Topical Corticosteroids

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Topical corticosteroids are used as anti-inflammatory agents in a variety of acute and chronic dermatoses[1]. They are less effective in granulomatous conditions or inflammatory reactions involving the deeper regions of the dermis as well as immediate type (wheat and flare) reactions. Topical corticosteroids also have an inhibitory effect on epidermal proliferative states such as psoriasis[2], although the development of tolerance and adverse effects limit the use of strong steroids in the latter condition. They may exacerbate skin infections and, although steroid antimicrobial combinations are used in secondarily infected dermatoses, there is a risk albeit small, of contact sensitisation and the development of drug resistance.

The clinical efficacy of topical steroids can be improved by enhancing the penetrating properties and potency of molecules. However both increased potency and the use of occlusion under polythene to enhance penetration increase the likelihood of adverse reactions[3,4]. Systemic adverse effects of topical corticosteroids include suppression of the adrenal pituitary axis after excessive absorption and growth impairment in children[5]. Local adverse effects include the appearance of striae, skin atrophy, bruising, rosacea-like dermatoses and secondary skin infections. Unrestricted use of strong corticosteroids under occlusion in some psoriatic patients may precipitate pustular psoriasis[6].

It is easy to forget that the advent of local corticosteroid treatments revolutionised the management of many skin conditions and used carefully they are one of the most effective forms of therapy in dermatology. Topical corticosteroids are usually classified into four main categories on the basis of strength: low potency (hydrocortisone, hydrocortisone-21-acetate); medium potency (triamcinolone acetonide); potent (betamethasone-17-valerate); and high potency (clobetasol dipropionate).

Low potency steroids are indicated in atopic or childhood eczema and in some cases of irritant contact dermatitis. They can also be used in moderation on the face or flexural areas. There have been no convincing reports that formulations containing one per cent hydrocortisone cause local or systemic toxicity as a result of excessive absorption except in infants[7].

The other more potent groups of corticosteroids induce a more rapid therapeutic effect but should not be used for long periods as tolerance may reduce efficacy. Many forms of eczema, including discoid eczema, respond well to these drugs. Some psoriatic lesions also improve on these regimes although tolerance and precipitation of an acute pustular phase may result from excessive use. Other dermatoses which may respond to the potent steroids include lichen planus, discoid lupus erythematosus, necrobiosis lipoidica and lichen simplex.

Adverse effects may follow excessive application of potent steroids to occluded sites, or in children. Topical corticosteroids are also contraindicated in primary skin infections and facial lesions.

Steroid combinations

Steroid antibiotic combinations

Examples include Neo-medrone lotion (methyl prednisolone and neomycin); Propaderm A (beclomethasone dipropionate and chlorotetracycline); Fucidin HC (hydrocortisone and fucidin); Gentacin HC (hydrocortisone and gentamicin). Secondary bacterial infection is common in eczematous dermatoses and in most cases is due to Staphylococcus aureus; it may be difficult to decide on purely clinical grounds whether infection is contributing to the skin condition. However, most studies have shown that steroid/antibiotic combinations are more effective than either ingredient alone in culturally confirmed infected eczema[8].

The use of antibiotic steroid combinations is limited by the risk of drug resistance or sensitisation. Little is known about the effect of the corticosteroid in these combined agents on the incidence of these reactions. The risk of drug resistance is a particular problem with gentamicin[9] which is useful for serious systemic infections. As most secondary skin infections are caused by Gram positive organisms such as Staphylococcus aureus the choice of an antibiotic steroid combination should be determined by the likely sensitivity range of the organism concerned. This allows the clinician to avoid using the important systemic drugs except in specific situations. The incidence of contact sensitisation to antibiotics following repeated and prolonged application is low but the prevalence in skin clinics is significant[10], particularly in certain sites which include the external ear and perianal area. The potentially harmful effects of topical antibiotic steroid
combinations can be limited if their use is avoided in a general hospital environment and if courses are restricted to a period of 10–14 days[11-13]. Other complications may be due to excessive absorption. For instance, application of topical gentamicin or neomycin to wide areas of skin is potentially ototoxic[14]. The risk of applying other antibiotics with potential systemic adverse effects such as tetracycline, particularly in infants, has not been recorded but is a further reason for avoiding excessive application.

Corticosteroid/antibiotic combinations are generally indicated in secondarily infected or exudative eczema and insect bite reactions. A weak steroid combined with an antibiotic may be useful in intertrigo. They should not be used in primary skin infections or in patients with a known hypersensitivity to the drug. Provided they are used sensibly and logically steroid antibiotic combinations have a defined but important role in the management of skin disease.

Other antimicrobial steroid combinations
Examples include Hydrocortisone vioform (hydrocortisone and cloquiolin); Quinoderm hydrocortisone (hydrocortisone and hydroxyquinoline); Remiderm (triacinolone and halquinol). Steroid antimicrobial (antiseptic) combinations usually involve the incorporation of an 8-hydroxyquinoline antiseptic with a steroid; more rarely benzalkonium chloride is used. These agents have broad spectrum antimicrobial activity but can only be used topically. Generally, the indications for their use in secondarily infected dermatoses are similar to those for antibiotic combinations, but their cost is low and drug resistance is not a problem. Sensitisation may, however, develop[15]. As with the antibiotic steroid combinations they should be avoided in primary skin infections. Logically these combinations have some attractions although they are not as strongly active against some bacteria and the tendency of hydroxyquinolines to turn yellow and produce staining on exposure to air is a drawback. They may also be irritant. Such combinations are most helpful in secondarily infected skin lesions where rapid elimination of organisms is not essential. However, studies comparing their use with steroid antibiotics preparations are clearly needed.

Steroid antifungal combinations
Examples include Nystan HC (hydrocortisone and nystatin), Daktacort (hydrocortisone and miconazole) and Canesten HC (hydrocortisone and clotrimazole). These combinations contain either a polyene such as nystatin which is active against candida or an imidazole (miconazole, clotrimazole) which inhibits dermatophytes as well. Although not necessarily of great practical application the imidazoles are also often active against Gram-positive bacteria. Resistance and sensitisation are not significant problems with these combinations, although the latter occurs[16]. Drug toxicity following systemic absorption has not been reported although widespread application of either groups of substances to infants should be avoided. There have been no reports of hepatotoxicity following topical application of imidazoles related to ketoconazole but prolonged widespread use is best avoided in patients with known hepatic disease. Percutaneous absorption of some imidazoles, which is usually negligible, can be enhanced by the presence of corticosteroids[17].

The main indications for steroid antifungal combinations are dermatoses such as eczema secondarily infected by candida, of which intertrigo is an example. The use of imidazole steroid combinations in bacterially infected eczema is of logical, but largely unproven, benefit and more comparative assessments here would be useful. Although it is possible that the combination of a steroid with an antifungal agent could be of benefit in inflammatory ringworm there are no conclusive data to support this. Indeed the uncritical use of these combinations in place of cultural confirmation of the diagnosis should be deplored. As with the antibiotics the steroid antifungal preparations are most effectively used in short courses.

Steroid and local anaesthetic combinations
Examples include Anugesic HC (hydrocortisone and pramoxine) and Ultraproct (fluocortolone and cinchocaine). These preparations are intended to provide rapid relief of pruritus, particularly in the anogenital area, and are only useful for short-term therapy. It is much more important to establish the cause of the itching which may include candidosis, threadworm infestation or fissure in ano. Contact sensitisation may follow prolonged application of these agents, especially cinchocaine[18].

Miscellaneous steroid combinations
Steroid-salicylic acid combinations are useful where there is significant hyperkeratosis combined with inflammation as in lichenified eczema, lichen simplex and foot eczema. In this situation the salicylic acid is incorporated for its keratolytic properties.

While caution should be adopted in applying these combinations to wide areas due to the possible risk of excessive absorption, the combination may prove very useful in localised disease.

Urea is a useful hydrating agent, although sometimes irritating. Its combination with hydrocortisone in Calmurd HC enhances penetration of the latter and there is a theoretical risk of systemic toxicity due to percutaneous absorption, especially in infants and small children. The combination is useful in lichenified dermatoses or limited areas of atopic eczema. Tar with corticosteroid combinations, e.g. Tarcortin (tar extract and hydrocortisone), can be used in tar responsive conditions such as psoriasis or lichenified eczema.

Conclusion
Topical corticosteroids when used carefully and rationally remain a highly useful group of compounds for the treatment of skin disease. The importance of limiting the length of courses to avoid tolerance and toxicity cannot be over-emphasised. The corticosteroid combinations are a logical approach to therapy although, with a few excep-
tions, they have not been critically evaluated against alternatives. In addition, few of them are suitable for chronic or repeated use without medical guidance. It is in the latter instance that many of their well publicised disadvantages such as sensitisation and the induction of drug resistance have become apparent: Topical corticosteroid combinations may prove useful in specific situations but it is important to remember that they still contain corticosteroids and the same care should be exercised in their use as would be employed with the pure steroid.

References
1. Maibach, H. I. and Stoughton, R. B. (1973) Medical Clinics of North America. 57, 1253.
2. Haynes, R. C. (1974) Clinical Pharmacology and Therapeutics. 16, 945.
3. Nater, J. P. and de Groote, A. (1983) Unwanted effects of cosmetics and drugs used in dermatology. Amsterdam. Excerpta Medica.
4. Cornell, R. G. and Stoughton, R. B. (1980) Pharmacology and Therapeutics. 11, 497.

Claud Bernard at St Julien en Beaujolais

Attendance at a recent French medical colloquium at Lyon provided an unexpected bonus in the form of a visit to St Julien en Beaujolais, situated some 5 km northwest of Villefranche, to the north of Lyon. St Julien is the village where Claud Bernard was born in 1813, the son of a humble vignerons. He spent his early formative years in and around the vineyards of St Julien until, in 1834, he proceeded to Paris where he was to achieve fame as the great experimental physiologist, pioneer of studies of animal and human metabolism and of the concept of le milieu intérieur.

Bernard retained happy memories of his youth in St Julien and when, in 1860, following a breakdown in his health, he was advised to leave Paris and take a prolonged convalescence in the country, he returned to his native St Julien where he spent the next two and a half years. In 1861, he purchased a spacious manor house and vineyards up on the hill adjacent to the Bernard family farmouse. Here he later loved to spend his holidays, usually at the time of the wine festival, when he proudly presented his own vintage Beaujolais. In some huts behind the house, he set up a simple laboratory where he conducted experiments on fermentation. It was also at St Julien that, during his convalescent stay, he wrote his masterpiece, Introduction to the Study of Experimental Medicine (1865), a milestone in the history of medicine.

Bernard had married in 1845 but conjugal disharmony finally led to separation from his wife in 1869. In that same year, a close and warm friendship began between him and Madame Hermann Raffalovich, the wife of a Russian Jewish financier in Paris. She was beautiful, intellectual and cosmopolitan but her relationship with Bernard remained purely platonic and resulted in a voluminous correspondence between them. Madame Raffalovich's letters were later destroyed, but some 450 of Bernard's letters, written from Paris and St Julien, have survived. In them, Bernard confided to Madame Raffalovich all his innermost thoughts—scientific, philosophical and personal—throughout the remainder of his life, until his death in Paris in 1878, aged 65. Thus, writing from St Julien, where he spent the duration of the Franco-Prussian War (1870-71), Bernard wrote of his involvement with the vintage—'These are familiar occupations to me. I was born to them, and they still please me—they are certainly much more agreeable than composing academic speeches.' And—'I have been busy... philosophical preoccupations are far from my mind and I can think of nothing but casks, wine prices and the yield of the vineyards.'

Bernard's estate at St Julien, now owned by the Fondation Marcel Mérieux (a French pharmaceutical company), has been skilfully and charmingly converted into the Claud Bernard Museum by Jacqueline Sonnolet, curator of the Musée d'Histoire de la Médecine, Paris. The larger manor house is devoted to the life and work of Claud Bernard himself. In the Bernard family farmouse, the rooms adjacent to the natal bedroom relate to the works of Bernard's pupils and disciples. The charming garden and vineyard make a suitably scenic setting to the museum and the vineyards still produce a good wine.

What better way to pay tribute to one of the greatest medical scientists of all time than to sit in his garden, more than a century after his death, and drink his own fine vintage Beaujolais of which he was so proud!

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