Editorial

The Field Effect

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If you talked to a child about the skin's function, you would tell him/her that the skin is the largest organ of the body, covering roughly 2 m^2 of surface area. To limit therapy and avoid side effects of systemic agents, one can lose sight of the true extent of the skin as an organ. One of the observations I have made in dermatology is that widespread disease rarely remits on limited topical therapy (ie, application to the affected area). I posit that the entire field of skin disease is far broader than the epidermal and dermal layers and merits therapy in surface areas beyond the 5% to 10% one would treat with creams.

The field you are treating in most skin diseases involves the surface area; the number of regions; and the structure, which consists of the keratinocytes, the barrier structure, the immune cells associated with the skin, and the neurovascular bundles of the skin. The immune cells associated with the skin include the skin-associated lymphoid tissue; dermal dendrocytes; and circulating white blood cells, such as polymorphonuclear cells. Other aspects of the skin include the appendages; dermal support structures; and circulating substances including hormones, vitamins, and cytokines. Treating the entire field of disease is the mechanism of action of biologic therapy for psoriasis and the reason that biologic therapies are effective as a class of therapy for psoriasis and psoriatic arthritis. Usage of systemic agents or phototherapy affects the broader and vaguer aspects of the skin (the parts of the skin that we cannot visualize with the naked eye), such as skin-associated lymphoid tissue or Langerhans cell activity, and gets to the pathogeneses of diseases more effectively. When the disease pathogenesis is well-elucidated, treating the field can be done using targeted agents, such as biologics; when the disease pathogenesis is not fully understood, usage of nonspecific therapies (eg, phototherapy) comes into play.

With these thoughts in mind, we can look at specific examples from my practice. Many of my pediatric patients with diffuse alopecia areata will experience subtotal or total hair loss. These patients are identified as having diffuse positive hair pull tests (loose hairs across the full scalp) and numerous areas of alopecia (>7 areas). When I started practicing, I would have parents chase the patches by applying a topical corticosteroid to the affected area only within a finger-width margin. This technique was and still is effective for treating limited disease (eg, marginal pull positive and <5 patches of alopecia). For diffuse recurrent alopecia areata, children would have constant disease activity and would not get holidays from drug treatment (ie, as one spot would regrow hair, new ones would emerge, and the patient would never have full hair growth). Today, as a practitioner, I consider the field of alopecia areata to include the "swarm of bees" around the follicular units, the follicular units of the terminal hairs of the scalp, and the cytokine milieu of the entire scalp. I, therefore, offer these patients therapy for the entire field of alopecia, usually for at least 3 to 6 months. Therapy for the entire field includes topical corticosteroids to the entire scalp (it takes 3–6 months to control hair loss over the full head) and topical immunomodulators such as squaric acid dibutylester or oral systemic agents, which can include minipulses of steroids once a week. Interestingly, field therapy can be either across the full head or part of regions (eg, treating the eyebrows with squaric acid dibutylester can promote eyelash regrowth). Although field therapies are more labor intensive, they offer the patient control of the regional cytokine milieu and regional immune activity, allowing for more effective control and remission times during which patients can come off therapy.[1]

Dermatologists do a great job treating the field in patients with acne vulgaris. The field in acne includes the pilosebaceous unit in specific blocks of skin (eg, face, chest, back), the cytokine milieu, the inflammatory cells that are attracted to the pilosebaceous unit in the disease (ie, the polymorphonuclear cells), and natural or dietary hormones.[2] In general, dermatologists prescribe agents to be used across the surface of the entire face and sometimes the chest and back; they address follicular plugging regionally (eg, retinoids), bacterial overgrowth (eg, benzoyl peroxide), and inflammation regionally (eg, topical antibiotics).[2-4] Usage of systemic agents in this disease

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The author reports no conflict of interest.

is the most effective way to address the entire field of disease. Oral antibiotics affect the movement of polymorphonuclear cells throughout the regions of involvement, while oral isotretinoin addresses follicular plugging, sebaceous gland activity, and inflammation of the pilosebaceous unit, effectively getting to all the root causes of acne at the cellular level and covering all regions of disease.[2-4] Other field therapies in our armamentarium are oral contraceptives[5] and the control of insulin release through a low-glycemic index diet.[6]

Generalized vitiligo vulgaris is a disease of broad pathogenesis that includes antibody-mediated (eg, to tyrosinase[7]) cellular cytotoxicity of the melanocyte, oxidative damage, and ultimately loss of pigment through melanocyte damage.[8,9] The factors that cause localized pigment loss such as antibodies, free radicals, and lymphocytes that attack melanocytes circulate globally and can cause new lesions at any time and essentially anywhere. The leading issue affecting quality of life in patients with this disease is the unpredictable course of illness.[8] Treating with local topical agents or excimer laser is wonderful for limited stable illness, but many patients have progressive pigment loss due to disease activity.[9] Therapeutically, some vitamins have been shown to be beneficial in limiting the course of disease, but the regimens are difficult to maintain. Therapeutically, narrowband UVB or psoralen plus UVA 2 to 3 times weekly can provide stabilization of illness after a 3- to 5-month interval.[10-12] Because there are no targeted biologic agents for vitiligo at this time, generalized phototherapy still represents the best way to treat the field of melanocytes that potentially would be affected by disease. When one considers the true field of disease—the entire pigmented skin surface—limited or local therapy may not offer the best disease control in all patients.

I hope that my conceptualization of the field of skin disease will help you to chart a course of therapy for your more challenging patients. As the complex pathogeneses of skin diseases are better elucidated, I look forward to seeing systemic agents that will specifically target the true field of our most therapeutically challenging illnesses.

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