

## The Power of Topical Steroids

Joerg Albrecht, MD, PhD

**Although topical steroids** are a ubiquitous part of dermatologic care, in recent years, they are rarely a major topic of discussion or investigation. It is telling that the US guidelines for the use of topical corticosteroids<sup>1</sup> have not been updated for a quarter century.

In their classification study in this issue of *JAMA Dermatology*, Bowie et al<sup>2</sup> meticulously assessed 3 international potency classification systems for topical steroids for agreement and correlation. The first step the authors undertook

←  
Related article page 796

was to identify a comprehensive list of topical steroid formulations as found in the Anatomical Therapeutic Chemical (ATC) classification system of the World Health Organization (WHO),<sup>3</sup> the Ontario Drug Benefit Formulary,<sup>4</sup> a recent Cochrane review on the use of topical steroids in eczema,<sup>5</sup> and elsewhere. Bowie et al<sup>2</sup> then compared 3 potency systems: (1) the ATC of the WHO<sup>3</sup>; (2) the US 7-category system; and (3) a system based on the British National Formulary (BNF) and extended in a recent Cochrane review.<sup>5</sup> Bowie et al<sup>2</sup> found that these 3 classification systems were incongruent, and their sources were not transparent. They urged authors of epidemiological studies to be clear about the potency systems they use. Because of the differences found, the authors go a step further and suggest using more than 1 system for sensitivity analysis.<sup>2</sup> This Editorial discusses the concept of steroid potency, compares and contrasts the 3 potency systems evaluated by Bowie et al, and discusses the implications of the findings for clinical practice.

### What Is Topical Steroid Potency, and What Determines It?

Topical steroids can be effective only if they penetrate the epidermal barrier. The first topical steroid, cortisone, could not do this and failed for that reason.<sup>6</sup> Only hydrocortisone managed to treat some steroid-responsive diseases. Through a long development process, topical steroid molecules became more clinically powerful.<sup>6</sup> The pharmacological potency of the steroid molecules determines the ATC/WHO potency. However, vehicles matter; beyond occlusion, the overall ability of the vehicle to deliver the corticosteroid is key. Advances have been made over the years such that ointments are not always the most potent formulations.<sup>7-9</sup> The resulting clinical potency and relative efficacy are measured by vasoconstrictor assays that determine the potency of topical steroids within the US 7-category system, or the 4-category potency classification system used by the Cochrane review.

Vasoconstrictor assays<sup>10</sup> are accepted despite their shortcomings, which include questions of clinical outcomes

and therapeutic index.<sup>11</sup> The US Food and Drug Administration (FDA) prefers these assays because they demonstrate a pharmacodynamic process, whereas clinical trials need larger numbers of patients and lack sensitivity.<sup>10</sup> Vasoconstrictor assays do not measure inflammatory activity directly, but it is reassuring that genes that modulate the expression of proinflammatory mediators (including interleukin [IL]-1, IL-2, IL-6, and interferon  $\gamma$ ) also influence vasodilatory effects.<sup>7</sup> Another strength of vasoconstrictor assays is that they have facilitated the entry of inexpensive generics on the market by avoiding costly trials.<sup>10</sup> Topical steroids—previously the most expensive drugs on the formulary of Cook County Hospital in the 1960s—currently remain relatively inexpensive. In sum, vasoconstrictor assays are useful and make sense.

### How Is Topical Steroid Safety Determined?

Although topical steroids have given dermatologists the ability to manage a multitude of skin diseases, the adverse effects of topical steroids are wide ranging.<sup>12</sup> Most feared is probably skin thinning, which is roughly similar to skin aging. Atrophy of the skin was quickly reported when topical steroids began to be used in the 1960s to 1980s. At that time, topical steroids were used in the treatment of chronic diseases without the help of potent immunomodulators, such as biologics. As a consequence, topical treatment was more aggressive than today—occlusion was ubiquitous to increase effectiveness.

Today, we use safer treatment regimens. When trials reported skin thinning, it occurred in less than 1% of patients with eczema, and some trials found none.<sup>5,12</sup> In addition, flexor telangiectasia in children with atopic dermatitis, atrophy due to mycosis fungoides, and aging skin may mimic steroid-related thinning and lead physicians astray.<sup>12</sup> In rare cases, steroids are problematic, particularly if high-potency steroids are freely available without prescriptions (or occultly present) in skin-bleaching formulations. However, when used under the guidance of a dermatologist, topical steroids are usually safe.

### ATC Classification System: Pharmacological Potency

Unlike the other systems compared in the study by Bowie et al<sup>2</sup> that rely on vasoconstrictor assays, the ATC classification system of the WHO separates drugs on the basis of their main pharmacological ingredient and their use, but not on their formulation. Triamcinolone is given a different code, depending on whether it is used for oral treatment (A01AC01), for hemorrhoids and anal fissures (C05AA12), or as a dermatological preparation (D07AB09), even if the same ointment or cream

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