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Topical Treatments for Scalp Psoriasis

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Contents

Abstract

Psoriasis is a common, chronic inflammatory skin disease that affects the scalp more commonly than any other site. Scalp psoriasis causes significant psychosocial disability as it is highly visible and can, on occasion, extend onto the face. Furthermore, current treatment regimens are messy, time consuming and, in some instances, ineffective, leading to a high level of non-compliance. The majority of current evidence for topical treatments for this condition comes from open-label, uncontrolled studies. From such studies, there are data to support the use of topical corticosteroids in a number of different formulations and topical vitamin D analogues. However, these studies have not addressed issues such as the need for keratolytics, which may be required to remove adherent scale before a topical corticosteroid or vitamin D analogue may prove efficacious. There is an urgent need for well designed, controlled trials to assess the efficacy of existing and new treatment regimens for scalp psoriasis. The aim of this review is to critically assess the relative effectiveness and tolerability of available topical therapies for this problematic condition and provide recommendations for selection of treatment.

1. Scalp Psoriasis

1.1 Epidemiology

Psoriasis is a distressing, chronic skin disorder affecting around 2–3% of the Caucasian population.[1] The scalp is the most commonly affected site in psoriasis, being involved in 50–80% of cases, and can often be the sole site of involvement.[2] Because of the visibility of both psoriasis and resulting scale found on clothing, this condition causes significant psychosocial distress to those with scalp psoriasis. An epidemiological study in the Netherlands, involving a questionnaire sent to 6000 psoriasis patients (1023 responded), found the most annoying signs and symptoms of scalp psoriasis to be visibility of lesions (34%) and itch (26%).[3] A more recent study evaluated the specific psychosocial effects that scalp dermatitis may have on a patient's life using 'scalpdex' – a quality-of-life (QOL) instrument based on symptoms, functioning and emotions.[4] Half of the patients assessed in this study had psoriasis, with over 40% of patients reporting itching, frustration and annoyance at their condition.[4] This novel QOL instrument may be useful in the future to validate efficacy of topical therapies used for scalp psoriasis.

1.2 Clinical Features

Psoriasis of the scalp characteristically extends to or just beyond the hair line (see figure 1). Its severity ranges from discrete involvement with localized plaques to covering of the entire scalp with either fine scaling or very thick scales attached for some distance along the hair shaft – known as pityriasis (or tinea) amiantacea. Persistent involvement of the scalp can lead to hair loss, development of telogen effluvium[5] and, rarely, scarring alopecia.[6-8]

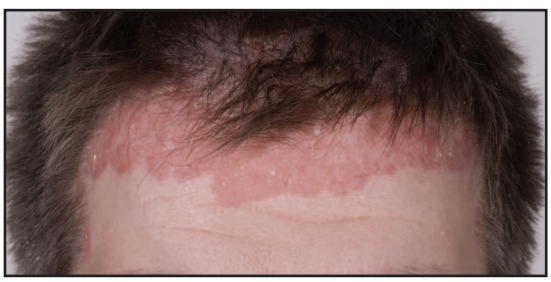

Fig. 1. Image of a scalp with clearly demarcated plaques of psoriasis visibly extending beyond the hairline onto the forehead. Courtesy of Dr R.J.G. Chalmers.

1.3 Differential Diagnosis

The major differential diagnosis of scalp psoriasis is seborrhoeic dermatitis, in its mildest form when only affecting the scalp, often referred to as 'dandruff'. The distinction between psoriasis and seborrhoeic dermatitis can be difficult – in some cases both clinical and histological features are virtually indistinguishable leading to the use of the term 'sebo-psoriasis'. Thorough clinical examination is required to try and separate these conditions. Seborrhoeic dermatitis is accepted to be a reaction to *Malassezia furfur* (formerly *Pityrosporum ovale*) infection,[9] although recently *M. globosa* has been found to be the predominant yeast in those experiencing dandruff.[10] Seborrhoeic dermatitis is a chronic dermatitis, characterized by yellowish red or dull, sharply marginated lesions covered with greasy-looking scales distributed in areas rich in sebaceous glands such as the face (nasolabial folds, eyebrows, and pre and post auricular regions), scalp and, in males, the upper trunk. In contrast, psoriasis typically involves the extensor surfaces of the body, often sparing the face and frequently leads to nail changes such as pitting and onycholysis, which do not occur in seborrhoeic dermatitis.

Other inflammatory skin conditions that can affect the scalp include fungal infections, lichen planus and systemic lupus erythematosus. Fungal infections, such as tinea capitis caused by *Microsporum* (e.g. *M. audouinii* and *M. canis*) or *Trichophyton* (e.g. *T. verrucosum*) species, are predominantly infections of children and cause scaling, hair loss and broken hairs sometimes leading to painful boggy nodules (kerion) and, if left untreated, scarring alopecia. Lichen planus of the scalp is characterized by scarring alopecia (lichen planopilaris) and violaceous perifollicular inflammation. Systemic lupus erythematosus produces both atro-

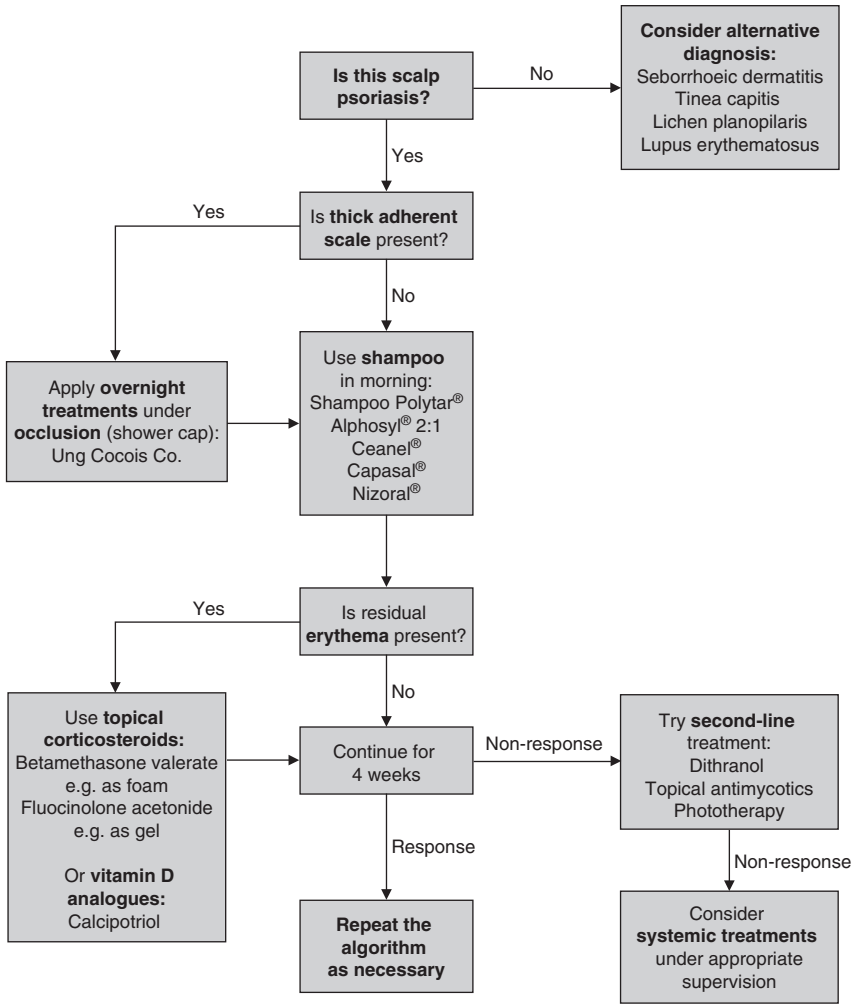

Fig. 2. A treatment protocol for scalp psoriasis.

phy and hyperkeratosis, frequently causing scarring alopecia.

2. Treatments

There is a wide range of topical therapies available for the treatment of scalp psoriasis; these include corticosteroids, dithranol, vitamin D analogues and coal tar, although few treatments have been investigated in well designed, placebo-controlled studies. Furthermore, treatment of scalp psoriasis is complicated by the relative inaccessibility of scalp skin due to the presence of hair, and the proximity of sensitive facial skin, which limits the use of the more irritant topical therapies. Other important characteristics of scalp skin are that it is more sensitive to chemical irritation than forearm (although not back) skin, demonstrating more erythema and barrier disruption. Furthermore, its capacity to absorb water is higher than forearm skin, factors that can be important when applying topical therapies.[11,12] Currently, there is a significant unmet need for patients with scalp psoriasis, namely, a clean, effective and safe topical agent. Figure 2 suggests a treatment protocol for scalp psoriasis

2.1 Corticosteroids

In psoriasis, corticosteroids act by reducing inflammation, modulating cutaneous immune responses and inhibiting epidermal proliferation.[13,14] They have been the most widely used topical formulations to treat scalp psoriasis for more than two decades. Despite this, historical evidence for their use is relatively sparse and studies have been uncontrolled with small numbers of patients.[15] However, recent advances in corticosteroid formulation[16] and the design of clinical trials, have confirmed their short-term efficacy.

The type of topical formulation is important for both compliance and efficacy. Ointments are often considered the most effective way to deliver topical corticosteroid therapy, although on the scalp this is often impractical. Recent studies have now shown that newer formulations, such as lotions, can increase the penetration of the corticosteroid and produce efficacy comparable to creams, which is clearly highly relevant to the use of corticosteroids for treatment of scalp psoriasis.[16,17]

A recent multicentre, randomized, vehicle-controlled study evaluated the efficacy and safety of 4 weeks' use of clobetasol propionate 0.05% shampoo versus its corresponding vehicle in 142 subjects aged ≥12 years with moderate to severe scalp psoriasis.[18] Recurrence of scalp psoriasis was assessed during a 2-week follow-up period. Results after 4 weeks demonstrated that clobetasol propionate 0.05% shampoo was significantly more effective than its corresponding vehicle in reducing pruritus, erythema, scaling and plaque thickening at 4 weeks ($p < 0.001$), with similar rates of adverse events in both groups. Fifty percent of patients in the clobetasol propionate 0.05% shampoo group maintained a good response during the 2-week follow-up period.[18] Furthermore, a 4-week, multicentre, randomized study compared the efficacy and safety of clobetasol propionate 0.05% shampoo versus a tar blend 1% shampoo in subjects with moderate to severe scalp psoriasis ($n = 162$).[19] The clobetasol propionate shampoo was superior to tar blend shampoo in all efficacy variables tested ($p < 0.001$)[19] and both treatments had a good safety profile and were well tolerated. A similar study in 151 subjects demonstrated that clobetasol propionate 0.05% shampoo was also superior to calcipotriol 0.005% solution over a 4-week treatment period.[20]

Some topical corticosteroids have become available in a low residue foam vehicle, potentially enhancing drug delivery. Franz et al.[21] were the first to report the superior efficacy of betamethasone valerate 0.12% foam over both betamethasone lotion and placebo in alleviating the primary signs of psoriasis (erythema, scaling and plaque thickness). Feldman and Housman[17] went on to show that the efficacy of a once-daily regimen is comparable to a twice-daily regimen and suggested this as the treatment schedule of choice. More recently, an open-label, multicentre, randomized, crossover study evaluated betamethasone valerate 0.12% foam versus 'standard therapies' (mometasone and betamethasone dipropionate or vitamin D analogues in 55% or 45% of cases, respectively) in 241 patients with moderate to severe scalp psoriasis.[22] After a 2-week run-in period, each active treatment was applied for 4 weeks with a wash-out period between the two active treatment phases of at least 4 weeks. Betamethasone valerate 0.12% foam was found to be more effective ($p < 0.001$) than the lotion-based 'standard therapies' with rates of complete or near clearance of 88% versus 66% for lotions.[22] In addition, patients found the foam to be more acceptable following evaluation using a questionnaire at baseline and following therapy.

The efficacy and tolerability of clobetasol propionate 0.05% foam has been assessed for psoriasis at scalp and non-scalp sites.[23,24] Scalp sites were assessed in a randomized, double-blind active and placebo-controlled study involving 188 subjects with moderate to severe scalp psoriasis allocated to receive 14 days of twice-daily treatment with either clobetasol propionate 0.05% foam, placebo foam, clobetasol proprionate 0.05% solution or placebo solution randomized (2 : 1 : 2 : 1).[24] Mean severity scores for erythema, scaling, plaque thickness and pruritus were all significantly improved ($p < 0.001$) by both clobetasol formulation groups versus placebo at 7 and 14 days. Seventy-four percent of patients

in the clobetasol propionate foam group and 63% in the clobetasol propionate solution were rated by investigators as completely clear or almost clear.[24]

Recently, an oil preparation containing the corticosteroid fluocinolone acetonide (0.01%) has been combined with an emollient in the vehicle base and been assessed in a randomized, double-blind, vehicle-controlled, multicentre study in patients with moderate to severe scalp psoriasis (n = 89).[25] At completion of the treatment period (21 days), all signs of psoriasis had improved in both treatment groups, with improvements in the fluocinolone acetonide group significantly greater than the vehicle-treated group ($p < 0.001$).[25] This is of particular interest as the corticosteroid formulation is low potency – its efficacy potentially being enhanced by the softening effects of the oil base of the vehicle.

Corticosteroids should be considered as the first-line topical treatment for scalp psoriasis, as their evidence base for short-term use is superior to other preparations. Long-term efficacy data are lacking, although it is possible that low potency formulations in suitable vehicles may enable extended use. Care is advised during the application of topical corticosteroids to the scalp. This area is more permeable to topical corticosteroids than other regions, and where the plaques migrate onto sensitive facial skin there may be a risk of skin atrophy and telangiectasia with more prolonged use, although evidence is lacking.

2.2 Vitamin D_3 Analogues

There are four vitamin D_3 analogues currently in use as topical agents in psoriasis: calcipotriol, tacalcitol, calcitriol and falecalcitriol. Their mechanism of action involves inhibition of keratinocyte proliferation, stimulation of keratinocyte differentiation and inhibition of inflammation.[26] Vitamin D_3 analogues are inactivated at low pH, which should be noted when they are used in conjunction with acidic topical therapies such as salicylic acid.[27,28]

2.2.1 Calcipotriol

Calcipotriol is now established as a first-line therapy for mild to moderate chronic plaque psoriasis affecting the trunk and limbs. It has been shown to be efficacious and have a good safety profile in several multicentre, randomized, controlled studies.[29] However, despite the high level of evidence for the use of calcipotriol on body-site psoriasis, evidence is lacking for scalp involvement with a predominance of open-label, uncontrolled studies. The one reported placebo-controlled study assessed twice-daily calcipotriol solution (50 g/mL) versus placebo over 4 weeks in 49 adult patients with scalp psoriasis.[30] At the end of the study period, 60% of patients receiving calcipotriol showed clearance or marked improvement versus 17% receiving placebo. Calcipotriol was also superior to placebo in both investigator and patient assessments ($p < 0.001$ for both).[30] Two further open-label studies have assessed twice-daily calcipotriol solution (50 g/mL) over 8 weeks duration and have shown a marked reduction in psoriasis signs and severity markers.[31,32] One of the studies included over 3000 patients, although both had no control group.[32]

The efficacy and safety of long-term twice-daily treatment of scalp psoriasis with calcipotriol scalp solution (50 g/mL) has been evaluated in a prospective, multicentre, open-label, uncontrolled study over 12 months in 202 patients.[33] One of the outcomes of scalp involvement was assessed by scoring the clinical signs of redness, thickness and scaliness from 0–5. Their sum was used to derive a total score. By week 28, mean total score for scalp psoriasis had reduced from 5.9 to 2.5 ($p < 0.001$). No further reduction was seen at week 52, although the number of patients assessing the severity of their scalp psoriasis as either moderate or severe had decreased from 72% to 21%.[33]

One uncontrolled study has compared the efficacy of calcipotriol solution (50 g/mL) and betamethasone valerate 1% lotion over a 6-week period in 42 patients with marked improvement and clearance rates of 72.8% and 72%, respectively. Both drugs were well tolerated, although two subjects in the calcipotriol group developed signs of irritation.[34]

2.2.2 Tacalcitol

Tacalcitol emulsion (4 μg/g) has been assessed versus placebo in 273 patients with scalp psoriasis in

a multicentre, prospective, randomized, double-blind study over an 8-week period. Response of psoriasis to treatment was evaluated using the sum score of erythema, infiltration and scaling. At the end of the study period, the median sum severity score had decreased by 53% in the tacalcitol versus 30% in the placebo group ($p < 0.0001$).[35] Treatment was very well tolerated and local reactions were transient and uncommon.

2.2.3 Calcitriol and Falecalcitriol

We found little data on the use of calcitriol and falecalcitriol for scalp psoriasis. However, they have both been shown to be an effective treatment for psoriasis at anatomical sites other than the scalp.[36,37]

2.3 Calcipotriol Combined with Corticosteroids

Calcipotriol can be combined with most other antipsoriatic therapies. Its use with topical corticosteroids is particularly notable in that corticosteroid-induced atrophy appears to be diminished by calcipotriol and irritation caused by calcipotriol inhibited by the corticosteroid. The combination of calcipotriol and betamethasone dipropionate is established as a first-line treatment for psoriasis involving typical body sites such as the extensor surfaces and trunk. Recently, an open-label observational study ($n = 10$) reported a significant improvement in scalp psoriasis in patients treated overnight with the two-compound ointment (betamethasone dipropionate 0.05% and calcipotriol 50 μg/g) under occlusion.[38] A further pilot study confirmed the efficacy of the two-compound ointment, but its greasiness may reduce acceptability and prevent wider use in scalp psoriasis.[39] A novel gel formulation of this combination product has been studied against betamethasone diproprionate 0.05% alone in a phase II study. The combination treatment had a faster onset of action, with both patients and investigators reporting greater efficacy versus betamethasone dipropionate alone.[40]

2.4 Keratolytics

There is little formal evidence for the efficacy of keratolytics such as salicylic acid for scalp psoriasis, although they have long been considered an important part of management if scaling is a dominant feature.

The keratolytic activity of salicylic acid has recently been quantified and it has been shown to be independent of the pH of its formulation. Therefore, similar levels of efficacy are achieved at neutral pH without producing skin irritation and barrier disruption.[41]

One study assessed the use of a salicylic acid 6% gel in patients with scalp psoriasis, reporting an improvement in the disease severity after 3 or 6 weeks as an inpatient or outpatient, respectively.[42]

2.5 Unguentum Cocois Co.

Unguentum cocois co. contains coal tar 12% solution, salicylic acid 2% and precipitated sulfur 4% in a coconut oil emollient base. It is a messy preparation, which is applied to clean hair and left on overnight under a shower cap to be washed off in the morning. The shower cap serves to improve penetration of the preparation and to protect bedclothes. The major objective of such a treatment is to remove adherent scale from the scalp to enhance the efficacy of topical corticosteroids or calcipotriol solutions, which can be applied the following morning after the unguentum cocois co. preparation has been washed off. Although there are little efficacy data available for this chemical debridement, there is anecdotal evidence supporting its use.[43]

2.6 Coal Tar

The antipsoriatic properties of coal tar are thought to involve inhibition of epidermal proliferation and various anti-inflammatory actions.[44] Crude coal tar derivatives are cosmetically unacceptable for scalp use, although coal tar shampoos, despite a lack of evidence, may have a role. One uncontrolled study of a gel containing refined coal tar solution demonstrated that the agent was effec-

tive in clearing psoriasis of the scalp in 83% of 112 patients when used for 5 days with vegetable oil soaking on the sixth day.[45] When this regimen was followed by the use of a tar shampoo, 30% of patients remained in remission 13 months later. A direct comparison of clobetasol propionate 0.05% shampoo versus a tar blend 1% shampoo in subjects with moderate to severe scalp psoriasis demonstrated the corticosteroid shampoo to be more effective.[19] Despite its positive effect on pruritus,[2] concerns over the mutagenic potential of coal tar products (as evidenced by the presence of benzo[a]pyrene in the urine of patients who had used a coal tar-containing shampoo)[46] their links to non-melanoma skin cancer,[47] and messiness, offensive aroma and staining properties all limit their use.

2.7 Dithranol

Dithranol has been known to have antipsoriatic properties for over 150 years and has been used for decades as a very effective treatment for chronic plaque psoriasis. Its exact mode of action is unclear but may involve the induction of free radicals leading to mitochondrial toxicity.[48] Despite its undoubted efficacy in the treatment of psoriasis, its widespread use is limited by staining (brown, black and notably blond hair purple) and burning of the skin, and, importantly for scalp psoriasis, most available formulations cannot be easily washed out of the hair. The efficacy of dithranol for scalp psoriasis has been studied in only a few trials, which have been limited in their design and size. Recently, a prospective, parallel-group study assessed 64 patients attending a daycare clinic. Patients were randomly allocated to one of three treatment groups: (i) dithranol in bio-wash oil; (ii) Micanol® [1] cream (a dithranol cream available in a lipid-stabilized base at 1% and 3% concentrations); or (iii) Micanol® cream in bio-wash-oil.[49] A greater reduction in modified Psoriasis Area and Severity Index at 3 weeks was seen in the dithranol bio-wash oil treatment group versus the other two treatments ($p < 0.05$).

Dithranol treatment of scalp psoriasis should be limited to those patients with recalcitrant disease and is more suitable in the setting of specialized daycare or inpatient dermatology departments.

2.8 Topical Antimycotics

Psoriasis of the scalp can coexist with and/or resemble (clinically and histologically) seborrhoeic dermatitis. One open-label study assessed the efficacy of urea 40% plus the antifungal agent bifonazole 1% in an ointment base applied nightly in 52 patients with scalp psoriasis and 17 patients with seborrhoeic dermatitis.[50] Over a 12-week period, the improvement of the scalp was scored as none (0), mild (0–25%), moderate (25–50%), marked (50–75%) and cleared (>75%). At 12 weeks, 24.6% and 42.1% of patients had marked improvement and cleared, respectively.

2.9 Zinc Pyrithione

Zinc pyrithione has antidandruff properties[51] and is an effective therapy for treating dandruff in combination with other antimycotics[52,53] and coal tar,[54] although is less so when used alone.[55] One study has shown histological evidence of reversal of features seen in psoriasis following zinc pyrithione use.[56] Given the overlap between scalp psoriasis and seborrhoeic dermatitis/dandruff, zinc pyrithione may be beneficial for the treatment of scalp psoriasis.

2.10 Phototherapy

Phototherapy is effective for psoriasis resistant to topical therapies; however, delivery of UV irradiation to the scalp is problematic. Novel devices to aid application, such as UVB combs[57,58] and hair blowers to part the hair prior to treatment,[59] have been used with success. One study comparing UVB comb phototherapy with betamethasone valerate solution (concentration not stated) in patients with scalp psoriasis (n = 44) found their efficacy was comparable after 3 weeks, with relapses occurring less frequently in the UVB comb group.[60]

1 The use of trade names is for identification purposes only and does not imply endorsement.

2.10.1 Topical Psoralen and UVA

Application of psoralen creams, ointments or lotions, followed by UVA irradiation (PUVA), is also effective but has several disadvantages. Non-uniform distribution may produce unpredictable phototoxic erythema reactions, and inadvertent application to uninvolved skin can lead to hyperpigmentation. Furthermore, the treatment does not prevent the development of new active lesions and may result in unacceptably high levels of psoralen in the plasma. Guidelines for topical PUVA have been published by the British Photodermatology Group.[61]

3. Discussion

Scalp psoriasis is common, symptomatic and highly visible. Affected patients have a high level of physical and psychosocial morbidity. There is an unmet need for effective long-term topical treatments for this condition. A meta-analysis of antipsoriatic topical treatments revealed that the only agents shown to be efficacious for the treatment of scalp psoriasis were potent topical corticosteroids and vitamin D_3 analogues.[62] The use of more 'traditional' topical therapies, such as coal tar and dithranol, are restricted by high levels of unacceptability to patients.[63] However, some promise is shown in therapeutic combinations and it is the authors' view that optimal topical regimens require more than one agent. For example, where there is a degree of scale present on the scalp, the use of an agent containing a coal tar solution and salicylic acid in a coconut oil emollient base is warranted before any topical corticosteroid application would be effective. Furthermore, overlap between scalp psoriasis and seborrhoeic dermatitis may require the use of antimycotic agents. Formulation of topical treatment is also key to obtaining a higher level of compliance and therefore treatment success.[17,64] We found direct comparisons between clinical trials difficult because of the lack of a universal, validated measure of scalp psoriasis severity. Future work should look to use consistent clinical and psychological outcome measures.

New vehicles for topical corticosteroids have advanced treatment for scalp psoriasis. Future therapies may involve successfully combining corticosteroids with other antipsoriatic agents in a cosmetically acceptable form, which retains both effectiveness and safety.

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