CLINICAL PRACTICE

Seborrheic Dermatitis

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.*

A 35-year-old man reports itching, redness, and scaling in his scalp, eyebrows, and external auditory canal. He has tried several over-the-counter dandruff shampoos, with only temporary relief, and he is increasingly embarrassed by this problem. Physical examination reveals greasy scaling on the scalp and erythema with yellowish scales in the nasolabial creases. How should his case be managed?

THE CLINICAL PROBLEM

Seborrheic dermatitis is a chronic, relapsing inflammatory skin condition with a predilection for areas rich in sebaceous glands.[1] The disorder is characterized by scaling and poorly defined erythematous patches, with large variations in extent and morphologic characteristics depending on the area of skin involved (Fig. 1 and Table 1). In the acute phase, the scales cover a slightly moist surface. The scalp is almost invariably affected; other common sites (in order of frequency) are the face, chest, and intertriginous areas. Blepharoconjunctivitis may occur in isolation or it may be associated with skin lesions. Infrequently, marginated lesions occur on the male external genitalia. Itching is moderate and usually limited to the scalp and the external auditory meatus. The disorder may be socially embarrassing, especially because of the scaling scalp, which may cause particular uneasiness because of a perceived association with uncleanliness.[2]

Seborrheic dermatitis is considered one of the most frequent skin disorders, although estimates of prevalence are limited by the lack of validated criteria for diagnosis or grading of severity. An infantile form, which usually involves the scalp (cradle cap), the face, and the diaper area, is particularly common. It affects as many as 70% of newborns during the first 3 months of life but usually disappears by 1 year of age.[3] The 1971–1974 National Health and Nutrition Examination Survey, which involved a representative sample of persons 1 to 74 years of age in the U.S. population, showed that the prevalence of seborrheic dermatitis, as assessed by a dermatologist, was 11.6% overall and 2.8% (2.6% for men and 3.0% for women) among persons with cases considered by the examiner to be clinically significant (i.e., warranting a visit to a physician). In this sample, the prevalence of clinically significant seborrheic dermatitis was lowest among persons younger than 12 years of age (<1%) and was highest among persons 35 to 44 years of age (4.1%).[4]

Seborrheic dermatitis is more common and more severe in persons infected with the human immunodeficiency virus (HIV), particularly in those with CD4 counts below 400 cells per millimeter,[5,6] than in uninfected persons, and it may regress with highly active antiretroviral therapy.[7] The skin condition is rare in African

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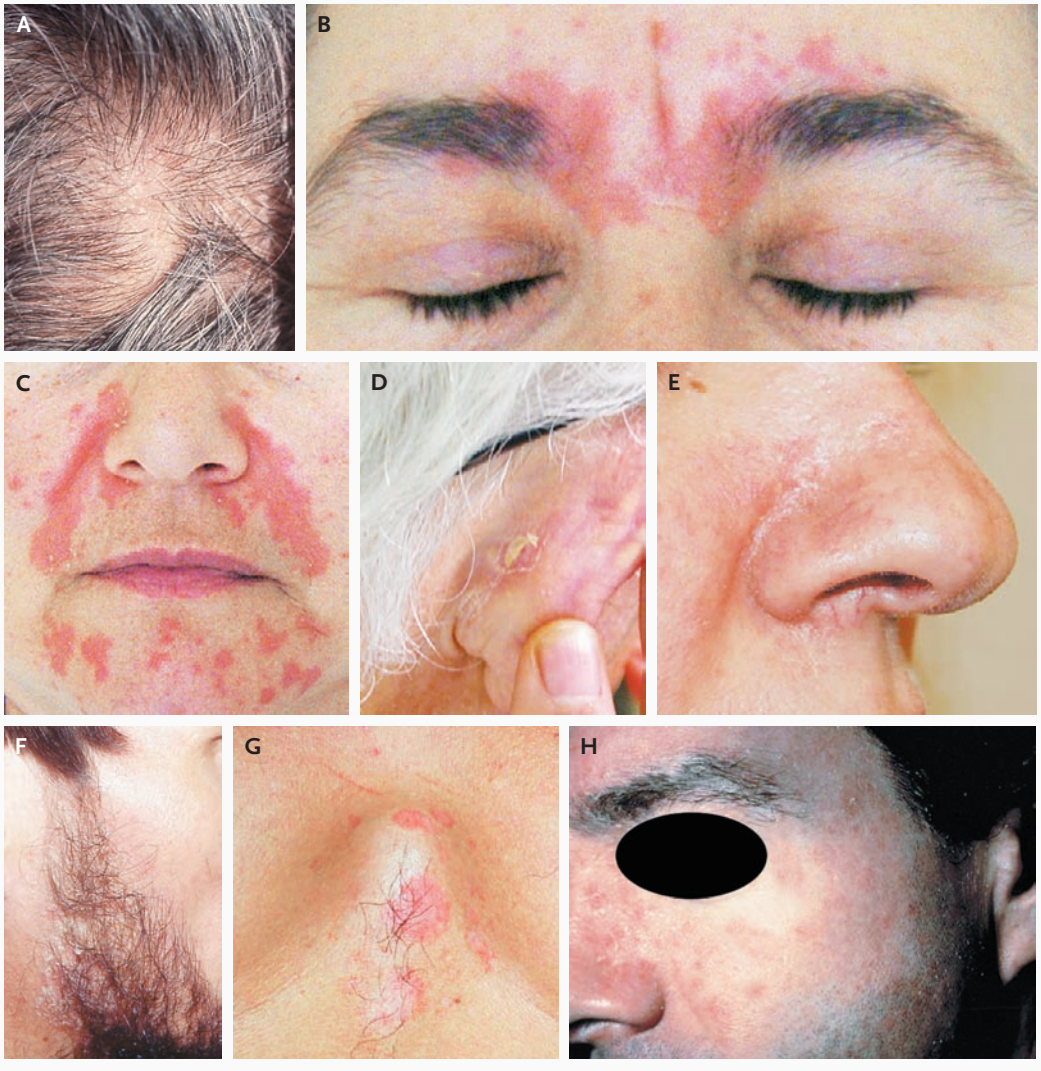

Figure 1. Clinical Manifestations of Seborrheic Dermatitis.

A typical patch of seborrheic dermatitis is erythematous with a yellowish hue, and it is covered with large greasy scales that can be detached easily. On the scalp, lesions may vary from dry scales (dandruff) to yellow, greasy scales and erythema (Panel A). On the face, the disease mainly affects the medial aspect of the eyebrows, the glabella (Panel B), the nasolabial folds (Panel C), the concha of auricle, and the retroauricular areas (Panel D). Lesions may vary in severity from erythematous patches to discrete fine scaling (Panel E). In men with a beard, moustache, or sideburns, lesions may involve the hair-bearing areas (Panel F), and they resolve if the areas are shaved. On the chest, and in the medial thoracic areas in men, the petaloid variety is the most prevalent and is characterized by circinate patches with a light-red scaling area in the center and darker red papules at their margin (Panel G). In HIV-infected patients, lesions are widespread and markedly inflamed and oozing (Panel H).

blacks; when it occurs in this population, it raises concern about HIV infection.[8] Seborrheic dermatitis has been reported to be associated with several conditions, including neuroleptic-induced parkinsonism, familial amyloidosis with polyneuropathy, and trisomy 21, but these associations have been poorly documented.[9-11]

Seborrheic dermatitis has been reported to be triggered by stress, but no controlled data are available. Patients with seborrheic dermatitis fre-

Table 1. Selected Clinical Variants of Seborrheic Dermatitis.*

Variant	Features and Comments
Adult variants	
Pityriasis capitis (dandruff)	Mild seborrheic dermatitis of the scalp with scaling as the most prominent feature; dandruff, which is not specific to seborrheic dermatitis, is a lay term for any scalp condition that produces fine scales
Blepharitis	Scaling and erythema of the eyelid margin, which may be associated with conjunctivitis; seborrheic dermatitis is the most common cause
Pityriasiform seborrheic dermatitis	Rare form involving the trunk and limbs, with a generalized erythematosquamous eruption
Flexural seborrheic dermatitis	Involves any body folds, especially the retroauricular areas, the inner thighs, the genitalia, and the breast folds, with intertriginous, sometimes oozing lesions
Pitirosporum (malassezia) folliculitis	Pruritic, erythematous follicular papules, sometimes pustules, typically in sites rich in sebaceous glands; may occur as a complication of seborrheic dermatitis, often observed in immunocompromised hosts
Erythroderma (exfoliative dermatitis)	Generalized redness and scaling of the skin with systemic manifestations; extremely rare complication of seborrheic dermatitis resulting from improper treatment of more localized forms of the condition with the use of contact irritants; consequences of skin failure such as tachycardia and disturbances in thermoregulation are regular features
Infantile variants	
Scalp seborrheic dermatitis (cradle cap)	Red-yellow plaques covered by scales on the scalp of infants; develops after a few weeks of age
Leiner's disease	Poorly defined entity that includes cases of primary immunodeficiency syndrome not related to seborrheic dermatitis
Pityriasis amiantacea	Thick, asbestos-like scales adhering to tufts of scalp hairs; may be associated with psoriasis, atopic dermatitis, or tinea capitis
HIV-related seborrheic dermatitis	Often more explosive, diffuse, and inflammatory than in otherwise healthy persons
Drug-related seborrheic-like dermatitis	Common in patients treated with erlotinib or sorafenib; also reported in patients treated with recombinant interleukin-2, psoralen plus ultraviolet A light, and isotretinoin; effectively treated with the same therapies as those used in spontaneous seborrheic dermatitis

* HIV denotes human immunodeficiency virus.

quently report improvement after exposure to sunlight.[12] However, an increased prevalence of seborrheic dermatitis has been reported among mountain guides who have a high level of long-term occupational exposure to solar ultraviolet radiation.[13] A seborrheic-like dermatitis of the face also may develop in patients treated for psoriasis with psoralen plus ultraviolet A light; this type of dermatitis can be prevented by masking the face during irradiation.[14]

The cause or causes of seborrheic dermatitis are incompletely understood. Despite its name, seborrheic dermatitis is not regularly associated with excessive secretion of sebum (i.e., "seborrhea"), nor are the sebaceous glands primarily involved. However, functioning sebaceous glands may be a permissive factor because seborrheic dermatitis occurs most often during periods of active sebum production (e.g., the neonatal period) and in areas of the skin where sebum is produced. There is no clear genetic predisposition.

Fungi of the genus malassezia (formerly called *Pitirosporum ovale*),[15-17] which are lipid-dependent, ubiquitous residents of the skin, have been considered potentially pathogenic, since they are present on affected skin, and antifungal agents are useful in treatment.[18,19] However, the absence of a correlation between the number of malassezia organisms and the presence and severity of clinical manifestations is perplexing. The inflammatory process may be mediated, in susceptible persons, by fungal metabolites — namely free fatty acids — released from sebaceous triglycerides.[18] The lipid layer of malassezia can also modulate proinflammatory cytokine production by keratinocytes.[20]

Table 2. Differential Diagnosis of Seborrheic Dermatitis.

Diagnosis	Clinical Findings	Diagnostic Clues
Common conditions		
Psoriasis	Scaling of the scalp common; facial involvement may mimic seborrheic dermatitis; well-demarcated erythematous flexural patches also observed in flexural inverse psoriasis	Plaques tend to be thicker, with silvery white scales, and more discrete and less pruritic than in seborrheic dermatitis; typically involves the nails, extensor, palmar, and plantar surfaces, and sacral area; arthritis present in approximately 10% of cases; uncommon in children, though sometimes occurs in a guttate eruptive variant
Tinea capitis	Infections, especially those associated with *Trichophyton tonsurans,* can present with scaling on the scalp in the absence of alopecia	Most commonly observed in children from developing countries; may occur in contacts of persons with the condition; findings on direct microscopical examination and culture are diagnostic
Atopic dermatitis	In infants, lesions are frequently observed on the face and scaling on the scalp may occur; dry scaling of the scalp and dry brittle hair may occur in adults	Later onset than seborrheic dermatitis, usually appearing after the third month of life; pruritus, irritability, and sleeplessness are common; extensor and facial involvement is common in infants, whereas localization to flexures increases in prevalence with age; xerosis is typical, and there is often a personal or family history of atopy (e.g., asthma or allergic rhinitis)
Contact dermatitis	Erythema and scaling may occur and may complicate seborrheic dermatitis as a reaction to topical agents used for treatment (especially in the ear canal or intertriginous areas)	Polymorphous features, including erythema, edema, vesiculation, and erosions in the acute phase and erythema, lichenification, and hyperkeratosis in the chronic stage; patch tests may be useful to confirm diagnosis; irritant diaper dermatitis is confined to the diaper area and, in contrast to seborrheic dermatitis, tends to spare the skin folds
Rosacea	Earliest stage of erythematotelangiectatic rosacea is a recurrent blush affecting the central facial area	Desquamation atypical; teleangectasias and recurrent edema may be associated; may occur with seborrheic dermatitis
Erythrasma	Characterized by well-demarcated erythematous patches on intertriginous areas	Caused by the saprophyte *Corynebacterium minutissimum*; lesions are stable and asymptomatic; with time, they are associated with fine wrinkling and the color fades from red to brown; bright coral-red fluorescence on illumination with a Wood's lamp
Rare conditions		
Langerhans'-cell histiocytosis	The acute diffuse variant, Letterer–Siwe disease, may occur in children younger than 1 year of age; skin-colored papules, scales, and crusts on the scalp, flexural areas of the neck, axilla, and perineum are common	Multisystem condition; features include osteolytic bone lesions and diabetes insipidus; besides papules, cutaneous involvement is characterized by pustules, vesicles, or both; the lesions tend to coalesce and become tender; petechiae and purpura are common; palmoplantar and nail involvement can occur
Wiskott–Aldrich syndrome	Dermatitis involving the face, scalp, and flexural areas develops during the first few months of life; exfoliative dermatitis occasionally develops	X-linked recessive disorder, occurring most often in boys; triad of atopic-like dermatitis, bleeding tendency due to thrombocytopenia, and recurrent sinopulmonary infections often observed
Lupus erythematosus	In infants, a form of subacute cutaneous lupus mainly affecting the face (especially periorbital skin) and the scalp may occur; in adults, "butterfly" rash of acute cutaneous lupus has a bilateral malar distribution similar to seborrheic dermatitis	Usually annular erythematous plaques in the case of subacute cutaneous lupus; photosensitivity is common; associated conditions include congenital heart block with or without cardiomyopathy, hepatobiliary disease, and thrombocytopenia; anti-Ro antibodies present in the child and usually the mother; "butterfly" rash rarely affects the nasolabial folds and often has a clear photodistribution; cutaneous lesions usually coexist with other clinical features of systemic lupus erythematosus
Dermatomyositis	Mild erythema and scaling of the posterior scalp can occur	Poikiloderma with intense pruritus and demonstrable hair loss; other cutaneous signs (e.g., well-marginated plaques on the elbows and knees and nail-fold changes) are present; there are usually clinical and laboratory signs of proximal extensor inflammatory myopathy

STRATEGIES AND EVIDENCE

DIAGNOSIS

The diagnosis of seborrheic dermatitis rests largely on the history and clinical examination (Table 2). The differential diagnosis depends on the patient's age, the site (or sites) involved, and the patient's race or ethnic group. Conditions commonly confused with seborrheic dermatitis include psoriasis, atopic dermatitis, and, in children, tinea capitis. Distinguishing severe seborrheic dermatitis from early facial psoriasis can be particularly dif-

ficult. Direct microscopical examination of a specimen of a superficial skin scraping prepared with potassium hydroxide may be useful to rule out tinea capitis. A skin biopsy is rarely needed for diagnosis, but it can be useful in occasional cases to rule out other diagnoses such as cutaneous lupus erythematosus.

MANAGEMENT

Topical agents are used in most cases of seborrheic dermatitis (Table 3). Randomized trials provide support for the use of several of these agents, not all of which are available in the United States.

Topical Antifungal Agents

Topical antifungal agents are the mainstay of treatment of seborrheic dermatitis. Well-studied agents include ketoconazole, bifonazole, and ciclopiroxolamine (also called ciclopirox), which are available in different formulations such as creams, gels, foams, and shampoos. There have been at least 10 randomized trials of ketoconazole, some limited to scalp treatment and others addressing the treatment of multiple areas of the body. In the largest double-blind trial, which involved 1162 people with mild-to-severe seborrheic dermatitis affecting multiple regions of the body, treatment was determined to be successful (on the basis of a global assessment score) at 4 weeks in 56% of patients who received ketoconazole foam twice daily, as compared with 42% who received placebo foam ($P<0.001$).[22] Similar results were obtained in a study comparing the drug with placebo in cream formulations.[22] In a trial comparing 2% ketoconazole in a gel formulation, used once daily, with placebo in 459 subjects with moderate-to-severe disease in different areas of the body, the skin of 25% of subjects assigned to active treatment and 14% assigned to placebo was considered cleared or almost cleared at day 28 ($P=0.001$).[30]

Intermittent use of ketoconazole can maintain remission. In one study, 312 patients with scalp lesions in whom dermatitis had initially cleared with twice-weekly shampoo containing 2% ketoconazole were subsequently enrolled in a 6-month placebo-controlled prophylactic trial; relapse rates were 47% among patients using placebo, 31% among patients using ketoconazole shampoo once every other week, and 19% among patients using the active treatment once weekly.[23]

Bifonazole has also been shown to be effective in the treatment of seborrheic dermatitis. In a randomized trial involving 100 patients, the skin of 43% of patients using 1% bifonazole cream once daily, as compared with 23% of those using placebo, was shown to be almost clear at 4 weeks according to a global improvement scale.[24] Bifonazole shampoo used three times weekly has also been shown to result in significantly greater improvement in scalp lesions than placebo.[31]

In a randomized trial comparing ciclopiroxolamine shampoo, used once or twice weekly, with placebo in 949 patients with scalp lesions, rates of clearance over a 4-week period were 45% and 58% with the once-weekly and twice-weekly active treatments, respectively, as compared with 32% with placebo ($P<0.001$ for both comparisons with placebo). Among 428 patients with a response who were subsequently randomly assigned to ciclopiroxolamine prophylaxis once weekly, ciclopiroxolamine prophylaxis every 2 weeks, or placebo for 4 months, relapse rates were 15%, 22%, and 35%, respectively.[25]

Limited data are available for comparisons of different antifungal agents. In a noninferiority trial involving 303 patients with facial seborrheic dermatitis, the use of ciclopiroxolamine cream twice daily for 28 days, followed by once-daily use for an additional 28 days, resulted in significantly higher rates of remission than the use of ketoconazole foaming gel used twice weekly for the first 28 days and then once a week (57% vs. 44% at 56 days in an intention-to-treat analysis, $P=0.03$). However, these results are difficult to interpret because of the much lower frequency of application for ketoconazole than for ciclopiroxolamine.[32] Local tolerance as well as overall acceptability were better with ciclopiroxolamine than with ketoconazole.[26] No major side effects have been reported with topical antifungal agents, although contact sensitivity has been reported with long-term use in rare cases.[33]

Topical Corticosteroids

Several randomized trials have directly compared short-term topical corticosteroids — including, in approximate order of increasing potency, hydrocortisone, betamethasone dipropionate, clobetasol 17-butyrate, and clobetasol dipropionate — with topical antifungal agents.[34,35] These trials have shown either no significant difference or a small difference in favor of the antifungal agent, but they have been underpowered, with the larg-

Table 3. Topical Agents for the Treatment of Seborrheic Dermatitis.*

Intervention	Formulation	Use	No. Needed to Treat†	Adverse Effects	Comments
Antifungal agents					
Ketoconazole	2% in shampoo, foam, gel, or cream‡	Scalp: twice/wk for clearance, then once/wk or every other wk for maintenance; other areas: from twice daily to twice/wk for clearance, then from twice/wk to once every other wk for maintenance	1.3–8.0 (higher values in larger studies) for clearance[21,22]; 4 for preventing relapse of scalp lesions at 6 mo with a once-weekly maintenance regimen[23]	Irritant contact dermatitis in <1% of patients; itching and burning sensation in about 3% of patients; pregnancy category C	Generic available; more data to provide support for efficacy are available for scalp lesions than for lesions elsewhere; some formulations such as foam are expensive
Bifonazole	1% in shampoo or cream	Scalp: 3 times/wk for clearance; other areas: once daily for clearance	5 for clearance[24]	Irritant local reactions in about 10% of patients	Not available in the United States; limited evidence available
Ciclopirox olamine (also called ciclopirox)	1.0% or 1.5% in shampoo or cream	Scalp: twice to 3 times/wk for clearance, then once/wk or every 2 wk for maintenance; other areas: twice daily for clearance, then once daily for maintenance	3–5 for clearance[25,26]; 5 for preventing a relapse of scalp lesions with once-weekly maintenance regimen[25]	Irritant contact dermatitis in <1% of patients; itching and burning sensation in about 2% of patients; rare cases of allergic contact dermatitis can occur; pregnancy category B	Generic available; studied in facial and scalp lesions and in short-term maintenance regimens; more expensive than ketoconazole
Corticosteroids					
Hydrocortisone	1% in cream	Areas other than scalp: once or twice daily	Insufficient data to estimate	Skin atrophy and excessive hair growth with prolonged, continuous topical use and systemic effects with extensive use; pregnancy category C	Generic available; limited evidence available
Betamethasone dipropionate	0.05% in lotion	Scalp and other areas: once or twice daily	Insufficient data to estimate	Skin atrophy and excessive hair growth with prolonged, continuous topical use and systemic effects with extensive use; pregnancy category C	Generic available; limited evidence available; potent topical corticosteroids should not be used on the face
Clobetasol 17-butyrate	0.05% in cream	Areas other than scalp: once or twice daily	Insufficient data to estimate	Skin atrophy and excessive hair growth with prolonged, continuous topical use and systemic effects with extensive use; pregnancy category C	Generic available; limited evidence available; potent topical corticosteroids should not be used on the face
Clobetasol dipropionate	0.05% in shampoo	Scalp: twice weekly in a short-contact fashion (up to 10 min application, then washing)	Insufficient data to estimate	Skin atrophy and excessive hair growth with prolonged, continuous topical use and systemic effects with extensive use; pregnancy category C	Limited evidence available; one of the most expensive options
Desonide	0.05% in lotion	Scalp and other areas of skin: twice daily	Insufficient data to estimate	Skin atrophy and excessive hair growth with prolonged, continuous topical use and systemic effects with extensive use; pregnancy category C	Generic available; limited evidence available
Lithium salts					
Lithium succinate plus zinc sulfate	Ointment containing 8% lithium succinate plus 0.05% zinc sulfate	Areas other than scalp: twice daily	Insufficient data to estimate	Irritant local reactions in about 7% of treated patients	Not available in the United States; effects studied in patients who have received ≤8 wk of treatment; only drug assessed, even in a small trial, in HIV-infected patients
Lithium gluconate	8% in gel	Areas other than scalp: twice daily	5 for clearance in the only available placebo-controlled trial[27]	Irritant local reactions in ≤10% of treated patients	Not available in the United States; effects studied in ≤8 wk treatment

Calcineurin inhibitors					
Pimecrolimus	1% in cream	Areas other than scalp: twice daily	Approximately 10 in the only available trial[28]	Higher rate of local reactions as compared with placebo (26% vs. 12%); possible increased risk of skin cancer with prolonged use; pregnancy category C	Limited evidence of effectiveness in moderate-to-severe facial lesions; possible advantage over topical corticosteroids is absence of atrophy with continuous use
Miscellaneous agents					
Selenium sulfide	2.5% in shampoo§	Scalp: twice weekly	4 in the only available trial[29]	Irritant local reactions in about 3% of treated patients; lightening and bleaching of hair color reported; pregnancy category C	Generic available; limited evidence available; less expensive than most other options
Zinc pyrithione	1% in shampoo¶	Scalp: twice weekly	Insufficient data to estimate	Irritant local reactions in about 3% of treated patients	Limited evidence available

* Shampoos, foams, and lotions are better suited for treatment of the scalp; creams, gels, and ointments are used for other areas of the body.
† The number needed to treat in order to benefit one patient was calculated on the basis of clearance and relapse with maintenance therapy.
‡ Ketoconazole is also available over the counter in the United States at a 1% strength; however, only a 2% strength, available by prescription, has been shown to be effective in randomized trials.
§ Selenium sulfide is also available over the counter in the United States at a 1% strength; however, only a 2.5% strength, available by prescription, has been shown to be effective in a randomized trial.
¶ Zinc pyrithione at a 1% strength is available over the counter in the United States.

est trial including only 72 people.[35] One randomized, placebo-controlled trial showed that 0.05% desonide lotion was superior to placebo in 81 patients with facial lesions associated with either atopic or seborrheic dermatitis, but the response rates among the patients with seborrheic dermatitis were not reported separately.[36] There is a consensus that topical corticosteroids are useful in the short term mainly to control erythema and itching. Data are not available to address the question of whether the combination of topical corticosteroids and topical antifungal agents confers a greater benefit than single-agent therapy. Skin atrophy and hypertrichosis are a concern with long-term corticosteroid use.

Selenium Sulfide Preparations

In a randomized trial involving 246 patients with moderate-to-severe dandruff, 2.5% selenium sulfide shampoo, 2% ketoconazole shampoo, and placebo were compared. All shampoos were used twice weekly. Reductions in the score for dandruff at week 4 were 67% with selenium sulfide, 73% with ketoconazole, and 44% with placebo; the reductions were significantly larger with both medicated shampoos than with placebo.[29] Itching and burning sensations were more common with sulfide shampoo than with ketoconazole. Trial data for the use of selenium sulfide in areas other than the scalp are lacking.

Topical Lithium Salts

Topical lithium succinate and lithium gluconate are effective alternative agents for the treatment of seborrheic dermatitis in areas other than the scalp. Their mechanism of action is poorly understood. In a crossover, placebo-controlled trial of lithium succinate involving two 4-week treatment periods separated by a 2-week washout period, twice-daily lithium succinate ointment was associated with significantly greater reductions in erythema, scaling, and the percentage of the area of the skin involved.[37] In a small, randomized trial involving 12 patients, lithium succinate was significantly more effective than placebo for the treatment of lesions in HIV-positive patients.[38] Twice-daily lithium gluconate was shown to be more effective than placebo in an 8-week trial involving 129 patients with facial lesions,[27] and it was shown to be superior to 2% ketoconazole in an 8-week noninferiority trial involving 288 patients with facial lesions; in the latter study, com-

plete-remission rates were 52% with the use of lithium gluconate and 30% with the use of ketoconazole, but ketoconazole was applied only twice weekly.[39] Skin irritation is the most common adverse effect associated with topical lithium salts.

Topical Calcineurin Inhibitors

Calcineurin inhibitors prevent T-cell activation by down-regulating the activity of type 1 and 2 T-helper cells. In a randomized trial involving 96 patients with moderate-to-severe facial seborrheic dermatitis, the mean change from baseline to 4 weeks in the total target-area score with twice-daily 1% pimecrolimus was significantly greater than with placebo in a per-protocol analysis but not in an intention-to-treat analysis.[28] Two small, randomized trials did not show significant differences between pimecrolimus and topical corticosteroids, but these trials had limited statistical power.[40,41]

Other Topical Therapies

Limited data are available to provide support for the use of topical zinc pyrithione. In one trial, 1% zinc pyrithione was less effective than 2% ketoconazole (both used as a twice-weekly shampoo) in reducing the severity of dandruff at 4 weeks (67% improvement in the severity score vs. 73% improvement, $P<0.02$).[42] Limited data are also available for metronidazole gel, with the largest trial failing to show a significant difference in outcome as compared with placebo.[43] Coal-tar shampoos are sometimes proposed in seborrheic dermatitis, although data supporting their use are scarce. In one randomized trial, 4% coal-tar shampoo, as compared with placebo, resulted in a significantly larger reduction in dandruff.[44]

High response rates have been reported in many trials with the use of a placebo alone. However, it remains uncertain whether these rates are due to a placebo response or to an emollient effect of the placebo.[22,28]

Phototherapy

Ultraviolet B phototherapy is sometimes considered as an option for extensive or recalcitrant seborrheic dermatitis, but it has not been studied in randomized trials.[45,46] Burning and itching may occur, and with long-term treatment, carcinogenic effects on the skin are a concern.

Systemic Antifungal Therapy

Data on the efficacy of systemic antifungal agents for seborrheic dermatitis are limited. In a randomized trial involving 63 patients with mild-to-moderate seborrheic dermatitis, a single weekly dose of 300 mg of fluconazole was no better than placebo after 2 weeks.[47] In a randomized, placebo-controlled trial involving 174 patients,[48] oral terbinafine (at a dose of 250 mg per day for 4 weeks) was no better than placebo in patients with lesions predominantly involving exposed areas of the skin, such as the face, whereas a difference was noted in patients with lesions predominantly involving areas of the skin that were not exposed, such as the scalp, sternum, and interscapular areas; however, conclusions based on subgroup analyses are problematic. The safety profile of systemic antifungal agents must be carefully considered in planning treatment for a chronic condition such as seborrheic dermatitis.

AREAS OF UNCERTAINTY

To improve the quality of evidence to guide treatment for seborrheic dermatitis, validated criteria for diagnosis and severity and validated, clinically relevant outcome measures are needed. Most trials of therapy are short-term and vehicle-controlled, in the case of topical agents, or placebo-controlled. There is a need for longer-term studies comparing different management strategies, including nonpharmacologic treatments, such as phototherapy, and simple interventions to remove scales, such as treatment with keratolytic agents. There are few data to guide treatment of infants with the disease. Similarly, data on the treatment of patients with HIV-related seborrheic dermatitis[38] and patients who do not have a response to conventional topical treatment are very limited.

GUIDELINES

Evidence-based guidelines, developed by the Finnish Medical Society Duodecim and revised in April 2007, are available through the National Guideline Clearinghouse (www.guideline.gov). Evidence-based guidance is also available in the Clinical Knowledge Summaries of the U.K. National Health System (cks.library.nhs.uk). The recommendations in this article are generally consistent with these guidelines.

CONCLUSIONS AND RECOMMENDATIONS

Patients should be educated about the chronic relapsing course of seborrheic dermatitis and should understand that treatment may not result in complete clearing of the skin. For a patient such as the one described in the vignette, I would recommend treatment of scalp lesions with shampoo containing 2% ketoconazole twice weekly for 1 month, with the goal of inducing a remission, followed by the use of this shampoo once every week or every other week. Similarly, facial lesions could be controlled with the use of cream containing 2% ketoconazole twice daily for 4 weeks, then twice weekly or less frequently, depending on the patient's response. Reasonable alternatives include shampoo containing 2.5% selenium sulfide or ciclopiroxolamine for scalp lesions, and ketoconazole foam or gel, ciclopiroxolamine cream, or ointment containing lithium salt for facial lesions. Decision making should take into account cost and the patient's preference for a given form of treatment.

An audio version of this article is available at NEJM.org

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REFERENCES

1. Hay JR, Graham-Brown RA. Dandruff and seborrhoeic dermatitis: causes and management. Clin Exp Dermatol 1997;22:3-6.
2. Hirt M, Ross WD, Kurtz R, Gleser GC. Attitudes to body products among normal subjects. J Abnorm Psychol 1969;74:486-9.
3. Foley P, Zuo Y, Plunkett A, Merlin K, Marks R. The frequency of common skin conditions in preschool-aged children in Australia: seborrheic dermatitis and pityriasis capitis (cradle cap). Arch Dermatol 2003;139:318-22.
4. Skin conditions and related need for medical care among persons 1-74 years, United States, 1971-1974. Hyattsville, MD: National Center for Health Statistics, 1978. (DHEW publication no. 79-1660.)
5. Coopman SA, Johnson RA, Platt R, Stern RS. Cutaneous disease and drug reactions in HIV infection. N Engl J Med 1993;328:1670-4.
6. Mallal SA. The Western Australian HIV Cohort Study, Perth, Australia. J Acquir Immune Defic Syndr Hum Retrovirol 1998;17:Suppl:S23-S27.
7. Dunic I, Vesic S, Jevtovic DJ. Oral candidiasis and seborrheic dermatitis in HIV-infected patients on highly active antiretroviral therapy. HIV Med 2004;5:50-4.
8. Mahé A, Simon F, Coulibaly S, Tounkara A, Bobin P. Predictive value of seborrheic dermatitis and other common dermatoses for HIV infection in Bamako, Mali. J Am Acad Dermatol 1996;34:1084-6.
9. Binder RL, Jonelis FJ. Seborrheic dermatitis in neuroleptic-induced parkinsonism. Arch Dermatol 1983;119:473-5.
10. Rocha N, Velho G, Horta M, Martins A, Massa A. Cutaneous manifestations of familial amyloidotic polyneuropathy. J Eur Acad Dermatol Venereol 2005;19:605-7.
11. Ercis M, Balci S, Atakan N. Dermatological manifestations of 71 Down syndrome children admitted to a clinical genetics unit. Clin Genet 1996;50:317-20.
12. Berg M. Epidemiological studies of the influence of sunlight on the skin. Photodermatol 1989;6:80-4.
13. Moehrle M, Dennenmoser B, Schlagenhauff B, Thomma S, Garbe C. High prevalence of seborrhoeic dermatitis on the face and scalp in mountain guides. Dermatology 2000;201:146-7.
14. Tegner E. Seborrhoeic dermatitis of the face induced by PUVA treatment. Acta Derm Venereol 1983;63:335-9.
15. Gupta AK, Boekhout T, Theelen B, Summerbell R, Batra R. Identification and typing of Malassezia species by amplified fragment length polymorphism and sequence analyses of the internal transcribed spacer and large-subunit regions of ribosomal DNA. J Clin Microbiol 2004;42:4253-60.
16. Xu J, Saunders CW, Hu P, et al. Dandruff-associated Malassezia genomes reveal convergent and divergent virulence traits shared with plant and human fungal pathogens. Proc Natl Acad Sci U S A 2007;104:18730-5.
17. Tajima M, Sugita T, Nishikawa A, Tsuboi R. Molecular analysis of Malassezia microflora in seborrheic dermatitis patients: comparison with other diseases and healthy subjects. J Invest Dermatol 2008;128:345-51.
18. DeAngelis YM, Gemmer CM, Kaczvinsky JR, Kenneally DC, Schwartz JR, Dawson TL Jr. Three etiologic facets of dandruff and seborrheic dermatitis: Malassezia fungi, sebaceous lipids, and individual sensitivity. J Investig Dermatol Symp Proc 2005;10:295-7.
19. Piérard-Franchimont C, Xhauflaire-Uhoda E, Piérard GE. Revisiting dandruff. Int J Cosmet Sci 2006;28:311-8.
20. Thomas DS, Ingham E, Bojar RA, Holland KT. In vitro modulation of human keratinocyte pro- and anti-inflammatory cytokine production by the capsule of Malassezia species. FEMS Immunol Med Microbiol 2008 August 21 (Epub ahead of print).
21. Carr MM, Pryce DM, Ive FA. Treatment of seborrhoeic dermatitis with ketoconazole: I. Response of seborrhoeic dermatitis of the scalp to topical ketoconazole. Br J Dermatol 1987;116:213-6.
22. Elewski BE, Abramovits W, Kempers S, et al. A novel foam formulation of ketoconazole 2% for the treatment of seborrheic dermatitis on multiple body regions. J Drugs Dermatol 2007;6:1001-8.
23. Peter RU, Richarz-Barthauer U. Successful treatment and prophylaxis of scalp seborrhoeic dermatitis and dandruff with 2% ketoconazole shampoo: results of a multicentre, double-blind, placebo-controlled trial. Br J Dermatol 1995;132:441-5.
24. Zienicke H, Korting HC, Braun-Falco O, et al. Comparative efficacy and safety of bifonazole 1% cream and the corresponding base preparation in the treatment of seborrhoeic dermatitis. Mycoses 1993;36:325-31.
25. Shuster S, Meynadier J, Kerl H, Nolting S. Treatment and prophylaxis of seborrehic dermatitis of the scalp with antipityrosporal 1% ciclopirox shampoo. Arch Dermatol 2005;141:47-52.
26. Unholzer A, Varigos G, Nicholls D, et al. Ciclopiroxolamine cream for treating seborrheic dermatitis: a double-blind parallel group comparison. Infection 2002;30:373-6.
27. Dreno B, Moyse D. Lithium gluconate in the treatment of seborrhoeic dermatitis: a multicenter, randomised, double-blind study versus placebo. Eur J Dermatol 2002;12:549-52.
28. Warshaw EM, Wohlhuter RJ, Liu A, et al. Results of a randomized, double-blind, vehicle-controlled efficacy trial of pimecrolimus cream 1% for the treatment of moderate to severe facial seborrheic dermatitis. J Am Acad Dermatol 2007;57:257-64.

29. Danby FW, Maddin WS, Margesson LJ, Rosenthal D. A randomized, double-blind, placebo controlled trial of ketoconazole 2% shampoo versus selenium sulfide 2.5% shampoo in the treatment of moderate to severe dandruff. J Am Acad Dermatol 1993;29:1008-12.
30. Elewski B, Ling MR, Phillips TJ. Efficacy and safety of a new once-daily ketoconazole 2% gel in the treatment of seborrheic dermatitis: a phase III trial. J Drugs Dermatol 2006;5:646-50.
31. Segal R, David M, Ingber A, Lurie R, Sandbank M. Treatment with bifonazole shampoo for seborrhea and seborrheic dermatitis: a randomized, double-blind study. Acta Derm Venereol 1992;72:454-5.
32. Chosidow O, Maurette C, Dupuy P. Randomized, open-labeled, non-inferiority study between ciclopiroxolamine 1% cream and ketoconazole 2% foaming gel in mild to moderate facial seborrheic dermatitis. Dermatology 2003;206:233-40.
33. de Pádua CA, Uter W, Geier J, Schnuch A, Effendy I. Contact allergy to topical antifungal agents. Allergy 2008;63:946-7.
34. Faergemann J. Seborrhoeic dermatitis and Pityrosporum orbiculare: treatment of seborrhoeic dermatitis of the scalp with miconazole-hydrocortisone (Daktacort), miconazole and hydrocortisone. Br J Dermatol 1986;114:695-700.
35. Stratigos JD, Antoniou C, Katsambas A, et al. Ketoconazole 2% cream versus hydrocortisone 1% cream in the treatment of seborrheic dermatitis: a double-blind comparative study. J Am Acad Dermatol 1988;19:850-3.
36. Freeman S, Howard A, Foley P, et al. Efficacy, cutaneous tolerance and cosmetic acceptability of desonide 0.05% lotion (Desowen) versus vehicle in the short-term treatment of facial atopic or seborrheic dermatitis. Australas J Dermatol 2002;43:186-9.
37. Efalith Multicenter Trial Group. A double-blind, placebo-controlled, multicenter trial of lithium succinate ointment in the treatment of seborrheic dermatitis. J Am Acad Dermatol 1992;26:452-7.
38. Langtry JA, Rowland Payne CM, Staughton RC, Stewart JC, Horrobin DF. Topical lithium succinate ointment (Efalith) in the treatment of AIDS-related seborrheoic dermatitis. Clin Exp Dermatol 1997;22:216-9.
39. Dreno B, Chosidow O, Revuz J, Moyse D. Lithium gluconate 8% vs ketoconazole 2% in the treatment of seborrhoeic dermatitis: a multicentre, randomized study. Br J Dermatol 2003;148:1230-6.
40. Rigopoulos D, Ioannides D, Kalogeromitros D, Gregoriou S, Katsambas A. Pimecrolimus cream 1% vs. betamethasone 17-valerate 0.1% cream in the treatment of seborrhoeic dermatitis: a randomized open-label clinical trial. Br J Dermatol 2004;151:1071-5.
41. Firooz A, Solhpour A, Gorouhi F, et al. Pimecrolimus cream, 1%, vs hydrocortisone acetate cream, 1%, in the treatment of facial seborrheic dermatitis: a randomized, investigator-blind, clinical trial. Arch Dermatol 2006;142:1066-7.
42. Piérard-Franchimont C, Goffin V, Decroix J, Piérard GE. A multicenter randomized trial of ketoconazole 2% and zinc pyrithione 1% shampoos in severe dandruff and seborrheic dermatitis. Skin Pharmacol Appl Skin Physiol 2002;15:434-41.
43. Koca R, Altinyazar HC, Eştürk E. Is topical metronidazole effective in seborrheic dermatitis? A double-blind study. Int J Dermatol 2003;42:632-5.
44. Davies DB, Boorman GC, Shuttleworth D. Comparative efficacy of shampoos containing coal tar (4.0% w/w; Tarmed), coal tar (4.0% w/w) plus ciclopirox olamine (1.0% w/w; Tarmed) and ketoconazole (2.0% w/w; Nizoral) for the treatment of dandruff/seborrhoeic dermatitis. J Dermatol Treat 1999;10:177-83.
45. Gambichler T, Breuckmann F, Boms S, Altmeyer P, Kreuter A. Narrowband UVB phototherapy in skin conditions beyond psoriasis. J Am Acad Dermatol 2005;52:660-70.
46. Pirkhammer D, Seeber A, Hönigsmann H, Tanew A. Narrow-band ultraviolet B (ATL-01) phototherapy is an effective and safe treatment option for patients with severe seborrhoeic dermatitis. Br J Dermatol 2000;143:964-8.
47. Cömert A, Bekiroglu N, Gürbüz O, Ergun T. Efficacy of oral fluconazole in the treatment of seborrheic dermatitis: a placebo-controlled study. Am J Clin Dermatol 2007;8:235-8.
48. Vena GA, Micali G, Santoianni P, Cassano N, Peruzzi E. Oral terbinafine in the treatment of multi-site seborrhoic dermatitis: a multicenter, double-blind placebo-controlled study. Int J Immunopathol Pharmacol 2005;18:745-53.