apparent leukonychia can be associated with subungual squamous cell carcinoma (SCC) or onychopapilloma.

In patients with total leukonychia or half-and-half nails, underlying conditions such as CKD (in uremic patients undergoing hemodialysis), Kawasaki's disease, or Behcet's disease should be considered. Terry's nails may indicate liver cirrhosis, CKD, congestive heart failure, diabetes mellitus, or simply normal aging.
Management of leukonychia involves determining the type of leukonychia present and ruling out fungal infection (pseudoleukonychia) in all cases. Further investigation into associated underlying conditions is warranted based on the type of leukonychia identified. Nail care practices should focus on avoiding cuticle manipulation to prevent trauma, limiting the use of nail grooming products, and applying moisturizer regularly.

2024 brightening agent trends decoded

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During the presentation, the speaker discussed various brightening agents. Cysteamine hydrochloride was noted for its potential irritation, while alternative forms such as N-propionyl-4-S-cysteaminylphenol or N-acetyl-4-S-cysteaminylphenol were mentioned as less irritating options. potassium azeloyl diglycinate (PAD), often referred to as a salt-form of azelaic acid or water-soluble azelaic acid, was highlighted for its mild nature and is regulated as a cosmetic ingredient globally. Bakuchiol, with its retinol-like action and ability to bind with cellular retinol-binding protein, was noted for enhancing dermoepidermal junction proliferation.
Ascorbic acid's instability was cautioned against, particularly older formulations containing erythrulose, which can cause skin tanning. The other forms of ascorbic acid such as ascorbyl palmitate and ascorbyl glucoside are more stable. While oral tranexamic acid is well-known for skin brightening, the efficacy of topical forms is limited due to its water-solubility. The cetyl tranexamate hydrochloride, a lipophilic form, may be more easily absorbed.

Isobutylamido thiazolyl resorcinol, a new brightening agent with high tyrosinase affinity and reversible inhibitory action, was introduced. Mercaptoicotinoyl glucine (2-MNG), discussed at the recent World Congress of Dermatology 2023, was highlighted for preventing UV-induced skin darkening by binding to melanin precursors. Rhododendrol (hydroxybutylphenol), associated with hypopigmentation and withdrawn from the market, was also mentioned.
Lastly, the presentation touched on chemical peels, favoring buffered agents like buffered trichloroacetic acid, or buffered glycolic acid to maintain an acidic pH and avoid degradation. Salicylic acid, commonly used in acne treatment, was noted for its poor solubility in water, leading to the modification to capryloyl salicylic acid, a lipophilic hydroxy acid (LHA) that is easier to dissolve in human skin lipid.