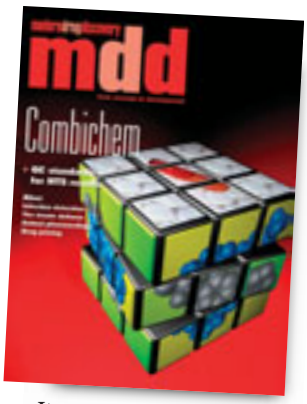
Beneath the skin

We wish to elaborate on some points made in the article "Vitiligo" (February, p 64) and enlighten readers about promising new therapies. Vitiligo is an acquired disease characterized histologically by the loss of melanocytes in affected depigmented areas. Clinically, these areas will appear as leukoderma, but leukoderma is not synonymous with vitiligo. Leukoderma is an acquired type of cutaneous depigmentation produced by a dermatosis or a specific substance. Occupational leukoderma may result from contact with or ingestion or inhalation of certain chemicals, such as monobenzyl ether of hydroquinone and phenol-containing compounds in the workplace. Postinflammatory leukoderma occurs after healing of various inflammatory dermatoses or infections, burns, or wounds. Achromia is another term for the absence or loss of melanin of the skin and iris that includes acquired conditions such as vitiligo as well as congenital disorders, such as albinism and piebaldism. It occurs from either defective melanin production, as in albinism and nevus depigmentosus, or from a lack of melanocytes as in piebaldism or vitiligo. Many etiologies must be considered in patients presenting with total or partial absence of skin pigment.



Vitiligo has a definite association with other autoimmune diseases such as autoimmune thyroid disease, diabetes mellitus, and Addison's disease. Numerous studies have demonstrated the presence of melanocyte-specific cytotoxic T cells infiltrating the border of a growing vitiligo lesion (see Hartmann, A.; Brocker, E. B.; Becker, J. C. Hypopigmentary skin disorders: Current treatment options and future directions. *Drugs* **2004,** *64*(1), 89–107). Topical corticosteroids may thus be helpful in treating vitiligo; however, their required prolonged use may result in unwanted side effects ranging from thinning of skin and striae (stretch marks) to systemic effects from percutaneous absorption of ultrapotent topical corticosteroids.

Recently, topical immunomodulators (TIMs) such as topical tacrolimus have shown promise in treating vitiligo (see Hartmann, A.; et al.). Tacrolimus and pimecrolimus bind with high affinity to macrophilin-12 (FKBP-12) and inhibit the calcium-dependent phosphatase calcineurin. As a consequence, they inhibit T cell activation by blocking the transcription of early cytokines. In particular, they inhibit interleukin-2 and interferon gamma (Th1-type) and interleukin-4 and interleukin-10 (Th2-type) cytokine synthesis in human T cells. TIMs avoid the skin atrophy and induction of acne and folliculitis that may occur with topical corticosteroids and the risk of iatrogenic Cushing's syndrome and hyperglycemia from percutaneous absorption of corticosteroids.

While these latest medications hold promise, more definitive therapy for vitiligo might be realized by inducing the growth of new melanocytes rather than halting their destruction. Future administration of melanocyte-stimulating growth factors by local application or via gene therapy could be used to treat not only vitiligo but also other hypo- or depigmented skin disorders.

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Past and future

"The ghosts of pharma past" (January, p 25) revived memories of seeking to recover sulfanilamide prescriptions—not unlike the sulfathiazole contamination with barbiturates a few years following. While the pharmacy I worked in did not carry that elixir in 1937, it did dispense some of the sulfathiazole tablets contaminated with barbiturates a few years later.

Because I worked on a poisonous gas program in the 1940s with the National Defense Research Committee chaired by James Conant and Vannevar Bush, "Identifying biowarfare agents" (January, p 47) stirred up a few memories as well. Ultimately, I ended up in Richmond, VA, with an interest in cancer research that was spurred after World War II. Finally, as a kind of career cap, the issue of inflammatory bowel syndrome and its cause and treatment has been of interest ("Left in knots", January, p 21).

Through it all, going back to the sulfa drugs, we have come a long way, but we are still struggling to get firm answers. Indeed, the antibiotics that followed the sulfas did add years to our collective lives. However, some of our approaches are back-ended, looking at an end-stage killing process and not really addressing why the dysfunction began in the first place. It is almost as if we have lost our way if we can't find a bacterium, virus, or prion to blame for the problem, or maybe a genetic foul ball to explain it all. One has to be really concerned about issues like rates of hospital infections that are 5 to 10 times as high as rates in Listerian hospitals 100 years ago. Is something driving us in the wrong direction?

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Corrections

On page 22 of the article "The cellular solution" (December 2003), the statement "CHO glycosylation is close to the human pattern, although it produces *N*-glycans terminating in *N*-glyconeuraminic acid" should have read "*N*-glycolylneuraminic acid". This has been corrected in the Web version of the article.

In the article "Pushing the frontiers of diagnosis" (April, p 33), PerkinElmer R&D Director Blas Cerda's name was misspelled. This has been corrected in the Web version of the article.