

P306

Vitiligo: The historical curse of depigmentation

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Vitiligo, the "small blemish" (from the Latin vitulum) was first described more than 1500 years BC. Both ancient Egyptian and pre-Hindu Vedic texts give a clear record of depigmented macules. A Vedic myth, for example, describes the human form of the sun-god developing vitiligo after being gazed upon by his illegitimate son. An accurate description also exists in Japanese Shinto prayers from 1200 BC. Leprosy is recorded as a pale swelling, distinct from vitiligo in the Ebers papyrus (an Egyptian collection of writings from 1500-3000 BC), but there is no such demarcation between the two diseases in either the Bible or in the first European description of the disease by Hippocrates. Sadly, this type of "nondiscrimination" persists in many communities in the world today, where vitiligo sufferers are sometimes shunned in the same age-old way as people with leprosy. Early attempts at treatment mirror contemporary therapies too, as both ancient Egyptian and Indian writings depict psoralen-containing plants applied to pale macules and then exposed to sunlight. We have much to learn from both the sociological and medical history of vitiligo, if we are to make progress in improving the management of this ancient disease in the modern world.

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P308

Novel noninvasive measurements of collagen formation using high-density ultrasound measurements

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In vivo skin high-density ultrasound measurements are being used to estimate the effect that skin care products have on collagen formation and skin elasticity. The general advantage of using the in vivo ultrasound measurements is to follow the formation of collagen without invasive biopsy techniques. Another advantage is to provide information on the rate of collagen formation as the products are continuously applied. Fifteen people applied different products to the lower forearm and the upper back for 6 weeks. Comparative data are presented for different products showing increases in collagen density and skin elasticity. Ultrasound and skin punch biopsy measurement were compared.

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BASIC SCIENCE

P400

A whole blood assay to assess peripheral blood dendritic cell function in human leprosy (Hansen disease)

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Leprosy (also called Hansen disease) is a chronic infectious disease caused by the intracellular bacillus *Mycobacterium leprae* (M lep) that is principally a disease of the skin and peripheral nerves. The lepromatous form of leprosy (L lep) provides a classic example of pathogen-specific failure of acquired T-cell immunity and therefore is a potentially informative model for understanding mechanisms of antigen-specific immune evasion. The antigen-presenting dendritic cells (DCs) of the innate immune system must first be activated by pathogens to prime T-cell immunity and therefore play a critical role in immune surveillance. This primary recognition of pathogens by DCs is via a system of pathogen-associated molecular pattern recognition receptors called toll-like receptors (TLRs). Of the 11 TLR members known in humans, TLR2 has been implicated in the recognition of M lep. These considerations have led to the hypothesis that defects in TLR2 signaling by DCs underlie the failure of initiation of M leprae-specific T-cell immunity in L lep. However, there are conflicting data concerning TLR2 and DC function in L lep patients. Current methods for examining activation and function in DCs are time-consuming and involve much potentially confounding ex vivo manipulation of these cells. We developed a rapid flow cytometry-based technique to assess TLR-mediated responses by DCs in whole blood and here report the application of this technique to evaluate TLR-stimulated DC function in leprosy patients and healthy controls. First, we demonstrate a concentration-dependent induction of TNF- α by DCs in whole blood in response to stimulation with either M tuberculosis (M tb) or M lep whole cell sonicates (WCS). By WCS concentration, we find that M lep is 100-fold less potent than M tb in activating DCs. Using a synthetic TLR2 ligand and the mycobacterial sonicates, we have performed an analysis of 11 leprosy patients and ethnically matched healthy controls so far recruited to our study. Our data suggest intact signaling via TLR2, but impairment in L lep of DC-1 expression of the lymph node homing receptor CCR7 in response to both M tb and M lep WCS. In conclusion, our data suggest that (1) M lep is intrinsically less immunogenic than M tb and (2) patients with L lep may have subtle defects in DC responses to mycobacteria that, together with the weak DC-activating properties of M lep, contribute to the failure to prime protective T-cell immunity.

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P307

Art review by cosmetic dermatologists

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Dermatology is a visual art. Cutaneous signs play a significant role in dermatologic illness and cosmetic dermatology (Al Aboud K, Al Hawsawi K, Ramesh V, Al Aboud D, Al Githami A. Cutaneous signs. *Skinmed* 2003;2:104-7). Learning to see what we look at enhances our appreciation of the world around us but also, quite specifically, makes us better dermatologists as well as better cosmetic dermatologists (Meakins JL. Surgical infection in art. *Arch Surg* 1996;131:1289-95). Art is ambiguous and multilayered, and its interpretation requires sensitivity, engagement, imagination, and reflection. Fostering these skills is also essential for clinical competence and professional development (Frich JC, Fugelli P. Medicine and the arts in the undergraduate medical curriculum at the University of Oslo Faculty of Medicine, Oslo, Norway. *Acad Med* 2003;78:1036-8; Shapiro J, Rucker L. Can poetry make better doctors? Teaching the humanities and arts to medical students and residents at the University of California, Irvine, College of Medicine. *Acad Med* 2003;78:953-7; Reilly JM, Ring J, Duke L. Visual thinking strategies: a new role for art in medical education. *Fam Med* 2005;37:250-2)3-5. Astute observation leads to early diagnosis and better results in the diagnosis of cutaneous diseases. What dermatologist can see beyond the canvas?

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P401

Advanced techniques for measuring skin hydration

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Optimal hydration of the stratum corneum (SC) is required to maintain flexibility of the skin and to facilitate the enzymatic reactions that drive SC maturation. Skin hydration is measured through correlation with the electrical properties of skin, such as conductance and capacitance. While it is widely accepted that these electrical measures directly correlate (although nonlinearly) with skin hydration, there are concerns about several confounding factors. These include the effects of other polar molecules in skin, temperature, and surface roughness. Additionally, it is evident that substances or treatments that interact with the keratin-water network of the SC can change the electrical properties of skin without actually altering water content. Techniques such as infrared spectroscopy directly measure the skin water content, and thus, many potential confounding factors are avoided. We developed near infrared (NIR) imaging-based technique and demonstrated its capability of detecting changes in skin hydration induced by skin moisturizers and cleansers. It is rapid, noncontact, and noninvasive and has the advantage of showing the degree of hydration as a function of location, for rapid assessment of change in hydration. We compared the NIR imaging technique with existing electrical methods. The visual assessment of skin dryness was used as the standard for the comparison of the techniques. Our results demonstrate that NIR imaging provides a more sensitive discrimination between treatments (moisturizers and cleansers) and controls (products whose effects on skin hydration are well established), as well as a strong correlation to the visual appearance of dryness. Confocal Raman spectroscopy has emerged in recent years as a useful tool to obtain detailed information about the molecular composition of the skin. It can provide depth-resolved information about water—that is, the gradient in water concentration throughout the epidermis—and other important skin constituents such as natural moisturizing factors. It can also provide information on exogenous molecules, such as glycerol, delivered from skin care products. In this presentation, we will review these spectroscopic techniques used in evaluating skin cleansing and skin care products. The results from recent clinical studies will be discussed to show the practical and potential use of spectroscopy in understanding skin condition and evaluating new technologies for skin care products.

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P402

Application of hydration mapping technique in skin research

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A hydration mapping technique, which presents an image of moisture distribution on the skin surface, is finding more and more applications in skin research. This technique not only measures surface hydration but also shows detailed microtopography of skin. This device consists of a digital sensor containing a large number of capacitor elements, arranged in a rectangular grid. Scalp lesions of the skin can be studied very well. Also, we can study the moisturization decay-rates of various products. After a single application of lactic acid (10% aqueous) on the face we followed the hydration levels for 6 hours. Distilled water was used as the control. The lactic acid site showed high hydration level at the 6-hour time-point, while the water site returned to baseline in only 15 minutes. We studied the skin microrelief in photodamaged versus relatively less photodamaged skin and found that the corner density parameter was inversely proportional to the amount of photodamage. The hydration images also showed the difference. Other topographic studies were done on lips, dorsal and volar forearms, nasolabial cheeks and V neck area of the chest. The skin hydration-mapping is a useful technique which can be utilized in studies of moisturizers, hyperkeratotic syndromes and photoaging.

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P403

Assessing the gentleness of a sonic skin care brush for daily use

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Gentleness of a sonic skin care brush was assessed comparing over-the-counter (OTC) exfoliants in 11 subjects who participated in a 4-arm, two-visit study. The treatments consisted of a sonic skin care brush with water (SB), a nylon facial pad with water (FP), a daily facial scrub (FS), and a negative control (no treatment [C]). Using an exfoliation tanning methodology, skin of the lower leg was stained with commercial self-tanning solution to darken pigment. Twenty-four hours after tanning, a standard skin color curve was constructed on the lower leg. Four 1-inch by 1-inch boxes were drawn within the tanned area using a surgical marking pen. The standard curve was created by placing multiple D-Squame strips in the same location, removing several cell layers until the tanned cells were lifted away. Above each box one of the following labels were placed: 0, 5, 10, 15 corresponding to the number of D-Squame tapes used. A 1-inch by 1-inch box was drawn outside the tanned borders as a control (labeled "U"). Four 2-inch by 2-inch boxes were drawn below the standard curve but within the tanned area and labeled according to the treatment applied within the borders of each test box. Prior to treatment, the following duplicate baseline measurements were recorded within the standard curve, treatment, and control areas; skin temperature (recorded using an infrared temperature scanner), melanin ([M] color intensity) and erythema ([E] redness) and triplicate measurements for transepidermal water loss (TEWL). Treatment was administered by an aesthetician and the same measurements were repeated after each treatment. A one-way ANOVA was used to assess the between-treatment group differences in the mean change in TEWL score. A mean TEWL difference was observed pre- to post- between all treatment groups ($P = .0007$). Comparisons of C to FS, FS to SB, and FS to FP were statistically significant. Analysis of variance was used to assess the between-group differences in the mean change in M and E. A mean M difference was observed pre- to post- between all treatment groups ($P = .0001$). Comparisons of C to FS, FS to SB, and SB to FP were statistically significant. No difference was observed in E pre- to post- between the treatment groups ($P = .4281$). The methodology used was able to assess the gentleness of the sonic skin brush for daily use. The sonic skin care brush was gentler than OTC facial products used.

Author disclosure: Presenter and principal investigator are employees of Pacific Bioscience Laboratories.

P404

Confocal Raman microspectroscopy—A new method for measuring the effects of topical moisturizers on stratum corneum water gradient, in vivo

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The stratum corneum (SC) water concentration gradient is fundamental to skin's role as a barrier, regulating its mechanical, physical, optical, and biochemical properties. Standard instruments that utilize changes in SC electrical properties to estimate SC water concentration provide simple, rapid measurements but cannot, by nature, provide true interval data as a function of depth. Confocal Raman microspectroscopy (CRS), in contrast, is a new technique that combines the well-attested method of Raman spectroscopy (the study of inelastic scattering of light, rather than its absorption) with confocal microscopy, allowing noninvasive, real-time, in vivo measures of molecular concentration profiles. A new confocal Raman microspectrometer equipped with a fiber-coupled laser source operating at a wavelength of 671 nm was used to obtain measurements in the high wave number region (~ 2400 – 4000 cm^{-1}). An air-cooled, high-sensitivity NIR detector system, equipped with a back-illuminated, deep-depletion CCD camera captured radiation scattered inelastically from focal planes within the skin in vivo (a high-precision, computer-controlled piezo-electric stage and objective allowing depth resolutions of less than $5 \mu\text{m}$, with oversampling). High-wave number data were analyzed to provide semiquantitative measures of water concentration ($[\text{water}]/[\text{protein} + \text{water}]$) across the SC. This new technique was used to study changes in SC water concentration gradients in human skin in vivo, in response to treatment with topical moisturizing products. This poster will report the results of a blinded, randomized 3-week study in human volunteers and, in particular, the significant ($P < .05$), unique effects of a topical moisturizer containing niacinamide (vitamin B_3) on SC water concentration gradient, as measured by CRS, in vivo. SC water gradient effects will be discussed in the context of the known SC barrier-augmentation properties of niacinamide and the utility of this new method will be compared and contrasted to existing methodology.

Author disclosure: All authors are employees of Procter & Gamble Company.

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