ABSTRACTS: DERMATOLOGY – MORE PRACTICE THAN BENCH

24 March 2004

SESSION 1

Chair: Professor J Rees, Professor of Dermatology, University of Edinburgh, Scotland

NEW OPTIONS FOR THE NON-SURGICAL TREATMENT OF SKIN CANCER

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Abstract

Non-melanoma skin cancer (NMSC) is the most common cancer in the UK, affecting around 2% of the population aged over 60. The incidence of NMSC continues to rise, increasing demand for timely treatment, especially surgery. In addition to service pressures, rising patient expectations over therapies have stimulated a search for novel non-surgical options for NMSC that combine high efficacy with good cosmesis. Emerging therapies are reviewed and the potential to prevent new cancers is assessed.

The literature is reviewed on the potential NMSC indications for topical diclofenac, imiquimod and photodynamic therapy (PDT) and initial results of the use of topical T4 endonuclease presented. The published evidence supporting tumour-prevention for certain therapies is examined.

Topical PDT is now approved for actinic keratoses (AK) and basal cell carcinomas (BCC). Several randomised controlled trials (RCTs) also confirm the efficacy of PDT in Bowen's disease (squamous cell carcinoma *in situ*). Pain can limit patient tolerance and analgesia/anaesthesia is required in certain patients. Topical imiquimod has now been extensively studied for AK and BCC, with approvals imminent, although irritation during therapy may limit patient tolerance. Case reports suggest efficacy in Bowen's disease and lentigo maligna. Topical diclofenac offers potential for thin non-hyperkeratotic AK. Topical T4 endonuclease was effective in reducing new AK and BCC, in patients with xeroderma pigmentosum. Field therapies, including PDT, also have reported efficacy in slowing the development of new cancers and pre-cancers, but larger studies are required. Disease sub-type, patient age, lesion size, number and location, and the cost, treatment protocol and local availability of these therapies will influence which is optimal for particular patients.

Several novel non-surgical approaches to skin cancer care now exist. Diclofenac may benefit certain patients with early AK. Topical PDT and imiquimod are likely to result in a significant change in our practice, especially for superficial cancer and pre-cancer. Topical therapies for cancer prevention still require further evaluation although may offer significant benefit to predisposed, immunosuppressed patients.

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Key words: Diclofenac, imiquimod, non-melanoma skin cancer, photodynamic therapy, topical T4 endonuclease.

Sponsors: Previous travel sponsorships from 3M Pharmaceuticals, Phototherapeutics Ltd and Galderma, manufacturers of imiquimod and PDT-related products, respectively.

Declaration: Current clinical investigator for several PDT clinical trials. No consultancies, nor stocks.

RECENT ADVANCES IN MELANOMA

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Abstract

Melanoma is one of the most rapidly increasing malignancies worldwide. Data in Scotland shows rising incidences for men and women and virtually static mortality rates. Over the last two decades Scottish data has shown a significant increase in the proportion of patients presenting with thin, good prognosis lesions and this largely explains improved overall five-year survival rates. Little progress has been made in the treatment of metastatic melanoma in 20 years, emphasising the importance of early detection. Much recent interest has been centred on the use of agents particularly interferon as adjuvant therapy and the introduction of sentinel lymph node biopsy as a staging technique.

Recent Scottish data shows a three-fold and two-fold increase in age standardised incidence rates for melanoma in men and women. The steepest rate of increase is being seen in men aged over 65 years. The trend to increasing numbers of thin, good prognosis melanomas recently may reflect the considerable public and professional educational exercises of the last 20 years. Despite this, we recognise a persisting number of patients presenting with thick, bad prognosis lesions. Over time, the site distribution of melanomas appears to be altering too.

Surgery remains the mainstay of melanoma management. More cases are now dealt with by dermatologists rather than surgeons. Guidelines have been produced to give appropriate margins of excision and avoid over zealous treatment. In recent years the technique of sentinel lymph node biopsy has been introduced as a staging technique. Its value remains to be proven.

Therapeutically, much interest has been directed to the use of interferon-alpha in high-risk melanoma. While there is evidence of some effect there is as yet no clear evidence of worthwhile survival benefit.

The epidemiology of cutaneous melanoma has changed markedly in the last two decades. The reasons for this remain unclear. Melanoma management has also changed with modification of surgical treatment and introduction of new techniques. The search for effective treatment for metastatic disease continues.

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Key words: Epidemiology, melanoma, surgery.

Sponsors: None.

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DERMATOLOGICAL SURGERY – A MEDICAL SPECIALTY – HOW BIZARRE!

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Abstract

Dermatology is an organ specialty which in the UK has traditionally, or certainly since the eighteenth century, come under the umbrella of the Colleges of Physicians. However it was not always so, many early surgical textbooks contained significant contributions on skin disease and John Hunter is regarded as one of dermatology's founding fathers. Nowadays in many parts of Europe, where there is less of a historical division between medicine and surgery, departments of dermatology have extensive surgical facilities and routinely do major tumour surgery and reconstructive surgery. Phlebology, including vein surgery, is also commonly found within dermatology departments. In many respects it is the UK, where often dermatologists have tended to focus more on the nosology of skin diseases rather than practical aspects of management, which is out of step with our international colleagues. For such an immediately visible organ with all its panoply of disorders it makes perfect sense for patients to be managed by one team with a common training.

If you define a surgeon as someone who incises and sutures then almost every dermatologist is a dermatological surgeon, as a skin biopsy is often a vital investigation of a rash. I think it is essential that a dermatological surgeon is first and foremost a dermatologist and there is a requirement for a thorough training in all aspects of skin disease to enable one to diagnose lesions accurately and plan management appropriately. The actual limits of dermatological surgery are hard to define, as it overlaps extensively with several surgical disciplines, including plastic and reconstructive surgery, maxillo-facial surgery, otolaryngology and ophthalmology. In the US and in Europe it is not unusual for post residency dermatologists to do Fellowships in these disciplines to broaden their training. Whilst I don't think this is ever likely to happen to any great degree in the UK, it does emphasise what may be possible.

The dermatological surgeon is ideally placed to be the initial referral base for suspected skin tumours. They have the necessary diagnostic skills to enable them to make an accurate clinical diagnosis and they are able to consider a range of treatment options which they can, except in the most advanced cases and excluding radiotherapy, administer themselves. We are all aware of cases where a benign pigmented lesion has been widely excised, having been misdiagnosed as a malignant melanoma, and of similar inappropriate surgery, with often disfiguring scars. Our aim should be to eliminate such practices and this is why 'one stop' tumour clinics are proving so popular. In

addition to considering formal surgical options, a dermatological surgeon would also be able to consider other techniques including cryosurgery, laser techniques or topical treatments, so the management of an individual lesion can be tailored appropriately.

There are certain surgical techniques which dermatologists can claim as ones which they have either developed or nurtured. Foremost of these is micrographic (Mohs') surgery. This was the idea initially of a general surgeon, but two dermatologists working with him developed the techniques on which current practice is based. Unfortunately, there is still some resistance to the technique amongst surgeons and others although it does now appear in official management guidelines as the treatment of choice for infiltrative basal cell carcinomas in 'awkward' sites. Dermatologists have been amongst the leading developers of the therapeutic uses of lasers. Dr Leon Goldman, a dermatologist from Ohio, is credited with the first clinical use of a laser and dermatological surgeons now use lasers and related light sources extensively to treat naevi, vascular lesions and tumours. Dermatological surgeons have advocated the use of secondary intention healing for years and, when used appropriately, it can save patients extensive reconstruction and produce excellent cosmetic results. Dermatological surgeons are much in demand for their aesthetic skills. Dermabrasion and peeling in general, hair transplantation, liposuction with tumescent anaesthesia and aesthetic uses of botulinum toxins are just four of many areas, in addition to the aesthetic uses of lasers, where dermatologists have made significant contributions to the development of techniques.

Dermatology is a medical specialty and I am first and foremost a dermatologist. The surgical skills which I and others have acquired complement our dermatology training to enable us to carry out procedures to better serve our patients and enable the specialty as a whole, and departments of dermatology in particular, to offer complete programmes of care.

Key words: Dermatological surgery, skin cancer.

Sponsors: None.

Declaration: No conflict of interest declared.

SESSION 2

Chair: Dr R Weller, Senior Lecturer, University of Edinburgh, Edinburgh, Scotland

BLISTERING DISEASES

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Abstract

Providing a barrier against the external environment is an important function of the human epidermis. To maintain this protection, its principal cells, the keratinocytes, are joined together by several types of adhesion junctions, including desmosomes and hemidesmosomes.[1,2] These complexes are composed of intricate networks of proteins and glycoproteins. Abnormalities in these structures result in skin fragility and blistering. Defects in their components can arise either through inherited gene mutations or through specific epitope targeting by acquired autoantibodies.

Methods include polymerase chain reaction (PCR), DNA sequencing, RNA analysis, transmission electron microscopy, immnuohistochemistry, immunoblotting and enzyme-linked immunosorbent assay (ELISA).

Over the last decade the precise macromolecular composition of desmosomes and hemidesmosomes in skin has been determined through a combination of microscopical, biochemical and molecular methods. However, the real biological significance of these structures has emerged from detailed studies on human subjects suffering from a spectrum of blistering skin diseases, both inherited and acquired.[3]

For the inherited blistering skin diseases, unravelling the molecular pathology and understanding genotype–phenotype correlation has led to more accurate diagnosis, improved genetic counselling, the feasibility of DNA-based pre-natal diagnosis, and a basis for the development of somatic gene therapy.

For the acquired blistering skin diseases, molecular studies have disclosed the pathogenic nature of certain skin anti-basement membrane zone autoantibodies, improved understanding of the mechanisms of blister formation, provided clues to predicting disease complications, and established a platform for the development of more selective approaches to immunosuppressive therapy and better disease management.

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Key words: Desmosome, hemidesmosome.

Sponsors: None.

Declaration: No conflict of interest declared.

ITCH

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Abstract

Not all itches arise in the skin. Itches that arise as a consequence of pathology in the central or peripheral nervous system can be said to have a 'neurogenic' or 'neuropathic' origin: the terms are often used interchangeably. In practice, 'neuropathic' is sometimes used to describe the particular character of itch or pain of neurogenic origin (e.g., co-existent stinging, burning, tingling, pain, formication, paresthesia, hypesthesia, hyperesthesia). Notalgia paresthetica and brachioradial pruritus are examples of two neurogenic itches that often, but not always, have a neuropathic character. The final pathway of certain metabolic itches, such as cholestatic pruritus, must of course involve the nervous system as well. Recognition of itches that arise from neural rather than cutaneous pathology has implications for the general approach to diagnosis and treatment of patients with pruritus.

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Note: This abstract and lecture are modified and updated from a lecture presented to the European Academy of Dermatology & Venereology, Prague 2002 (*J Eur Acad Dermatol Venerol* 2002; **16(s1):**1).

Key words: Brachioradial pruritus, itch, neuropathy, notalgia paresthetica, pruritus.

Sponsors: None.

Declaration: No conflict of interests declared.

SESSION 3

Chair: Professor C Munro, Consultant Dermatologist, Southern General Hospital, Glasgow, Scotland

MODERN VIEWS ON THE MANAGEMENT OF PSORIASIS

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Abstract

Modern 'biologicals', engineered antibodies to cytokines or elements of the antigen presentation system, are being strongly promoted in the US as treatments for psoriasis, and are beginning to be used off-license in the UK. While undoubtedly effective and useful in some patients, they have not yet been compared against currently used systemic agents or phototherapy. Using data from the published literature on the efficacy of biologicals, and our own experience in the dedicated Edinburgh psoriasis clinic, I will try and define the place for these new drugs, and what, if any, advantages they have within a very different healthcare model from the US.

Key words: Biologicals, psoriasis, therapy.

Sponsors: None.

Declaration: No conflict of interest declared.

THE MANAGEMENT OF ATOPIC DERMATITIS IN CHILDREN

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Abstract

Standard management for childhood atopic eczema includes emollients, topical steroids, antibacterial agents and sedative antihistamines at night. Parents are always keen to try allergen avoidance and complementary therapy. The role of the new topical immunomodulators is not yet clear. Patients with very severe eczema may be helped by phototherapy or longer term systemic therapy with steroids, cyclosporin or azathioprine. Unfortunately the evidence base for eczema treatments is very limited,[1] none are reliably effective, and many have adverse effects.[2, 3] Effective delivery of care[4] and empowerment of patients[5] are essential considerations in managing this common, chronic condition.

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5 http://www.eczema.org/ and http://www.eczemapro.org/

Key words: Allergen, atopic, compliance, dermatitis, eczema, emollient, steroid.

Sponsors: None.

Declaration: I have participated in phase three trials of tacrolimus ointment funded by Fujisawa. My department receives sponsorship from several other pharmaceutical companies on the understanding that we do not endorse or promote their products.

FUNGAL INFECTION – A LOGICAL BASIS FOR TREATMENT

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Abstract
In financial terms antifungals represent by far the largest therapeutic area in dermatology. These drugs are available as prescription only medicines (POMs), prescribed medicines (PMs) and over the counter (OTC) products. They are all generally used without laboratory confirmation of infection even when given systemically and are almost certainly over prescribed.

Ideally, all infections should be confirmed before treatment is instituted. However, in the real world, this is not absolutely necessary and there are many fungal infections where diagnosis by therapeutic trial is a perfectly respectable approach. Most infections which can be treated topically do not require laboratory confirmation, hence the reason that the majority of topical agents are available without prescription. Athlete's foot, the commonest of all fungal infections, can now be treated over durations as short as one week with very high cure rates and the same can be said for small areas of infected glabrous skin.

Systemic treatment is necessary in areas where the keratin is especially thick namely the scalp, palms, soles and nails. Laboratory confirmation of infection should be obtained in all of these areas, because of the duration of treatment and the risk, admittedly low, of adverse events. In scalp infections, laboratory diagnosis plays an important role in the aetiology of the disease and in the possible identification of an animal vector.

Terbinafine, both topically and orally, is the most potent antidermatophyte agent available. It is not active against *Candida albicans* when given systemically where azoles are the drugs of choice. A large percentage of the cost of antifungal therapy results from the systemic treatment of nail infections. It should be remembered that the optimum treatment period for finger and toenails is 9 and 12 weeks respectively. There is little utility in using more prolonged courses in cases of treatment failure. The reasons for such failure should be identified and countered.

Key words: Antifungals, laboratory confirmation, systemic treatment, terbinafine, therapeutic area.

Sponsors: None.

Declaration: No conflict of interest declared.

SESSION 4

DEBATE

Chair: Professor D Weller, Professor and Head of General Practice, University of Edinburgh, Edinburgh, Scotland

WHY DERMATOLOGISTS LOVE GENERAL PRACTITIONERS

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Abstract
Not love them, perhaps, but dermatologists ought at least to be grateful to general practitioners (GPs). In the UK, the majority of dermatological service provision occurs in primary care. Dermatologists are relieved of the burden of many relatively minor conditions which form the basis of dermatological practice in Europe and the US. British dermatologists can focus on the management of major skin disorders, interesting or challenging cases, and tertiary services. Erosion of the gatekeeper function in the face of rising expectations puts pressure on this system, and highlights a need for better training in dermatology for primary care.

A minority of GPs consistently make inappropriate demands on specialist dermatology units in both the volume and quality of their referrals, which result in inefficient use of specialist time and unnecessary waits for patients. However, it is demonstrable that knowledge of dermatology does not reduce referral rates, and waiting lists tend to re-establish themselves despite GP education, consultant expansion or demand

management measures. As politicians respond to waiting lists, dermatologists should recognise that over the decades GPs – whether or not they have interest or ability in dermatology – have been unfailing drivers of a gradual expansion in specialist dermatology.

Sponsors: None.

Declaration: No conflict of interest declared.

WHY GENERAL PRACTITIONERS LOVE DERMATOLOGISTS

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Abstract

Why do GPs love dermatologists? This is an interesting question, but this statement is based on the premise that GPs actually do love dermatologists. We can turn to anecdotes. Taking matters literally, in Leeds there is a GP married to a consultant dermatologist and hopefully they love each other!

If GPs recognise themselves as the engine of the NHS what do they think of dermatologists?[1] There are also quite a number of GPs who have become dermatologists probably because they loved dermatology. This may, however, be due to the facts that patients with skin disease did not call you out during the night and did not die.[2] They may also feel that life would be so much easier if patients were contracted to have only one condition at a time.[3] General practicioners may easily adapt to a life of dermatology, as there is some evidence that the impact of skin disease on the quality of life of patients seen in primary care is comparable with patients seen in secondary care.[4]

In my own career, spanning 25 years as a GP and hospital practitioner, most comments about dermatologists from GPs have been complementary however a few dermatologists' ears could have burnt. John Morgan was a dermatologist on Teesside, Scotland, between 1956 and 1982. He was truly loved by GPs, patients and staff. Reasons given included being hard working, kind, accessible and an excellent diagnostician. John entertained GP registrars to lemon tea on the lawn after clinics. Common topics of conservation were the Staithes lifeboat and steam trains in India! John had a head start on other dermatologists for the hearts of GPs, as his father was a GP.

In the days of evidence-based medicine one is required to dig deeper into the views of GPs. Quantitative research would be of little value in measuring such an emotive subject as 'love'. Qualitative research looked the way forward; however, GPs had to overcome their anxiety about giving their views of consultant colleagues. Over 50 GPs in five large practices were asked for their views. The GPs were clearly advised that their views would be anonymous. These views will be presented during the debate.

The views of today may not be the views of the future. The demographics of both dermatology and general practice are changing. These days dermatology is changing from a male dominated specialty to a female one. Part time working if not the norm already in this specialty, will be the way of the future. Will this affect relationships between GPs and dermatologists?

Most GPs prefer to manage the majority of dermatological problems themselves, with support from the department when necessary.[5] General practitioners with a special interest may be able to provide care for most patients with common skin diseases. This along with tele-dermatology may reduce contact between GPs and dermatologists.

Are dermatologists the last generalists in secondary care? Are they a dying beloved breed? In the future will we send patients to a dermatological geneticist, paediatric dermatologist, dermatological surgeons or laser specialist? Will the love affair between GPs and dermatologists continue?

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Key words: Dermatologists, general practitioner, love.

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Declaration: No conflict of interest declared.