## European Academy of Dermatology and Venereology Conference Review

#### Making Education Easy

#### 6-10 October 2010, Gothenburg, Sweden

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## **Welcome** to our review of the 19<sup>th</sup> Congress of the European Academy of Dermatology and Venereology (EADV) – a locally focused summary of some of the latest and most exciting developments in dermatological and venereological research presented at the congress.

This Review has been created to allow those unable to attend, but with a keen professional interest, to access a summary of significant presentations made that are likely to affect current practice. Selection and review of the research has been carried out independently by Associate Professor Peter Foley, a dermatologist with the Skin and Cancer Foundation, who attended the congress in Gothenburg, Sweden during October 2010.

I hope you find this conference review stimulating, and I look forward to your feedback.

Kind Regards

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#### EADV Gothenburg 2010 report

The International Psoriasis Council presented a Meet the Experts session, chaired by Prof Wolfram Sterry from University Hospital Charite in Berlin. This was a case-based learning forum on difficult-to-treat psoriasis patients held in a room with a capacity of 72, but containing at least 200 delegates. The experts, Prof Knud Kragballe from Aarhus University Hospital, Denmark, Assoc Clin Prof Craig Leonardi from St Louis and Prof Alan Minter from Dallas, presented a series of difficult cases to illustrate their approach and highlighted the experiences they have gained over the years.

Gems to be gleaned from the discussion included a recommendation of switching methotrexate from oral to weekly subcutaneous administration in patients intolerant of oral dosing or showing lack of efficacy. Dosing subcutaneously is apparently equivalent to the oral dose with enhanced bioavailability and therefore response. All agreed this route of administration was preferable to both oral and intramuscular administration. In Australia, the TGA-indicated route is intramuscular rather than subcutaneous.

The discussants revealed some early data on golimumab – an anti-TNF monoclonal antibody approved in Australia for rheumatoid arthritis – with PASI 75 response rates at week 14 of 40% and 58% with the 50mg and 100mg doses, respectively.

The need to vaccinate patients pre-immunosuppression was discussed. Live and live-attenuated vaccines – flu mist (nasal), TY21; (oral typhoid), smallpox, yellow fever, BCG, measles/mumps/rubella, varicella, rotavirus and oral polio – should all be given pre-immunosuppression. A normal antibody titre response to pneumococcus and influenza vaccinations has been reported in patients on adalimumab.

The suggestion was made that it may be possible to use anti-TNF agents in patients with hepatitis B who have been cleared, as long as serology and liver function are closely monitored. Obviously comanagement with a gastroenterologist/hepatologist is mandatory.

A richly rewarding session, this Meet the Expert forum finished too soon for all present in the auditorium.



**PBS Information:** Authority required for the treatment of adults with severe rheumatoid arthritis, severe psoriatic arthritis, ankylosing spondylitis, Crohn's disease and severe chronic plaque psoriasis. This product is listed on the PBS as a Section 100 item for polyarticular juvenile idiopathic arthritis. Refer to PBS Schedule for full authority information.



#### Abbott sponsored symposium Real-world challenges in psoriasis: current choices, future possibilities

The Abbott sponsored symposium was a well-attended and highly entertaining 90-minute session hosted by Professor Kristian Reich.

Professor Reich spoke on the efficacy (PASI 75) of briakinumab - a new anti-IL 12/23 monoclonal antibody, including 12-month data, with a superior response to methotrexate. A further look was undertaken at the currently available methotrexate data, which suggest a response rate of around 40%.

Professor Richard Langley from Dalhousie University, Halifax, Nova Scotia, gave an overview of management strategies that can help patients maintain a positive long-term therapeutic outcome. This included how to deal with treatment interruptions – for

#### **European Society for Photodermatology Day**

The European Society for Photodermatology held their annual symposium on the day preceding the opening of the EADV Congress. With the symposium taking place in the morning, rather than the traditional afternoon location, attendance numbers were down. This did not detract from the typical high standard expected from chair Professor John Hawk who was in his usual good form and high spirits.

Gillian Murphy, a recent visiting guest at the Australasian College of Dermatologists' Annual Scientific Meeting, spoke on the management of actinic keratoses. She reminded the audience of the role of chemical peels and ablative laser resurfacing as options for field therapy for actinic damage. Professor Murphy also mentioned a paper from a decade ago on the potential for severe (potentially life-threatening) adverse reactions in patients treated with 5-fluorouracil (5-FU) who have dihydropyrimidine dehvdrogenase (DPD) deficiency, an autosomal recessively inherited condition. Current research suggests that nearly 8% of the population has at least partial DPD deficiency. A diagnostic determination test for DPD deficiency is available, and it is expected that with a potential 500,000 people in North America using 5-FU, this form of testing will increase. Quoted complete response rates for 5-FU are around 50%, with recurrence rates of more than 50%. A recent study looking at 0.5% 5-FU and 10% salicylic acid suggested a higher response rate (but more irritation) than diclofenac in hyaluronic acid. The Europeans are quite excited by the prospect of the Australia-originated PEP 005 (ingenol mebutate) being introduced in the near future. Inducing apoptosis, necrosis and antibody dependant cellular cytotoxicity, this agent, which can cause quite pronounced short-term local skin reactions, appears to have acceptable complete response rates.

Rolf-Markus Szeimies spoke on photodynamic photorejuvenation, first described by Ruiz-Rodriguez in 2002 using 20% amino-levulinic acid (ALA) and IPL. A number of subsequent publications have looked at ALA and/or methyl aminolevulinate (MAL). Improvement is noted in texture, (telangiectasia), sallowness, mottled pigmentation and skin roughness, although oedema, erythema, crusting, scaling, purpura and pain can be an issue. ALA plus PDL can increase dermal collagen production, while MAL plus Aktilite decreases elastotic tissue (elastolysis) and increases collagen production by fibroblast stimulation, neocollagenesis and collagen remodelling. Microneedling can enhance drug penetration, whilst pretreatment with Fraxel increases fluorescence with MAL.

The European Society for Photodermatology plenary presentation was by Jan van der Leun who spoke on climate change and skin cancer. He pointed out that climate change is associated with changes to temperature, cloud levels, rainfall and the melting of snow and ice. In experimental animals, enhanced skin carcinogenesis has been reported with higher environmental temperature (with stable UV exposure). In the US, data have been reported as showing an increased risk of nonmelanoma skin cancer with a rise in mean ambient temperature.

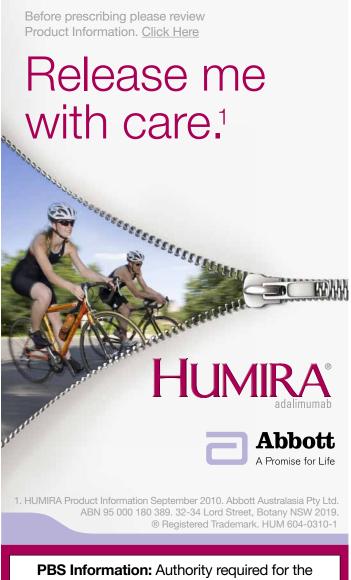
Han Christian Wolf spoke on population UV exposure. Typical daily standard erythemal dose (SED) exposure for an indoor worker is 0.7 (annual 132) whilst a gardener receives 1.3 (224/year). It has been predicted that sunbathing increases exposure by 15% in children and up to 51% in adults.

Skin photoageing was discussed by Sewon Kang (outside in) and Jean Krutmann (inside out). Dr Kang focussed on the effects of UVR on fibroblasts with increased production of matrix metalloproteinases, collagen fragmentation, change in fibroblast shape and modified procollagen and MMP-1 synthesis. He compared scanning electron microscope findings of long intact collagen fibres in photoprotected sites (hip) and fragmented collagen fibres with a decreased percentage of cells in contact with collagen fibres, decreased cellular processes, decreased cell surface area and decreased procollagen 1 at photoaged sites (forearm). Prof Krutmann discussed changes in the mitochondria as a result of photoexposure. There are five mitochondrial enzymes involved in oxidative phosphorylation. Mitochondrial DNA mutations (including the common 4977 deletion) results in premature ageing.

example with pregnancy or surgery. Three-year data show >75% of Humira-responders maintained their response with continuous therapy out to 3 years.

Professor Ulrich Mrowietz explained how data from new therapies will allow these agents to fit into current evidence-based guidelines and treatment algorithms. He introduced the Progressive Psoriasis Initiative, which was established to define treatment goals for psoriasis based on consensus from representatives of 19 European countries.

This was an interesting and stimulating symposium on issues relevant to psoriasis management.



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#### Lasers for vascular, pigmentary and hair disorders

#### Current status of laser assisted hair removal Lapidoth M

Summary: This lecture described the current and future systems for laser- and light-assisted hair removal. Focus was on emerging low-energy and home-use devices, and discussing the myths versus reality and associated side effects to enhance clinical knowledge and highlight some of the more unusual side effects.

#### 19th Congress of the EADV 2010; Symposium 08; Presentation S08.3

#### Laser literature review for 2010

Haedersdal M

Summary: This presentation reviewed current (2010) literature on new treatment indications for laser dermatological treatments and new treatment approaches for conditions commonly treated with lasers.

#### 19th Congress of the EADV 2010; symposium 08; Presentation S08.5

**Comment:** The session 'Lasers for vascular, pigmentary and hair disorders' had the learning objectives of: describing laser procedures used in vascular, pigmented and hair removal procedures; avoiding complications with these laser treatments; and having an updated knowledge on scientific literature regarding these laser chapters.

#### Vascular lasers

Superficial red blood vessels are best dealt with using lasers in the 530-600nm range. Larger deeper vessels absorb more in the near infrared range. Pulsed dye lasers have seen an increase in purpura threshold with an increase in the number of micropulses. (In 2009, Candela brought out a vascular laser with eight micropulses.) Combined wavelength devices, for example 595nm pulsed dye lasers and 1064nm long pulsed Nd:YAG used sequentially increase efficiency (presumably by converting haemoglobin to methaemoglobin, which is in turn targeted by the Nd:YAG). The new long-pulse alexandrite (755nm) and long-pulse Nd:YAG (106nm) also appear to have synergistic properties. New generation IPL systems appear to have a better action on leg veins (0.5-2mm in diameter).

#### Pigmentation lasers

- Pigmentation and tattoos: alexandrite 775nm targets red.
- Café au lait macules are best targeted with Q-switched Nd:YAG (532nm).
- Melasma the gold standard is 4% hydroquinone and sunscreen although IPL and ablative Fraxel are catching up.
- Becker's naevus-erbium: YAG and Q-switched Nd:YAG.
- New tattoo pigment (Freedom Ink) is biocompatible black and red pigments with absorption wavelengths compatible with currently available lasers.

#### Laser hair removal

This is the most common laser procedure and ranks third behind Botox and hyaluronic acid fillers as the commonest cosmetic procedure. Vaniga in combination with laser appears to increase efficacy. A new home-use device is yet to have safety and efficacy confirmed.

Laser therapy complications may be the result of patient factors - dysmorphic, medication (for example isotretinoin, gold), tendency to hypertrophic/keloid scars, noncompliance and laser specific - e.g. highest risk of scarring with Nd:YAG and lowest risk with PDL, ruby and alexandrite.

Complications of epilation include reticulate erythema, paradoxical hyperpigmentation and koebner phenomenon, whilst tattoo removal may be associated with hypo- and/ or hyperpigmentation, milia, pigment darkening, scar formation, burns, allergic reactions and pigmentation in lymph nodes.

Mistakes may be a result of lack of training, wrong indication, wrong diagnosis, wrong time, wrong physical parameters and lack of follow up.

'What's new in vascular lasers' saw the recommendation of pulsed dye lasers as the treatment of choice in port-wine stains with >50% clearance with 1-3 treatments in most. However, 20% are poor responders. Long pulsed dye lasers tend to be better than IPL for port-wine stains. New high powered IPLs are on the way and next on the list will be the addition of topical rapamycin for vascular lesions.

Melasma is best treated with triple ingredient topical bleaching creams with adjunctive benefits from peels and laser, especially the new 1550nm nonablative fractional laser. Four sessions, every 2 weeks, appear to be effective.

Combined with Vaniqa, IPL and LPDL may have good responses for hair removal with 40% and 34% showing good responses out to 6 months, respectively.

Finally, new home-use devices have been developed for laser hair removal - low level IPL and diode lasers with transient effect, requiring repetitive or continuous use and good eye safety.

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**Diagnosis and management for autoimmune bullous diseases** 

In the workup of the patient with suspected autoimmune bullous disease, direct immunofluorescence is still the gold standard, although this requires a second biopsy, special transport medium for the fresh specimen, and specialised laboratory equipment. In bullous pemphigoid, 100% of patients show C3d staining on immunohistochemistry, with 82% of patients showing C3d and C4d in pemphigus. ELISAs in bullous pemphigoid (BP180-NCI6A) show sensitivity compatible with indirect immunofluorescence and specificity >90–95%. An estimated 50% of bullous pemphigoid patients relapse within 12 months of treatment cessation. Predictive for relapse is BP180, age >82 years, positive immunofluorescence and high titre BP180 Elisa (positive predictive value 91%). BP230 (BPAG1) correlates poorly with disease activity, has lower sensitivity than BP180 and has no supplementary value.

#### Mucous membrane pemphigoid/ocular cicatricial pemphigoid

Mild disease involving oral mucosa only can usually be managed with topical corticosteroids and systemic dapsone. Extensive oral or mild ocular cicatricial pemphigoid has dapsone, sulphasalazine and tetracyclines as first-line therapies, then mycophenolate mofetil (60–70% control), cyclophosphamide (75% in remission after 18–24 months) and azathioprine. Severe OCP/MMP is treated with dapsone, sulphasalazine, corticosteroids, mycophenolate mofetil, cyclophosphamide and

#### How to manage atopic dermatitis successfully

This session commenced with an emphasising of the recently published ETFAD/ EADV guidelines in 2009. The speakers emphasised that the components of atopic dermatitis management include education of the patient, regular checks of compliance, website or printed information and instruction sheets – particularly relating to emollients (40% of mild atopic dermatitis can be managed with emollients alone), topical corticosteroids, topical calcineurin inhibitors, consideration of quality of life and psychological counselling. In assessing severity, physical symptoms and quality of life should be considered. When basic therapy fails, it may be due to severe disease, noncompliance, infection, complicating disease, stress and economy. Systemic therapies include glucocorticosteroids (no controlled data), ciclosporin (2.5-5 mg/kg/day), azathioprine (helps pruritus and sleep disturbance), methotrexate (few studies, but high response rates) and mycophenolate mofetil, which can also be utilised. To date, various biologicals have been unsuccessfully trialled in atopic dermatitis. These therapies have been based on well-known raised levels of interleukins (IL)-4, IL-17, 1L-22, and interferon- $\gamma$ . Therapies not

#### **Urticaria**

## The EAACI/GA<sup>2</sup>LEN/EDF/WAO guidelines on urticaria – classification and diagnosis

#### Czarnecka-Operacz M

**Summary:** Guidelines for urticaria compiled jointly by the EAACI Dermatology Section, GA<sup>2</sup>LEN, EDF and WAO, and acknowledged and accepted by the European Union of Medical Specialists, section of Dermato-Venereology, were presented. The guidelines provided an updated definition and classification of urticarias, and also provided recommendations for diagnostic approaches for common subtypes.

19th Congress of the EADV 2010; Symposium 41; Presentation S41.1

## The EAACI/GA<sup>2</sup>LEN/EDF/WAO guidelines on urticaria – treatment modalities

#### Sabroe RA

**Summary:** A case-based approach was used to highlight the main points of the European urticaria guidelines, and also compare them with other guidelines. The key points raised were: i) avoidance of relevant physical stimuli, avoidance of specific drugs, eradication of infective agents and dietary manipulation where appropriate; ii) nonsedating H1-receptor antagonists have the highest level of evidence for treatment, followed by increasing the dosages of these agents, then the addition of a leukotriene antagonist, with ciclosporin, H2-receptor antagonists, dapsone and omalizumab having variable evidence (level IV); iii) avoidance of routine use of sedating antihistamines and long-term oral corticosteroids; and iv) the need for additional well-designed trials.

19th Congress of the EADV 2010; Symposium 41; Presentation S41.4

azathioprine, with IV immunoglobulin (IVIG; 2 g/kg over 2–5 days), etanercept and rituximab being relatively new. Steroids and IV cyclophosphamide are used if there is a lack of response or laryngeal cicatricial pemphigoid.

#### Pemphigus vulgaris (PV)/pemphigus foliaceus (PF)

A correct diagnosis is made on history, examination, H&E examination, direct immunofluorescence and indirect immunofluorescence – with IgA/IgG reactivity against defined autoantigens by Elisa/immuoblot – PV desmoglein 3 and PF desmoglein 1. Atypical pemphigus is associated with desmocollin 1, 2, 3, whilst paraneoplastic pemphigus is associated with periplakin, endodoplakin, BP180/230 and 170kD antigen. Evidence-based treatment for widespread disease recommends systemic corticosteroids (1–2 mg/kg/day) prednisolone), adjuvant immunosuppression with azathioprine (up to 2.5 mg/kg/day), mycophenolate mofetil (2 g/day) – faster, more prolonged response, cyclophosphamide (1000 mg/m<sup>2</sup>), ciclosporin, methotrexate and chlorambucil. Second-line options include systemic corticosteroids plus IVIG, rituximab, and immunoabsorption. In the future, targeted therapies, e.g. anti-CD20 and IVIG, may become treatments of choice.

#### 19th Congressof the EADV 2010; Symposium 03

found to be helpful include anti-IgE (omalizumab), anti-T cell agents (efalizumab, alefacept), anti-B cell (anti-CD20) agents (rituximab), anti-TNF (infliximab), anti-IL-4/17 (nuvance, pitrakinra,  $T_{\rm H}^2$  targeted cytokines) and anti-IL-5 (mepolizumab, eosinophils). Future targets may include IL-31 and thymic stromal lymphopoietin (TSLP).

#### Antibiotic resistance

Impetigo is now most commonly caused by *Staphylococcus aureus*. Communityacquired methicillin-resistant *S. aureus* (MRSA) is increasing in prevalence and virulence. The presenter suggested topical mupirocin or topical fusidic acid. Additional therapies for MRSA include chlorhexidine body wash, mupirocin nasal ointment, systemic antibiotics such as daptomycin and linezolid, along with improved personal hygiene, antibacterial hand sanitisers, regular showers, no shared items, early detection of community-acquired MRSA and surgical drainage of abscesses rather than relying on systemic antibiotics.

#### 19th Congress of the EADV 2010; Workshop 01

#### **Physical urticarias**

#### Maurer M

**Summary:** This presentation provided an overview of physical urticarias. It described their physical and mechanical triggers, and the importance of distinguishing them from other forms of urticaria. It covered the main diagnostic goal and preferred treatment options (nonsedating antihistamines, with higher dosages or omalizumab necessary for the large proportion of unresponsive patients), along with the important fact that it is often not possible to treat the underlying cause and provide a cure.

#### 19th Congress of the EADV 2010; Symposium 41; Presentation S41.3

#### Autoreactive urticaria

#### Gratton CEH

**Summary:** The role of autologous serum skin testing (ASST) for defining autoreactive urticaria was discussed in this presentation. While a negative ASST has a very high negative predictive value for the absence of a positive basophil histamine release assay (BHRA), and as such is a good indicator of idiopathic chronic urticaria, a positive ASST has only moderate sensitivity and specificity for detecting basophilic histamine release in healthy donors, and therefore should not be used to test for autoimmune urticaria. A positive ASST on its own does not predict a good response to immunosuppressant therapy, although those who also have a positive BHRA are more likely to respond than those with a negative BHRA. It was concluded that the main reason for identifying autoreactivity is to show patients with chronic urticaria that vasoactive factors, rather than a food allergy, are responsible for their condition.

19th Congress of the EADV 2010; Symposium 41; Presentation S41.5

#### **Contact urticaria syndrome**

#### Giménez-Arnau AM

**Summary:** Contact urticaria syndrome, contact urticaria and protein contact dermatitis are characterised by the development of eczematous or urticarial lesions minutes after contact with the trigger substance, and systemic involvement can also occur in contact urticaria syndrome. Overall, there is inadequate documentation regarding these conditions, but latex allergy is known to have a prevalence of 5–10%, and there is a high frequency of contact urticaria syndrome in the occupational setting. New compounds responsible for these immediate skin reactions were presented, as were suggestions for further investigation.

19th Congress of the EADV 2010; Symposium 41; Presentation S41.6

#### **Urticarial vasculitis**

#### Wallengren J

**Summary:** This overview of urticarial vasculitis noted that it occurs in 2–20% of patients with chronic urticaria, and 40% of these patients will also have associated angio-oedema. Leucocytoclastic vasculitis on skin biopsy confirms the diagnosis. A number of laboratory tests are indicated, including complement levels as these determine classification of the disease as normocomplementaemic or hypocomplementaemic urticarial vasculitis syndrome. For disease limited to the skin, treatment may include antihistamines, dapsone, hydroxychloroquine or colchicine, and there are several agents that can be tried for patients with systemic involvement. Treatment withdrawal should be undertaken with caution, as the disease can persist for years.

#### 19th Congress of the EADV 2010; Symposium 41; Presentation S41.2

**Comment:** The urticaria symposium saw a packed auditorium, and addressed the learning objectives of:

- 1. making the proper diagnosis in patients with urticaria
- 2. proposing the most appropriate treatment
- 3. diagnosing and treating difficult types of urticarias.

The session opened with two presentations on the updated EAACI/GA<sup>2</sup>LEN/EDF/WAO guidelines on urticaria: the first on classification and diagnosis; the second on treatment modalities (<u>http://www.euroderm.org</u>).

The physical urticarias and their diagnoses were discussed by Marcus Maurer from Berlin. He recommended testing on the upper back or a forearm for symptomatic dermatographism ( $\geq$ 50% of physical urticaria diagnoses), ideally with a dermographometer at 36 g/mm<sup>2</sup> or a blunt object. Delayed pressure urticaria (deep swelling 4–12 hours later) is best tested with a 7kg weight over the shoulders or a weighted rod. For cold contact urticaria, an ice cube in a clear plastic bag can be applied to the lower forearm and read 10 minutes later. Most cases have a threshold of 23–27°. The higher the threshold, usually the more severe the urticarial disease. It was recommended that solar urticaria be elicited on the buttock.

#### **Evolving strategies in STI prevention**

**Summary/comment:** The speaker introduced the current sexually transmitted infection (STI) treatment guidelines (<u>http://www.iusti.org/sti-information</u>).

Recent reports from the Melbourne Sexual Health Centre suggest that in women aged <28 years, there is already a decrease in the number of new clients with HPV infection. Gardasil vaccination started in 2007 for 12–26-year-old women, with now 80% coverage.

It was suggested that circumcision may decrease HIV prevalence as the foreskin is rich in target cells. However circumcision does not provide protection against herpes simplex, syphilis or gonorrhoea.

Questions for the future include, who is at risk of STIs, who should pay, can we influence sexual behaviours and should prevention strategies be targeted or universal.

#### 19th Congress of the EADV 2010; Plenary lecture 7

Autoreactive urticaria was presented by Chris Grattan from London. If the autologous serum skin test shows no reaction, the negative predictive value is 92.8% (95% Cl 81.4–100%). Patients with this condition need high doses of antihistamines. Associations have been reported with hyperthyroidism, rheumatoid arthritis, coeliac disease, positive ANA and HLA-DR4.

Contact urticaria can be divided into four stages: i) contact urticaria, immediate dermatitis or nonspecific itching, burning and stinging; ii) generalised; iii) systemic; and iv) anaphylaxis. This condition is most common in the food industry, especially bakers, and healthcare workers, latex and protein contact being the main culprits. In Australia (as reported by Jason Williams), natural latex rubber, food stuffs and ammonium persulfate are the most common allergens. Treatment is generally with oral corticosteroids and nonsedating antihistamines, topical corticosteroids and calcineurin inhibitors.

Angio-oedema can be divided into hereditary (C1-esterase inhibitor deficiency) and nonhereditary - allergic IgE-mediated, NSAID-induced, ACEI-induced, associated with idiopathic urticaria, and idiopathic with no urticaria. With hereditary angiooedema, androgens enhance C1 inhibitor whilst new agents ecallantide (kallikrein inhibitor) and icatibant (bradykinin-B2 receptor antagonist) have recently been approved as treatments. In nonhereditary angio-oedema, it is recommended to avoid ACE inhibitors and NSAIDs; consider adrenaline [epinephrine], antihistamines and oral corticosteroids; avoid allergens; consider carrying an Epipen; and, if idiopathic (+ urticaria), consider steroids or steroid-sparing agents such as ciclosporin.

Anaphylaxis is treated with adrenaline, antihistamines and corticosteroids. It can be divided into immunological, idiopathic and nonimmunological. Immunological may be IgE dependent - foods, metals, wasp and bee stings (biological), natural latex rubber and radiocontrast or non-IgE dependent – dextran, infliximab and radiocontrast (also). Nonimmunological triggers include physical (cold, heat, UV) and other – drugs, such as NSAIDs, and alcohol.

The final presentation reminded the audience that urticarial vasculitis is a form of leucocytoclastic vasculitis that may show deposits of IgG, IgM or IgA and C3 in blood vessel walls and on the basement membrane (80%). Urticarial vasculitis may be subdivided into normocomplementaemic and hypocomplementaemic with/without systemic manifestations. Whilst many cases are idiopathic, urticarial vasculitis may be associated with autoimmune conditions such as lupus, Sjögren's syndrome, cryoglobulinaemia, physical urticarias, drugs such as cimetidine, diltiazem, fluoxetine and methotrexate, infectious diseases such as hepatitis B, hepatitis C, infectious mononucleosis and Lyme disease, and haematological diseases such as hypocomplementaemia, leukaemia, and PRV. Recommended investigations include biopsies for H&E and direct immunofluorescence, complement levels (if low C3 and C4, test C1q and anti-C1q, IgG, IgA, IgM), full blood examination, ESR, urea and electrolytes, liver function, urinalysis and consider ANA, anti-double stranded DNA, ENA, cardiolipin, antiphospholipid, hepatitis B, hepatitis C, Lyme disease, C3 nephritic factor, chest x-ray and forced expiratory volume if there are pulmonary symptoms. The long list of treatments include, cooling the skin, reducing alcohol and tobacco, treatment of underlying disease, antihistamines, indomethacin/NSAID, dapsone, colchicine, hydroxychloroquine, prednisolone, azathioprine, cyclophosphamide, methotrexate, pentoxifylline, ciclosporin, mycophenolate mofetil, etanercept and rituximab.

#### **EADV** Conference Review

This review of the 19th Congress of the European Academy of Dermatology and Venereology (EADV) has been carried out independently by

Associate Professor Peter Foley, a dermatologist at St Vincent's Hospital Melbourne and has teaching responsibilities for both undergraduate and postgraduate students. He also works for the Skin and Cancer Foundation (Vic) and in a private dermatology practice.



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#### An overview of stem cells in dermatology

#### Barrabdon Y

**Summary:** Advances in stem-cell technology have resulted in the ability to reprogramme them in a number of ways. It is foreseeable that molecules specifically targeting the fate of stem cells or the microenvironment in which they exist will become available in the near future. These exciting developments are likely to have major implications for our understanding of many dermatological diseases, and should also provide us with new therapeutic options.

#### Targeted therapies for cutaneous malignancies Hauschild A

**Summary:** Agents with molecular targets for treating skin cancers and inflammatory skin diseases were discussed in this presentation. The roles of rituximab for cutaneous B-cell lymphomas and imatinib (Glivec) for dermatofibrosarcoma protuberans were covered. Recent data on the oral inhibitor of the sonic-hedgehog signalling pathway, GDC0449, in unresectable basal-cell carcinomas was mentioned, and other agents targeting this pathway are also currently being evaluated in Gorlin-Goltz syndrome. Genetic alterations in the various subtypes of melanoma primary tumours represent a significant breakthrough in the treatment of metastatic melanomas. Recent important findings include: i) a response rate of 70% with PLX4032, an oncogenic B-RAF inhibitor, in an early clinical trial; and ii) reduced tumour sizes in >50% of patients with C-KIT-mutated melanomas treated with imatinib. There are also ongoing studies of several other agents with molecular targets for metastatic melanoma.

**Comment:** The presenter commenced by stating that if this presentation was given 2 years ago, the range of treatment options would have included: surgery, interferon and chemotherapy for melanoma; surgery, imiquimod and photodynamic therapy for BCC; surgery for SCC; and surgery for DFSP. However, in 2010, we have targeted therapies for melanoma with B-RAF, C-KIT and MAGE-A3 as possible targets. For BCC there are new hedgehog inhibitors, whilst EGF receptor inhibitors have been reported for SCC and imatinib for DFSP.

We are all aware of the use of rituximab (an anti-CD20 monoclonal antibody) to treat cutaneous B-cell lymphoma (CD20 positive). Recent reports suggest that in advanced nonresectable SCC, blockade of EGF receptors by cetuximab (dose 400 mg/m2 then 250 mg/m2/week) has a remission rate of 69%. Grade 1–2 toxicity is seen in 78% while 22% experience grade 3–4 toxicity.

Mutations in the Patched gene or activation of Smoothened may result in the induction of BCC. Several agents targeting this pathway have been developed, with the most successful showing a 54.5% partial or complete response rate.

The speaker proposed the idea that there may be a group of tumours more correctly termed 'the melanomas' than simply melanoma. In Caucasians, 65% of mutations in melanoma cells are of B-RAF, whilst 15% are of C-KIT CCND1. Imatinib may be affective in C-KIT-mutated melanomas. PLX4032 has been shown to be effective in 81% of B-RAF-mutated tumours. New trials are being undertaken to compare B-RAF inhibitors with dacarbazine.

19th Congress of the EADV 2010; Plenary lecture 9; Presentation PL09.1

## New strategies for the biological therapy of psoriasis

**Summary/comment**: New agents in development include tasocitinib, an inhibitor of Janus kinase 3 which is being investigated in rheumatoid arthritis, psoriasis and inflammatory bowel disease. BMS have a P38 MAPK inhibitor that is being investigated for psoriasis, rheumatoid arthritis and arthrosclerosis.

Recent data suggest that the TNF antagonists have a mean rate of hospitalisation for infection of 1.43 (relative risk [RR]) in the first year, 1.15 in the second year and 0.82 in the third year.

Psoriasis has an increased risk of nonmelanoma skin cancer (RR 3.2), BCC (1.2), non-Hodgkin's lymphoma (2.2), Hodgkin's disease (3.3) and lung cancer (1.5). The skin rashes that many develop on anti-TNF therapy include palmoplantar pustulosis, new psoriasis, AGEP, lupus and erythema multiforme. TNF blockade increases interleukins 1B, 6, 17A, 21 and 22. This may be a result of decreased T-regulatory cell Foxp3.

Data on briakinumab suggest that after a loading dose of 200mg subcutaneously at weeks 0 and 4, 100mg at 4- or 12-week intervals may be effective in the management of chronic plaque psoriasis. No increased rates of malignancy or infection were seen with this agent.

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**Comment:** Stem cells are defined as being capable of self-renewal, that is, cells with the capacity to generate differentiated progeny for an extended period of time. Stem cells have a typical lifecycle of self-renewal, asymmetrical growth, rest, differentiation and then death. Breakthroughs have meant that it is possible to manipulate stem cell fate. Potential adult stem cell sources include blood, gastrointestinal cells and epidermal cells. The hair follicle is just one of the stem cell sources in the skin, with epidermal stem cells and sweat gland stem cells also possibly being inducible into pluripotent cells.

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**PBS Information:** Authority required for the treatment of adults with severe rheumatoid arthritis, severe psoriatic arthritis, ankylosing spondylitis, Crohn's disease and severe chronic plaque psoriasis. This product is listed on the PBS as a Section 100 item for polyarticular juvenile idiopathic arthritis. Refer to PBS Schedule for full authority information.

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