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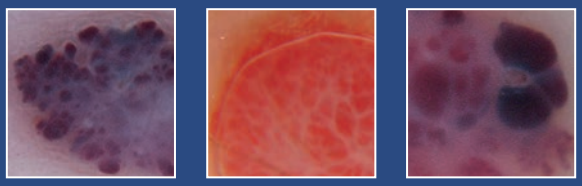

Spring 2018

Primary Care Dermatology Society

PCDS Bulletin

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Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.mhra.gov.uk. Adverse events should also be reported to Dermal.

References:
1. Gallagher J. *et al.* Poster presented at EADV Congress 2009.
2. Dermol Range – Total Unit Sales since launch. Dermal Laboratories Ltd. Data on file.

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Chairman's Report

Dr Stephen Kownacki
Executive Chairman of the Primary Care Dermatology Society

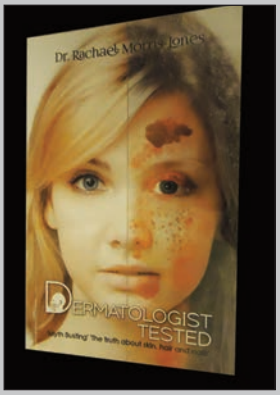
Greetings.

2018 continues with the guarded optimism that working with the RCGP and the BAD was developing last year. Very soon the General Practitioner with Extended Role (GPER) accreditation programme will be rolled out and details are to be found within Tim Cunliffe's article in this Bulletin. In addition there will be a launch (date yet to be set) of the Dermatology section of the "RCGP Educational Library delivered in partnership with the BAD and PCDS" which gives access to the latest dermatology elearning resources, national guidelines and RCGP accredited courses via the >elearning. rcgp.org.uk/Dermatology< website. This joint venture not only gives direct access to the pcds website for most of its content but also places our educational meetings in front of >56k possible users and has already made an increase in attendances for Essential Dermatology 1 and 2 (ED) and Dermoscopy For Beginners (DFB.) Most of all it means we will be reaching a huge increase of healthcare workers and so benefitting ever more patients with skin disease. The fundamental aim of the PCDS!

That's the good part but sadly the difficulties for the NHS and provision of healthcare generally show no signs of improvement and I am hugely sympathetic to the GPs struggling with ever increasing workloads and pressure from CCGs, the government and worst of all, the press! Not surprisingly we are seeing more GPs looking for relief from the daily grind by developing expertise in dermatology either as staff grades in secondary care or as GPERs in community-based provider clinics and federations. There is no doubt that, as happened in my old GP practice, encouraging partners all to develop a special interest helps to break up the week and reduce the risk of burnout. Not only does it benefit the practitioner but the increased knowledge and skill provides patients with the best service. Remember the salaried partners and nurse practitioners may also become invigorated and better integrated by a degree of specialisation and reduces the risks of de-skilling those not involved.

Over the years I have authorised questionnaires asking you to share your knowledge and circumstances to inform policy and treatment. You will also find the research column in this Bulletin which repeats a study we sent by email recently regarding Dermoscopy usage. I hope you feel able to contribute when appropriate and you can be reassured that only non-promotional NHS based topics will drop into your inboxes. Any Sponsors questionnaires require you to respond directly if you wish to work for them and will be clearly "sponsored."

The executive committee will be joining me, many friends and honorary members in Manchester at the Spring meeting to learn a lot and to enjoy the company of dermatology people who, as our sponsors all agree, are the friendliest group of doctors! This Bulletin may arrive after the event but the summer meeting in London on 28th June will be an opportunity for me to say goodbye and good luck to as many members as can make it. I will avoid staining this copy with tears as I may get another to write before my retirement at the end of June but after 18 years as Chair and a founder member of the PCDS (1994) I feel a huge sense of gratitude to all our members, past and current, for their support and company on the journey so far. There is more for my successor, Angelika Razzaque, to do.



Book Review: Dermatologically Tested

Review by **Brian Malcolm**
Associate Specialist in Dermatology & PCDS Executive Committee Member

Having had my curiosity awakened by both title and cover, I settled down to read "Dermatologically Tested", a paperback of just in excess of 200 pages written by Dr Rachael Morris-Jones, Consultant Dermatologist at Kings College, London.

The book itself is an easy read attempting to cover a disparate number of perpetually topical dermatological issues such as treatments for scars and dietary supplements for hair and nail disorders, most of which raise more questions than answers. Speaking as a clinical dermatologist who does no private or cosmetically orientated practice, the book was of limited value and added very little to my knowledge base or working practice and only served to underline the lack of robust research in issues that are largely related more to the field of cosmetology rather than dermatology. However, Dr Morris-Jones had clearly reviewed the literature base comprehensively and this in itself is very useful when communicating confidently with patients on such issues.

On finishing the book, I was left with a sense of confusion as to who is the intended target audience. It flits between more scientific/technical language regarding double blinded trials etc and explanations for the lay person in a style that is somewhat top heavy with anecdote and jokey "one-liners". Perhaps the idea was to cast a wide net to the reading public and see what interest was captured. Certainly, some of the content may be of interest to those involved in the ever-burgeoning beauty sector, clinicians in skin disease including primary care or indeed the general public.

The book itself is marketed at an economy price of £8.50. Unfortunately, the cheap price is reflected in the product. There was no contents page, glossary, index or referencing. Illustrations and photos were sparse and not of very good quality and there were basic type setting and spelling errors and most surprisingly, in my copy, the pages were in the wrong order!

One last concern for me was, in a new publication, that the ABCDE rule pertaining to the recognition of melanoma still purported the now outdated and misleading dogma, D for diameter, that "melanomas are usually larger than 6mm". In the brave new world of dermoscopy, such statements can induce a false sense of security as melanomas are often melanomas from the start; it was simply our lack of ability to recognise them as such previously that led to such teaching historically and the key to surviving this condition as also emphasised in this book, is diagnosis at the earliest possible stage!

"Dermoscopically Tested" is available through Austin Macauley Publishers and Amazon.

Editorial Spring 2018

Sara Ritchie
PCDS Bulletin Editor

We are all well and truly into 2018 now, with hours of daylight finally increasing perceptibly day by day, so a very warm welcome to the first bulletin of the year.

It was great to get back up to my homeland for the Scottish meeting in November last year (the PCDS meetings are the only reason I go back to beautiful Scotland now!) – and I have written up a summary of this inside this bulletin for those who could not make it.

I am delighted to introduce our feature article this time on topical Calcineurin inhibitors. As we all know well these are used in practice for a variety of conditions in dermatology, despite their license being only for eczema. So Dr Daniel Lichtenstein has written for us an extremely interesting review article outlining current evidence on their use in conditions other than eczema. Daniel has very helpfully included also some information on usage under 2 years of age in other countries of the world which differ from the UK, and such interesting facts as the use of topical Protopic on the nailbeds even potentially helping nail psoriasis in some patients.

I am also delighted to introduce a case report from Dr Jaya Aiyengar on a case of fixed drug eruption due to Mefenamic acid. Jaya includes a clear explanation for the reason that fixed drug eruption can be reactivated at the same body site following re-exposure to the culprit drug - explaining that it is a type IV hypersensitivity reaction in which the T cells can persist for years even in completely faded lesions. And although the common triggers are anti-infective medications, analgesics including other NSAIDs, and anticonvulsants, it's worth remembering this also occurs infrequently with Mefenamic acid.

Emma Le Roux's research column this time highlights a link to an initial survey underway on hyperhidrosis where you can register your views for research priority setting, and a similar second survey also now open on lichen sclerosus. Emma also invites you to take part in an interesting and important survey also underway about your views and personal current use of dermoscopy in primary care.

Thank you also to Julian Peace for yet another interesting journal watch. So here are a few highlights to entice you to the back pages.. A literature review on terbinafine induced liver injury has shown that patients generally had some symptoms of this for a mean of 14 days before seeking medical advice, and that routine monitoring of LFTs in the absence of symptoms is not considered necessary. A case report from South Korea highlights success in using Picato to treat pyogenic granuloma in a 4 year old. And a second case report highlights a possible link between chronic urticaria and nail varnish.

And lastly but very interestingly we also have a most informative book review by Brian Malcolm, and an interesting update by Tim Cunliffe on current progress in GPwER accreditation. So to finish just a quick reminder that we offer £50 for anyone submitting a case report – so do think about writing up and sending in any interesting cases you come across!

Sara Ritchie PCDS Executive Committee Member

Saturday 18th & Sunday 19th November 2017

PCDS Scottish Meeting
Westerwood Hotel, Nr Glasgow

A huge thanks indeed to Iain Henderson, the PCDS Scottish Representative, for once again arranging the Scottish meeting in November. Iain will be stepping down from this role, so I really would like to say a very huge thank you on behalf of everyone at the PCDS for all the meetings he has arranged in Scotland over the years.

We had a great line up of talks over the weekend, (not to mention an amazing ceilidh band on Saturday evening!) Dr Girish Gupta kicked off with two fascinating talks on non-melanoma skin cancer, and we will be publishing his feature article on actinic keratosis, so I will just cover the other parts of his talk here.

We probably all knew to remember to consider treating the field rather than just individual actinic keratosis, however Dr Gupta helpfully emphasized that subclinical AKs with surrounding microscopic field change is common, and that the aim in treating AKs is long-term disease control rather than clearance.

The annual rate at which a specific AK may change into SCC has been estimated at 1.83%, although it is still not possible to predict exactly which will do this. It was previously thought that AKs had to progress to become thick AKs before becoming an SCC, however recent research has shown that all stages of AK even early thin ones can develop directly into an SCC, and that the thickness of an AK is not a good predictor of what is happening microscopically in the skin. Despite this, high risk features are still currently thought to be having large numbers of AKs, multiple thick large confluent AKs, a history of previous skin cancer, or immunosuppression, and the decision to treat should probably be based on high-risk features, symptoms and patient choice.

Dr Gupta gave us a reminder of treatment options including Efudix (or Picato if available) for small field <25cm, and Efudix, PDT, or Zyclara for large field >25cm, with Ingenol Disoxate being a newer version of Picato which will be licensed for larger areas than Picato. And if topical agents don't work to control actinic keratosis, low dose Acitretin 10-20mg can be considered, eg for organ transplant patients.

PDT should also be considered for multiple bowens disease on the lower legs, and although cutaneous horns can have SCC in the base, this can normally be suspected by being painful, having an indurated base, or a low height to base ratio, so others can be treated with cryotherapy, rather than having to biopsy all of these.

In terms of SCCs, these are considered high-risk SCCs if there are 2 or more of the following: >2cm diameter, poorly differentiated, extension into subcutaneous fat, or perineural involvement. This indicates a higher risk of recurrence, so the margins are paramount, adjuvant radiotherapy should be considered, and follow-up should be for at least 2 years (whereas patients with low risk SCCs can be discharged).

With regards to BCCs, there is a 17-fold increased risk of BCC after one BCC, and Gorlins syndrome should be considered if 2 BCCs occur under age 20. And for Merkel cell carcinoma there is still a dismal survival rate, so at least 2cm margins are needed, or Mohs, with radiotherapy also to the nodal basin even if the nodes are negative.

Dr Brian Malcolm gave us the next talk on leg ulcers, which personally I found thrillingly informative. The key take-home point was never to forget that a leg ulcer is not a diagnosis – it is a manifestation of some underlying disease process, and

that we always need to ask ourselves the cause of every leg ulcer. The causes are protean, but include venous, arterial, mixed, neuropathic, malignancy, vasculitis, pyoderma grangrenosum (which can koebnerise to surgical wounds and give negative histology), and of course medications. Nicorandil can cause excuisitely painful unusual ulcers, which may develop years after starting the drug, and both NSAIDS and beta blockers can delay ulcer healing.

Arterial ulcers are painful, with venous and neuropathic ulcers being painless, however in diabetics an arterial ulcer may be painless due to lack of sensation. If you don't have a Doppler don't forget the value of history and examination in distinguishing these. Arterial ulcers will have pale surrounding skin, poor pulses, and a deep edge, Venous ulcers will have dusky surrounding skin, good pulses, a shallow edge, and possibly atrophie blanche (little white stellate scars), although both pathologies can coexist.

Other tips to remember are if ulcer does not start in the gaiter area (from ankle to below-knee), suspect a non-venous cause. If ulcers are multiple consider vasculitis or pyoderma gangrenosum. And in multiple superficial ulcers in the immunocompromised/elderly/diabetics consider rarer causes such as cutaneous CMV.

Essential investigations for everyone with a leg ulcer should be FBC, U&E, TFTs, albumin, urinalysis and a Doppler. A swab does not need to be routine if there is no redness, heat or pain, as biofilm bacteria will be picked up which are not necessarily pathogenic.

Vasculitic ulcers can be due to medications, or an autoimmune cause, and require more extensive investigation, although even after extensive investigation in 50% an underlying cause is never found. All patients with vasculitic leg ulcers however need BP + urinalysis repeatedly over a few weeks to look for systemic involvement.

In terms of treatment the type of dressing is not a major factor in wound healing, however a venous ulcer won't heal in the presence of oedema. Compression here is key, although the evidence for which types of compression are better than others is still unclear, but any compression is better than no compression. Potassium permanganate for a few days and then Dermovate for 2 weeks under zipzoc stockings can work wonders for sloughy leg ulcers. And another couple of really useful tips in this talk were Dermovate for at least 2 weeks to treat overgranulation, and Beconase nasal spray to treat peristomal eczema. If a leg ulcer is failing to improve at 3 months, or not healed at a year, consider referral, and remember that healing the ulcer is not the end point – it is important to prevent more ulcers.

Dr Andrew Pink from St Johns Institute in London gave us a very interesting talk on treatment of atopic dermatitis, and the St Johns website has leaflets for patients on application of creams. He encouraged us to think about Milton antiseptic bleach baths twice weekly as an alternative to Dermol (instructions for parents on the St Johns website), and highlighted evidence that daily emollients from 3 weeks of age can prevent eczema in high risk children. A clean spatula or spoon should be used to apply emollients, as studies show that infection can occur in the pot from fingers even after 4 days.

Pre-treating with topical steroids for at least 3 days before using topical calcineurin inhibitors can reduce burning over the first 2 weeks. And Milton bleach baths, decreasing greasiness of emollients, and applying topical steroids in the direction of hair growth can all help to reduce the risk of folliculitis from topical steroids.

Stubborn hand eczema can be helped by Hydromol soaks (15 mins in water), and potent topical steroids with occlusion (eg clingfilm or gloves at night). The special Dermovate 60% with 40% Propylene glycol (if available) enables increased penetration of the dermovate.

Lichen Simplex requires a super potent topical steroid, if possible under Duoderm Thin dressings until these falls off. Tar preparations are also good for lichenified eczema. For nodular prurigo also treat with Dermovate under Duoderm extra Thin dressings until these fall off, or alternatively occlude under Zipzoc stockings (easier than standard wraps). And if you do use a week of oral steroids in severe eczema, consider a reducing course thereafter as otherwise it might re-flare.

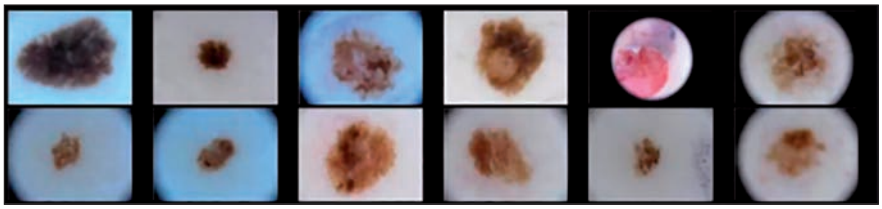
Dr Robert Dawe from Ninewells Hospital in Dundee reminded us that PUVA is still as good as most of the biologics in psoriasis, and is cheaper with less side effects. He offered us the following statistics that approximately 1 in 20 patients treated with > 200 PUVA exposures will develop an SCC, whereas biologics carry a 1 in 200 risk of death every year due to a side effect. And Mr Ross Milligan gave a very interesting talk about clinical photography. He reminded us that images are patient identifiable data, and the BAD website has guidance on use of mobile devices in clinical photography.

Written consent to take images is mandatory, and these should be deleted straight away from mobile devices after emailing them securely via nhs.net. All digital folders to store photos should be password protected, and our employers technically own the copyright for images. He also reminded us that the use of Whatsapp to send photographs breaches the data protection act.

And finally Dr Liz Ogden gave an absolutely wonderful talk on creepy crawlies and the skin, with some brilliant tips for managing these. Body lice can survive in seams of clothing up to 10 days away from the body, and can only be cleared by getting rid of the clothing. Bedbugs can hide not just in beds but literally anywhere in a room, including behind paintings, radiators, and seams of chairs, and can last a whole year without a meal. Vibrations from walking on the floor can cause flea pupae to hatch, the fleas can be prompted to jump by changes in light and dark, and can jump up to 18cm. In scabies we should consider in everyone now treating the face, scalp, neck and ears too, and if exposed to ticks you should really check your entire body not only on the day after walking in woodland, but also the day after too.

Dr Rob Ellis Consultant Dermatologist, South Tees

Notes From a Small and Then a Big Island



International Society for Digital Imaging of the Skin (ISDIS)

I was recently re-invited to present to the PCDS during the summer meeting at "the Belfry". As always, I thoroughly enjoy these meetings, although this year my head was a little thick following in depth science discussions with some of the Committee in the bar the night before. I was also disappointed to realise the golf clubs I brought with me were redundant!

I am currently writing this bulletin in Brisbane following a great victory for the Wallabies over the All Blacks. The stiff competition between the two nations extends past the rugby field, and into the world of skin cancer and melanoma care. I have been attending the 9th Society of Melanoma Research where I have managed to keep up to date with the ever-changing field of skin cancer. I was also fortunate enough to make a flying visit to Tauranga, on the Bay of Plenty, New Zealand, as a stop-over to visit my old SpR, and major inspiration in my career choice, Dr Neil Mortimer who runs a state of the art Skin Cancer Centre. I think some of the experiences I have had these past 10 days are going to have a major impact on my future skin cancer care, and although I love the rain and smog of Teesside it wouldn't seem too much of a hardship to battle the scourge of skin cancer on its home turf!

Although I am sat in the Sunshine State, the sun has been hiding this week and I have been subject to ridicule for bringing the British weather with me. I have however taken a keen interest in the UV index throughout the day. This scale is used by the WHO to report on UV radiation levels around the world, and ranges from 0 – 11+. In the UK, 8 is a rare phenomenon, with 7 only occurring on exceptional days around the summer solstice. It is the middle of October, and although there are clouds in the

sky, the UV index here in Brisbane is 10! It was completely overcast yesterday, and it still hit 8. You can really feel it when the clouds move and the death rays from the sky hit your skin. No wonder you burn in minutes.

The first NZ/Aussie debate was who has the highest rates of melanoma. The latest data sets for Queensland suggest an invasive melanoma rate of ~80 per 100,000 per year. With up to 50% of melanomas excised in Australia being in situ at diagnosis, this takes the figure much higher. The Australian registry data for skin cancer is much more robust than Tauranga's, but their local figures do seem to be consistent with Queensland's.

In terms of non-melanoma skin cancer (I'm sure we should start calling this keratinocyte cancers), the Australian registry suggests rates of SCC at 271/100,000 per year, BCC 770, all keratinocyte tumours (including AK and Bowen's) 1531 and keratinocyte cancers in > 80 year-olds ~6000/100, 000 per year! (data taken from the Neville Davis and Gerald Milton Lecture by Adele Green, SMR 2017)

A striking difference for me, and to be fair I've not seen much of either country on this trip, is the general condition of the two populations skin. The urban Brisbanite tends to have pretty good quality skin. I am finely attuned to people watching, and spotting skin pathology at 30 paces (my friends' kids call me the Derminator); but all seemed generally good in Oz. However, the average New Zealander seems to have much more background solar skin changes. This was confirmed during my time in Dr Mortimer's Tauranga skin clinic where everyone seemed to be riddled with sun damage, AKs and BCCs. A select population I know, but it was the same in the coffee shops (I'm also a coffee addict and the Flat White originates from New Zealand) and bars.

Dr Mortimer runs a Moh's micrographic surgery service for a large catchment on the North Island. The process of Moh's is essentially to excise narrow clinical margins around keratinocyte cancers (generally BCCs) and then assess frozen sections of the tissue almost immediately following surgery. The patient can the undergo wider margins as necessary on the same morning, and closure of the remaining defect. Moh's remains the gold standard for skin cancer excisions for this reason. It is however costly and has limited availability in the UK at present.

During microscopic analysis of the Moh's sections, a typical UK BCC would be surrounded by relatively "clean" epidermis. Conversely, the BCCs I saw in NZ seemed to be sat in a sea of varying degrees of keratinocyte dysplasia, with evidence of actinic keratosis being completely passé and an expected part of older NZ skin.

One of the most pleasing elements of the congress was a presentation of the evidence behind the long-standing Slip, Slop, Slap "SunSmart" campaign in Oz. Perhaps this has something to do with the differing general skin phenotypes? Cost benefit analysis of this campaign has consistently shown health economic benefits from skin cancer reduction – with an overall saving of AU$2.30 per dollar invested in the campaign[1]. Interestingly, sunbeds have also been completely banned across Australia since 2013 – hopefully, this will also reap further rewards from forward thinking policy makers.

The UK has a long tradition of tattooing. The northern inhabitants of Brittania were known as Picts, or painted people, by the Romans. This was probably due to their habit of applying blue, woad (*isatis tinctoria*) based "war paint", which was also used to dramatic effect in Braveheart. Since then, the tradition has continued throughout the years, with a major influence from maritime pursuits, and more recently footballers, fashionistas and the famous.

Generally, tattoos seem to be less popular in Australia, and appear to be an eclectic mix of designs and placement. There is however a long history of tattooing and scarification of the skin amongst the Aboriginal peoples. In New Zealand the tattoo appears to be ubiquitous. Initially, this followed the early inhabitation of the Islands by Polynesians who brought their tattooing culture with them. Following discussions with a couple of Māori tattooists on my travels it appears that the original South Sea Islanders' straight-line designs have gradually morphed into the swirls and intertwining motifs that appear similar to Celtic designs. Traditional Māori *tā moko* is also different to tattoo, as the skin is carved with a *uhi* (chisel) rather than punctured. There is also great symbology and meaning behind *tā moko* which has led to a degree of resentment following increased global awareness and demand for this art form, which is a major part of the Māori cultural identity that they are keen to keep undiluted.

As I have previously reported in a PCDS bulletin, I do wonder whether there are other factors that cause melanoma. UV exposure is clearly the biggest factor, but many questions remain as to why the rates around the world are still going up. A further element to my *heavy metal*

hypothesis is the possibility of tattoo pigments as a causative agent in cancer. Schreiver et al.[2] have identified that tattoo pigments easily find their way into lymph nodes, and given the variation of heavy metals such as copper, cadmium and titanium found in pigment chemicals, and my previously discussed role of these in melanomagenesis may lead to an interesting further route of investigation (which we are looking at!). Similarly, a presentation by Margaret Karagas (New Hampshire) at the SMR suggested a variation in tumourigenicity between different colour pigments found in tattoos (unpublished).

As in many fields of medicine, it seems that the follow up regimes of melanoma patients seems to have developed overtime with a limited evidence base. The role and timing of melanoma follow up depends on many variables, including the local healthcare economy (whether follow-up is State or privately funded), available providers of follow-up, the baseline risk of an individual of developing a further primary melanoma and the availability and cost of radiological screening methods. It seems that in the privately funded sectors, once you are diagnosed with a melanoma you will always be in follow-up (as you will be paying someone for it). Some of the evidence presented during the SMR suggests that the majority (up to 77%) of primary and second primary melanomas are detected by the patient or a friend, questioning the all-powerful role of clinical follow-up, and that most countries utilise GPs to undertake melanoma follow up rather than relying on secondary care practitioners. Our follow up regimes in the UK do seem to be rather arbitrary, but my group have just been awarded an NIHR Health Technology Grant in conjunction with Dr Tim Cunliffe to assess the current follow-up of AJCC stage I melanoma patients; hopefully, resulting in some evidence based changes to the current system.

In terms of developing melanoma care pathways, we heard from the American National Comprehensive Cancer Network, the Australian "wiki" system for guideline development, the Germans' strictly evidence based guidelines and British NICE regime. Overall, the British system seems to be less reactionary to changes in international management of melanoma, but it does place a great emphasis on standardisation of care across the board. This has its strengths, in terms of highlighting areas of concern, but it does limit the role that some skilled clinicians play in the care pathway. In many countries, and certainly in NZ, there is an understanding that care should be undertaken by the appropriate individual based on their skill set, not title/position. During my NZ excursion I witnessed numerous surgical procedures undertaken by GPs and nurses, and there is no necessity that skin cancers are treated in secondary care only.

One of the biggest differences I saw in the Antipodes was the huge role played by teledermatology for lesions. This was probably, initially, down to the huge geographical distances involved, but has now become a major part of their practice. It is also morphing into a whole new technological world , with high quality photographic screening and distance "neural learning" of automated systems of pattern recognition that appear to be as accurate at diagnosing skin cancer as a trained Dermatologist. We are still very reluctant to embrace teledermatology in the North East, but as an antonym to G.O.T "summer is coming…" and I think that the computer/camera will become a much greater part of our diagnostic array in the future.

As always, dermoscopy itself made an ongoing appearance at the meeting with varying experiences of different tumour sites and 1001 different models to buy. Interestingly, the International Skin Imaging Collaboration: Melanoma Project, led by Harold Kittler, and encompassing a range of academic and industry partners are compiling a huge database of clinical and dermatoscopic images of melanoma to help develop digital imaging standards and creating a public archive of skin lesions; it's well worth a look (http://isdis.net/isic-project).

Overall, I think my trip to the southern hemisphere opened my eyes to the sheer volume of skin cancer seen in Australasia; but also how well the health care systems have adapted to this demand with forward thinking and acceptance of meritocracy. I am concerned that we are hanging on at the moment in the UK in terms of skin cancer care, but I predict that this will likely fall off a cliff edge soon given the reductions in Dermatologist numbers and the inability of the NHS to change gears at an appropriate pace. Hopefully I'm wrong, but there is always going to be plenty of work in Tauranga…

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Dr Tim Cunliffe GPwSI in Dermatology and Skin Surgery
Clinical lead for the National Accreditation of GPwER in Dermatology and Skin Surgery (the longest title I have ever had!)

An Update on the Accreditation of GPwER in Dermatology and Skin Surgery

At the time of publication of this bulletin it is very likely that the new guidelines on the Accreditation of General Practitioners with Extended Roles (GPwER) in Dermatology and Skin Surgery will be finalised, or almost across the finishing line. For those unaware, the term GPwER is replacing GPwSI.

The new **dermatology framework,** which will be accompanied by a **generic framework,** is ground breaking in that it is the first national GPwER speciality guideline. The RCGP, who are the accrediting body, have worked closely with members of the PCDS and British Association of Dermatologists (BAD) to develop the framework. Together, this working group has also taken advice from NHS England, and the General Medical Council (GMC), as well as keeping the medical defence up to date.

As things stand I am unable to divulge certain information, however, I can share below some of the key points about the guidelines.

- It focuses on the **accreditation of the individual,** not the service, making it transferable to anywhere in the country.
- To be accredited through the RCGP an individual must still be in **active General Practice,** meaning a minimum of 40 sessions per year, however, for most it is likely that career portfolio's will have a good mixture of generalist and specialist work.
- There will be **no grandfather clause** ie all existing GPwSI will have to go through the process. The good news is that the concept of reaccreditation every five years, which is currently the case, has been scrapped – **once an individual is accredited there will be no more hoops to jump through.**
- The guidelines, including the curriculum, **are likely to be similar** to the last GPwSI guidelines in 2011, as such the process for formerly accredited GPwSI should be relatively straightforward.
- The clinical supervisor, who signs off the competences, may be a consultant dermatologist, however, other appropriately competent individuals, such as **experienced GPwERs can also now act as supervisors.**
- The accreditation documents will be submitted electronically to the RCGP and then **assessed** by both a generalist and a specialist. The assessors then pass their recommendations to a panel, which is to be held quarterly.
- Those accredited will receive a certificate, which will hopefully be kite marked by the GMC and defence unions.
- Accredited GPwER will usually have an **annual performance review in the specialist area,** usually by the clinical supervisor, which can then be fed in to the whole scope of practice annual review performed by the GP appraiser.
- Five years of successful appraisal will lead to **revalidation,** which will act as reaccreditation.

The **homepage of the PCDS website** will flag up as soon as the accreditation process goes live.

Emma Le Roux GP with a Dermatology interest and Researcher

Primary Care Dermatology Research News Column

Once again, we are looking for GP and nurse involvement to give us your ideas and experiences to help shape the future of research into dermatological conditions. Priority Setting Partnerships (PSPs) enable clinicians, patients and carers to work together to identify and prioritise uncertainties about the effects of treatments that could be answered by research. There are several PSPs currently ongoing in dermatological conditions.

The first is the Hyperhidrosis PSP in collaboration with a team at De Montfort University, Leicester. Hyperhidrosis (excessive sweating) is a common condition with limited satisfactory treatments. It is often undiagnosed and untreated because many people with the condition are too embarrassed to seek help. There is currently an **initial survey** underway which would benefit hugely from GP and nurse contributions. To have your say and **complete the survey** please visit the hyperhidrosis PSP https://cambridge.eu.qualtrics.com/jfe/form/SV_8dDDUdANnsojlnn

Lichen sclerosus is a chronic, inflammatory skin condition that mainly affects genital skin, and there is a lack of published high quality evidence around treatments and prevention of this condition. Fortunately, there is another PSP for this condition which is now into the second survey stage. It is being funded by the *British Society for the Study of Vulval Disease (BSSVD)* and co-ordinated through the Centre of Evidence Based Dermatology, in Nottingham. Over 650 participants responded to the first survey. Their questions have been collated and **the second survey is now open** for people to vote on those that are most important to them. They are also collecting **expressions of interest** from patients, carers and parents, clinicians and healthcare professionals to **attend a final workshop in June.** To **participate in the survey** and subsequent activities please visit the website: http://nottingham.ac.uk/research/groups/cebd/projects/5rareandother/ls-psp/index.aspx

I am involved with the Psoriasis PSP which is well underway. It is being led by a team from the University of Manchester and supported by the Psoriasis Association. The

first survey had an excellent response with over 2,000 questions collected from 795 respondents. The second survey (to vote on the questions collected) will be released in May 2018. Please see the website here: **https://www.psoriasis-association.org.uk/research/psp** for further updates.

Moving away from PSPs to malignant melanoma excisions and dermoscopy use in primary care. Current guidelines require GPs in the U.K. to refer all suspected malignant melanomas for management in secondary care[1]. In other comparable countries where melanoma incidence is higher including Australia and New Zealand, initial management of melanoma is largely a primary care activity and supported by their national guidelines[2]. A recently published study looked at melanoma mortality following excision by GPs or in-hospital in a whole Scottish sample[3]. They explored the association between morbidity and mortality and setting of primary melanoma excision (primary versus secondary care), and found no meaningful difference. Although these results are not definitive, they may invite discussion around the role of GPs in the management of suspicious skin lesions, particularly in this era of increasing melanoma incidence and burgeoning secondary care clinic lists.

While there is not yet sufficient evidence for the safe use of dermoscopy in routine primary care, many dermatologists feel that, with training, it can be safely and accurately used to reduce referrals via urgent or routine pathways. A group at the primary care unit, Cambridge University are currently conducting a systemic review of the evidence for dermoscopy use in primary care. Alongside this, they are very keen to understand more about primary care clinicians' views about dermoscopy use. They would be very grateful if **GPs and practice nurses could complete a survey** about their use of dermoscopy in routine practice. Please either follow this link to the survey: Take the Survey, or copy and paste this URL into your internet browser: **https://cambridge.eu.qualtrics.com/jfe/form/SV_8dDDUdANnsojlnn?Q_DL=6fFY0kbxDnqrqFD_8dDDUdANnsojlnn_MLRP_cNqUmy7lkgorHQV&Q_CHL=email&Q_JFE=qdl**

I wanted to highlight a recent study that has explored the **views and experiences of patients seeking information and help for vitiligo.**[4] This was a qualitative study of free text responses in an online survey distributed to members of the Vitiligo Society. Participants expressed concerns about the credibility of online information on vitiligo and often viewed GPs as their primary information source. Where GPs appeared sympathetic or signposted towards further information this was appreciated, even where people felt their GP had not seemed knowledgeable. They found that the information and help-seeking needs of people with vitiligo currently appear to be poorly met, even amongst members of the Vitiligo Society, who are likely to have received more information than others.

The **UK Dermatology Clinical Trials Network (UK DCTN)** is a collaborative network of clinicians and health service researchers which supports the development of research ideas into future funded studies. Each year they award fellowships to GPs and nurses with an interest in Dermatology. Through my own experience of being an award holder, there are a wealth of activities offered including attending the Getting to Grips with Evidence Based Dermatology Course, joining the Network Steering Committee and undertaking critical appraisal training with UK DCTN Chair, Professor Hywel Williams. The 2017 UK DCTN GP Fellowship has been awarded to Dr Mitesh Patel. Mitesh is a GP academic clinical fellow (ACF) based in Nottingham and has a research interest in cellulitis. More information about the fellowships and the UK DCTN can be found at their website **www.ukdctn.org**

Finally, for those of you interested in the latest evidence around Acne and Hidradenitis Suppuritiva, there is an **Annual Evidence Based Update Meeting on Wednesday 9th May 2018,** held by the Centre of Evidence Based Dermatology at the East Midlands Conference Centre, Nottingham. Chaired by Professor Hywel Williams, the programme for the meeting includes presentations by European experts of recently conducted randomized controlled trials and systematic reviews, plus clinical viewpoints. For details of this and previous meetings, including some useful presentations, please see **www.ukdctn.org/events-and-meetings/evidence-based-update-meetings.aspx**

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Topical Calcineurin Inhibitors - Beyond Atopic Dermatitis

Pimecrolimus (Elidel) and tacrolimus (Protopic), the topical calcineurin inhibitors, are immunomodulatory agents that affect the T-cell and mast-cell function and inhibit the synthesis and release of multiple pro-inflammatory cytokines, including interferon-gamma, tumor necrosis factor-α, and interleukins 4, 5, and 10. They were initially developed for the treatment of atopic eczema and are licensed as second line treatment for this condition.

Their main advantages compared to topical corticosteroid therapy are more selectivity in their mode of action, no risk of skin atrophy and negligible systemic absorption.

Topical tacrolimus is available in 0.1% and 0.03% potency, the weaker preparation usually prescribed to children aged 2–16 years. In adults the usual strength is 0.1%. The lower 0.03% strength may sometimes be suitable in adults on the face or eyelids, as it can be just as effective and has a lower risk of initial irritation.

In the UK 0.03% tacrolimus ointment and 1% pimecrolimus cream are not licensed for children under 2 years old. Israel allows pimecrolimus use in children as young as 6 months old and in New Zealand pimecrolimus is approved for atopic dermatitis in patients that are over 3 months of age.

Although licensed for atopic dermatitis only, pimecrolimus and tacrolimus have been tested on a number of other inflammatory dermatoses, especially those involving sites more prone to deleterious side effects of topical steroids (in particular atrophy) such as the face, flexures, and genital areas.

They were found to be efficacious for facial or flexural psoriasis, seborrhoeic dermatitis, vitiligo, lichen sclerosus, morphea, contact and hand eczema and cutaneous lupus erythematosus.

Psoriasis

Early investigations in the late 1990's demonstrated that tacrolimus induced very mild improvement in psoriasis, which was not better than placebo[1]. It was suggested this was due to low penetration of the drug into thick plaques and prompted the use of 6% salicylic acid gel to enhance it[2]. The results demonstrated a statistically significant decline in erythema, scaling, and pruritus in the treated group versus placebo.

These observations suggested than tacrolimus may be more effective in areas devoid of thick scale. Subsequently, 10 patients with anogenital and facial psoriasis were given tacrolimus 0.1% ointment BD for 10 days with a 12 week follow-up. There was notable improvement in all subjects by the end of the first week, and no adverse effects[3].

A multicenter randomized double-blind placebo-controlled trial investigated the efficacy of tacrolimus 0.1% ointment in 167 patients with inverse psoriasis for 8 weeks. By the end of the trial, 65.2% of patients treated with tacrolimus 0.1% ointment were clear or almost clear of their psoriasis, compared to 31.5% treated with placebo[4].

An open-label study investigated the safety and efficacy of tacrolimus in the management of genital psoriasis in males. 12 participants, applied tacrolimus 0.1% ointment BD for 8 weeks and were followed up for a further 4 weeks. The mean male genital PASI was significantly reduced from 15.8 at the beginning of the trial to 1.2 at week 8[5].

Steele published a retrospective case study of 13 paediatric patients, aged 22 months to 16 years with facial and intertriginous psoriasis treated with tacrolimus 0.1% ointment twice daily[6]. Within 2 weeks 12 of the participants achieved complete clearance of lesions. Patients were followed up for 2 years and instructed to apply the ointment if there was any recurrence of skin lesions.

Another study of 11 patients (aged 6-15 years) demonstrated the efficacy of tacrolimus 0.1% ointment for treatment of facial and inverse psoriasis[7]. All patients had excellent improvement of psoriasis after 30 days of treatment. Several participants who experienced a relapse following cessation of treatment regained adequate control upon re-application.

Tacrolimus 0.1% ointment produced good results when used in a 12 week randomized controlled open-label study, involving 21 patients with nail psoriasis. Participants were randomized to either the treatment or placebo group and were applied the ointment to their nails once daily at bedtime[8]. Severity of nail psoriasis was measured using the Nail Psoriasis Severity Index (NAPSI). At the end of the trial participants who received treatment had a mean significant reduction in NAPSI score of 13, compared with a mean reduction of 3 points in the placebo group.

A number of reports suggest that topical tacrolimus treatment is effective for generalized pustular psoriasis[9,10] palmoplantar pustular psoriasis[11], and oral psoriasis[12, 13].

Seborrheic Dermatitis

A Cochrane Database from 2014 reported on 7 randomized controlled trials which examined the use of calcineurin inhibitors[14]. Outcomes of interest were total clearance of symptoms, erythema, scaling, pruritus and adverse effects.

Steroids and calcineurin inhibitors were found comparable in all other assessed efficacy outcomes (5 trials, 237 participants). Adverse events were less common in the steroid group compared with the calcineurin group.

In one study, a calcineurin inhibitor was more effective than placebo in reducing erythema and scaling. In another study, it was comparable with an azole when erythema, scaling, or adverse effects were measured for longer-term treatment.

The group's conclusion is that calcineurin inhibitors show benefit over placebo in reducing erythema and scaling and that they seem to be comparable with azoles and steroids concerning efficacy. Steroids have less adverse effects.

Vitiligo

For patients with localised vitiligo, mid-to high-potency topical steroids are the first-line therapy and agents with negligible systemic or local side effects, such as mometasone furoate, are preferred.

The efficacy of tacrolimus and pimecrolimus for the treatment of non segmental vitiligo has been evaluated in several randomized trials by the Cochrane Group[15].

In a randomized trial, 100 children (55 suffered from facial vitiligo) were treated with clobetasol propionate 0.05%, tacrolimus 0.1%, or placebo for six months[16]. Among patients with facial vitiligo, re-pigmentation (>50 percent from baseline) was the same in the topical steroid and tacrolimus groups (58 percent). Among those with non facial vitiligo, the success rate was higher in the topical steroid group compared with the tacrolimus groups (39% versus 23%).

Another randomized trial including 44 adult patients with stable vitiligo compared 0.1% tacrolimus ointment BD, 1% pimecrolimus cream BD, and NB-UVB phototherapy three times a week for 24 weeks[17]. At the end of the study, re-pigmentation rates for the three treatment arms did not differ significantly.

In a 12-week open, randomized study, 53 patients with vitiligo were treated with 308 nm monochromatic excimer light (MEL) twice weekly plus 0.1% tacrolimus and oral vitamin E daily, 308 nm MEL twice weekly plus daily oral vitamin E, or daily oral vitamin E alone[18]. At the end of the study, good to excellent re-pigmentation was achieved in 70% of patients in the MEL plus tacrolimus and vitamin E group, 55% of those in the MEL plus vitamin E group, and in none of the patients in the vitamin E group.

In another open trial, 40 children with vitiligo were treated with 0.1% mometasone furoate cream OD or 1% pimecrolimus cream BD for three months[19]. Moderate or marked responses were seen in 55% in the mometasone furoate group and in 35% in the pimecrolimus group. This difference was not statistically significant.

Twice-daily application of 0.1% tacrolimus provided better results compared with once-daily applications[20].

Good results were obtained in an open study performed with 1% pimecrolimus cream[21]. 0.05% clobetasol propionate induced a comparable rate of re-pigmentation. The best results were observed on sun-exposed areas.

A prospective comparative study has shown that tacrolimus monotherapy in the absence of UV resulted in little re-pigmentation[22]. This is interesting because labeling recommends that calcineurin inhibitors should not be used in combination with ultraviolet light therapy.

Nowadays, some dermatologists consider topical calcineurin inhibitors as the preferred first-line therapy in patients with limited disease involving the face or intertriginous areas.

Lichen Sclerosus

Topical calcineurin inhibitors appear to have efficacy for vulvar lichen sclerosus (LS), but are less potent than clobetasol propionate. Given the high therapeutic efficacy of topical steroids for LS, topical calcineurin inhibitors are second line treatment if topical steroid therapy is ineffective or poorly tolerated.

A three-month randomized trial in which 58 female children and adults with vulvar LS were randomly assigned to treatment with tacrolimus 0.1% ointment OD or clobetasol propionate 0.05% ointment OD found that although both treatments improved vulvar LS, clobetasol propionate was more effective[23]. At study end, 19 of 28 tacrolimus-treated patients had residual clinical signs of LS compared with only 9 of 27 patients in the clobetasol propionate group. In addition, significantly more patients had no clinical signs or symptoms of LS in the clobetasol group.

In a 12-week randomized trial of 38 women with vulvar LS that compared pimecrolimus 1% cream BD to clobetasol 0.05% cream OD, both agents significantly reduced patient symptoms and improved histopathologic inflammation[24]. The degree of reduction of inflammation in biopsies was higher with clobetasol, supporting the position of potent topical steroids as the preferred choice for initial therapy.

Other pruritic vulvar dermatoses including lichen simplex chronicus[25], chronic pruritus[26] and allergic contact dermatitis[27] have responded to topical calcineurin inhibitors

The impact of topical calcineurin inhibitor therapy on risk for SCC in patients with vulvar LS is unknown and long-term safety data on topical calcineurin inhibitors use for vulvar LS are lacking. Topical pimecrolimus may exhibit a better long-term tolerability profile[28].

Morphea

Topical tacrolimus 0.1% ointment may be effective for active, inflammatory morphea.

In a randomized trial of 10 adults with active circumscribed morphea, one lesion on each patient was treated with tacrolimus ointment and a second lesion with petrolatum, both given twice daily for 12 weeks[29]. Significantly greater improvement occurred in lesions treated with tacrolimus.

A few additional open label studies lend support to the use of topical tacrolimus for morphea [30,31, 32].

Discoid Lupus Erythematosus (DLE) and Subacute Cutaneous Lupus Erythematosus (SCLE)

Topical steroids are first line therapy for DLE and SCLE. Topical calcineurin inhibitors are an alternative on facial lesions but are slower to act.

An 8 week trial examined 10 patients with DLE who were treated with either pimecrolimus 1% cream or betamathasone17-valerate 0.1% both applied BD[33]. Mean severity scores decreased by 86% and 73% respectively and adverse effects were within the same range for both agents.

Another trial compared tacrolimus 0.1% ointment and clobetasol proprionate 0.05% ointment[34]. In the 5 patients who suffered from DLE or SCLE efficacy was similar and adverse affects (telangiectasiae) were more common in the clobetasol group.

Conclusion

The extended role of the topical calcineurin inhibitors is an important addition to our arsenal of dermatological therapeutics.

The adverse effects profile of the calcineurin inhibitors is well known. Both agents are usually well tolerated and occasionally cause transient irritation or stinging at the start of use. As use becomes wider we will most likely recognize hitherto unknown side effects akin to the rosacea-like eruption[35, 36] which has been reported for both pimecrolimus and tacrolimus, and we will need to warn our patients about them.

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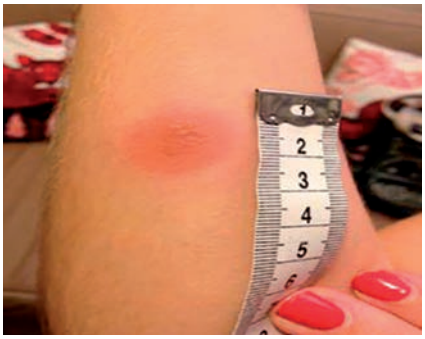
Case Study: A Case of Fixed Drug Eruption



Ms X presented with history of an itchy rash that appeared overnight, 16 months ago, on her right forearm which resolved in some days. She reported intermittent flare up in the same area every month during her periods. The rash would get itchy, inflamed and ooze and needed topical steroids on a couple of occasions. She was prescribed mefenamic acid (MFA) for dysmenorrhoea which she used every single period but recalled developing a rash even when she did not take MFA. There was no history of eczema or any other trigger. She had no medical issues and was allergic to codeine. On examination, there was a 10p size pigmented macular rash on her right forearm without any sinister features under the dermatoscope.

The working diagnosis was fixed drug eruption (FDE) following MFA. Though the rash flared up even when she did not take the medication, it appeared that MFA was the trigger on most occasions. Discoid eczema and insect bite was considered but the history and presentation did not fit with the picture. She was due for a period and it was proposed to avoid taking MFA. She resisted until the 3rd day of her period and with one dose developed a flare up on the same area the following day. Provoking the rash with the assumed causative drug helped establish the diagnosis. This was confirmed with a biopsy which showed interface inflammation with scattered colloid bodies, pigment deposits in the dermis with perivascular infiltrate of mature lymphocytes. The appearance was consistent with FDE. She was advised to consider other methods to deal with dysmenorrhoea.

FDE represents a drug reaction of the skin and mucous membranes of type IVc[1] characterised by inflamed lesions at the identical location after repeated exposure to the responsible drug. Intraepidermal α β TCR$^+$ and CD8$^+$ T cells possessing a phenotype resembling effector memory T cells are responsible for the epidermal damage[2,3]. The T cells persist for years in completely faded lesions[4] and can be reactivated following re-exposure to the drug. FDE is characterised by sudden appearance of defined erythematous macules on the skin and mucous membrane[5,6]. The lesions can blister particularly in the mucous membrane. Common sites are palms, soles, the medial aspects of the limbs, abdomen, oral mucosa and glans penis. The lesions are often pruritic and occasionally systemic symptoms can occur. It resolves with hyperpigmentation that can persist for months. FDE is common between 20-40 years and an association with HLA-B22 has been reported[7]. The common triggers are antibiotics, antifungal drugs, analgesics, anticonvulsants and barbiturates[6,8]. MFA is a non-steroidal anti-inflammatory drug that acts via inhibition of prostaglandin synthesis and mainly prescribed for dysmenorrhea. FDE has been commonly associated with non-steroidal inflammatory drugs but reports of MFA as a trigger are infrequent[9-15]. Provocation test with the implicated drug represents the gold standard in diagnosis[16]. Local patch testing is reported but is limited by lack of standardisation of the tests as the results depend on the concentration and penetration of the test substance[17].

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Journal Watch

November 2017 – January 2018

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GPSI Sheffield & PCDS Treasurer

Welcome to your new Journal Watch, it's 2018, so we are already in the cutting edge of future aspirations – when Marty McFly went Back to the Future in the second film, that was three years ago! We may not have hover boards, but we do have some learned journals to examine.

We will, as we so often do, start with a set of guidelines. Who doesn't love a set of guidelines. To paraphrase Elizabeth Barrett Browning, How do I love thee, Guidelines, let me count the ways… Anyway, our first set[1] in this edition gives us advice on the management of pemphigus vulgaris (PV). PV is an uncommon, but potentially life-threatening disease that requires specialist care and immunosuppressive treatment. First line treatment with oral corticosteroids is well established and cessation of blistering can be expected within 2-3 weeks – although healing may take up to 8 weeks. Once remission is achieved, then the steroid dose can be tapered, although there is no consensus in the rate at which the steroids are reduced. As PV is a long term, but not lifelong disease, both bone protection and a steroid sparing agent must be considered at the outset, with azathioprine being the most common first line choice, followed by mycophenylate mofetil if azathioprine is not appropriate or tolerated. Inevitably, given recent advances in other fields, there is now a biologic agent to consider, with Rituximab, a monoclonal antibody directed against B-lymphocyte-specific antigen CD20 showing significant promise. Further advice is limited by the lack of high-quality evidence to support the use of the usual suspects, such as methotrexate, dapsone, tetracyclines and cyclophosphamide. Given that PV is, thankfully, uncommon, the large scale trials necessary to clarify the situation further are unlikely to happen any time soon.

We live in worrying times, and the move to restrict the prescription of various medications – including, it seems, emollients, is a seemingly retrogressive step in the management of many skin diseases. Emollients are vital both in the primary treatment of many diseases, but also as adjuvant agents that reduce the dose of corticosteroids necessary to achieve clinical improvements. A Cochrane systematic review[2] attempts to add some evidence to the debate but, sadly, falls short of any substantive conclusions. Whilst most moisturisers demonstrated some beneficial effects – such as flare reduction and corticosteroid sparing – no one moisturiser works better than another.

This emphasises what we have taught for many ears, not only is the best emollient the one that the individual patient prefers, it is also necessary to maintain a range of such agents to allow the propagation of patient choice. Perhaps those holding the purse strings would be well served by reading this article…although I fear it may fall upon deaf ears.

We have previously looked at the use of terbinafine in the treatment of onychomycosis. Previously, use was limited by the rather prohibitive cost of this treatment, but since it dropped off patent, the unit cost of a course of terbinafine has fallen enormously. Concerns, however, still arise around the small risk of terbinafine induced drug-induced liver injury (DILI). Helpfully, a critically appraised topic[3], looking at exactly this topic is next on our list. A literature search produced case reports of 69 symptomatic patients, the mean duration of treatment to reaction was 30 days, and patients generally had symptoms – pruritus, a flu-like illness, dark urine and jaundice being the commonest presentations – for a mean of 14 days before seeking medical assistance. Significantly, all patients with DILI were symptomatic, and no asymptomatic patients were identified if hepatic monitoring had been performed. At no time point was monitoring deemed to be meaningful, and, consequently, monitoring of liver function tests on terbinafine is not considered necessary.

Now, the treatment of verrucas cannot, really, be considered 'cutting edge', but, as they remain one of the commonest dermatological pathologies seen in Primary Care, new research[4] into treatment options seems to be rather welcome. Clearance rates for cryotherapy and salicylic acid keratolysis hover around the 14% mark, which is, frankly, poor. This study looks at the Falknor needling technique, first described in the 1960s, and recently attracting some renewed interest. It involves anaesthetising the verruca, and repeatedly inserting a needle into the verruca and through in to the subcutaneous fat layer. Clearance rates are impressive, around 65%, in the one randomised trial previously published, but the numbers of subjects included are very small – only 33 patients. The trial we are looking at today compares this needling technique with callus debridement. Sadly, needling was neither clinically better, nor more cost effective than traditional methods. It was, however, considered to be less painful – perhaps the local anaesthetic had something to do with that… The Holy Grail of cheap, simple and effective verruca treatment remains obscure, for now.

From the simple, to the slightly obscure – bullous pemphigoid (BP). Current treatments of BP revolve around the long term use of topical and systemic corticosteroids. These are, sadly, associated with a high level of adverse events and an excess rate of mortality. Corticosteroid sparing agents are back in the 'news' after studies looking at the use of Doxycycline in the treatment of BP – which we discussed a couple of editions ago. Doxycycline was found to be non-inferior to oral corticosteroids, so now attention turns to azathioprine and dapsone[5] – a couple of more traditional steroid sparing agents. The data – looking at safety and efficacy of dapsone, compared with azathioprine, both of which are combined with methylprednisolone – supports dapsone as the more effective agent. As often, however, the 'lower than expected' number of patients mean that the results are classed as 'barely significant'. This is not a level of statistical scrutiny that I had previously been aware of. Using steroid sparing agents, however, does lead to a significant reduction in 1 year mortality in this rather vulnerable patient population.

A continuing theme of this Journal Watch is that evidence cannot be assumed – even when it appears to be self-evident. Increasingly, we are using patient reported methods – such as the Dermatology Life Quality Index (DLQI) – to compare the efficacy of varying treatments and also to measure disease severity. As the relentless march of technology continues, these indices are often used in electronic formats, rather than paper based versions. As the same information is presented in a similar format, it is often assumed that these two formats are comparable, without formal evidence. Thankfully, this study[6] demonstrates that there is high concordance, and therefore high equivalence between the electronic and paper versions of the DLQI. Patients also clearly prefer the electronic version.

One of the most interesting developments in the recent past has been the emergence of treatment options for Hidradenitis Suppurativa (HS). Whilst we are some way off an easy, simple and effective treatment for this most distressing of conditions, the discovery of an active pro-inflammatory cytokine makes future, targeted therapies increasingly likely. A group from Switzerland have been looking at[7] the levels of Interleukin-32 (IL-32) in skin samples from healthy controls, and patients with HS, psoriasis and atopic dermatitis (AD). They have found that Il-32 is overexpressed in HS, in both lesional skin and serum compared to all three control populations. Targeted treatment against Il-32, therefore, represents a potential new therapeutic option, specifically for HS.

Whilst the potential for the development of hepatic toxicity, and hepatic fibrosis has long been noted in patients where Methotrexate (MTX) is used as a long term therapeutic option, the need for monitoring this with serial measurement of procollagen-3 N-terminal peptide (PIIINP) levels remains controversial. In the region in which I work, and, it seems, many other regions, Dermatologists regularly measure PIIINP levels, whilst rheumatologists do not. Recent reports seem to suggest that the incidence of liver fibrosis in patients taking MTX for psoriasis is actually relatively low, and in those who do develop fibrosis, either steatohepatitis or other stigmata of the metabolic syndrome are most significant factors in the fibrogenesis. A research letter, here[8], also suggests that psoriasis itself may be an independent predictor for the development of hepatic steatosis (we have discussed, at length, the co-existence of psoriasis and the metabolic syndrome). Whilst PIIINP measurement does reduce the necessity for performing liver biopsies, MTX administration may not be the only risk factor for the development of liver fibrosis. The use of PIIINP to monitor liver disease evidently needs further investigations. Perhaps the rheumatologists are right?

A case report from South Korea[9] provides a potential new application for topical Ingenol mebutate (IM). The case describes the use of IM in the successful treatment of a facial pyogenic granuloma (PG) in a 4 year old. Whilst this is obviously out of license usage in the UK, two, three day applications, separated by a week led to complete resolution of the PG with no recurrence at 5 months of follow up. Other treatment options may be cheaper, in isolation, but would require either sedation or general anaesthetic. Other topical options are available – such as topical timolol – but the short duration of treatment and rapid resolution engendered by IM could be key features if this was, after further study, to prove a useful addition to our armamentarium.

In these enlightened times, when a disease presents itself, with no apparent mechanism of initiation, it comes as a bit of a shock. Frontal fibrosing alopecia (FFA), is such a disease. Despite many theories and associations, the aetiology remains obscure but with each bit of evidence, the field narrows… Some finding suggest a hormonal mechanism – it is a disease more prevalent in post-menopausal women – and some studies suggest a response to antiandrogenic drugs. This study[10] looks at serum sex hormone levels in pre-menopausal women diagnosed with FFA. Looking at 43 women, 39 were considered to be 'normal', whilst the remaining 4 were considered to be either entering the menopause, or actively peri-menopausal. The conclusion reached is that serum hormone levels are not directly related to the development of FFA. A negative result, as we well know, can be just as valuable as a positive one.

The incidence of Squamous Cell Carcinoma (SCC) is increasing, probably as a result of chronic Ultra Violet (UV) light exposure. Invasive SCCs present with different grades of differentiation and different depth of invasion. Identifying these at an early stage would facilitate earlier removal and, therefore, potentially better outcomes. Sadly, however, SCCs do not come with a little flag in them giving their grade of differentiation. Although dermoscopy can be helpful, histological reports are the gold standard for determining grade – but there may be patterns to be found with careful study… We thus turn to a study[11] from Australia – where they seem to have experience of both chronic UV exposure, and high levels of SCCs. Looking, retrospectively, at clinical and histological data, they assessed the grade of differentiation, histological diameter and depth of invasion in various sites across a study population of 1666 SCCs. Increased rates of poorly differentiated SCCs were found on the forehead and cheek for both sexes, men had more poorly differentiated SCCs on the (bald) scalp and the ears. Tumour diameter and depth tended to increase as the grade moves from well to poorly differentiated. In addition, poorly differentiated tumours, with an increased depth of invasion were found on the ears of men, and in facial sites in both sexes. Applying the knowledge of anatomical sites that have a higher incidence of SCC with high risk factors may help to identify these tumours early in the disease process. Early detection optimises outcomes, it's a win/win situation.

Moving on to another favourite topic – markers of disease severity. Prolactin has been suggested as a marker of psoriasis activity before, in fact, I think we have looked at it in a previous edition. Previous studies have shown mixed results, but a meta-analysis[12] looking at prolactin levels in patients with psoriasis and in healthy controls provides interesting reading. Prolactin levels were consistently higher in patients with psoriasis and the levels appear to correlate with disease severity.

We now turn to a second case report. Whilst allergic contact dermatitis (ACD) secondary to acrylates and methylacrylates in gel nail varnish is well recognised, here[13] is a report of a 50 year old lady who presented with hand dermatitis exacerbated by gel nail varnish on a background of chronic urticaria (CU). She was advised to avoid all nail

varnishes, and both the allergic contact dermatitis AND the chronic urticaria improved. The cause of chronic urticaria is rarely identified, this case is the first to link nail products with both CU and ACD.

Whilst isotretinoin is undoubtedly our most potent and effective treatment for acne, the controversy linking it with depression and suicide refuses to go away. Prospective studies have failed to clarify this situation and, in fact, some studies have demonstrated an improvement in mood in some patients taking isotretinoin. Whilst a randomised, controlled trial would go some way towards answering the question, the difficulties associated with 'blinding' isotretinoin, a drug with such well recognised adverse effects, makes such a study difficult to arrange. A team from Australia[14] have designed such a study and undertaken a feasibility study. Very small numbers of eligible patients agreed to enter the study – this is something that is hard to get around, when you are potentially delaying a treatment that the patient may have waited a long time to access – but the study, a triple blind study no less, does appear to be possible. We await the next steps.

We will return to isotretinoin shortly, but first, another set of guidelines – this time having particular relevance to primary care. Pruritus is a difficult condition to manage, especially so in the absence of an underlying dermatosis. Having sage advice[15] on how best to manage and investigate this troublesome problem seems particularly valuable. The management of pruritus depends upon the treatment of any underlying disease, where no disease can be identified, symptomatic measures may be appropriate. As we all know, the causes can be many and varied, so a systematic approach will help us all. Pruritus may be caused by iron deficiency, or iron overload alongside haematological malignancies, so a full blood count and iron studies (including ferritin) is a good place to start. Endocrine diseases are rarely associated with pruritus, so routine endocrine investigations are rarely needed, unless there are other signs or stigmata of endocrine dysfunction. Both liver disease and renal disease are, however, likely culprits, so liver function and urea and electrolytes are needed, alongside an ESR, and immunoglobulins. Consideration should be given to other underlying causes – such as solid malignancies, neuropathic pruritus, infections, infestations and drug-induced pruritus. When it comes to treatment where no cause can be found, emphasis is now clearly on using non-sedating anti-histamines, updosing where necessary. Topical treatments, other than emollients, are rarely of any benefit – especially calamine lotion or crotamiton cream, but there is some good evidence to support the use of paroxetine, mirtazapine, gabapentin and pregabalin in selected cases. In a secondary care setting, phototherapy can be useful, but as can be seen from the above, this is a condition that can be mostly managed in primary care. Referral should be considered where diagnostic doubt exists or those in whom there is significant distress despite primary care management. As always, I advise reading these guidelines in their entirety – they are well worth it.

And so, as promised, we return to isotretinoin, specifically to a systematic review[16] looking at both efficacy and adverse effects of oral administration of isotretinoin. Amazingly, this is the first comprehensive review of the evidence of the use of isotretinoin in acne. Fortunately, efficacy was not called in to question, with every study demonstrating a significant benefit against control. Adverse effects experienced by those taking isotretinoin, however, were around twice that experienced by those taking controls. More than half the adverse effects were dermatological, with dryness being the most common. Severe adverse events – necessitating withdrawal from medication occur in around 3.2% of trial participants. With European guidelines for the management of acne recommending the early use of oral retinoids (to reduce our dependence upon antibiotics), fresh evidence of efficacy is timely.

I will admit, that prior to reading the journals this month, I had never come across Lindioil before. Although it sounds like a hair product for swing dancers, it is the refined formulation of Indigo naturalis and has significant activity in treating psoriasis. The active ingredient in Lindioil is indirubicin, and here[17] we have a study looking at the efficacy of differing concentrations of indirubicin in Lindioil ointment as a topical treatment for psoriasis. The conclusion reached was that a concentration of 200µg/g indirubicin in Lindioil ointment was considered both effective and safe. New topicals for psoriasis are few and far between, this is a little 'left field' for Pharma, but is encouraging nonetheless.

Moving on…we know that UV causes melanoma, sunscreen prevents sunburn, and this DNA damage, so, by extension, regular sunscreen use should prevent melanoma – but by how much? Using a 'plausible health intervention scenario' of incremental increases in sunscreen prevalence over a 10 year period, the results[18] are really quite striking. The regular use of sunscreen could reduce the incidence of melanoma by around 10% in high risk populations, such as the United States (US) or Australia.

Whilst 10% doesn't sound a lot, this represents over 230,000 fewer melanomas in the US, and over 28,000 fewer melanomas in Australia in the years up to 2031. A theoretical maximum possible intervention would more than triple those numbers. Why are we aiming for plausibility, when we could be aiming for maximal benefit?

Talking of maximal benefit, pre-existing evidence suggests that indoor tanning may have addictive properties. A new instrument, the Behavioural Addiction Indoor Tanning Screener (BAITS) has been developed[19] to specifically look at this issue. Comparing the BAITS with other indices of potential tanning addiction, it does seem to be valid and reliable. As it mainly consists of binary questions (yes/no answers), it is easy to use in large numbers, and its brevity is also strongly in its favour! Results suggest that 20% of current indoor tanning users screen positive for a potential tanning addiction. These are big numbers, and represent a public health catastrophe in the making.

Finally, let's have another look at cutaneous warts. (I know, sometimes I spoil you…). Despite their seeming ubiquity, warts have a cure rate, after therapy, of no more than 50%. A team form the Netherlands[20] have been looking at patient and morphological wart characteristics to see if these predict human papillomavirus (HPV) types in individual warts and whether these characteristics predict a favourable response to treatment. The black dots of capillary thrombosis strongly predict the presence of HPV in a wart. The alpha subtype of HPV (HPV 2, -27 and -57) are associated with a poor treatment response. In addition, when cryotherapy alone was used as a therapy, HPV type did not play a role in predicting success, but cryotherapy was less successful in the presence of callus or if the wart was located deeper in the skin. It seems that morphological characteristics of warts, and HPV genotype do influence treatment outcomes and can, therefore, potentially influence future treatment options for cutaneous warts.

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