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New topical developments and preventive mechanisms

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Primary prevention of atopic dermatitis (AD) was discussed. Studies have showed that oral probiotics given in the 3rd trimester and continued in first six months of life may have beneficial effect in prevention of AD development. Cochrane review of 39 randomised controlled studies examining probiotics for treatment of AD did not appear to be effective. Dietary restriction and house dust mite reduction are also not recommended in the prevention of AD.

There is evidence indicating that early barrier impairment predisposed to AD development. Studies had showed increase transepidermal water loss in early life in patients with AD. Whole body daily application of topical emollient continuously after birth is proposed to prevent AD in high-risk children with some positive studies previously. The latest outcome of a large randomised controlled multicentre trial (The Barrier Enhancement for Eczema Prevention [BEEP] trial) however failed to show significant benefit in prevention of AD.

There is also evidence of skin microbiome changes preceding the onset of AD. Commensal bacteria have an important anti-inflammatory role and the loss of skin microbiome diversity is well documented in active AD. Emollient use increases bacterial diversity and may help in prevent of AD and disease flares. Early studies have shown that commensal organisms such as *Roseomonas mucosa* reduce severity of AD, which support the commensals' inhibition of pathogenic *Staphylococcus aureus* colonisation. This may provide a new strategy for prevention of AD.

New topical agents inhibiting phosphodiesterase-4 (PDE4, a major regulator in inflammatory cytokines production) have been showed to be effective in treating AD. PDE4 is increased in AD lesions and PDE4 inhibitors such as difimilast, crisaborole, roflumilast and E6005 have been showed to reduce disease severity. Further studies to determine long-term disease control, efficacy of maintenance and proactive therapy are to follow.

Tapinarof is a small molecule natural aryl hydrocarbon receptor (AhR) agonist. AhR affects the balance of T17 and Treg cells, plays an important role in development and maintenance of skin barrier. Tapinarof moderates the expression of proinflammatory cytokines in CD4 T cells and keratinocytes. A phase 2 study of topical tapinarof published early this year has shown efficacy in treating adolescent and adult AD patients.

Topical JAK inhibitors are being actively studied in treatment of AD. Topical tofacitinib (JAK1/3 inhibitor), topical ruxolitinib (JAK1/2 inhibitor), topical delgocitinib (JAK1/2/3 inhibitor) have been shown to be efficacious for treatment of AD in early studies with no severe adverse reaction.

Learning points:

Newly developed topical therapeutics such as PDE4 inhibitors, tapinarof and JAK inhibitors offered new modalities of treatment for AD. Modification of skin microbiome may be a new strategy for prevention of AD.

Nail update

Speakers: BM Piraccini,[1] B Richert,[2] P Chang[3]
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Almost all nail melanoma is adult onset with single digit involvement. The features are longitudinal melanonychia with or without Hutchison's sign, longitudinal melanonychia with nail plate abnormality, ulceration or nodules of nail bed, ulceration with Hutchison's sign. Dermoscopy will help to delineate the malignant features such as multicolor lesions, interrupted lines of melanonychia and micro-Hutchison's sign.

There has been an increasing use of biologics in the treatment of nail psoriasis. Apart from TNF alpha inhibitors such as adalimumab, IL-17 inhibitor and IL-23 inhibitor have been shown to be efficacious. Acrodermatitis continua of Hallopeau can also be treated with biologics such as adalimumab.

There are a significant number of patients with connective tissue diseases have proximal nail fold changes that can be observed under dermoscopy. The changes in nail fold capillaries are categorised into morphology, diameter, architecture and density. In systemic sclerosis, early disease shows limited number of giant capillaries, active disease shows numerous giant capillaries and frequent microhaemorrhages, while late disease shows marked loss of capillaries and extensive avascular area. In dermatomyositis, apart from scleroderma pattern, the most typical feature are tortuous and arborescent capillaries.

Learning points:

Dermoscopy is very helpful in the diagnosis of nail melanoma and connective tissue diseases. The clinical signs in nail bed and nail fold can be picked up with dermoscopy under experienced eyes.

Toxic epidermal necrolysis: to treat or not to treat? Immunotherapy vs. supportive therapy

Speakers: CH Hu,[1] T Shiohara,[2] P Wolkenstein,[3] S Oro[4]
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Controversies existed as to whether treatment with immunotherapy for toxic epidermal necrolysis (TEN) and Stevens Johnson syndrome (SJS) will improve outcome and survival benefit. There have been no large controlled trials to support or disprove the benefit of treatment. There has been also no consensus on which immunotherapy should be used. Systemic corticosteroids, IVIg, cyclosporine and anti-TNF-α all have been used to treat TEN or SJS.

Systemic corticosteroids have been used widely as first-line treatment. A number of regimens have been used, including pulse methylprednisolone which decreases several pro-inflammatory cytokines. There have been a few reports of infectious complications, which is the major drawback. The outcome of IVIg treatment is inconclusive. Non-comparative studies showed no benefit on mortality or progression. There seemed to be more deaths observed in elderly and patients

with renal impairment. Thus IVIg treatment should be avoided in elderly or those with renal impairment. Cyclosporine failed to show beneficial effect in a retrospective cohort of 174 patients. However, most severe patients did not receive cyclosporine or were not included in the analysis. Etanercept has been reported in a Taiwan study recently showing earlier skin and oral mucosa healing compare with corticosteroid, while the mortality has no significant difference.

Systemic corticosteroid use and withdrawal may cause immune reconstitution inflammatory syndrome in the hosts that may result in significant morbidity and mortality. There are three types mediators involved in the evolution of TEN/SJS, namely phenotype associated mediators (sFasL, granulysin), severity associated mediators (IL-4, 6, 8, IP-10, TNF-α and resolution associated mediators (IL-10, 12). It is therefore suggested that sFasL and granulysin are useful for predicting disease progression but not disease severity. Pro-inflammatory cytokines IL-6, 8, IP-10 and TNF-α are useful for monitoring disease severity. It is proposed that if proinflammatory cytokines and IP-10 are not elevated despite marked elevation of sFasL and granulysin, these patients should not be treated with immunosuppressive therapy that may increase risk of infections. Instead they should be managed with supportive therapy. However, the speaker also admitted that identifying all the cytokines concerned is not readily available in most centres and treatment is still highly dependent on the clinical condition and experience of the clinicians.

Learning points:

Systemic corticosteroid has been used widely as first line treatment in TEN but infectious complication is the major drawback. IVIg should be avoided in elderly or patients with renal impairment. Pro-inflammatory cytokines IL-6, IL-8, IP-10 and TNF-α seems useful in monitoring disease severity while sFas L and granulysin are useful to predict disease progression.

Atopic dermatitis: does early aggressive therapy change the natural history?

Chair: Omar Lupi da Rosa Santos[1]
Discussant: D Thaçi,[2] L Eichenfield[3]
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Birth cohort longitudinal studies have shown that there are distinct phenotypes in atopic dermatitis (AD) that display different disease trajectories. These can range from early onset-early resolving, early onset-late resolving, early onset-persistent, mid-onset-resolving to late-onset-resolving disease. There is evidence that the development of allergic rhinitis and food allergy correlates with baseline severity of AD. Neuropsychological comorbidities such as attention deficit hyperactivity disorder in younger children may have a "dose-dependent" relationship with severity of AD. Depression and anxiety in teenagers and adults may also have a positive correlation with severity of AD. Early aggressive therapy and long-term disease control of AD will improve the clinical signs and symptoms of these conditions. The course of the disease and some of the comorbidities such as allergic rhino-conjunctivitis, asthma, attention deficit hyperactivity disorder may be improved as well although we still do not know how much the natural history of atopic dermatitis is actually altered. The National Institute of Allergy and Infectious Diseases of the US recommends infants with severe atopic dermatitis, egg allergy or both to have introduction of age-appropriate peanut containing food as early as 4-6 months of age to reduce risk of peanut allergy. Referral to allergist may be required if a serum IgE screen is positive in these infants.

Learning points:

Early aggressive therapy and long term disease control for AD may improves neuropsychological comorbidities, clinical signs and symptoms of AD, as well as allergic rhinoconjunctivitis and asthma. However, how much the natural history of AD is actually altered by treatment is still unknown.