"Tar smarts" may have a new meaning for atopic dermatitis and psoriasis

Warren R. Heymann, MD
Marlton, New Jersey

Coal tar therapy has been used for more than 2000 years to treat skin disorders, most notably eczema and psoriasis. Despite its efficacy, crude coal tar is not universally embraced by clinicians or patients because of concerns regarding cosmesis and safety. *Crude* is an appropriate adjective because coal tar contains more than 10,000 organic compounds preventing comprehension of its molecular mode of action. Even with dramatic therapeutic advances in atopic dermatitis (AD), such as the biologic dupilumab, topical therapy remains the cornerstone of treatment for AD, utilizing topical steroids, calcineurin inhibitors, and crisaborole. In this age of steroid phobia, any new valuable topical agents are welcome.

Recent studies have elucidated the mysteries of coal tar's benefit. Through use of organotypic skin models with primary keratinocytes from patients with AD and controls, it has been demonstrated that coal tar activates the aryl hydrocarbon receptor (AHR), resulting in induction of epidermal differentiation, restoration of filaggrin expression, and counteraction of type 2 helper T cell cytokine—mediated downregulation of skin barrier proteins. Coal tar interferes with type 2 helper T cell cytokine signaling via dephosphorylation of signal transducer and activator of transcription 6, most likely as a result of AHR-regulated activation of the nuclear factor, erythroid 2 like 2 antioxidative stress pathway. These findings suggested that the therapeutic effect of AHR activation could lead to the development of new mechanism-based drugs for AD.[1]

Tapinarof is a bacteria-derived polyphenol that acts on the AHR and nuclear factor erythroid 2—related factor 2 (a basic leucine zipper protein) that protect against inflammatory-induced oxidative damage. Tapinarof also has free radical scavenging ability.[2] In a study using a mouse model of imiquimod-induced psoriasiform skin lesions, topical treatment of AHR-sufficient mice with tapinarof led to compound-driven reductions in erythema, epidermal thickening, and tissue cytokine levels. Tapinarof had no impact on imiquimod-induced skin inflammation in AHR-deficient mice. This study clearly demonstrated that the anti-inflammatory properties of tapinarof are due to AHR agonism.[3]

In this issue of the *Journal of the American Academy of Dermatology*, Peppers et al[4] performed a double-blind, vehicle-controlled, randomized, 6-arm trial (with varying concentrations and dosing schedules compared with vehicle alone) in patients with AD age 12 to 65 years with body surface area involvement between 5% and 35%. Of 363 screened patients, 191 (77%) completed the 12-week treatment phase. The most effective treatment was the 1% formulation applied twice a day, with a statistically significant treatment success (clear or almost clear, with a minimum 2-grade improvement) rate of 53% compared with 24% for the vehicle alone. Treatment-emergent adverse events were reported in 51% of patients overall. They were considered treatment related in 13% of patients, leading to discontinuation of therapy in 5% of participants. The most frequently reported adverse reaction was nasopharyngitis; others noted in at least 5% of participants included folliculitis, worsening or flare of AD, headache, acne, and impetigo. The authors concluded that tapinarof cream is efficacious and well tolerated in adolescent and adult patients with AD of varying severity. They recommend further studies to determine the full efficacy and safety profile of tapinarof.[4] These studies are also warranted for psoriasis.

Tar smarts refers to the immediate burning or stinging sensation when tar-treated sites are exposed to ultraviolet A or sunlight.[5] The benefit of activating the AHR, either by coal tar, tapinarof, or yet-to-be discovered agents, gives "tar smarts" a new meaning.

From the Division of Dermatology, Cooper Medical School of Rowan University, Marlton.
Funding sources: None.
Conflicts of interest: None disclosed.
Reprints not available from the author.
Correspondence to: Warren R. Heymann, MD, Division of Dermatology, Cooper Medical School of Rowan University, 100 Brick Rd, Suite 306, Marlton, New Jersey 08053. E-mail: wrheymann@gmail.com.
J Am Acad Dermatol 2019;80:56-7.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2018.10.057

Future studies may demonstrate that the oldest therapeutic approach may be the smartest of all!

REFERENCES

1. van den Bogaard EH, Bergboer JGM, Vonk-Bergers M, et al. Coal tar induces AHR-dependent skin barrier in atopic dermatitis. *J Clin Invest*. 2013;123:917-927.
2. Vakharia PP, Silverberg JI. New therapies for atopic dermatitis. *J Am Acad Dermatol*. 2018;78:S76-S83.
3. Smith SH, Jayawickreme C, Rickard D, et al. Tapinarof is a natural AhR agonist that resolves skin inflammation in mice and humans. *J Invest Dermatol*. 2017;137:2110-2119.
4. Peppers J, Paller AS, Maeda-Chubachi T, et al. A phase 2, randomized dose-finding study of tapinarof (GSK2894512 cream) for the treatment of atopic dermatitis. *J Am Acad Dermatol*. 2019;80:89-98.e3.
5. Diette KM, Gange RW, Stern RS, Arndt KA, Parrish JA. Coal tar phototoxicity: characteristics of the smarting reaction. *J Invest Dermatol*. 1985;84:268-271.