

Dermatology

in practice



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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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Debunking dermatology

“ With the Keogh review over and our new executive medical director in post, I have escaped to Wales for a couple of weeks of walking, eating, reading and chatting. I had promised to write this editorial on the first rainy day – so here we are on Day 3! That’s actually a bit unfair as it was sunny this morning, so we played tennis and then walked into Beaumaris for lunch.

This issue of *Dermatology in practice* has a mixture of the common, the rare and the puzzling. Christina Green starts us off with a practical guide to peanut allergy, debunking many of the misconceptions often held by parents of children we see in the clinic. It is refreshing to read such a clear explanation of concepts like allergy and sensitisation; the interpretation of specific IgE levels; and the relationship between Type 1 and Type IV reactions. The article is worth sharing with patients and could shorten some of those tricky consultations.

Similarly, the article by Reena Shah and colleagues on stress and the skin summarises what we all know: for many patients, the skin disease is merely one manifestation of some inner torment that the patient is going through and it is difficult, if not impossible, for us to dissect them. I have

often thought that it would be useful to have a psychology input into the dermatology outpatient clinics, but I have failed to achieve it. I was encouraged to read that providing leaflets with basic psycho-education and simple relaxation techniques has been shown to be effective in increasing patients’ insight and reducing their distress. Some dermatology departments show educational videos in the waiting areas. Perhaps we should also show relaxation techniques? Psychological support has traditionally been an area for dermatology specialist nurses, but maybe we should develop dermatology specialist psychologists?

Tracy Adni and Adrian Heagerty’s article is a useful introduction to epidermolysis bullosa but, more than that, it explains the rationale behind NHS Specialised Services. With the push to develop more community-based dermatology, it is important to bear in mind more specialised services like biologics,



■ Maybe we should develop dermatology specialist psychologists for patients with stress-related skin conditions?

complex patch testing, Mohs surgery and these very specialised services only required by small numbers of patients. One of the benefits of the NHS is that, to some extent, it functions as a massive risk-sharing scheme for those with rare but costly conditions. As the current reforms

are implemented, it is important that this aspect does not get lost.

Barry Monk’s articles on the ‘orphan drug’ dapsone, exploring its use and history,

make interesting reading. As a trainee, I was often puzzled about why a ‘trial of dapsone’ had been suggested – it seemed that learning the role of dapsone was one of those mysterious initiation rites one goes through on the journey to become a ‘proper’ dermatologist. History often teaches us lessons to equip us for today’s challenges, and Barry’s ‘Monk’s moments’ feature reminds us of the origin, and importance, of research ethics committees – and thus goes some way to relieving the pain of the preparation and submission processes. Part of my time, nowadays, is spent listening to enthusiastic doctors who want to introduce new techniques or treatments. It’s great to witness their enthusiasm, but equally important to challenge them to ensure that the patients’ interests are protected.

Neill Hepburn, Editor

Correction

In the last issue of *Dermatology in practice*, in the article ‘Dealing with artefactual skin disorders’, author Reena Shah’s name and qualifications were listed incorrectly. These should have read: Reena Shah BSc MSc DClinPsych CPsychol

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Peanut allergy and the dermatologist

It does not usually fall within the remit of a dermatologist to diagnose and manage patients with peanut allergy, particularly children. However, there is an important overlap with the work of consultant allergists who generally manage such patients, both with regards to sensitisation to peanuts and managing patients with eczema who also have food allergies. In this article, I hope to raise awareness of food allergy as a concomitant problem for children with atopic eczema, help point out the pitfalls of arriving at the correct diagnosis, and discuss some research which points towards possible new ways of managing such patients in the future.

The number of young children with a diagnosis of peanut allergy doubled between 1997 and 2002.¹ There are many theories as to why this increase has occurred, but at this time there are no

definite answers. A possible clue may be found in the work of Du Toit *et al*, who reported a large joint study between Israel and the UK where a nearly tenfold increase in incidence of peanut allergy among UK children was noted compared with Israeli children.² It was found that Israeli children were given peanut-containing foods at a much younger age than those in the UK. Following these observations, the Learning Early About Peanut Allergy (LEAP) prospective study was devised and results are expected in 2014.³ Presently, paediatric associations in the UK recommend delaying the introduction of peanuts until the age of three, but this advice could be revised depending on the outcome of the study. This work opens up the intriguing question of whether there exists an early period in an infant's immunological development where tolerance to food allergens may be established.

Sensitisation

Food allergies are more common in atopic individuals than in the non-atopic population, with around 23% of children with eczema under one year of age showing immunoglobulin E (IgE) sensitisation to peanuts.³ Only a proportion of these children show symptoms related to peanut allergy and, as with any other Type 1 allergy, it is important to make the distinction between sensitisation and frank allergy. The route of sensitisation has



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attracted a lot of attention in recent years, particularly with the finding of the filaggrin mutation in a proportion of children with atopic eczema.⁴ This results in a protein abnormality in the upper epidermis, which impairs the integrity of the skin as a barrier, allowing allergens to cross more readily.

Peanuts may be ingested whole, or often in the form of peanut butter, but less obvious contact can occur with peanut particles on surfaces or in the form of oils (arachis or groundnut), where they can be absorbed through the skin as a route of sensitisation. Peanuts are legumes, not nuts, and share allergens with other members of the legume family, which includes peas, chickpeas and soy peas, lentils, fenugreek and lupin (the last being commonly used commercially as flour to improve baking). It has been speculated that sensitisation to peanuts may occur by contact with other members of the legume family, but there is no good evidence to support this at present and clinical cross-reactions are not that common, apart from to lupin flour. This raises the question of whether we should restrict the use of emollients containing soya; for example, Balneum® (Almirall) products and Zerogent® (Thornton & Ross), in infants with atopic eczema as well as those who are already allergic to peanuts. The manufacturers try to minimise risk by heating soya to denature the protein, but they do still warn patients with peanut sensitivity about cross-reactivity on the packaging, although they are not aware of any reported major reactions.⁵

Diagnosis

Reactions to peanuts usually occur within minutes of contact with peanut allergen. This is a Type 1 reaction where specific IgE cross-links with the allergen on the mast cell to release histamine. As dermatologists, we often request IgE tests, but perhaps do not always have the expertise to interpret the results. It is a commonly held misconception that the higher the total amount of specific IgE, and the higher the 'class' of reaction reported by the lab, the more severe the allergy is likely to be. Over the past 20 years, a lot of work has been done to try to assess how levels of IgE relate to the predictive risk of a clinical allergy. From Table 1, it can be seen that the level of IgE needed to provoke clinical symptoms is different for varying food allergens.⁷ The absence of specific IgE is often much more clinically useful than a positive figure. A positive test should be interpreted as 'sensitisation', but it is not necessarily 'allergy'. The level of IgE can be used in conjunction with the information shown in Table 1 as a guide to whether a clinical reaction is likely.

Another theoretical pitfall is that the commercial tests measure only IgE directed to a restricted

Table 1. Levels of specific IgE antibodies yielding PPVs of 95% and NPVs of 90% for a positive, double-blind placebo-controlled food challenge⁶

Food	Specific IgE (k μ /l) >95% PPV	Specific IgE (k μ /l) <90% NPV
Egg	6	0.6
Cow's milk	32	1.0
Peanut	15	0.35 (>85% NPV)
Fish	20	5
Soy	65 (50% PPV)	5
Wheat	100 (75% PPV)	79

IgE = immunoglobulin E; NPV = negative predictive value; PPV = positive predictive value

Adapted from Sampson *et al*⁶

number of protein epitopes, and the epitope to which the child is reacting may be low or not included in the test. For example, peanuts have several recognised epitopes termed Ara h 2–8. Therefore, allergists often back up IgE measurement with skin prick tests (SPTs), which may use the food itself as the substrate (known as prick-to-prick testing) or a different commercial testing kit. SPTs are, therefore, usually performed alongside IgE measurements as a complementary test. In a child with a positive test of uncertain meaning, or a strongly suggestive history but negative tests, a food challenge can be performed – usually around school age under medical supervision.

Clinical reactions

The reaction to skin contact in peanut allergy is a weal at the site of itch, erythema and swelling. If peanut-containing food is swallowed, or inhaled, the reaction may be systemic, particularly in children with asthma. Anaphylactic symptoms such as bronchospasm, hypotension, widespread urticaria or angio-edema, flushing, abdominal pain and vomiting may ensue and, rarely, there may be a fatal outcome. The provocation of eczema by peanut contact is listed as an outcome in many of the patient guides and websites, but is largely unfamiliar to dermatologists. As with some other Type 1 reactions where skin contact is made (for example, from sitting on the grass), there may be an initial immediate weal, which if scratched and rubbed gives rise to a delayed eczematous reaction in children with atopic eczema. Some other food allergies, such as those to milk, may be more directly associated with flares of eczema, usually in children aged under two, although the mechanism of this reaction remains opaque.

Treatment of peanut reactions

Apart from avoidance of peanuts, and any cross-reacting legumes, it is advised that peanut-allergic individuals should also avoid nuts, as 35–40% of such individuals go on to have nut allergies and

there may be cross-contamination with other nuts in the factory. There is also some protein homology with sesame seeds. Not all those with peanut allergy will have clinical reactions to all of these other foods. If a child is eating a food to which they are sensitised without difficulty, the advice is to let them continue to do so. Each child should have a personal management plan, which includes oral antihistamines for mild attacks and the addition of an adrenaline pen for intramuscular administration in more severe episodes. The guideline for adrenaline dosage is 10 µg/kg, which means that a junior pen delivering 150 µg is given to children under 30 kg and, thereafter, an adult pen is prescribed that delivers 300 µg. Adrenaline becomes less active with time and each pen has a 'use-by date', after which a new pen should be prescribed. Adrenaline pens need to be carried only by those who need them, under the advice of a practitioner with the expertise to diagnose and manage such conditions. Once adrenaline is used, the individual should attend the emergency department in case further adrenaline or life support is required.

Impact

The striking characteristic of parents attending an allergy clinic is their almost palpable sense of anxiety regarding the risk of their child dying of an anaphylactic attack due to the inadvertent ingestion of peanut, or one of the cross-reacting legumes. This often leads to exaggerated parental vigilance and increased anxiety when the child goes to school. Teenagers may not ever remember having had anaphylactic symptoms and consequently let their guard down when out with friends. A careful history may reveal that the child has actually ingested peanuts without any reaction. Up to 20% of children who develop peanut allergy before the age of two will 'grow out' of it by school age, although another 20% may have worsening symptoms over time.⁸ The rest continue to have a similar degree of peanut allergy throughout their lives. Thus, families who have to cope with managing the skin of an often miserable child with atopic eczema may also have the extra burden of worry regarding their child's diet.

The effect of both of these aspects can sometimes result in social isolation, both for the child and the rest of their family. It is important, therefore, for such children to be reviewed at intervals in an allergy clinic where they can be supported by the dietitian and the allergy team. 'Food allergies' may be erroneously cited by parents, who are constantly on the lookout for something to blame for their child's eczema, making it very important to be able to sort out the real causes from the imagined ones.

The future

As well as the LEAP study, which is assessing the effect of *when* peanuts are introduced into an infant's diet, the EAT (Enquiring About Tolerance) study is looking at six other food allergens in a similar way. The study is assessing infants from the general population, comparing early introduction of food allergens alongside continued breastfeeding with breastfeeding alone. It should be reporting in 2015. Other groups are trying to genetically engineer peanuts to remove the proteins that trigger allergies. Perhaps of more immediate clinical value are the attempts to switch off the allergy once it has developed, using an escalating dose regime of very tiny amounts of peanut protein to desensitise a patient.⁹ This strategy is not without risk, but could be attractive to families who have extreme difficulty living with peanut allergy.

Last, as new tests become available to measure IgE to specific peanut epitopes, it may be possible to refine the prognosis given to a child and their family. For example, higher levels of antibodies to Ara h 2 appear to be an indicator of severe peanut allergy, whereas higher levels of IgE to Ara h 8, which are more common, may be predictive of milder reactions or the development of tolerance ■

Declaration of interest
None declared.

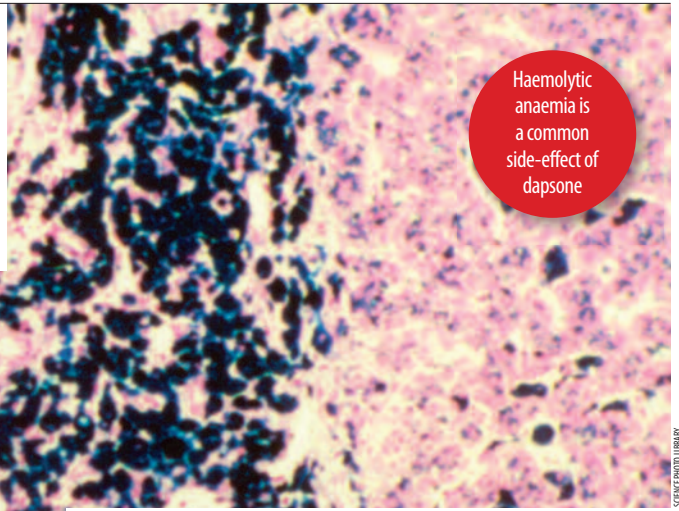
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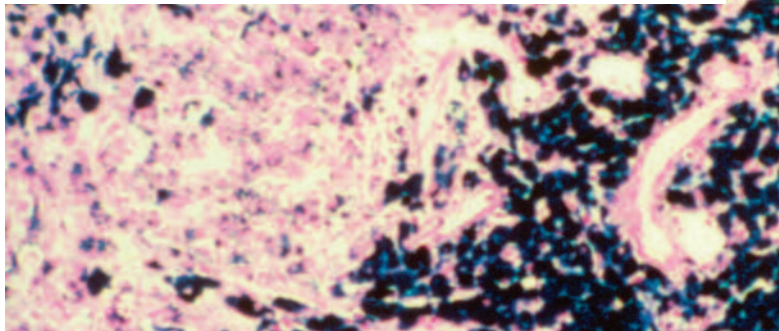
Key points

- Consider food allergy when managing a child with atopic eczema.
- The diagnosis and management of food allergy should be under the supervision of a practitioner with expertise in the area.
- A detected level of immunoglobulin E to a specific allergen denotes sensitisation – clinical allergy needs to be established by other means.
- The impact of peanut allergy on the child's family must not be underestimated.
- There are exciting new developments occurring in this field.

Dapsone: what you need to know



Haemolytic anaemia is a common side-effect of dapsone



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Bedford

Although dapsone was first synthesised in 1908, it was only in 1950, when being used under the mistaken impression that dermatitis herpetiformis (DH) is caused by a bacterial infection, that its remarkable efficacy in this disorder was discovered.

Today, the licensed indications for dapsone are, in addition to DH, as part of the multidrug treatment of leprosy and in the prophylaxis of pneumocystis infection in patients with HIV. However, although dapsone is an antimicrobial, it is the drug's rather poorly understood anti-inflammatory effects that have led to its use in a wide range of dermatoses (see Box 1). In some of the rarer conditions, the evidence of efficacy inevitably relies on case reports and anecdotes, rather than coming from controlled trials. It is not an uncommon experience in dermatology clinics, when faced with a difficult therapeutic problem in a patient with a chronic inflammatory disorder in which first- or second-line treatments have already been tried but have failed, to find that 'a trial of dapsone' is suggested.

Many of the disorders dapsone is used to treat are chronic ones. So, although dapsone therapy is rarely likely to be initiated in primary care, GPs may, from time to time, encounter patients who are on the drug and be asked to participate in the monitoring or prescribing of it. For this reason, it is important for them to be aware of some of the important side-effects that may be encountered, especially as these can be a little unusual.

Dapsone-induced haemolysis

Haemolytic anaemia is a common side-effect of dapsone. Its severity is dose-related and it is much more common and more severe in subjects who have G6PD deficiency – accordingly, patients from areas with a high prevalence of this (such as Mediterranean littoral and Africa) need screening

Box 1. Indications for dapsone therapy

- Leprosy*
- Dermatitis herpetiformis*
- Pneumocystis*
- Pyoderma gangrenosum
- Leucoclastic vasculitis
- Urticarial vasculitis
- Acne
- Hidradenitis suppurativa
- Sweet's disease
- Epidermolysis bullosa acquisita

* Licensed indications

before treatment. Regular monitoring of full blood count (including reticulocytes) is required in long-term dapsone therapy, and a falling haemoglobin level, or rising mena corpuscular volume or reticulocyte count, are a warning sign. If mild, this may be managed by dose reduction rather than withdrawal of the drug.

Methaemoglobinaemia

Dapsone may cause methaemoglobinaemia. Patients present acutely short of breath and apparently cyanosed, but with a normal pO₂. Intravenous methylene blue effects a dramatic cure. The problem is usually dose-related and the drug may be reintroduced at a lower dosage.

Cutaneous reactions

Dapsone may be associated with a variety of acute skin reactions, ranging from a generalised maculopapular rash, or erythema multiforme, to toxic epidermal necrolysis or a systemic drug reaction with eosinophilia. Such reactions commonly occur shortly after the initiation of therapy and require immediate withdrawal and appropriate supportive measures ■

Author's note

The information in this article is for guidance only. Please refer to the current *British National Formulary*.

Declaration of interest

The author declares that there is no conflict of interest.

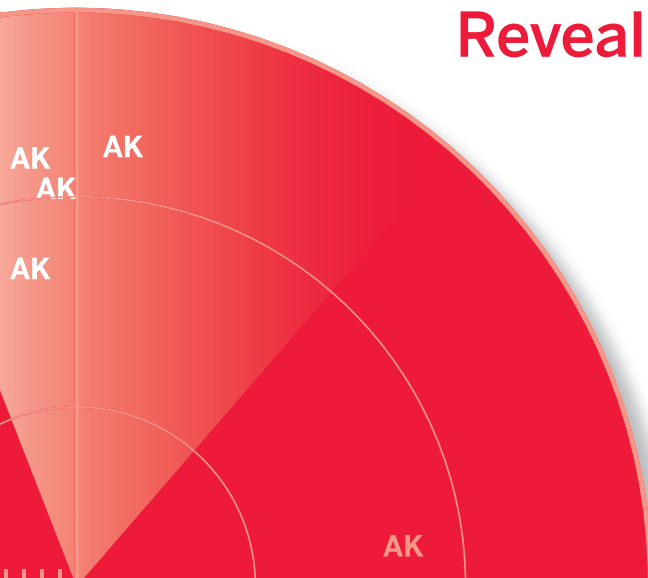


Learn about the dark history of dapsone on page 18

For Actinic Keratosis



Reveals and treats clinical and subclinical AK lesions¹⁻⁴



Zyclara 3.75% cream (imiquimod). **Indications:** Zyclara is indicated for the topical treatment of clinically typical, nonhyperkeratotic, nonhypertrophic, visible or palpable actinic keratosis (AK) of the full face or balding scalp in immunocompetent adults when other topical treatment options are contraindicated or less appropriate. **Dosage:** Treatment should be initiated and monitored by a physician. Apply up to 2 sachets, once daily, before bedtime to the skin of the affected treatment area for two treatment cycles of 2 weeks each separated by a 2-week no-treatment cycle or as directed by the physician. The treatment area is the full face or balding scalp. The safety and efficacy of imiquimod in AK in children and adolescents below the age of 18 years have not been established. For external use only. Contact with eyes, lips, and nostrils should be avoided. The treatment area should not be bandaged or otherwise occluded. Apply as a thin film to the entire treatment area and rub in until the cream vanishes. Partially-used sachets should be discarded and not reused. Leave on the skin for approximately 8 hours; after this time it is essential that the cream is removed by washing the area and the hands with mild soap and water. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Warnings and precautions:** Lesions clinically atypical for AK or suspicious for malignancy should be biopsied to determine appropriate treatment. Not recommended until the skin has healed after any previous medicinal products or surgical treatment. Use of sunscreen is encouraged, and patients should minimise or avoid exposure to natural or artificial sunlight. Not recommended for the treatment of AK lesions with marked hyperkeratosis or hypertrophy as seen in cutaneous horns. During therapy and until healed, affected skin is likely to appear noticeably different

from normal skin. Local skin reactions are common but generally decrease in intensity during therapy or resolve after cessation of therapy. Rarely, intense local inflammatory reactions including skin weeping or erosion can occur after only a few applications. There is an association between the complete clearance rate and the intensity of local skin reactions. These local skin reactions may be related to the stimulation of local immune response. Imiquimod has the potential to exacerbate inflammatory conditions of the skin. If required by the patient's discomfort or the intensity of the local skin reaction, a rest period of several days may be taken. Treatment can be resumed after the skin reaction has moderated. The intensity of the local skin reactions tend to be lower in the second cycle than in the first treatment cycle. Flu-like systemic signs and symptoms may accompany, or even precede, intense local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, and chills. An interruption of dosing or dose adjustment should be considered. Use with caution in patients with reduced haematologic reserve. Patients with cardiac, hepatic or renal impairment were not included in clinical trials. Caution should be exercised in these patients. Use with caution in immunocompromised patients and/or patients with autoimmune conditions and consider balancing the benefit of treatment for these patients with the risk associated either with the possibility of organ rejection or graft-versus-host disease or a possible worsening of their autoimmune condition. No data are available on re-treating AK that have cleared after two cycles of treatment and subsequently recur. Stearyl alcohol and cetyl alcohol may cause local skin reactions. Methyl parahydroxybenzoate (E 218), and propyl parahydroxybenzoate (E 216) may cause allergic reactions (possibly delayed). No interaction studies have been performed but use with caution

in patients who are receiving immunosuppressive drugs. Avoid using with any other imiquimod creams in the same treatment area. No data are available on the use of Zyclara during pregnancy or breast-feeding and there are no data on the risk to human fertility. There is no or negligible influence on the ability to drive or use machinery. **Side effects:** Herpes simplex, skin infection, lymphadenopathy, haemoglobin, white blood cell and platelet counts decreased, anorexia, blood glucose increased, insomnia, depression, headache, dizziness, nausea, diarrhoea, vomiting, erythema, scab, skin exfoliation, skin oedema, skin ulcer, skin hypopigmentation, dermatitis, erythema multiforme, Stevens Johnson syndrome, cutaneous lupus erythematosus, skin hyperpigmentation, myalgia, arthralgia, application site effects, including erythema, scabbing, exfoliation, dryness, oedema, ulcer, discharge, reaction, pruritus, swelling, burning, irritation and rash, fatigue, paresthesia, influenza like illness, pain, chest pain. Consult the Summary of Product Characteristics before prescribing, particularly in relation to side effects, precautions and contraindications. **Legal Category:** POM. **Package quantity and basic NHS price:** Pack of 28 sachets £113.00. **Product licence number:** EU/1/12/783/002. **Marketing authorisation holder:** Meda AB, Pipers väg 2A, 170 73 Solna, Sweden. **Date of preparation of prescribing information:** January 2013. UK/ZYC/13/0003

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

References: 1. Zyclara 3.75% Cream, Summary of Product Characteristics; Meda, August 2012. 2. Stockfleth E and Alomar A. Poster Presented at 6th World Meeting of Interdisciplinary Melanoma Skin Cancer Centres & 8th EADO Congress 2012, Barcelona. 3. Swanson N *et al.* J Am Acad Dermatol 2010; 62(4): 582-590. 4. Hanke CW *et al.* J Drugs Dermatol 2011; 10(2): 165-170.

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A guide to national networking on epidermolysis bullosa

Epidermolysis bullosa (EB) is an umbrella term used for a group of genetic skin fragility disorders characterised by blister formation in response to minimal trauma.¹ While there are currently 29 separate conditions identified, involving abnormalities of 14 genes, EB can be classified into three main categories: EB simplex (EBS), involving intraepidermal separation with the genetic defect arising in keratin 5 or 14;² junctional EB (JEB), comprising separation in the lamina lucida with the genetic abnormality in the collagen XVII gene and laminin-332; and dystrophic EB (DEB), with sublamina separation and a genetic abnormality occurring in the collagen VII gene type (see Figure 1).³ EBS may affect only the hands and feet, but can, on occasion, be more widespread, whereas DEB and JEB are usually more generalised.⁴ The inheritance may be either autosomal dominant or autosomal recessive, the latter group usually having far more severe symptoms with more far-reaching consequences.

Blistering and other problems

Patients with EB have no problems in healing, but before this occurs they frequently experience

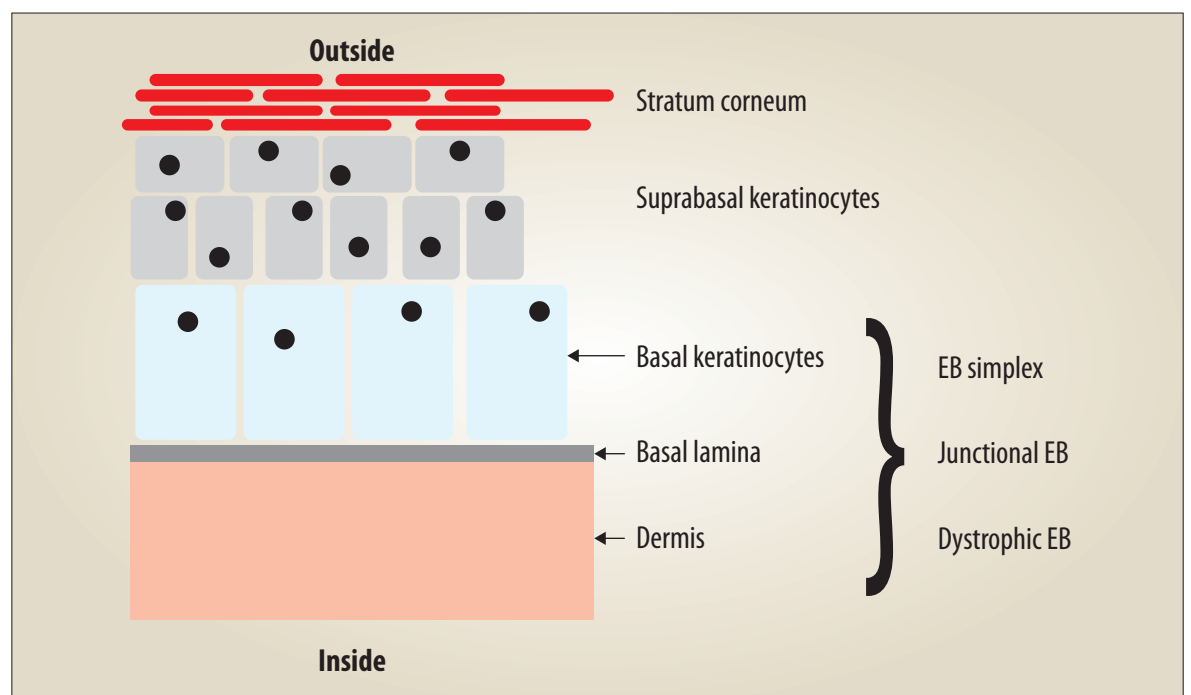


■ Dystrophic epidermolysis bullosa



■ Pseudosyndactyly

■ **Figure 1.** Diagram of the skin to show different levels of split in types of epidermolysis bullosa (EB)



If you suspect a patient has epidermolysis bullosa (EB)

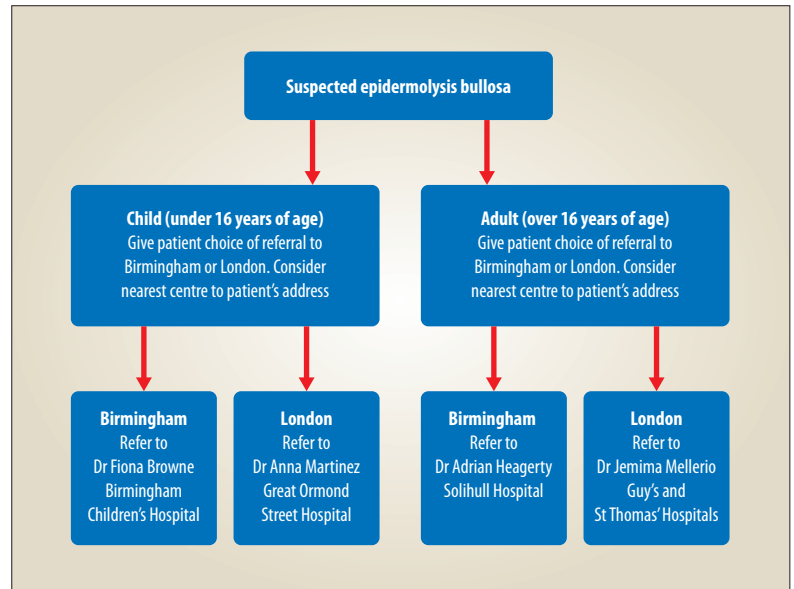
- Check patient history
 - Does the patient have a lifelong history of blistering?
 - Does the patient have a family history of EB?
- If yes to either of the above, refer to the appropriate EB centre for diagnosis

discomfort, if not pain. The problem is severely exacerbated if the blister roofs are lost. Dressings are of prime importance in the management of EB, with the avoidance of adhesive products that can further traumatise the skin. Provision of sufficient quantities of different types of dressing, antiseptics and sterile needles for rupturing blisters can be a logistical and expensive nightmare. Recurrent pain is almost inevitable in all forms of EB, frequently causing stress, anxiety and problems with carrying out normal daily activities. This is compounded by poor gait, which can severely debilitate patients.

Depending on the type of EB present, there may be many other effects on the patient as a consequence, either directly or indirectly, of the blistering. Perhaps the most common issue is skin infection and, in the case of a form of DEB, scarring. Recurrent skin infection may give rise to sepsis and, on occasion, renal failure, usually in the severe types (JEB and DEB), while scarring may be so pronounced that the patients develop webbing of the fingers and, finally, an inclusion of the hands in a scarred encasement known as pseudosyndactyly. Scarring may be one of the reasons why patients with severe dystrophic disease are at increased risk of developing particularly aggressive squamous cell carcinomas (SCCs) over a long period of time, which may be life-threatening.

Dysphagia, following repeated blistering and scarring in the oesophagus, is remarkably common, together with microstomia and poor dental hygiene, due to the difficulties in cleaning the mouth and teeth without further blistering. Dysphagia can lead to poor nutrition, the main problem being that of iron deficiency, giving rise to post-cricoid webs and low vitamin D levels, as well as poor protein intake. In addition, patients are particularly susceptible to reflux as well as constipation, secondary to pain and bleeding on defecation.

As mentioned earlier, recurrent pain related to blistering is almost invariable, especially in the severe types of EB, causing problems such as stress



■ **Figure 2.** Epidermolysis bullosa referral pathway

and anxiety. Studies looking at the psychological and social impact of EB have highlighted significant issues that need to be addressed within a multidisciplinary setting.⁵

Patient groups

Some 30 years ago, a group of parents of patients with EB in the UK established a patient self-help group, later to be known as the Dystrophic Epidermolysis Bullosa Research Association (DEBRA), to stimulate knowledge of, and interest in, EB for the benefit of those with the condition as well as their families, and to fund medical research. Following this, national DEBRA organisations have been established in more than 40 countries that act individually, but are co-ordinated by DEBRA International, to ensure that people living with EB have access to the best quality support and medical care, while also driving the development of effective treatments and cures for the condition. Local DEBRA groups were responsible for the co-ordination of the provision of care, particularly in the community, while supporting research. As this has progressed, it has become evident that co-ordinated healthcare is something best achieved under the umbrella of the NHS.

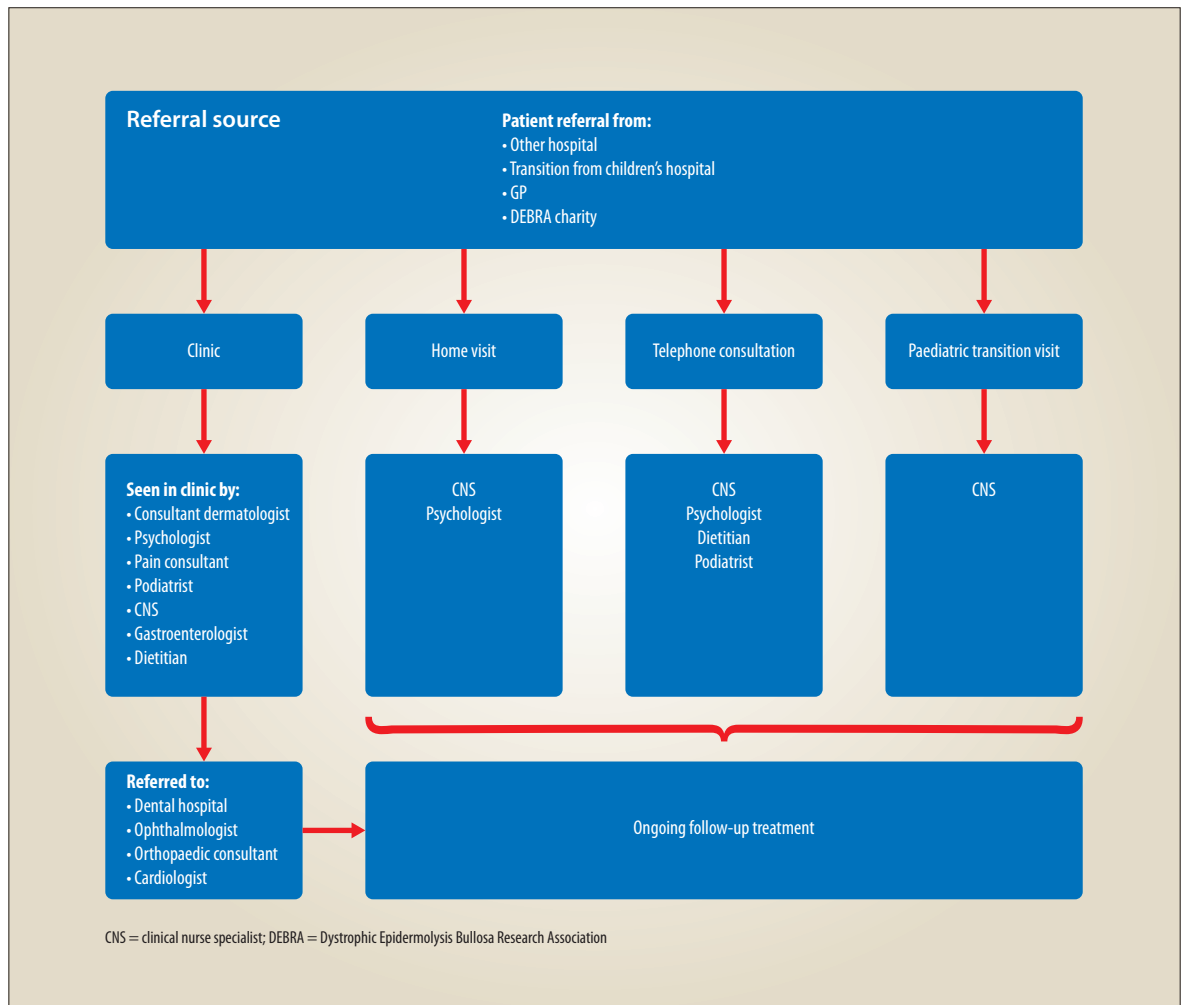
National network

Four specialist EB centres have evolved in the UK, with St John's Institute of Dermatology at Guy's and St Thomas' Hospitals being the first to see patients with EB, followed by Great Ormond Street Hospital and Birmingham Children's Hospital. Finally, the Heart of England



Recurrent skin infection may give rise to sepsis and ... renal failure

■ Figure 3.
Epidermolysis bullosa
patient pathway



NHS Foundation Trust provides medical, nursing, psychological and surgical support at Solihull Hospital, with laboratory services being provided at St John's Institute, London and Ninewells Hospital, Dundee. Initially, care was funded as in any other NHS service, but it soon became financially burdensome to diagnose and treat patients from throughout the country. Luckily, support for rare disease groups exists, funded by the Department of Health. EB was considered an appropriate member of one of these groups some ten years ago.

Patient and public involvement is a key factor in these developments

Since then, the overarching organisation has been rebadged and changed somewhat, currently being part of the NHS Specialised Services. This is the national organisation responsible for the commissioning of specialised services that help improve the lives of children and adults with rare diseases or disorders. A specialised service is defined by law as a service that covers a planning population (catchment area) of more than a million people. Each clinical commissioning group contributes some of its budget to funding specialised services and, consequently, the GP surgery referring the patient is not charged for the patient referral and care. Patients enter the service largely through ter-

tiary referral from consultant dermatologists, but previously unseen individuals from families known to be affected are frequently referred by their GPs to access the specialised services (see Figure 2 and Figure 3).

Conferences held throughout the country by members of national teams, as well as scientists involved in gene therapy research, have generated considerable interest from patients, resulting in

Key points

- Epidermolysis bullosa (EB) can be classified into three main categories: EB simplex, junctional EB and dystrophic EB.
- EB patients suffer many side-effects, including pain, infection, scarring, pseudosyndactyly and increased risk of aggressive squamous cell carcinoma.
- The first patient self-help group for patients with EB was established 30 years ago.
- There are four specialist EB centres in the UK, which form a national network providing care to children and adults with this rare disease.

heightened awareness of the national service and an influx of referrals for diagnostic investigation and up-to-date management.

To provide a specialist network of dermatology care for EB patients, the four national centres' core members meet quarterly to discuss service provision and new therapy developments. Service developments are discussed, and projects to improve the quality of services provided across the centres are established. This ensures they evolve and address the areas that have the most positive impact on patients. Patient and public involvement is a key factor in these developments, with user feedback driving the need for change.

One of the advantages of a co-ordinated national service is the identification of homogeneous groups of patients who may be treated in specific ways. Examples of this are the treatment of severe recessive dystrophic patients with intralesional allogeneic fibroblast therapy; the identification of large homogenous pedigrees of patients with identical keratin defects for developing therapy with small inhibitory RNA fragment technology in the simplex group; and the identification of patients for gene therapy and protein therapy. The rare but more aggressive skin tumours (in particular, SCCs in dystrophic patients) may be identified early and newer therapies considered. DEBRA International currently funds research across the world by active groups, usually for two- or three-year projects. The single national service allows UK patients to be identified for inclusion in these.

Conclusion

Knowledge about EB has expanded almost exponentially over the last 50 years. With this has come the need to address the many problems experienced by patients, couched with understanding of the underlying genetic defects, as well as the experience gleaned by clinicians specialising in the care of EB patients. The creation of a network of centres linked to two diagnostic laboratories, all funded by the NHS, has dramatically improved the care provided, by helping comprehensive multidisciplinary teams to address the issues experienced by this unfortunate patient group ■

Declaration of interest

The authors declare that there is no conflict of interest.

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Bookshelf

Oxford Handbook of Medical Dermatology

Susan Burge, Dinny Wallis. Oxford: Oxford University Press, 2011: £27.99

The elation of passing finals in 1984 and, by some quirk of the examination system, getting my MB ChB with honours was rapidly dampened when I started as a house physician at Manchester Royal Infirmary – I felt truly inadequate for the task. My colleagues clearly knew considerably more than I and I listened with amazement to their 'war stories' in the junior doctors' mess at meal times. I read the 'houseman's handbooks' available at the time and carried a book on 'medical emergencies' in my white coat pocket – but neither provided the handy resource I needed.

When the *Oxford Handbook of Clinical Medicine* was published a few years later, its success indicated that I had not been alone. There are now over 50 Oxford Handbooks in an ever expanding series that clearly meets a need for junior (and not so junior) doctors.

The *Oxford Handbook of Medical Dermatology* is a useful pocket reference offering accessible, practical advice. I particularly like the chapter 'What is the diagnosis?', which considers practical problems that often cause confusion; for example, 'red-leg' syndrome. Surely diagnosis is the most difficult part of our daily practice. The book goes on to consider how to manage common, and not so common, conditions by discussing the following questions: 'What should I ask?', 'What should I look for?' and 'What should I do?'

The advice is, as you would expect from Susan Burge, sensible, practical and applicable. Practical tools, such as the Psoriasis Area and Severity Index, are described and it also offers some background information to help answer questions in clinic; for example, 'Why is this sunscreen ineffective?'

I would have liked to see more line diagrams; for example, the measurement of the ankle brachial pressure index is well explained, but a diagram would have made it easier to assimilate quickly and, for me at least, more memorable. The same goes for fingertip units.

I tried to keep the book with me in clinic for a week to see how I got on using it. Perhaps the best testimony was that it disappeared on the Thursday – was the culprit one of my consultant colleagues, a specialist doctor, a GP registrar, or a medical student? I am sure all would have found it interesting and useful ■



Content:	★★★★
Teaching:	★★★★
Reference:	★★★
Illustrations:	★★★
Readability:	★★★★

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■ Stress may exacerbate skin conditions such as psoriasis



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Stress and the skin

The skin is the largest organ of the body and, if not covered, is the one immediately on show. Not only does it represent an external barrier between our internal being and the outside world, but it is also a key feature we use to assess the well-being of those we come into contact with. Health and illness are caused by many different factors, producing multiple effects. The biopsychosocial model illustrates how health and illness are consequences of interactions between biological, psychological and social factors.

The prevalence of patients seen with skin disease in primary care services is approximately 36.5% (patients with at least one skin problem). For 59% of patients, the skin condition was their main complaint to their GP.¹ Given the rise in skin cancer statistics, it is fair to say that the percentage of skin disease is on the rise. Those who have physical health problems are more likely to develop mental



health issues. Therefore, to provide true holistic care, it is crucial to recognise the impact that skin disorders can have on individuals and their families. The psychological factors could be perpetuating, or precipitating, the skin condition and could also be severely affecting the patient's quality of life (QoL). Treating the skin condition in conjunction with the psychological factors can enhance the therapeutic relationship with the patient, which will, in turn, increase their adherence to treatment.

Causation and consequence

People vary in their susceptibility to developing a disease in the presence of psychological and social

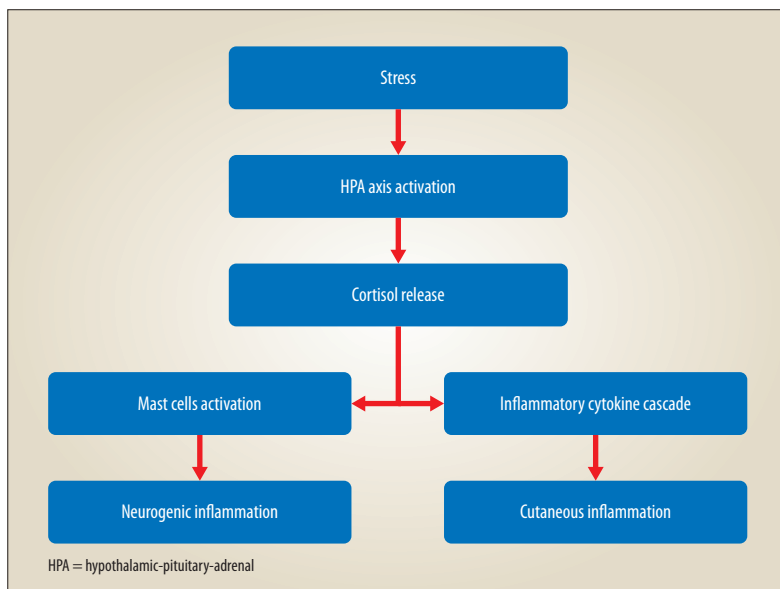
stress. The diathesis-stress model proposes that some people have a predisposition to developing psychopathology or illness; if the combination of the predisposition and stress (any environmental life event disrupting the person's equilibrium) exceeds the person's threshold, they could go on to develop a disorder.² Together with biological factors, psychophysiological elements have also been shown to influence the itch sensation, which is a major factor in many skin disorders.³

There is a biological basis to the link between stress and the skin (see Figure 1). The hypothalamic-pituitary-adrenal (HPA) axis represents a neuroendocrine system, regulated by a feedback mechanism – the activity of which results in a hormonal cascade. This is more commonly known as the 'stress axis'. The main hormone produced from this cascade is corticotrophin-releasing hormone (CRH) and this is released in response to stress activation of the HPA axis. The brain is activated by stress to produce hormones that can have both positive and negative effects on the body. Both acute and chronic stress can activate the HPA axis. The tendency for acute stressors, however, is to induce temporary activation, while chronic stressors lead to adaptation of the HPA axis to function at a heightened level. The sustained release of cortisol (the 'stress hormone') in response to raised CRH levels, in higher than 'normal' amounts, is damaging to tissues. A chronically active HPA axis acts as a pro-inflammatory system by:

- Stimulating mast cell-mediated inflammation
- Prolonging inflammation
- Inducing pro-inflammatory cytokine production (for example, interleukin 18) to produce cutaneous inflammation.

The role of CRH and its product (cortisol) has been demonstrated in atopic dermatitis, psoriasis, alopecia areata, skin cancers, contact dermatitis/urticaria and acne/seborrhoea.⁴ Although the exact mechanisms are not fully understood, there is a body of evidence to show the negative effects of stress on the skin, mediated by the HPA axis, high cortisol levels and sustained inflammation. Activation of the inflammatory pathway is linked to most skin diseases.

A link between stress and the exacerbation of skin disorders has been confirmed by research.⁵ For example, people with eczema have reported having flare-ups when stressed. Also, people with vitiligo have reported that they have noticed new patches when they feel stressed. It is difficult to ascertain which element comes first – the physical or the psychological. One theory is that a vicious cycle occurs, with the spread of the condition being an increasing cause of both worry and fear



■ **Figure 1.** Diagram to show the link between stress and the skin

of rejection, consequently exacerbating a psychological problem such as anxiety or depression.

Stigma is a huge problem in our society and having unblemished skin is thought to be an attribute of a beautiful person – a line of thought arguably perpetuated by the media. Hence, people with skin disorders may take various steps to maintain a 'sense of self'. This may be due to the belief that other people may stigmatise or reject them because of how they look. Living this way, day in, day out, can sometimes lead to the development or exacerbation of mental health problems, depending on personal experiences and coping strategies.

Studies have shown that 30% of patients have clinically significant levels of psychological distress.⁶ It is important to recognise that the severity of a visible difference does not correlate with the

It is crucial to recognise the impact that skin disorders can have

amount of psychological distress and dysfunction experienced.⁷ For example, a person with a small patch of vitiligo could feel the same way about their condition as someone who has eczema all over their body. Reasons for the psychological distress could be due to various factors, such as past experiences, difficult relationships, personal beliefs and one's upbringing. A recent survey within a general dermatology clinic in the NHS indicated that 28% of females and 23% of males scored within the clinical range for anxiety, with 46% of females and 36% of males reaching the borderline range.⁸ Interestingly, 40% of females and 24% of males had a high degree of appearance-related concerns and approximately 40% of males and females reported poor QoL. The most widely cited difficulties are those around social anxiety, social skills and self-concept, which can impact on all kinds of relationships, with friends, sexual partners or family.

Primary care intervention

Although the link between the psyche and the skin has been established for decades, it is only comparatively recently that clinical guidelines have addressed this association; for example, for psoriasis.⁹ The All Party Parliamentary Group on Skin has been campaigning, and producing evidence, to facilitate changes within services since 2003.^{10,11}

Within the NHS, there is a drive to enhance primary care services and to provide more support in the community, rather than referring to hospitals. Together with the financial constraints, producing and providing low-cost interventions with maximum output and minimum therapist time will be crucial. There are numerous studies indicating the efficacy of self-help.

Primary care would benefit from having specialised clinical psychologists

However, in relation to skin disorders, there is only one recent study that proposed that providing self-help to those with social anxiety associated with vitiligo is clinically effective in reducing psychological distress and enhancing coping with the condition.¹² Within clinical practice, providing leaflets, containing basic psychoeducation and often simple relaxation techniques, has been shown to be effective, in terms of increasing insight, reducing distress and reducing long waiting lists. It can also minimise the time needed in individual psychological therapy at a later stage, and often patients have reported that further support is not necessary. Further research is required to establish whether guided self-help would be effective, as this could potentially provide an additional tier between self-help and face-to-face psychological therapy.

There is a plethora of psychological therapies that might help people with skin conditions. However, more quality research to guide best practice is needed. Some intervention studies have

shown the benefits of cognitive behavioural therapy (CBT) (an approach that aims to change maladaptive ways of thinking, feeling and behaving) for psoriasis, acne, eczema and vitiligo, to name a few. For conditions that lead mainly to scratching (rather than an appearance-related problem), habit-reversal therapy may help to reduce the desire to scratch, which exacerbates the condition. This has been shown to be effective for people with eczema and skin-picking.¹³

Working in collaboration

To provide holistic care, primary care would benefit from having specialised clinical psychologists able to provide psychological assessment, therapy, consultation and impact on service development, especially to cater for their patients with skin disorders. Within secondary care, a large proportion of patients display symptoms of psychological distress. Many patients report that they have never been asked (in either primary or secondary care) about their well-being in relation to their skin disorder.¹¹ This raises the question: if this was addressed in primary care, could this reduce referrals to secondary care? Patients who require psychological care might feel as though their needs had been met without referral. Further, offering psychological support and psychoeducation early in the process (including when giving a diagnosis, to help a patient adjust to a new condition) might help to reduce the stigma and enhance the established link between the skin and the mind. In clinical practice, some children with eczema have been shown to have low confidence and poor treatment outcome due to scratching. Interestingly, parents have often rejected psychological support due to the stigma of mental health conditions and many appear to believe it may be their fault as parents. Hence, providing psychoeducation can help to reduce the fear of psychology and help to ensure the child sees a psychologist or counsellor.

Conclusion

Overall, the link between the mind and the skin has long been established and psychological interventions are slowly being adapted specifically for skin disorders. Good quality research on interventions is limited, although clinical practice indicates there are a number of effective therapies.¹³ However, due to the limited budget in the NHS, the provision of psychological healthcare for people with skin disorders is seen as inadequate.¹⁴ In some areas of the UK, psychological services are offered. Paradoxically, perhaps due to the stigma attached to being referred to mental health services, some pa-

■ Stress and mental health issues have been shown to have a direct link to skin problems



ANDREW WICKACKOSKI/PHOTO LIBRARY

tients have reported that they prefer to see someone within dermatology. New national guidelines (for example, for vitiligo and skin cancer) and increased media coverage emphasising the importance of psychological interventions for people with skin conditions, may create an impetus for change and lead to the development of psychological services within the NHS. Change should be considered at all stages of the patient's journey, starting within primary care ■

Declaration of interest

The authors declare that there is no conflict of interest.

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Key points

- People with physical health problems are more likely to develop mental health issues.
- Many patients feel stigmatised in modern society due to their skin problems and this can significantly contribute to mental health problems.
- A patient's predisposition to experience psychological distress due to their skin condition can be related to experiences from their past.
- Simple measures in primary care, such as distributing information leaflets on the issue, can reduce stress associated with skin conditions further down the line.
- There is evidence to suggest that it would be beneficial to primary care to have specialised clinical psychologists to cater for patients with skin disorders.

PCDS

Over the weekend of the 14–16 March 2014, the Primary Care Dermatology Society (PCDS) will be celebrating its 20th anniversary at the Chesford Grange Hotel in Warwickshire. This should be a great meeting with an opportunity to meet many members – both old and new! While the PCDS has flourished over the years, we are always pleased to welcome new members.

Dermatology provides a significant proportion of a GP's daily work and the vast amount of cases can be managed in primary care. There has been a move to bring services for those who cannot be managed in primary care into the community, enabling patients to easily access dermatological care closer to their home.

For those with skin cancer there has been the development of referral pathways (such as two-week referral rules) ensuring patients are seen and managed quickly. One drawback has been that some patients with inflammatory skin conditions have not seen the desired improvements because skin cancer dominates, and takes a large proportion of the available clinic time.

When the PCDS started, the internet was in its infancy. The PCDS has embraced new technology and has developed an excellent website full of useful information for those interested in dermatology in primary care. Do not just take my word for it, log on and see what is available. See below for website details.

The PCDS not only has regular meetings for its members, but also runs 'Essential Dermatology' one-day courses for GPs, or GP registrars, who are interested in learning more about dermatology. Sadly, the amount of dermatological education that the future GP receives is less than that they would have had 20 years ago. Those with the least knowledge have the most to learn and gain by attending an Essential Dermatology course.

Dermoscopy has been one of the major developments in the last 20 years. It is a tool that can provide extra information on new and/or changing lesions. I prefer to think of it as supplementing one's clinical skills, providing an extra check and increasing diagnostic accuracy. Once a GP has become proficient at dermoscopy, it can help to reduce unnecessary referrals. The PCDS provides both beginner and advanced dermoscopy courses. All current dates and venues can be seen on the PCDS website.

Over recent years, fewer GPs have been performing skin surgery, but those who do are becoming more skilled and perform a wider range of procedures. The PCDS provides regular skin surgery courses at differing skill levels.

Much has been achieved in the last 20 years, but the society needs to continue to expand and respond to the rapidly changing face of dermatology in primary care for the next 20 years ■

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An uncomfortable truth

Dapsone is an unusual drug, with a range of indications from leprosy to vasculitis. Yet, it has an even more unusual history.

Dapsone (diaminodiphenylsulfone) was first synthesised in 1908, but it was many years before its therapeutic potential was recognised. During the Second World War, Germany found itself at a significant disadvantage in lacking access to the newly discovered penicillin, which was available to the British and US troops. Much effort was directed into investigating derivatives of the early sulphonamide preparations, which had much weaker antibacterial effect.

Josef Vonkennel was a leading dermatologist in Leipzig, an ardent Nazi and adviser on dermatology to the Schutzstaffel (SS). He established a research centre at Buchenwald concentration camp and began experimenting with the effects of dapsone on experimentally induced poison gas burns in inmates. His studies did indeed show that the agent had some therapeutic effects, albeit at the expense of the lives of many of his hapless victims.

We should not lose sight of what has been done in the name of medicine

Some years later, in 1950, a group of Portuguese dermatologists, mistakenly believing that dermatitis herpetiformis was a bacterial infection, studied the use of dapsone and discovered its remarkable therapeutic efficacy in that condition.

After the war, Vonkennel was arrested as a war criminal, but managed, aptly, to save his own skin by giving evidence against some of his physician colleagues at the Nuremberg Doctors' Trials. Subsequently, while never denying or apologising for his Nazi connections, he was appointed Professor of Dermatology at

the University of Cologne and established himself as one of the leading figures in German dermatology. In 1962, the German dermatology journal *Der Hautarzt* published an article by his fellow Nazi Professor Heinrich Gottron (whose name is remembered eponymously in the characteristic papules of dermatomyositis) extolling Vonkennel's professional achievements.

However, the following year, 1963, the German government announced an investigation into Vonkennel's wartime activities and he committed suicide rather than facing the consequences.

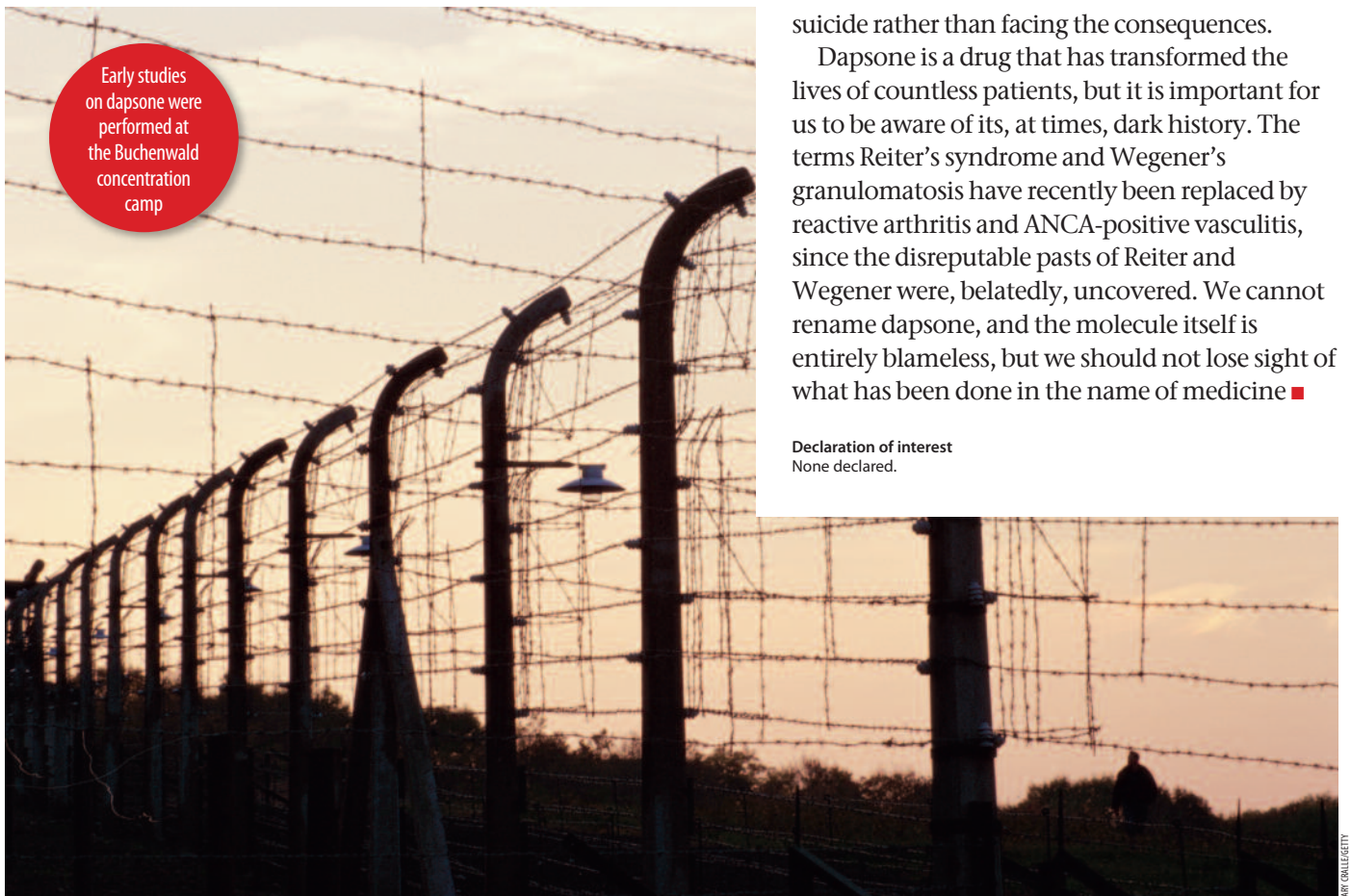
Dapsone is a drug that has transformed the lives of countless patients, but it is important for us to be aware of its, at times, dark history. The terms Reiter's syndrome and Wegener's granulomatosis have recently been replaced by reactive arthritis and ANCA-positive vasculitis, since the disreputable pasts of Reiter and Wegener were, belatedly, uncovered. We cannot rename dapsone, and the molecule itself is entirely blameless, but we should not lose sight of what has been done in the name of medicine ■

Declaration of interest
 None declared.



Read about the indications for, and side-effects of, dapsone on [page 8](#)

Early studies on dapsone were performed at the Buchenwald concentration camp



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Can telemedicine ease growing healthcare costs?

A teledermatology service launched in Cardiff seeks to be at the forefront of remote diagnosis, reducing the need for many outpatient appointments.

As the demand for healthcare spending inexorably rises, the use of new technology to improve quality of healthcare provision for patients, but at a lower cost, becomes a political imperative. How can telemedicine help towards this objective?

There is an enormous unmet need and demand for dermatology care. On average, one in six consultations in general practice is for a skin complaint and yet fewer than one in ten GPs receive any dermatology training after medical school. Any way of reducing the number of GP consultations for skin care, or increasing the GP's ability to manage skin complaints, would release resources. Teledermatology can do this by assisting with diagnosis and management, and with GP education.

Since 2005, the Welsh Institute of Dermatology has offered a teledermatology service in the Cardiff area. Some 3,000 dermatology referrals are processed in this way each year, compared with approximately 12,000 cases that are referred and seen in the traditional way. Of these telereferrals, 70% are handled by offering advice for the GP to continue managing the patient in primary care. About 18% are given routine outpatient appointments and 12% receive urgent appointments for suspected malignant neoplasms. Feedback from GPs and patients has been overwhelmingly positive. Telemedicine, for some, is anathema in that a face-to-face consultation with an experienced consultant is the highest quality form of consultation, but personalised medicine comes at a cost that seems increasingly unaffordable. The challenge for the NHS, given its experience of IT developments that have overrun in time and cost, is to be able to access a solution that provides a secure, scalable and consistent platform for the adoption of this kind of service.

Time for Medicine (www.timeformedicine.com) is a spin-out company from the University Hospital of Wales in Cardiff. Founded, and mainly funded, by clinicians, the company's mission is to deliver



healthcare in a more affordable fashion, closer to people's homes, reducing the need for hospital visits and, thus, reducing waiting times. It has developed a digital 'telehealth' platform, which is capable of providing a remote diagnostic solution in many areas of medicine, covering the symptom complexes that are most often referred to outpatient services. The software was developed by over 40 senior clinical consultants and others, and features:

- Templates of the questions that a consultant would normally ask a patient in the relevant outpatient clinic and the appropriate tests and examinations that may be required
- A digital platform that can present templates to patients in a primary care setting, capture the patients' responses and the results of tests, and make this available to consultants in their offices
- A platform that can be hosted securely within the NHS firewall.

The technology platform makes more efficient use of clinical consultants' time by:

- Gathering patient history and test results remotely from the consultant
- Allowing the consultant to access patient data remotely via the NHS 'Health Cloud', significantly reducing the number of patients needing consultations in person
- Mechanising the consultant's information review and diagnostic output process, such that an opinion letter back to a GP can be electronically created in five to ten minutes, saving clerical costs.

Teledermatology is the first service deployed by the company, with further modules planned. A crucial design feature of the company's software is that NHS bodies, without complicated and expensive interface issues, can easily access its web architecture. Local providers of community dermatology services can, therefore, use it; for example, as a platform for the delivery of teledermatology solutions.

Compliance with appropriate governance provisions is important for any such service provided to patients and the recently published *Quality Standards for Teledermatology* is a professional consensus that provides a welcome contribution to such services¹ ■

Reference

1. www.pcc-cic.org.uk/article/quality-standards-dermatology (last accessed 23/08/13)

Let's help children cope better with itchy skin



Hi! I'm Qool Vince, but my friends call me **QV**

Like you, I do everything I can to help children with sore and itchy skin. From a gentle wash to an intensive ointment, my range of cleansers and moisturisers provides a course of **total emollient therapy** – morning, noon and night.

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