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The art and science of photodermatology – beyond the surface of the skin

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According to popular wisdom medicine is both an art and a science. Among the medical specialties this is particularly true for dermatology. The science of dermatology includes pathophysiological understanding, classification, and evidence-based treatment of skin disease; the art is related to the individualized, patient-oriented application of its science. In addition to this, dermatology is an art of observation, where the experienced doctor is able to recognize the numerous clinical variations that nature produces on our integument as manifestations of different diseases. However, these clinical features that are so helpful for diagnosis are only superficial signs of disease processes that happen well below the surface of the skin.

The current issue of *Photochemical & Photobiological Sciences* is devoted to photodermatology, a subspecialty of both photobiology and dermatology. Photodermatology deals with the interaction of human skin with electromagnetic radiation within the range of the terrestrial solar spectrum. The resulting effects can lead to tissue damage and disease (photodermatoses) but can also be used for diagnostic purposes (photodiagnosis) and for therapy (phototherapy). According to the first law of photochemistry (named after the 19th century photochemists Theodor Grotthuss and John W. Draper), light must be absorbed in order for a photochemical reaction to take place. In the skin the major chromophores (mainly DNA, some amino acids, pigments, and small molecules) reside in subsurface cellular and interstitial structures. According to Grotthuss' and Draper's law, absorption by these chromophores results in photochemical reactions that may be followed by photobiological responses and – under certain conditions – will ultimately produce visible signs on the skin surface to aid the dermatologist in applying both the art and the science of his field. Ultimately, research efforts in photodermatology must be focused on patients and improving patient care. Research efforts in photodermatology can impact on patients through a better understanding of their photosensitivity diseases, improved application of phototherapies, better strategies for photoprotection and greater understanding of holistic elements of patient care. We are grateful to the authors who have contributed to this issue with perspectives and original articles which illustrate the above remarks and cover some of the most recent advances in photodermatology.

Scientific progress is usually gradual and builds on advances made in the past. It thus makes sense to open this issue with a scholarly perspective on the history of phototherapy by Hönigsmann (DOI: 10.1039/c2pp25120e) who introduces us not only to the major developments of the past but also to the individuals behind it.

Without doubt photodynamic therapy (PDT) is among these achievements which has inspired research in experimental as well as in clinical photomedicine. This is reflected by a number of articles in this issue that cover basic aspects of PDT as well as clinical experience on its use in large patient cohorts: Valentine *et al.* (DOI: 10.1039/c2pp25271f) demonstrate how basic research in PDT can be utilised to improve its clinical application. A step further into the clinic Fabricius *et al.* (DOI: 10.1039/c2pp25128k) present the results of a study in healthy volunteers showing that the extent of PDT-related adverse effects is dependent on the concentration of the methyl aminolevulinate (MAL), a commonly-used photosensitizer in dermatology approved for superficial variants of non-melanoma skin cancer (NMSC). The response of the various stages of squamous cell carcinoma, a common form of NMSC, to oxidative stress from PDT and other sources is the topic of an experimental study by Barrette *et al.* (DOI: 10.1039/c2pp25064k). From their results the authors conclude that susceptibility to oxidative stress is maintained even in cells from advanced tumours.

Although not formally approved, PDT is also used for a variety of dermatoses other than NMSC. Calzavara-Pinton *et al.* (DOI: 10.1039/c2pp25124h & 10.1039/c2pp25125f) provide valuable evidence from a large Italian case collection on the practical experience of MAL-PDT in a broad range of oncologic, infectious, inflammatory and cosmetic indications. Eichner *et al.* (DOI: 10.1039/c2pp25164g) lead us into a potential future application of PDT. They show that a group of clinically relevant disease-causing bacteria and fungi can be rapidly and

efficiently killed by PDT and propose its further development for hand hygiene in health care.

Investigation of the mechanisms underlying the effects of phototherapy is an important line of research that will add not only to our understanding of the treatment modalities but also of the pathophysiology of the treated disease. For example, Wolf *et al.* (DOI: 10.1039/c2pp25187f) demonstrate in a clinical study on the treatment of polymorphic light eruption, a common but poorly understood photosensitivity condition, that prophylactic treatment with 311 nm UVB (photohardening) leads to changes in the cytokine milieu in the skin that inhibits the subsequent development of the disease. Psoriasis is another disease where UVB may be of therapeutic benefit. Weatherhead *et al.* (DOI: 10.1039/c2pp25116g) have reviewed the literature from which UVB therapy for psoriasis has evolved and offer new insights into the application of keratinocyte apoptosis as a biomarker for response to UVB. They describe how keratinocyte apoptosis might be combined with a systems biology approach to provide insight into which wavelengths of UV are most effective at clearing psoriasis. Photopheresis is another form of phototherapy where specialist equipment is used to expose blood components to 8-methoxypsoralen and UVA in a system outside the human body (extracorporeal). Its development, mechanistic aspects and clinical results are reviewed by Trautinger *et al.* (DOI: 10.1039/c2pp25144b). In another clinical study, Wolf *et al.* (DOI: 10.1039/c2pp25203a) present initial evidence on the efficacy of photopheresis in the treatment of severe refractory atopic dermatitis.

It is increasingly apparent that the benefit of ultraviolet irradiation for the treatment of skin disease is explained by both suppression of adaptive immune responses and induction of innate immunity. Until recently, the latter has been relatively neglected. The two sides of this issue are illustrated by contrasting papers from Manchester and Delhi. Felton *et al.* (DOI: 10.1039/c2pp25158b) describe how ultraviolet radiation of the skin leads to induction of the innate immune system by induction of antimicrobial peptides. They describe how these small peptides are increasingly recognised as providing a pivotal link between the adaptive and innate immune systems and may even contribute to photosensitivity reactions by dysregulated responses to ultraviolet irradiation of the skin. In contrast, Sharma *et al.* (DOI: 10.1039/c2pp25186h) provide a comprehensive review of the scourge of parthenium dermatitis, a skin condition characterised by deranged adaptive skin immunity. Chronic exposure of the skin to the ubiquitous non-indiginous weed *Parthenium hysterophorus* leads to contact dermatitis, a type IV hypersensitivity reaction. This has become the most common plant dermatosis in India and is not infrequently complicated by chronic actinic dermatitis, one of the most severe and persistent acquired photosensitivity syndromes. In a second paper from Delhi, Sharma *et al.* (DOI: 10.1039/c2pp25182e) describe the clinical features of photosensitivity syndromes in pigmented skin, a hitherto neglected area of the art of clinical photodermatology.

A number of papers in this issue focus on effects of UVB and UVA on the skin. Kiss and Anstey (DOI: 10.1039/c2pp25275a) provide an up-to-date review of photodermatoses mediated by UVB. Most of these conditions are rare, but their study has provided important insights into normal photobiological responses within the skin. This is particularly so for xeroderma pigmentosum (XP), a congenital photosensitivity syndrome which is comprehensively reviewed in a perspective by Fassihi (DOI: 10.1039/c2pp25267h). Although much is known about XP, management remains difficult and complex due to the absence of effective therapies other than rigorous photoprotection. Fassihi highlights gaps in our understanding of XP, including a failure to understand why some patients with XP do not show the characteristic exaggerated sunburn response.

Rizwan *et al.* (DOI: 10.1039/c2pp25177a) have studied the psychological impact of a broad range of photodermatoses, recognising that collectively photosensitivity conditions are common and are known to significantly impact on patients' quality of life. This study demonstrates the high psychological comorbidity of photodermatoses; the authors emphasise the need for greater awareness of the psychological impact with adoption of a biopsychosocial approach to management. Broadening from this focus on photosensitivity diseases, Sklar *et al.* (DOI: 10.1039/c2pp25152c) have reviewed the effects of ultraviolet radiation, visible light and infra-red radiation on cutaneous erythema and pigmentation. They conclude by stating that current evidence reveals a good understanding of the cutaneous effects of ultraviolet radiation; however, they also emphasise that much remains to be learned about how visible light and infrared affect skin erythema and pigmentation. Prevention of ultraviolet damage to skin with sunscreens is the focus of a study by Wang *et al.* (DOI: 10.1039/c2pp25112d); the evolution of sunscreen products in the United States of America was studied in a 12 year cross-sectional study. They conclude by stating that the past decade has seen sunscreen products undergoing fundamental improvements, the most significant of which is broader protection against UVA1. The significance of this is highlighted by Tewari *et al.* (DOI: 10.1039/c2pp25323b), who show that UVA1 (340–400 nm) generates pyrimidine dimers, especially thymine dimers, and that the rate of DNA damage increases with greater skin penetration of the UVA1. They go on to explain that UVA1 may be more carcinogenic than was previously assumed.

Protection from sunburn and chronic photodamage (including photocarcinogenicity) can be achieved with avoidance of exposure, clothing and sunscreens. Investigations on sun-exposure behaviour and sunscreen use under real-life conditions are thus important to guide educational campaigns with the aim of reducing the global burden of skin cancer. The studies by Thieden *et al.* (DOI: 10.1039/c2pp25138h) and Petersen *et al.* (DOI: 10.1039/c2pp25127b) demonstrate that – at least in the population

studied – individual sun-exposure habits remain unchanged over an observation period of years and that, if measured under real sun holiday conditions at the beaches, sunscreens are used in a way that their intended protective effect is compromised.

Finally, the paper by Jin *et al.* (DOI: 10.1039/c2pp25070e) describes an innovative approach combining nanomedicine and photophysics for the advancement of skin regeneration. Scaffolds of nanofibers were generated from photovoltaic polymers, seeded with fibroblasts and stimulated with visible light upon which cell growth was significantly stimulated.

In summary, the aim of this issue was to showcase a cross-sectional sample of papers from around the world in the field of photodermatology. We have attempted to demonstrate that – although often only visible with the various tools provided by scientific research – much is happening within and beyond the skin following exposure to UV, visible light and infra-red radiation that merits research. Our thanks go to all contributing scientists, the editorial staff of *Photochemical & Photobiological Sciences* for their support and the editor-in-chief for his untiring help, inspiration (and patience) in putting this issue together. We hope that this small collection of articles, representing as it does only a fraction of the scientific achievements in photodermatology, makes for an interesting read and is able to stimulate interest and new ideas in those who are less familiar with this field.

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