ACD 50th Annual Scientific Meeting Conference Review™

Making Education Easy

6-9th May 2017, Sydney, Australia

In this review:

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Welcome to our review of the 50th Annual Scientific Meeting of the Australasian College of Dermatologists (ACD), held in Sydney in May 2017.

The meeting was well attended and offered an excellent opportunity to update knowledge and renew acquaintances. The 10-minute update format of much of this year's meeting meant that a lot of dermatology was covered over 4 days. A/Prof Amanda Oakley (Hamilton, NZ) and Dr Warren Weightman (Adelaide, Australia) attended the meeting and found the following sessions to be particularly interesting. More information about the meeting can be found online at http://www.acdasm2017.com/program-at-a-glance/.

I hope you find the Conference Review interesting and I look forward to your feedback.

Dr Chris Tofield

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Nevogenesis: insights gained from dermoscopy

Presenter: Dr Ash Marghoob (New York, USA)

Summary and comment (AO): Dr Marghoob told us how the finding of small brown dots on dermoscopy of normal skin had led to the discovery of small naevus-cell nests on histology. Nearly all of these cells carry BRAFv600E mutations and are thought to be the origin of Clark naevi (dysplastic naevi). Dr Marghoob pointed out that Unna's theory (1893) that naevus cells drop down from the epidermis and Cramer's theory (1984) that they climb up nerve fibres do not fit with the evidence. Molecular genetic studies have found distinct subsets of naevi characterised by presence of P16 (dysplastic naevi), HRAS (Spitz naevi) and NRAS (congenital melanocytic naevi) among others. These correspond with dermatoscopic variations in pattern. The symmetrical growth of a dysplastic naevus is predictably associated with peripheral globules on dermoscopy. It ends up 4 or 5 years later as a reticular or homogeneous naevus as it enters clinical senescence. The starburst pattern of growth in the Reed naevus is also symmetrical, and it too eventually becomes homogeneous and stops growing. On the other hand, a melanoma grows asymmetrically with or without peripheral globules, and does not enter a senescent phase. Dr Marghoob described how naevi involute. A childhood globular naevus becomes homogeneous in adult life and gradually shrinks and fades over decades, disappearing by the age of 60 years. The halo form of involution of a globular or homogeneous naevus is quicker, taking 8 years to return to normal skin over a period of 8 years. A halo around any other dermoscopic pattern may indicate melanoma. Grey peppering is due to melanophages and also indicates involution. An uncommon form of involution in acral naevi involves transepidermal elimination via pagetoid spread.

ACD 50th Annual Scientific Meeting 2017. Plenary session 1; May 6

Independent commentary by Associate Professor Amanda Oakley

Associate Professor Oakley is a specialist dermatologist at Waikato Hospital and is an Adjunct Associate Professor at Waikato Clinical Campus (Auckland University School of Medicine). **For full bio CLICK HERE**.

Independent commentary by Dr Warren Weightman

Dr Warren Weightman has practiced Dermatology for over 25 years and is currently Head of the Department of Dermatology at the Queen Elizabeth Hospital, Adelaide and a Senior Lecturer with Adelaide University. **For full bio CLICK HERE**.

Benefits of leveraging technology towards melanoma detection

Presenter: Dr Marghoob (New York, USA)

Summary and comment (AO): The world of technology for melanoma detection is very exciting. Early detection is essential; despite the increasing efficacy of new drugs to treat advanced melanoma, we can't afford them. Currently, we train physicians to spot ugly ducklings and watch out for new changing naevi in patients with multiple and/or atypical naevi. Dermoscopy training, total body photography and digital dermatoscopic surveillance has led to sensitivity and specificity gains, a reduction in the number needed to treat (NNT), reduced benign to malignant ratios, and the excision of thinner tumours. Dr Marghoob described the latest technology for whole body scanning in which multiple cameras coupled with sophisticated software can detect new and changed lesions and distinguish naevi from seborrhoeic keratoses. But less than 3% of changing naevi are melanoma. Until now, a human armed with a dermatoscope has been required to choose lesions for excision – but in the best centres NNT remains 4 to 7 and it's a time consuming process. A few researchers armed with confocal microscopy, optical coherence tomography, electrical impedance and molecular tests have claimed to reduce NNT further. In February 2017, a remarkable paper published in *Nature* described how computers have been reported to equal or better the experts in melanoma diagnosis when provided with macroscopic photographs of skin lesions. This may change everything. To improve the results further, international collaboration and big data are required, i.e. literally millions of images of skin cancers and every other skin spot. The future of artificial intelligence (AI) is intelligence augmentation (IA) for the clinician.

ACD 50th Annual Scientific Meeting 2017. Registrars and Fellow update session 1; May 6

Update on the use of topical and oral sirolimus in paediatric dermatology

Presenter: Dr Anne Halbert (Nedlands, Western Australia)

Summary and comment (AO): Dr Halbert described rapid response of early, small angiofibromas and hypopigmented "ash leaf" macules in tuberous sclerosis to treatment with 0.003–1% sirolimus cream or ointment. Crushed sirolimus tablets or powder can be used to make 50g of 0.1% ointment for about $AU60. Dr Halbert told us that 0.1% sirolimus in petrolatum dramatically reduced nosebleeds and requirement for iron transfusions in a patient with hereditary haemorrhagic telangiectasia. Topical sirolimus has not been shown to be very effective in vascular malformations but multiple publications attest to the efficacy of oral sirolimus in vascular malformations. There is a long list of side effects associated with oral sirolimus, but it can be considered in Kasabach-Merritt syndrome (after using corticosteroids), lymphatic malformations if sclerotherapy is ineffective, venous malformations, and in complicated proliferative infantile haemangiomas unresponsive to propranolol.

ACD 50th Annual Scientific Meeting 2017. Paediatric Dermatology; May 8

Livedo racemosa: the relationship between lymphocytic and neutrophilic vasculitis

Presenter: Dr Robert Kelly (Melbourne, Australia)

Summary and comment (WW): Livedo racemosa always indicates underlying pathology as opposed to livedo reticularis, which is often a physiological response. In Dr Kelly's case series of 16 patients, lymphocytic thrombotic arteritis (LTA) involving small to medium arteries was associated with livedo racemosa when it had a widespread distribution. However, when it had a localised distribution a neutrophilic vasculitis consistent with cutaneous polyarteritis was found. It is important to make this distinction, as LTA is benign and has no significant systemic involvement although one case had peripheral neuropathy and another had testicular infarction. LTA is chronic, indolent, less destructive and less amenable to immunosuppressive therapy but responds to aspirin and pentoxifylline. This response is similar in livedoid vasculitis which is a related disorder but affecting small vessels.

ACD 50th Annual Scientific Meeting 2017. Plenary session 2; May 7

The role of inflammation in epidermolysis bullosa, its contribution to carcinogenesis and other complications and novel anti-inflammatory therapies

Presenter: Prof Dedee Murrell (Sydney, Australia)

Summary: A number of specific targeted therapies (gene, protein and cell) are underway in trials or preclinical work for certain types of epidermolysis bullosa (EB), but another approach is to target the inflammation. The anti-inflammatory agents doxycycline and minocycline have been used *ad hoc* in reducing inflammation in EB, and trimethoprim has been shown to reduce inflammation by reducing bacterial load. Colchicine and thalidomide have also shown promise in cases with junctional EB. A number of randomised controlled trials are underway for new topical anti-inflammatory agents for EB.

Comment (AO): Dr Murrell has been involved in research and the care of children and adults with EB for many years. There are several genetically distinct types of EB, in which protein abnormalities contribute to separation of the epidermis from the dermis. Dr Murrell told us about presentation and complications of severe forms of EB, such as junctional EB, in which laminin is missing from the basement membrane. Cutaneous and mucosal surfaces are involved resulting in contractures/stenosis and nutritional deficiencies that eventually lead to an early death. To reduce the suffering of EB patients, she recommends bathing in saline/diluted bleach and applying dressings while moist to reduce pain and secondary infection. Bathing regimens may take up to 2 hours each day. Children with more severe forms of epidermolysis bullosa have persisting inflammation associated with painful erosions without fever, exudate or finding organisms. It can be difficult for the patients and their clinicians to identify cutaneous infection, when antibiotics are indicated. Persistent ulceration in dystrophic EB – in which there is loss of collagen 7 – may lead to pseudosyndactyly and squamous cell cancer (SCC) at a young age – and constant vigilance is required to identify these early. The inflammatory cascade involves metalloproteinase expression, and can be reduced by gentian violet topically and tetracyclines/colchicine orally. Dr Murrell questioned whether reducing inflammation could lead to reducing the incidence of SCC. Topical treatments under evaluation in EB include allantoin cream, oleogel (derived from birch bark tree), diacerein (derived from rhubarb root) and sirolimus.

ACD 50th Annual Scientific Meeting 2017. Oral Presentations; May 10
Abstract

Stress induced epigenetic remodelling as a mechanism of adaptive resistance in melanoma

Presenter: A/Prof Helmut Schaider (Brisbane, Australia)

Summary: One of the most important mechanisms leading to acquired drug resistance in cancer patients is the acquisition of genetic mutations leading to heterogeneity and growth advantage. The transition from a drug-sensitive to a drug-tolerant state is characterised by an epigenetically-driven distinct H3K4me3 slow cycling growth-arrested reversible drug tolerant state in cancer cells that precedes permanent resistance. Identifying and targeting the drivers of this epigenetically-forced transition will prevent permanent resistance and facilitate sustained remission in melanoma patients.

Comment (AO): Helmut Schaider described how targeted drugs have led to dramatic extension in survival (yet not to cure) in many patients with advanced melanoma, due to the adaptation of the tumour to treatment. The example was given of a patient with numerous cutaneous metastases that completely resolved within days of commencing vemurafenib, only for them to recur in the same sites a few months later. Response is better with combinations of BRAF and MEK inhibitors (and there are fewer side effects). However, in patients that showed early partial or complete response, relapse is detectable at about 45 days, and clinically obvious at about 90 days. Several groups are investigating methods to avoid this acquired adaptive response, which includes development of new tumour gene mutations, activation of different pathways, changes to the microenvironment of the tumour and dysfunctional apoptosis. A marker called H3K4me3 appears to be driving this process. We heard that research has shown that inhibitor drug tolerant colonies (IDTC) are selected out by treatment, and if they can be eliminated at a very early stage (e.g. before 45 days when the cell cycle of IDTC is slow), resistance might be reversible. Researchers have postulated that early drug holidays or intermittent courses of treatment may reduce IDTC escape. Survival appears better if programmed death (PD)-1 inhibitors are added, but the mechanism for this is unclear. PD-1 inhibitors often lead to autoimmune diseases, including skin diseases in 35% of treated patients.

ACD 50th Annual Scientific Meeting 2017. Oral Presentations; May 10
Abstract

Pathomechanism of severe adverse drug reaction

Presenter: Riichiro Abe (Hokkaido, Japan)

Summary: Although high-dose corticosteroids, intravenous immunoglobulin and plasmapheresis have been used in the treatment of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), the mortality rate is still high. Dr Abe reported that keratinocyte death in SJS/TEN can be triggered by the interaction of annexin A1 and formyl peptide receptor (FPR)-1. Annexin acts on FPR-1, located on the surface of the skin cells, to cause necroptosis, a programed form of cell death. Research into the development of an FPR-1 antagonist is currently underway.

Comment (AO): Dr Abe reminded us that SJS and TEN are now classified together (SJS/TEN): TEN has more extensive skin loss (>30%) and mortality (25%) than overlap SJS/TEN (10–30%) or SJS (<10%). Histology shows death of keratinocytes. The mechanism of cell death is independent of the cause of the reaction (which is usually a drug). The process involves antigen presenting cells, peripheral blood monocytes (PBMC), cytotoxic CD8+ T cells, perforin, granzyme B and natural killer cells. Researchers have discovered that PBMC carry a soluble anti-drug factor to the keratinocytes. Supernatant of PBMC from patients with a history of SJS/TEN kills keratinocytes from SJS/TEN patients *in vitro*, whereas supernatant of PBMC from a control does not, indicating the keratinocytes are specifically sensitised to the drug. This mechanism is independent of caspase, which is a component of the apoptosis pathway, therefore death of keratinocytes is not due to apoptosis. Instead, it is an inflammatory, programmed death pathway called necroptosis and involves tumour necrosis factor, annexin A1, and FPR-1. Anti-FPR-1 drugs are being sought.

ACD 50th Annual Scientific Meeting 2017. Oral Presentations; May 10
Abstract

Update on hidradenitis suppurativa

Presenter: Dr Erin McMeniman (Brisbane, Australia)

Summary and comment (WW): Hidradenitis suppurativa remains a difficult disease with the pathogenesis not completely understood and treatment options not always effective. There are 3 main types including the classical axillary/groin and inframammary type as well as a follicular type resembling acne and a gluteal type where the patients are less likely to be obese and Crohn's disease needs to be excluded. The role of inflammatory mediators is becoming better understood with interleukin (IL)-1 and IL-17 playing important roles which may lead to newer biologic treatments. IL-6 has been associated with a worse prognosis and a gamma secretase mutation has been found to be a cause in some patients. Assessment of these patients includes looking for obesity, metabolic syndrome and smoking as well as checking for arthritis and enthesitis, chronic lymphoedema, and anaemia. A biopsy should be done to exclude Crohn's disease. With regard to treatment, zinc gluconate 90 mg/day may be worthwhile as an adjunct to other treatments. Resorcinol 15% in aqueous cream twice daily to flaring nodules can be helpful. In Dr McMeniman's institution the use of rifampicin has been banned due to concern about increasing resistance to tuberculosis so the clindamycin/rifampicin combination can't be used. Adalimumab has a 60% benefit and there may be other biologics available in the future. A video of deroofing and healing by secondary healing was shown which looked to be a simple procedure with reasonable cosmetic results.

ACD 50th Annual Scientific Meeting 2017. Registrars and Fellow update session 1; May 6

Acne session

Chair: Dr Jo-Ann See (Sydney, Australia)

Summary and comment (WW): The acne breakfast session discussed various aspects of acne. Jill Cargnello spoke on hormonal acne which is more common in older women. Her favourite drug is spironolactone which at doses of 50–100 mg/day is effective with few side effects. There is no need to measure potassium levels unless the patient is older and on other treatments. The 3rd and 4th generation oral contraceptive pills have antiandrogenic properties and are preferred but carry an increased risk of thrombosis. We were reassured by Marius Rademaker that isotretinoin can be started at birth and continued until death. Jo-Ann See discussed a new nitric oxide gel and 2 new sebum reducers for the treatment of acne which show promise and are on the horizon. Professor R. Paus discussed the biology of the pilosebaceous unit. The sebaceous gland is one of the major sites of steroid synthesis and metabolism in the body and is a target of neurotransmitters and neuropeptides. It produces adipokine, has a role in skin ageing and wound healing and harbours immunocytes. The opening of the sebaceous gland duct is the acne hotspot rather than the gland itself.

ACD 50th Annual Scientific Meeting 2017. Acne session; May 7

Psoriasis symposium

Chair: Dr John Sullivan (Sydney, Australia)

Summary and comment (WW): The Australasian Psoriasis Collaborative presented 3 talks on psoriasis. These talks gave practical and evidence-backed advice in the management of psoriasis. Marius Rademaker gave the first talk on methotrexate in psoriasis. The main points were that liver function tests only need to be done every 3–6 months after the initial period. The best test to predict risk of liver irritation is body mass index and abdominal girth rather than a liver function test. A test dose is of little value and above a dose of 25mg it is best to split the dose. Methotrexate has a short half-life unless polyglutamated which takes 5–6 months which is when the maximal effect is seen. Tests for infections such as tuberculosis and hepatitis (as is done for biologic treatment) are worthwhile doing at screening. The second talk was given by Diana Rubel regarding malignancy in psoriasis. The main risk factor for malignancy is related to the comorbidities. Haematologic malignancy (mainly non-Hodgkin lymphoma and especially T-cell lymphoma), solid organ, and non-melanoma skin cancer were increased but not melanoma. There is an inherent increased risk of malignancy in psoriatic patients. There should be age-appropriate cancer screening. A previous cancer is not a contraindication to starting biologics. The third talk was by Meagan Andrews who spoke about psoriasis in those planning a family, pregnancy or breastfeeding. There are fewer births in patients with psoriasis but no increase in birth defects. Two-thirds improve during pregnancy but it is worse in 25% and there is a post-partum flare in 65%. If one parent has psoriasis there is a 16% chance of the child developing psoriasis but if 2 parents are affected the risk increases to 50%. Folic acid is recommended if planning a pregnancy, as levels are low if UVB or methotrexate has been given recently. The biologics are being prescribed more frequently by rheumatologists and gastroenterologists due to the greater risk of complications if they are ceased and the underlying disease flares and are not showing significant safety signals in pregnancy. Stopping biologics in the third trimester should be considered to reduce the risk of immunosuppression of the newborn.

ACD 50th Annual Scientific Meeting 2017. Psoriasis symposium; May 7

Genital dermatology session

Chairs: Dr Catherine Drummond (Canberra, Australia) and Dr Ian McCrossin (Nowra, Australia)

Summary and comment (WW): Dr Deen started the session with a discussion on the use of imiquimod for penile intraepithelial neoplasia. The drug had a complete response of 63% in treating penile intraepithelial neoplasia. The average duration of treatment was 40 days with 5 days a week application but less frequent applications and longer overall duration gave better results. Dr Dawes-Higgs informed us that low and high grade squamous intraepithelial neoplasia (LSIL and HSIL) are the new terminology for vulval intraepithelial neoplasia (VIN). Low grade refers to flat condyloma or human papilloma virus infection, with HSIL corresponding to the old terms of VIN 2 and 3. Dr Nguyen discussed the risk of chronic vulvovaginal candidiasis in past or present users of levonorgestrel-releasing intrauterine systems, and recommended treatment with fluconazole 50–100mg daily for 12 weeks. A/Prof Hall and A/Prof Fischer discussed female and male genital dermatology. In females with lichen sclerosus, 50% will develop scarring and 5% will get cancer. However, this doesn't occur if treated. Topical corticosteroid usage should be titrated to disease severity; long term management with topical corticosteroids is safe. In males the aetiology of lichen sclerosus is unknown. One theory is that it is due to urinary incontinence and chronic urine occlusion but this is not proven. There is a negative association with autoimmune disease in men but an association with hypertension, higher body mass index and metabolic syndrome. Circumcision has limited efficacy as two-thirds have ongoing lichen sclerosus after circumcision. 25% of patients go into complete remission. The red burning scrotum has normal investigations, and computed tomography scans or magnetic resonance imaging are not indicated. It is a difficult disorder to treat but usually responds well to treatment with low dose tricyclics (antidepressants). Other medications that can be tried include gabapentin, selective serotonin reuptake inhibitors. Topical calcineurin and topical lignocaine are other therapeutic options

ACD 50th Annual Scientific Meeting 2017. Genital Dermatology session; May 8