

CLINICAL PRACTICE

Scabies

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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 author's clinical recommendations.

A 30-year-old man notes diffuse, intense itching. He reports that his girlfriend has the same itching. Examination of the skin reveals interdigital lesions, with small papules, vesicles, and excoriations on the hands, and indurated nodules on the genitalia, all suggestive of classic scabies. How should this case be managed?

THE CLINICAL PROBLEM

NATURE OF THE INFECTION

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Scabies is a common parasitic infection caused by the mite *Sarcoptes scabiei* variety *hominis*, an arthropod of the order Acarina. The worldwide prevalence has been estimated at about 300 million cases yearly, although this may be an overestimate. Scabies occurs in both sexes, at all ages, in all ethnic groups, and at all socioeconomic levels. In an epidemiologic study in the United Kingdom, scabies was shown to be more prevalent in urban areas and among women and children and more common in winter than in summer.¹ Scabies is generally a nuisance on account of itching, rash, and its ability to spread among people; superinfection may also occur. The risk of severe outbreaks and complicated scabies is particularly high in institutions (including nursing homes and hospitals) and among socially disadvantaged populations and immunocompromised hosts.

The mite is an obligate parasite that completes its entire life cycle on humans. Only female mites burrow into the skin (Fig. 1). The maturation process lasts about 15 days, with the larvae emerging 2 to 3 days after the eggs are laid.² About 5 to 15 female mites live on a host infected with classic scabies, but the number can reach hundreds or even millions in cases of crusted scabies. The skin eruption of classic scabies is considered a consequence of both infestation and a hypersensitivity reaction to the mite. The incubation period before symptoms occur is three to six weeks for primary infestation but may be as short as one to three days in cases of reinfestation.

TRANSMISSION

Mites cannot fly or jump but crawl at the rate of 2.5 cm per minute on warm skin. They can survive for 24 to 36 hours at room temperature and average humidity and remain capable of infestation and epidermal burrowing.³ The more parasites on a person, the greater the likelihood of transmission, either direct (i.e., skin-to-skin contact) or indirect (e.g., through infested bedding, clothing, or other fomites).

The predominant route of transmission is direct skin-to-skin contact. Transmission by means of shared clothing or other indirect method is rare with classic scabies but may occur with crusted scabies (e.g., in immunocompromised hosts). Transmission among family members and in institutional settings is common.

Sexual transmission also occurs. In a study of risk factors for scabies in a clinic for sexually transmitted infections,⁴ high-risk persons included men who have sex with men and men with sporadic sexual contact. There is no evidence to suggest that mites can transmit infection with the human immunodeficiency virus (HIV).

STRATEGIES AND EVIDENCE

DIAGNOSIS

The diagnosis of scabies rests largely on the history and examination of the patient, as well as on the history of the family and close contacts. Classic manifestations of scabies include generalized and intense itching, usually sparing the face and head. Pruritus is worse at night. The lesions are located mostly in the finger webs (Fig. 2A), on the flexor surfaces of the wrists, on the elbows, in the axillae, on the buttocks and genitalia (Fig. 2B), and on the breasts of women (Fig. 2C). Inflammatory pruritic papules are present at most sites. Burrows (Fig. 2D) and nodules (generally in the genital regions and axillae) are specific for scabies but may be absent. Nonspecific secondary lesions, including excoriations, eczematization (Fig. 2E), and impetiginization, may occur anywhere.

In a report from a sub-Saharan region where there is a high (13 percent) prevalence of scabies, the presence of diffuse itching and visible lesions associated with either at least two typical locations of scabies or a household member with itching had 100 percent sensitivity and 97 percent specificity for the diagnosis.⁵ Such data are lacking from areas with a lower prevalence of scabies.

Scabies occasionally presents in atypical forms⁶ (Table 1) that are more difficult to diagnose than the classic forms and, therefore, may be more likely to lead to outbreaks. Atypical presentations in infants often involve the face, scalp, palms, and soles. Atypical papular scabies occurs in the elderly, localized or generalized crusted scabies in immunocompromised patients, and impetigo in patients whose scabies is superinfected (Fig. 3A through 3F).

DIAGNOSTIC TESTS

Definitive diagnosis relies on the identification of mites, eggs, eggshell fragments, or mite pellets. Multiple superficial skin samples should be obtained from characteristic lesions — specifically, burrows or papules and vesicles in the site of bur-

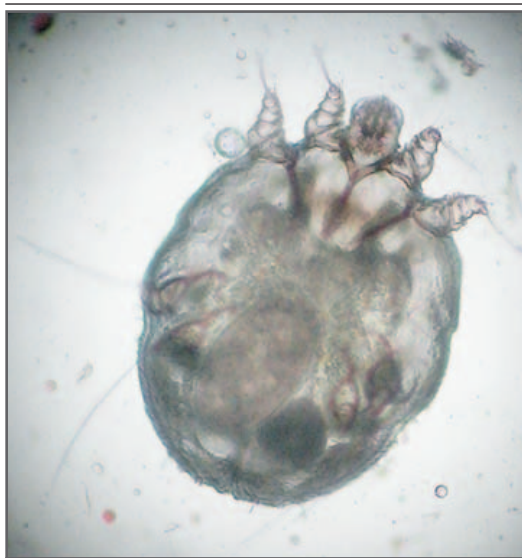


Figure 1. Adult Gravid Scabies Mite.

This mite was seen on direct examination of skin scrapings. The female mite dissolves the stratum corneum of the epidermis with proteolytic secretions and burrows downward. It is translucent, with brown legs; is 0.2 to 0.5 mm long; and is usually too small to see with the naked eye.

rows — by scraping laterally across the skin with a blade, taking care to avoid bleeding. The specimens can be examined with a light microscope under low power (Fig. 1). Potassium hydroxide should not be used, because it can dissolve mite pellets. Since the number of mites is low in cases of classic scabies, this technique is highly operator dependent. Failure to find mites is common and does not rule out scabies.

In atypical cases or when direct examination is not possible, a skin biopsy may potentially confirm the diagnosis (Fig. 4). However, mites or other diagnostic findings are frequently absent, and the histologic examination usually shows a nonspecific, delayed hypersensitivity reaction.⁷ Despite the relatively low sensitivity of diagnostic testing, empirical treatment is not recommended for patients with generalized itching and should be reserved for patients with a history of exposure, a typical eruption, or both.

TREATMENT

Infested persons and their close physical contacts should be treated at the same time, regardless of whether symptoms are present. Topical or oral products may be used, although there are few rigorous studies to guide their use. Table 2 summa-

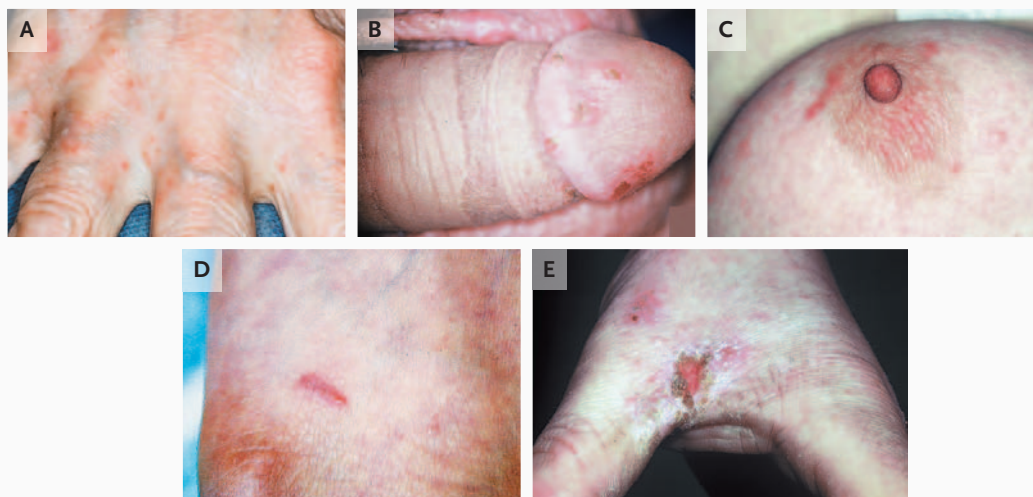


Figure 2. Classic Scabies.

Typical scabies in the finger webs evoke the diagnosis (Panel A). Nail involvement is uncommon in classic scabies but common in crusted scabies. Panel B shows involvement of the male genitalia in a patient with excoriated and papular scabies. The genitalia should be examined in all instances of suspected scabies infestation, especially when the patient reports itching. Panel C shows the breast of a woman with papular scabies lesions on the nipple and areolar area — a common location for scabies in women. Given this woman's family history of pruritus, scabies was easily identified by the finding of scabies in this location. Panel D shows a typical, specific, scabious, linear burrow with a tiny vesicle at the distal end. Such an obvious lesion is rarely seen, because it is usually obscured by eczema, impetigo, or both. The more common presentation of scabies with eczematization of the scratched lesion is shown in Panel E. The chronic pruritus of scabies rapidly leads to scratching and explains why eczema is frequently observed. The localization and epidemiologic context lead to the diagnosis.

rizes doses and side effects of agents commonly used to treat scabies.

Topical

Permethrin and lindane are the two most studied topical treatments for scabies. A Cochrane meta-analysis of four randomized trials comparing these agents indicated that permethrin (given as a single overnight application) was more effective than lindane (odds ratio for clinical failure, 0.66; 95 percent confidence interval, 0.46 to 0.95).^{8,9} However, there was considerable heterogeneity in effects among studies in the meta-analysis. In the largest trial, there was no difference in clinical cure rates; at an average of 28 days after treatment, complete resolution had occurred in 181 of 199 patients treated with permethrin (91 percent) and in 176 of 205 patients given lindane (86 percent).¹⁰

Nevertheless, the potential neurotoxicity of lindane, especially with repeated applications, has limited its use¹¹; the product is no longer available in the United Kingdom or Australia. In an

in vitro model assessing systemic exposure during conditions of overuse, the risk of adverse effects with the use of 5 percent permethrin cream was estimated to be lower by a factor of at least 40 than the risk associated with the use of 1 percent lindane lotion.¹² In patients, the rate of central nervous system side effects reported by physicians to be at least possibly related to permethrin was low in a 1996 report (1 per 500,000 U of distributed permethrin), with no serious events.¹³ Despite its higher cost than lindane, 5 percent permethrin is recommended by the Centers for Disease Control and Prevention (CDC) as first-line topical therapy for scabies.¹⁴ Mass treatment with permethrin has also been effective in controlling scabies in communities in which it is endemic.

Other topical treatments include benzyl benzoate (not available in the United States) and cro-tamiton. In a randomized trial performed in Vanuatu, in the South Pacific, where scabies is a major public health problem, the cure rate at three weeks was 51 percent (19 of 37 patients) with 10 percent

Table 1. Special Forms of Scabies.

Variable	Major Clinical Features
Involved subpopulation	
Infants and young children	Lesions are vesicles, pustules, and nodules, but their distribution may be atypical. Eczematization and impetigo are common; scabies may be confused with atopic dermatitis or acropustulosis. Pruritus may be so severe that infants can be irritable and eat poorly.
Homeless people	Eczematization and impetigo are common. Extensive excoriated lesions are not necessarily indicative of scabies in homeless people but pruritus in a homeless shelter should suggest a diagnosis of scabies.
The elderly	Atypical presentation is common. Scabies epidemics are reported frequently in nursing homes, where a single patient with crusted scabies may be the index patient leading to infection of other residents, as well as health care workers and their families.
Immunocompromised patients	Severe scabies (i.e., atypical papular scabies or crusted scabies) develops predominantly in patients receiving topical or systemic corticosteroids, those with human immunodeficiency virus infection, organ-transplant recipients, and patients of advanced age. Pruritus may be mild or absent (i.e., scabies incognito).
Indigenous communities	Scabies, whether crusted or not, may be endemic (e.g., risk factors include poor nutritional status, inadequate medical facilities, and overcrowding). The burden of the disease may be very high among Aboriginal people in northern Australia, children in Africa or the Solomon Islands, and resettlement colonies in New Delhi, India, for example. Because of the high rate of scabies superinfection, Australian Aboriginal communities have the highest rate of post-streptococcal glomerulonephritis in the world.
Atypical presentation	
Scabies of the scalp	Scabies may accompany or simulate seborrheic dermatitis or dermatomyositis on the scalp; infants, children, the elderly, patients with the acquired immunodeficiency syndrome, and patients with crusted scabies may be affected.
Nodular scabies	A few violaceous, pruritic nodules are often localized on the groin, axillae, and male genitalia; they represent a hypersensitivity reaction to mite antigens and persist weeks or months after treatment.
Crusted scabies	Generalized crusted scabies is a psoriasiform hyperkeratotic dermatosis of the hands and feet with involvement of the nails and an erythematous scaly eruption on the face, neck, scalp, and trunk. Crusted scabies may be localized, affecting only the scalp, face, fingers, toenails, or soles. Crusted scabies occurs in immunocompromised patients and persons with such developmental disabilities as Down's syndrome. Because of the very large number of mites, crusted scabies is highly contagious, including through indirect transmission; it causes outbreaks among family members and among patients in hospital wards when no preventive measures are instituted. It may go undiagnosed. The plaques of crusted scabies can be misdiagnosed as psoriasis, eczema, Darier's disease, contact dermatitis, ichthyosis, or an adverse drug reaction.
Scabies mimicking immunologically mediated diseases	Bullous pemphigoid, urticaria, chronic lymphocytic leukemia, B-cell lymphoma with monoclonal infiltrate, CD30+ lymphoid proliferations, necrotizing vasculitis, and lupus erythematosus can all mimic scabies.

benzyl benzoate, similar to the cure rate of 56 percent with a single oral dose of ivermectin of 200 μg per kilogram of body weight.¹⁵ However, a third of the patients treated with benzyl benzoate reported burning or stinging, as compared with 7 percent of those treated with oral ivermectin. In France, where permethrin is not available, benzyl benzoate is considered first-line local treatment, mainly on the basis of professional experience.

The Cochrane Review concluded that data were insufficient to compare the effectiveness of either benzyl benzoate or crotamiton with lindane or permethrin.⁸ However, limited data from a randomized trial suggest that crotamiton has significantly less efficacy than permethrin at four weeks (61 percent vs. 89 percent).¹⁶

Pyrethrin has also been used as an aerosol spray (e.g., allethrin) to treat scabies. However, this treat-



Figure 3. Special Forms of Scabies.

Panel A shows scabies in an infant. Localization on the sole is not atypical in this form of scabies, nor is involvement of the face, scalp, and palms. Panel B shows a patient with scabies superinfection presenting as impetigo. In such patients, the risk of glomerulonephritis associated with nephritogenic strains of streptococcus is of concern in developing countries. Panel C shows atypical papular scabies in a very old woman, who also had similar lesions on her back. Frequently, scabies goes unrecognized in such patients because itching is attributed to senile pruritus. Panel D shows localized crusted scabies in a young woman who was being treated with an immunosuppression regimen after renal transplantation. She presented because of a symptomless hyperkeratotic toenail; many mites were found in skin scrapings. Panels E and F show generalized crusted scabies in the finger webs and on the sole of the foot, respectively. This form of scabies is highly contagious, leading to outbreaks in institutions, including hospitals and nursing homes.

ment was associated with severe bronchospasm in two girls with asthma who had head lice and was fatal in one. Such a formulation of pyrethrin should never be prescribed to persons with a history of asthma.¹⁷ Sulfur, topical ivermectin, and tea tree oil¹⁸ have been suggested as treatments, but data are lacking to support their use.

Oral

Topical treatments may be poorly tolerated by some patients (e.g., they are messy, may be difficult to apply, and may cause burning or stinging, especially when the skin is excoriated or eczematous, and potential percutaneous absorption may pose a risk). An alternative approach is the use of oral ivermectin,¹⁹ an agent that has been used extensively for several parasitic infections, including onchocerciasis, lymphatic filariasis, and other nematode-related infestations. Ivermectin is thought to interrupt glutamate-induced and γ -aminobutyric acid-induced neurotransmission in parasites, leading to their paralysis and death.²⁰ In humans, ivermectin does not cross the intact blood-brain

barrier, whereas in collies, central nervous system toxicity and associated sudden death have been described.²¹

Several controlled trials have assessed the efficacy of a single dose of ivermectin (200 μ g per kilogram) for the treatment of scabies. In one placebo-controlled trial, 37 of 50 patients treated with ivermectin (74 percent) were cured, as compared with 4 of 26 patients in the placebo group (15 percent).²² In small studies, no significant differences in clinical cure rates were found between ivermectin and 10 percent benzyl benzoate,¹⁵ or between ivermectin and lindane.²³ In one randomized trial comparing oral ivermectin with an overnight application of 5 percent permethrin,²⁴ a single dose of ivermectin cured 70 percent of patients, as compared with a 98 percent cure rate with permethrin ($P < 0.003$), but a second ivermectin dose taken two weeks later increased the cure rate to 95 percent. The lower efficacy of single-dose ivermectin could reflect the lack of ovicidal action of the drug.

Randomized trials and clinical experience have

suggested that ivermectin is safe. Encephalopathy has been reported in patients who are treated with this agent and who have onchocerciasis and are heavily infected with *Loa loa* microfilariae.²⁵ No serious adverse effects were noted in a program of mass treatment with ivermectin for children with scabies in the Solomon Islands.²⁶ In one study, an excess risk of death was reported among elderly patients who received ivermectin for scabies,²⁷ but selection bias and confounding factors were possible explanations; this observation has not been confirmed in other studies, including studies of residents in nursing homes.²⁸

Ivermectin may be used as first-line therapy, but its higher cost in some countries supports consideration of initial therapy with topical agents. Ivermectin should be routine therapy for patients who have no response to a topical scabicide, and it may be the appropriate first choice for the elderly, patients with generalized eczema, and other patients who may be unable to tolerate or comply with topical therapy.

Assessing the Response

Patients should be advised that itching can persist for up to four weeks after the end of correctly administered scabicide therapy. After that time, the cause of itching should be reinvestigated (Table 3).

Control of Infectivity

Classic scabies is transmitted most commonly by prolonged skin-to-skin contact with the infested person. Persons who have contact of this nature, but not those with more casual contact, should be treated. Prescriptions should be provided for all household members and any sexual contacts, even if they are asymptomatic. The time course for the eradication of parasites after treatment for classic scabies has not been extensively studied, but there is some concern that patients treated with ivermectin may remain contagious longer than those treated with topical therapies.

Crusted scabies is very easily transmissible, and treatment of persons who have been even minimally exposed is warranted. In institutional settings, patient care staff and support staff (e.g., cleaning staff and laundry employees) should be considered to have been exposed to infested persons.

The spread of classic scabies without direct person-to-person contact is rare. However, the recovery of live mites from chairs and couches in the

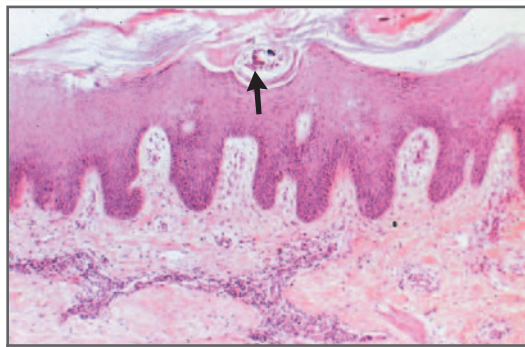


Figure 4. Adult *Sarcoptes scabiei* in Its Burrow (Arrow) at the Upper Part of an Acanthotic Epidermis (Hematoxylin and Eosin).

homes of patients with scabies supports the use of environmental measures,²⁹ even though data are lacking to confirm the efficacy of such measures in reducing transmission. Ideally, clothes and bed linens should be machine washed at 60°C and machine dried the day after the first treatment³⁰; insecticide powder or aerosolized insecticide is generally reserved for materials that cannot be laundered. Items may also be kept in a sealed plastic bag for at least 48 to 72 hours. On the basis of the survival of mites, only clothes and linens that were in contact with the patient during the previous 48 to 72 hours warrant these cleaning procedures.

AREAS OF UNCERTAINTY

A sensitive and specific method for the diagnosis of scabies is lacking. Newer approaches are under investigation, including measurement of specific circulating IgE levels or molecular tools such as polymerase chain reaction followed by enzyme-linked immunosorbent assay or DNA fingerprinting.³¹ Preliminary studies have suggested that epiluminescence microscopy³² and noncomputed dermoscopy³³ — noninvasive techniques allowing detailed inspection of the skin — may be useful. The role of these tests in practice remains uncertain.

Optimal therapy for classic scabies is not certain. Topical treatments may be poorly tolerated. Oral ivermectin is convenient, but the optimal dosing regimen remains uncertain, post-marketing surveillance is mandatory, and the cost is generally higher than that of topical treatments. Limited data suggest that one dose of 200 µg per

Table 2. Current Treatments for Scabies.*

Generic Drug Name	FDA Approval for Treatment of Scabies	Dose	FDA Pregnancy Category [†]	Major Side Effects or Contraindications	Comments
Topical treatment [‡]					
Permethrin [§]	Yes	5% Cream, rinsed off after 8–14 hr	B	Itching and stinging on application; may be used in infants and nursing mothers	First-line topical therapy in the United States; a second administration 1 wk after the first often routinely prescribed; treatment failure potentially attributable to incorrect application or a failure to treat all contacts
Lindane	Yes	1% Lotion or cream, rinsed off after 8 hr	B	Seizures, muscle spasms, aplastic anemia; not for use in infants or pregnant or breast-feeding women	Second- or third-line topical therapy; available by prescription in the United States and some parts of Europe
Benzyl benzoate [¶]	No	10% or 25% Lotion, rinsed off after 24 hr (several other regimens possible)	None	Burning and stinging when applied to exoriated skin, pruritic cutaneous xerosis, or eczematous lesions post-treatment	Not currently available in the United States; approved in Europe
Allethrin	No	0.6% Aerosol, rinsed off after 12 hr	Should be B	Not for use in patients with asthma	Not currently available in the United States; approved in Europe
Crotamiton	Yes	10% Cream applied to the nodules for 24 hr, rinsed off, and then reapplied for an additional 24 hr	C	None	Not very effective; often used on scabies nodules in children
Precipitated sulfur	No	3–6% Lotion or 5%, 10%, or 40% in petrolatum applied for 24 hr and then reapplied every 24 hr for the next 2 days (with a bath taken between each application)	None	None	Often used in children under 2 mo of age and pregnant and breast-feeding women; limited data to support efficacy and safety

Oral treatment	No	Single dose of 200 µg/kg of body weight (commercially available as 3-mg tablets); 2nd dose recommended 14 days later	C	Excess risk of death for elderly patients not confirmed	Approved in France, the Netherlands, and Mexico; cost may vary widely and could be a limitation for use; post-marketing surveillance of various age groups (e.g., children and the elderly) and large populations needed
Ivermectin**					

* FDA denotes Food and Drug Administration.

† For drugs in FDA pregnancy category B, there is no evidence of risk in humans. Drugs in pregnancy category C have had toxic effects in studies of animals, but the results of studies in humans are inadequate.

‡ The correct application of topical drugs is crucial to a cure. After the patient dries off after a tepid bath or shower, the product should be applied from head to toe (because scalp involvement may be a cause of relapse), including the groin. Special care should be taken at the mucocutaneous junctions to avoid contact between the agent and the mucosa.

§ Permethrin has been approved for use in infants two months of age or older. When a nursing mother with scabies infestation of the breasts has to be treated with permethrin, she should bottle-feed her infant and discard pumped breast milk until residual cream has been thoroughly washed off.

¶ No alcoholic beverages should be consumed for at least 48 hours after application, because of a potential disulfiram-like effect of the interaction.

|| Pyrethrin is in FDA pregnancy category B. Since allethrin belongs to the family of pyrethrins, it too should probably be in category B.

** The single dose of 200 µg per kilogram equals a dose of 12 mg for a person weighing 60 kg. The absorption of ivermectin may be improved if taken with a fatty meal. The regimen is not approved for children weighing less than 15 kg or for pregnant or lactating women. The drug could be useful in patients with classic scabies, and multiple doses in combination with topical therapy could be useful in patients with the acquired immunodeficiency syndrome who have extensive scabies and in patients with crusted scabies.

kilogram may be insufficient.²⁴ Alternative approaches include repeating the dose on day 14 or giving a single dose of 400 µg per kilogram.³⁴ The elimination half-life and the incubation time of 15 days to egg hatching suggest that administration of a second dose of ivermectin on day 14 might be more effective than a single dose, although comparative studies are lacking.

Further study of treatments for crusted scabies is also needed, including the roles of isolation of the index case, combined oral and topical therapy, repeated administration of therapy, and the use of a softening agent both to treat hyperkeratosis and to increase the efficacy of topical scabicides. The potential emergence of ivermectin-resistant scabies mites should be assessed,³⁵ along with the risk of cross-resistance of other parasites, notably in developing countries. Tolerance of mites to permethrin has been demonstrated in vitro, but there has not been in vivo evidence of tolerance or resistance.³⁶

GUIDELINES

Recommendations for the detection and management of scabies have been issued by several organizations. A fact sheet for patients that is available from the CDC¹⁴ recommends examining skin scrapings to confirm the diagnosis and the use of 5 percent permethrin as standard therapy, with crotamiton or oral ivermectin as alternatives; these recommendations also apply to HIV-infected patients with classic scabies. When oral ivermectin is prescribed, the CDC recommends a dose of 200 µg per kilogram, repeated two weeks later.³⁷ National guidelines in the United Kingdom recommend screening for other sexually transmitted infections in patients who present with scabies at clinics for genitourinary medicine.³⁸ Guidelines in the United Kingdom recommend permethrin as the treatment of choice.

SUMMARY AND RECOMMENDATIONS

Patients with scabies should be informed that scabies is benign but transmissible and that several treatments are available (Table 2). Treatment should be recommended on the basis of a confirmed diagnosis. Topical permethrin is reasonable first-line therapy in the United States. Where permethrin is not available (e.g., in France), topical benzyl benzoate or oral ivermectin are good

Table 3. Main Causes of Itching after Scabicide Therapy.*

Cause	Management	Prevention
Cutaneous irritation		
Overtreatment	Intensive use of emollients, with or without mild topical corticosteroids	Limited topical treatment or oral ivermectin
Severe eczematous scabies	Intensive use of emollients	Nonirritant scabicide or oral ivermectin
Contact dermatitis	Topical corticosteroids	Nonallergic scabicide or oral ivermectin
Treatment failure		
Poor compliance or failure to follow instructions correctly	Supervised application of scabicide or ingestion of oral ivermectin	Clear instructions and evaluation of the patient's understanding
Resistance	Use of another scabicide	
Relapse or reinfestation	Further use of scabicide (including application to the scalp) or oral ivermectin and simultaneous re-treatment of all contacts	Head-to-toe application or second dose of ivermectin, as well as simultaneous retreatment of all contacts
Delusions of parasitosis†	Psychiatric referral	
Nonscabietic origin	Treatment of the underlying cause	

* Adapted from Chosidow.¹⁷

† These psychiatric disorders, including acarophobia, occur in persons who have been successfully treated for scabies or who have never had scabies.

choices. Oral ivermectin is preferred for patients who cannot tolerate topical therapy and those who are unlikely to adhere to a regimen of such therapy.

If ivermectin is used to treat the man described in the vignette, limited data and my professional experience would lead me to recommend administration of a dose of 200 μg per kilogram, repeated two weeks later. Close contacts of the man should also be treated, and I would provide a prescription to treat his girlfriend at the same time,

even if she were asymptomatic. I would also recommend machine washing and drying recently worn clothes and bed linens. The patient should be followed to confirm resolution of itching, which may take up to four weeks.

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