

75th American Academy of Dermatology (AAD) Annual Meeting Conference Review™

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Welcome to this review of the 75th Annual Meeting of the American Academy of Dermatology (AAD).

The meeting brought together dermatologists and healthcare professionals in dermatology-related specialties from around the world. Independent commentary for this review was provided by Associate Professor Anthony Hall, a dermatologist from Geelong, Victoria. I hope you find this conference review interesting and the content useful in your clinical practice.

Kind Regards,

Dr Janette Tenne

Medical Research Advisor

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New and emerging therapies for atopic dermatitis

Author: Cohen D

Summary/Comment: Topical corticosteroids have been the mainstay of treatment of atopic dermatitis since 1% hydrocortisone was introduced in 1952. Recent trials have demonstrated the risk of developing atopic dermatitis may be reduced by the early introduction of regular application of a topical emollient, particularly petrolatum (soft white paraffin or vaseline) applied at least once daily to neonates at high risk for atopic dermatitis within 3 weeks of birth. Advances in non-corticosteroid preparations include topical crisaborole 2% ointment, a PDE-4 inhibitor. When topical crisaborole 2% ointment is applied twice daily studies suggest up to 50% of patients with atopic dermatitis clear within 4 weeks. Patients with severe atopic dermatitis will be greatly helped by new targeted therapies including dupilumab (an IL4 inhibitor) given by subcutaneous injections every 1 to 2 weeks and lebrikizumab (an IL13 inhibitor).

Atopic dermatitis – advances in understanding leading to new treatments

Author: Guttman-Yassky E

Summary/Comment: There has been ongoing debate as to whether atopic dermatitis is caused by a barrier defect (innate immune system) or by abnormalities of the acquired immune system. The discovery of mutations in the filaggrin gene in patients with atopic dermatitis in 2006 led many to believe this was the cause of atopic dermatitis. Advances in understanding of the immunologic basis of psoriasis led to development of targeted (“biologic”) therapies for psoriasis. Atopic dermatitis is now known to be a systemic disease with immune responses similar to psoriasis with increased T-cell activity and circulating cytokine activity. The two most important T-cells are Th2 and Th22. This new understanding of the immune basis of atopic dermatitis resulted in the development of the first targeted therapies for atopic dermatitis. Dupilumab blocks IL4 and is given as weekly injections. Dupilumab reverses the inflammation of atopic dermatitis and corrects the barrier function defect. Dupilumab has a good safety profile but is not yet approved for use by the (US) FDA. Dr Guttman-Yassky concluded atopic dermatitis is a reversible immune disease like psoriasis. “This (dupilumab) is a game-changer and a life-changer”. New trials are underway with lebrikizumab (an IL13 inhibitor) and nemolizumab (an anti-IL31-receptor monoclonal antibody). Another trial has targeted IL22, involved in epidermal hyperplasia and barrier defects. The next question to be addressed is could the “atopic march” (eczema, asthma, hay fever and urticaria) be prevented by immunological manipulation of atopic dermatitis.

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Evolving mechanistic and therapeutic concepts for alopecia areata

Author: Norris D

Summary/Comment: A productive field of research is re-purposing of immunological drugs from other auto-immune diseases. There are case reports of success with new drugs in different immunological skin diseases, such as alopecia areata. The specificity of immune response in alopecia areata is not completely known but alopecia areata is driven by cytotoxic T-cells. Pigmented anagen hair follicles appear to be targeted. Janus kinase (JAK) inhibitors have been shown to block T-cell function without killing T-cells, leading to blunting of their effect. Some JAK-inhibitors (e.g. ruxolitinib) have shown efficacy in alopecia areata and show promise for the future.

New and emerging therapies in infections of the skin

Author: Rosen T

Summary/Comment: Professor Rosen provided an extensive update on infectious diseases including a discussion on arboviruses. Zika virus results in asymptomatic infection in 80% of people. Symptomatic disease includes fever and a non-specific cutaneous eruption. Important complications include microcephaly and miscarriage. Death has been reported in some infected individuals. The persistence of virus detectable in semen for up to 6 months after exposure means infected individuals need to avoid sexual contact for this period. Strategies to control the Zika epidemic include genetically modified mosquitoes using sterile male mosquitoes. Treatments under trial include daptomycin, an antibiotic successfully used for methicillin-resistant staphylococcus aureus (MRSA) infections.

An Ebola vaccine has been shown to be 100% successful in trials while the Dengue fever vaccine has not proven successful. The new nano-valent HPV vaccine (Gardasil 9) will provide wider coverage against HPV types. Newer treatments for external genital warts include ranpirinase that degrades DNA, a nitric oxide topical gel and (off label use) of ingenol mebutate that is proving effective with one application. The HPV quadrivalent vaccine has been shown to be effective treatment for recalcitrant palmar or plantar warts in children. Intralesional purified protein derivative has been reported from India as a treatment for recalcitrant extra-genital warts.

HIV self-testing is now available, as a blood test or oral swab. The likelihood of developing HIV infection has been shown to be very significantly reduced by use of pre-and post-exposure prophylaxis with anti-retroviral drugs.

Resistance to the topical antibiotic bactroban is increasing. A new topical antibiotic ozenoxacin 1% cream may be useful for superficial skin infections.

Most STDs are on the rise in the US, including syphilis. Bicillin (an effective treatment for syphilis) is becoming harder to obtain. A Chinese study demonstrated minocycline 100 mg taken twice daily for 28 days for syphilis to be superior to bicillin.

Topical ivermectin was effective for treatment of scabies in an Egyptian trial and may prove an alternative treatment to topical permethrin or oral ivermectin. Topical 1% ivermectin cream available for treatment of rosacea could be utilized as a treatment option for scabies applied to the whole body but would be very expensive.

Advances in understanding of pruritus

Author: Yosipovitch G

Summary/Comment: Valuable advice was offered to help manage patients who present with itch. If a patient complains of itchy palms without rash, consider primary biliary cirrhosis or cholestasis. If lichen simplex chronicus of extensor aspects of forearms, think of brachio-radial pruritus. Cervical canal stenosis (C4-C7) may be an underlying cause. In peri-nasal itch without visible skin change consider trigeminal trophic syndrome or narcotic use. In an adult with new onset of widespread itch but no history of atopy, think of possible lymphoma.

Newer developments for treatment of itch have heralded the "end of the oral anti-histamines era". Newer topical anti-itch treatments include topical pramoxine for facial or genital itch, strontium 4% gel and topical ketamine 2.5-5% alone or combined with amitriptyline 5% gel. Topical ketamine 5-10% can be combined with amitriptyline 5% and lidocaine 5% in a lipoderm base. Possible local adverse effects include burning, redness, allergic contact dermatitis, itch (itself) and dizziness. Systemic drugs that target itch include gabapentin and pregabalin. Side effects of gabapentin and pregabalin include drowsiness, increased appetite, leg swelling and constipation. Mirtazapine is another alternative with potential side effects including drowsiness and increased appetite. Butorphanol analgesic inhaler (kappa opioid) is approved for acute pain and may be used for itch. New biologic agents for chronic itch include dupilumab, omalizumab, TNF-inhibitors and secukinumab. Finally the concept of "stress to itch" was raised. Itch may benefit from the simple technique of progressive muscle relaxation, requiring only a brief 5 minutes of exercise daily.

Vitiligo pearls

Author: Desai S

Summary/Comment: Vitiligo may be classified into acute-progressive (increase in depigmentation of 2% body surface area per month), stable (no depigmentation over at least 12 months) and refractory or resistant vitiligo. Stabilizing vitiligo can be achieved by oral mini-pulse (OMP) therapy using dexamethasone 4 mg daily on 2 consecutive days per week (often weekends) and continuing for a few weeks. For children, a half dose of dexamethasone should be used. It is important to warn of potential adverse events but OMP therapy with dexamethasone results in less HPA suppression. An alternate to OMP therapy is intramuscular triamcinolone 60 mg monthly for 3 months and then transitioning to OMP. Consider supplemental vitamin D. Anti-oxidants such as alpha-lipoic acid 100 mg daily can be added to NB-UVB treatment for vitiligo and enhance re-pigmentation. Polypodium leucotomos (an anti-oxidant) may help in re-pigmentation of vitiligo. Topical tacrolimus may be combined with NB-UVB. Tacrolimus 0.03% on the face and tacrolimus 1% for the body are safe. Cryotherapy may help with re-pigmentation of vitiligo. Treatment of trichromate vitiligo may be enhanced by early use of UVB combined with intra-lesional triamcinolone at the periphery. Finally JAK inhibitors may be of hope for future treatment of vitiligo.

Independent commentary by Associate Professor Anthony Hall

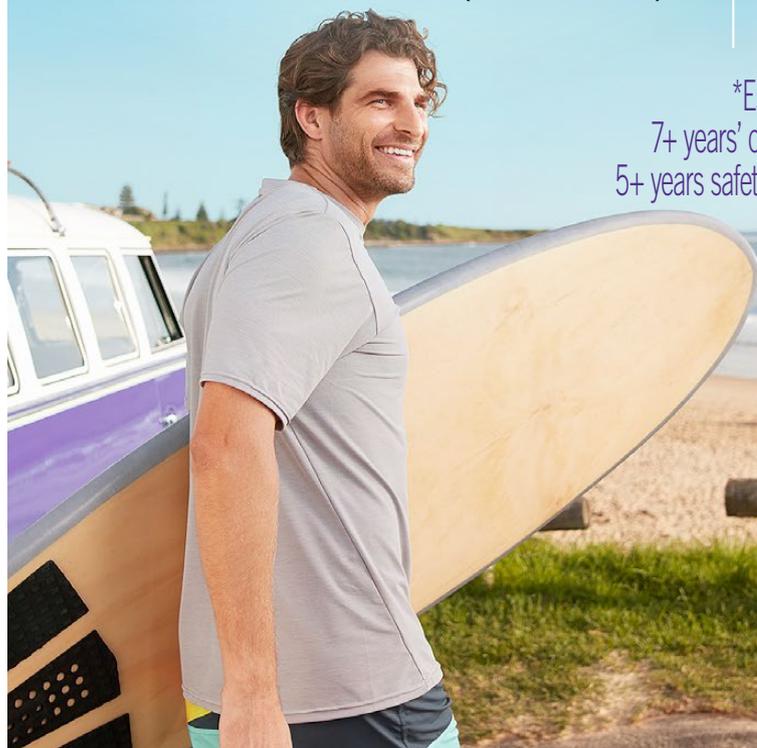
Tony is currently in full-time clinical dermatology practice in Geelong. After graduating from Monash University he completed the Fellowship with Royal Australian College of General Practitioners and worked full-time in general medical practice. After 14 years in general practice Tony was appointed to the dermatology program of the Australasian College of Dermatologists to pursue his love of skin disease. After completing dermatology training in 2002 he spent time working at the Vienna General Hospital before commencing full-time dermatology practice in Geelong. His special interests include genital dermatology and medical teaching. Current appointments include dermatologist to the Male Genital Dermatology Clinic at the Skin and Cancer Foundation (Inc) and Associate Professor, School of Medicine, Deakin University. More recently Tony has begun visits to the Solomon Islands to help treat dermatology patients. Outside of medicine he is an amateur naturalist with a keen interest in volcanology while playing tennis and golf poorly.





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*Estimated 777,000+ patient-years of cumulative exposure from 7+ years' clinical use.^{1,2} In psoriasis: 5 years PASI 75/90 response data,^{1,3} 5+ years safety observations,^{1,3-5} 4 times a year dosing (after 2 initial doses).¹



PBS Information: Authority Required. Refer to the PBS Schedule for full details.

Please refer to the Product Information before prescribing (available from http://www.janssen.com.au/Stelara_PI)

PASI: Psoriasis Area and Severity Index. **STELARA® ustekinumab (rnc) vials MINIMUM PRODUCT INFORMATION (Plaque psoriasis, psoriatic arthritis, *Crohn's disease) INDICATIONS:** Moderate to severe plaque psoriasis in adults who are candidates for photo- or systemic therapy; signs and symptoms of active psoriatic arthritis in adults where response to previous non-biological DMARD therapy has been inadequate; *moderately to severely active Crohn's disease in adults who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a TNF α antagonist or have medical contraindications to such therapies. **DOSE:** **Psoriasis:** Subcutaneous injection. 45 mg at Weeks 0 and 4, then every 12 weeks. Alternatively, in patients weighing >100 kg, 90 mg at Weeks 0 and 4, then every 12 weeks. If inadequate response, consider treatment every 8 weeks. Discontinue if no response after 28 weeks. **Psoriatic Arthritis:** Subcutaneous injection. 45 mg at Weeks 0 and 4, then every 12 weeks. Some patients weighing >100kg received a 90mg dose in clinical trials and observed a clinical benefit. Discontinue if no response after 28 weeks. ***Crohn's Disease:** Single initial intravenous tiered dose based on body weight using STELARA 130 mg vial (weight \leq 55kg = 260 mg [2 vials]; weight > 55kg to \leq 85 kg = 390 mg [3 vials]; weight > 85 kg = 520 mg [4 vials]). Then subcutaneous injection. 90 mg 8 weeks after the intravenous dose, then every 8 weeks. In some patients a subcutaneous dose of 90 mg 8 weeks after the intravenous dose, then every 12 weeks may be acceptable according to clinical judgment. Consider discontinuing if no evidence of benefit by Week 16. **CONTRAINDICATIONS:** Severe hypersensitivity to ustekinumab or to any of the excipients. Do not administer to patients with a clinically important active infection. **PRECAUTIONS: Serious infections:** STELARA may increase risk of infections and reactivate latent infections. Serious bacterial, fungal and viral infections have been observed. Use with caution in patients with chronic or recurrent infections. **Tuberculosis (TB):** Evaluate for TB prior to initiating treatment. Do not administer to patients with active TB. Treat latent TB before administration. Consider anti-TB therapy in patients with suspected TB. Monitor patients for TB. **Malignancies:** STELARA may increase risk of malignancies. Malignancies have been observed. Use with caution in patients with known malignancy or history of malignancies. Patients should be monitored for the appearance of non-melanoma skin cancer. **Hypersensitivity reactions:** Discontinue immediately if serious hypersensitivity reactions including anaphylaxis and angioedema occurs. **Immunisations:** Do not give live bacterial or viral vaccines. Consider secondary transmission of live vaccines from contacts. **Immunosuppression:** STELARA should not be used in combination with photo- or systemic therapy. **Immunotherapy:** Use with caution in patients receiving allergy immunotherapy. **Reversible Posterior Leukoencephalopathy Syndrome (RPLS):** If RPLS is suspected, STELARA should be discontinued and appropriate therapy instituted. **Serious Skin Conditions:** Physicians should be alert for symptoms of erythrodermic psoriasis or exfoliative dermatitis. STELARA should be discontinued if a drug reaction is suspected. **Use in Pregnancy:** Category B1. **ADVERSE EFFECTS:** Serious: serious infections and malignancies. Common: URTIs, nasopharyngitis, dizziness, headache, *oropharyngeal pain, diarrhoea, nausea, *vomiting, pruritus, back pain, myalgia, arthralgia, fatigue, injection site erythema, injection site pain. See full PI for other adverse effects. Adverse events: serious cardiovascular events, suicidality, hypersensitivity (including rash, urticaria), serious hypersensitivity reactions including anaphylaxis and angioedema. **PRESENTATION:** Pack of 1 single use 45 mg vial for subcutaneous use, and *pack of 1 single use vial for intravenous use (Crohn's disease only). Store at 2°C – 8°C. Refrigerate. Do not freeze or shake. Protect from light by storing in original carton. **Date of preparation:** 8 March 2017

*Please note changes to Product Information as **italicised text*

REFERENCES: 1. STELARA (ustekinumab) Approved Product Information 28 February 2017. 2. Janssen data on file. 3. Kimball AB et al. J Eur Acad Dermatol Venerol 2013;27:1535-1545. 4. Langley RG et al. Br J Dermatol 2015;172:1371-1383. 5. Papp KA et al. Br J Dermatol 2013;168:844-854. © Janssen-Cilag Pty Ltd 2017. Trademarks and brand names are the property of Johnson & Johnson, its affiliates or third party owners. Janssen Cilag Pty Ltd, ABN 47 000 129 975. 1-5 Kharoum Road, Macquarie Park NSW 2113. Phone: 1800 226 334. Date of preparation: April 2017. MKT-STE-AU-0137 JANS1868/EMBC



Unmasking facial pigmentation

Author: Rodrigues M

Summary/Comment: A comprehensive approach to facial pigmentation was discussed, based on history taking and examination. Important aspects of history include age of onset, whether other sites are affected, if there is a preceding inflammatory process (suggestive of post-inflammatory hyperpigmentation), current treatments used and sunscreen usage. Both distribution of hyperpigmentation and whether hyperpigmentation is brown or blue-grey are important. Melasma is central facial hyperpigmentation that spares eyelids, nose tip, nasolabial folds and photo-protected sites such as below earlobes. The aetiology of melasma is unknown but both genetic and environmental factors (hormonal, UV light and visible light) are important.

Lichen planus pigmentosa occurs in the third to fourth decade, and is predominantly seen in Indian and Middle Eastern people. Itch may be a feature. Skin biopsy is useful to confirm diagnosis. Erythema dyschromicum perstans is seen in intermediate skin type people mostly from South America. The cause of acquired dermal melanosis is widely debated. Naevus of Ota may appear in infancy or at puberty, mostly in people of Asian or African descent. Naevus of Ota involves the first or second division of the fifth nerve (V1-V2) and mucosae may be involved. Hori's naevus is seen in Asians over 20 years of age, mostly involving zygoma with no mucosal involvement. Minocycline-induced pigmentation can occur at any age and diagnosis is based on history. Drug-induced hyperpigmentation may also be caused by amlodipine and hydroquinone. A history of recurrent annular plaques at the same sites in patients on certain medications (e.g. NSAIDs) is key to diagnosis of fixed drug eruption. Mucosal involvement is common. Exogenous ochronosis is rare, occurring mostly with unsupervised prolonged use of higher concentrations of hydroquinone (> 4%). Maturation dyschromia occurs in middle aged Indians and Sri Lankans involving the forehead and cheekbones. Maturation dyschromia may be a variant of acanthosis nigricans and may indicate early insulin resistance. Treatment principles for facial pigmentation are based on correct diagnosis, eliminating triggers, use of photo-protection including visible light exposure and cosmetic camouflage. Hydroquinone is gold standard for active treatment, showing a response within 6 weeks and can safely be used for 6 months. Hydroquinone may be used in combination (e.g. triple therapy of 5% hydroquinone, 0.1% tretinoin, 0.1% dexamethasone). Topical retinoids require prolonged use beyond 6 months. Other topical therapies include ascorbic acid and kojic acid. Use of lasers in post-inflammatory hyperpigmentation, melasma and Hori's naevus was discussed. New treatments include tranexamic acid (only available as a systemic agent) proving useful for melasma with minimal reversible adverse reactions. Repeated shorter courses may be necessary.

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Dealing with difficult patient encounters

Author: Prose N

Summary/Comment: Five clinicians presented insights into different strategies for dealing with difficult patient encounters. Dr Neil Prose offered his advice, emphasizing that the "ideal" patient encounter starts before entering the consulting room. He observed that doctors are infinitely distractible, a trait carried into the consulting room. Take a deep breath before entering the consulting room and make a conscious effort to concentrate. Imagine each patient is your favourite patient. Sit down with your patient as this gives the perception of a longer consultation. Even on wards sit down on your patient's bed. Turn away from your computer and listen. Make eye contact by turning your whole body towards your patient. It is important to point your knees in the direction of your patient, rather than simply rotating your head to face your patient. The first question should be "Tell me how you are getting on (since last seen)" or "What bothers you?" If you want to interrupt your patient, ask permission to interrupt. Dr Prose feels all doctors are "explain-oholics" so ask permission to explain what you think is the "cause" of your patient's concern. Summarizing the story back to your patient demonstrates that you were listening. Acknowledge your patient's frustration with treatments (e.g. "I will talk about side effects of isotretinoin and then we will make a decision together"). End the consultation with "what questions do you have? (Rather than "do you have any questions?"). The patient then has the vote to end the consultation.

Surgical tips

Author: Siegel D

Summary/Comment: Dan Siegel described himself as the son of a plumber and offered many effective and cost-saving tips for dermatologic surgery, sometimes utilizing materials from a hardware store. If taking a skin biopsy from a patient with multiple risk factors for bleeding, insert a deep needle below the planned biopsy site and, leaving the deep needle in situ, insert a biopsy punch down to the deep underlying needle. After removing the skin biopsy, tighten the underlying suture, to achieve a bloodless biopsy. Inexpensive stainless steel rings (from a hardware store) can be applied to a wound site for compression if a bleeder is encountered. This facilitates a bloodless field and allows time to control a bleeding vessel. Many chemical haemostatic agents as alternatives to suturing were discussed. "Wound seal powder" is useful for granulating wound sites (cheaper than suture material), "wound clot" (gauze dressing), "Celox" (a prawn derivative) and "Arista" (a potato extract that has become more expensive) were all suggested as haemostatic agents. Skin closure of wounds can be achieved using 5-0 or 6-0 plain catgut covering the wound with gentian violet and left for 7 to 10 days. Gentian violet (crystal violet) is cheap and useful with a low risk of adverse reactions apart from temporary stinging. Running sutures are faster to apply but don't strangle tissues. Monocril sutures are more expensive but can also be used as buried sutures. Manuka honey is expensive whereas common honey (the thicker the better) is equally as effective. Lava soap (powdered pumice) is effective for paring warts. As silicone gel is very expensive, use of commercial silicone (from a hardware store) was suggested. Using a commercial silicone gel gun, squeeze silicone into a zip-lock pack and make flat sheets of silicone over-night to be used next day. Finally always have available cheap head loupes for lighting that can be used in a power failure.

Volunteers abroad

Summary/Comment: A broad overview of medical volunteering was presented by a panel of dermatologists and dermatopathologists, all involved in medical volunteering. Before embarking on medical volunteering issues to be considered include framework, statement of purpose, partnership with local health workers, site selection, assessment of social value of the work and finally outcomes review. Assess ethics of medical volunteering. Consider the ethical rationale for global health and whether equity is sustainable. The question as to whether medical volunteering is always good was raised. An experienced volunteer dermatological surgeon stressed the importance of making needs assessment for surgery, a plan for dermatological surgery and finally a plan for prevention. One experienced volunteer felt the biggest challenge was to look a patient in the face and say "No, I cannot help you". It is important to visit and introduce oneself to local pharmacists and assess medications available. Training local doctors in dermatopathology is important. In Vietnam, a digital pathology service has been established where digitalized histopathology slides can be viewed live in Texas (teledermatopathology). The limiting factor is expense of digital scanners (US\$50,000 to \$100,000). One experienced medical volunteer stated unashamedly that the greatest benefit of volunteer medical work is personal – in taking two sons (now in their teens) with him on visits to Yucatán Peninsula in Mexico. "It has made them fine young men with a conscience".

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