

## Recommendations for the Treatment of Scabies Infestations in Israel

Kosta Y. Mumcuoglu PhD<sup>1</sup> and Leon T. Gilead MD PhD<sup>2</sup>

<sup>1</sup> Department of Parasitology, Hebrew University-Hadassah Medical School, Jerusalem, Israel

<sup>2</sup> Department of Dermatology, Hadassah University Hospital, Jerusalem, Israel

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Scabies is an intensely pruritic disorder induced by an allergic response to infestation of the skin by the mite *Sarcoptes scabiei*. The female mite penetrates the skin and excavates a burrow in the stratum corneum/epidermal junction. During the next 2–3 weeks it lays three to four eggs daily, which hatch after 3–4 days. Newly hatched larvae exit the burrows and appear on the surface of the skin where they continue their development until they reach the adult stage.

Generally, prolonged skin-to-skin contact is required for transmission (a quick handshake or hug will usually not spread infestation). Infestation is easily spread to sexual partners and household members. Infestation may also occur by sharing clothing, towels and bedding. In Israel, 20,000–25,000 units of scabicides are sold yearly.

The burrows of the female are found mainly on hyperkeratotic areas on the sides of hands and fingers, finger webs and flexural areas of wrists but also on elbows, feet (mainly in infants), genitalia, buttocks, around nipples and in axillae. The allergic response usually starts 3–4 weeks after initial infestation with mites and is accompanied by intense pruritus. The itching may affect all parts of the body and is particularly bad at night. The symptoms begin to appear within a day or two on recurrent infestations.

A polymorphic, mainly papular, rash is typically visible in areas such as around the waist, inside the thighs, on the lower buttocks, lower legs, ankles and wrists, as well as on the interdigital webs and sides of the fingers and palms. Typical locations in females appear around the nipples and in males on the penile shaft and on the glans penis. Secondary infections are common.

Nodular lesions develop in about 7% of scabies-infested patients. The lesions appear during active scabies and consist of itchy, round, reddish-brown, smooth nodules, 5–8 mm in diameter, sometimes topped with a typical burrow. They characteristically persist after the rest of the eruption has cleared with treatment. Such nodules may develop on the front folds of the axillae and around the naval, and in males also around the groin and on the penis. Nodules are considered to be a reaction of the reticuloendothelial system to mite antigens.

Crusted scabies (also known as Norwegian scabies) is a severe widespread infestation characterized by the involvement of all parts of the body including the head and neck. The nails are often affected, resembling onychomycosis. Crusted scabies may

begin as ordinary scabies with burrows, papules and vesicles in the same places but later a keratotic reaction develops. It has been found that those infested usually suffer from Down's syndrome, mental deficiency or neurologic disorders, or from immunosuppression due to corticosteroid treatment, radiation or AIDS. In people who are severely immunocompromised the burden of mites can reach several thousand.

The diagnosis of scabies is made clinically by the typical distribution of the rash, as previously described, and by examining the rash for evidence of typical burrows. The diagnosis is confirmed by scraping the burrows with a scalpel blade and identifying the mites or eggs under a microscope. A positive diagnosis may also be made without scraping, using a dermatoscope surface microscope. A negative result on skin scraping is not always conclusive as the infested person may have few mites (on average 10–15). It should be emphasized that scabies may be difficult to recognize, particularly if scratching, inflammation or infection has obscured the presentation [1].

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### Treatment of choice

Permethrin dermal cream, 5%, is considered the treatment of choice; it has an excellent safety record for all ages including pregnant women [2–8]. This excellent record has recently been damaged, as an association was found between maternal exposure to household, garden and anti-louse insecticides (pyrethroids) during pregnancy and increased risk for leukemia in their offspring [9]. The following points are important when prescribing treatment:

- Apply the cream to clean, dry and cool skin. A bath or shower immediately prior to treatment is not necessary
- Ensure that the entire surface of the body is covered from the hairline on the head to the soles of the feet. Remember to remove all jewelry
- Pay special attention to the areas behind the ears, between

the fingers and toes, wrists, under the arms, external genitalia, buttocks and under finger and toe nails

- Do not over-treat by applying the cream until detectable layers remain on the surface
- Wash the whole body thoroughly 8–12 hours after treatment
- Reapply any cream washed off during the treatment period, e.g., after hand-washing
- Where possible, ask someone else to apply the medication on the skin as this makes it easier to get to difficult-to-reach parts of the body
- Immediately after treatment, change bed linen and wear freshly laundered clothes.

### Further measures regarding treatment

- 5% permethrin dermal cream is suitable for use by adults, including the elderly and children. However, children aged between 2 months and 2 years and pregnant women should be treated under medical supervision and maternal benefit should be weighed against fetal risk
- It is important that all household members and close contacts be treated at the same time
- When treating children apply the medication to the face, avoiding the area around the eyes
- For severe infections a second treatment after 7–8 days might be necessary
- It may be necessary to prescribe two tubes of cream to ensure all areas of the body are covered thoroughly because very dry areas of skin will absorb more cream
- The itch may persist for a week or more after treatment. This does not necessarily imply a failure of treatment or re-infestation. However, if fresh spots appear or lesions still remain after 4 weeks after treatment, a second treatment should be considered
- Permethrin formulations could lead to irritation. The use of moisturizer and emulsifiable oil baths can help settle this type of itch. Special care should be taken in those allergic to chrysanthemum or permethrin
- Clothing, towels and bedding used by the infested person in the 48 hours prior to treatment should be laundered using the hot cycle, or dry-cleaned. Alternatively, items may be placed in a dry place for about one week before they are reused as mites cannot survive lengthy periods off the human body
- The treatment for those with crusted scabies should also include their face, scalp and ears
- For crusted scabies, treatment with oral ivermectin should be considered
- Secondary infections should be treated with appropriate oral antibiotics
- *Sarcoptes scabiei* of animal origin such as dog, cow or goat may penetrate the human skin. However, it cannot develop and dies within a few days without reproducing itself. Accordingly, it is necessary to treat the animal

with scabicides and the patient with anti-pruritic medication.

In Israel, two preparations based on 5% permethrin are available – namely, Lyclclear® (Glaxo Wellcome, Germany) and Mite-X® (Fischer Pharmaceuticals, Israel). According to the manufacturers' instructions, Lyclclear should be applied for a period of 8–24 hours and Mite-X for 8–14 hours. If necessary, a second application may be given. Children aged 2 months to 2 years old and adults over 70 years old should be treated under medical supervision. Burning, itching and stinging may occur after application.

Ivermectin was first used for the treatment of scabies in farm animals [10]. It was introduced in humans in 1982 for the treatment of onchocerciasis [11] and later for strongiloidiasis. It was first reported to be effective in human scabies infestations in 1991 [12] and has since been extensively studied and found to be highly effective and safe [13]. The recommended dose is 200 µg/kg body weight repeated after 1–2 weeks [14]. Ivermectin has not been tested in children weighing less than 15 kg and therefore should not be given to such patients. Although it has never been approved by the United States Food and Drug Administration, ivermectin is considered together with 5% permethrin to have revolutionized the treatment of human scabies infestations [15].

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### *Ivermectin and 5% permethrin have revolutionized the treatment of human scabies infestations*

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Two subgroups that deserve special attention are pregnant women and infants under 2 months old. These subgroups are considered more sensitive for toxic side effects (i.e., fetus in pregnant women and small babies) and for skin irritation (small babies). Five percent permethrin has been shown to be safe and effective in both groups [16], but its long-term leukemia risk [9] may require reevaluation of its use in these subgroups. A second choice is the old-fashioned application of 5% precipitated sulfur in petrolatum twice daily for a week, which is considered safe but messy and less effective [17].

### Other scabicides

#### Crotamiton

Crotamiton (10%) was effective after two applications over a 24 hour period, but the success was less than 100% [18]. Poor results were reported by several investigators [19–21]. Crotamiton is odorless, non-greasy, non-irritating and has anti-pruritic properties and therefore is a good medication for the persistent post-scabietic itch. It has been advocated for the treatment of children [22] but it apparently requires prolonged application. In Israel, the instructions for Scabicin® lotion (10% crotamiton)

(Fischer Pharmaceuticals, Israel) are to apply once for 24 hours, to reapply thereafter for 48 hours and to take a bath only at the end of the second application. The medication is not recommended for pregnant and breast-feeding women or for infants and children. According to the instructions, the application of Eurax® lotion or cream (10% crotamiton) (Novartis, Switzerland) should be repeated once daily, preferably in the evening, for 3–5 consecutive days. The patient could take a bath between applications and at the end of the treatment.

### Sulfur

According to the literature, a 5–10% sulfur ointment is a safe and effective treatment for scabies both in adults and children and is considered as first-line treatment for scabies-infested infants in the U.S. [1,17]. One of the scabicides on the Israeli market is Duo-Scabil® (Agis, Israel), which is a combination of 10% crotamiton and 8% sulfur. To our knowledge, there are no published data on the clinical efficacy of such a combination. The cream should be applied once daily for 3–5 days. Forty-eight hours after the last application the entire body should be washed in a warm bath. Local irritation, rash or inflammation has rarely been observed.

### Benzyl benzoate

Benzyl benzoate is a relatively old treatment for scabies. It is generally accepted that 10–25% of an aqueous emulsion of benzyl benzoate yields reliable results. The emulsion should be applied to the body after a bath or shower and left for 5–10 minutes to dry before getting dressed. Benzyl benzoate could cause skin irritation in general and especially scrotal irritation, and should not be used if there is any broken surface on the skin. It is also a conjunctival irritant and should therefore be used with special care in infants and young children [1]. Caution has been advised in the use of benzyl benzoate in early childhood scabies as well as during pregnancy and nursing because of possible intoxication/problems following systemic absorption of benzyl alcohol (the metabolite of benzyl benzoate) [23]. Comparative studies have shown it to be slightly less effective than most of the other topical scabicides. In Israel, the instructions for use of Scabiex® (25% benzyl benzoate emulsion) (Rekah, Israel) are to apply the medication to the entire body after a 10 minute hot bath, repeat the treatment twice with an interval of 12 hours and take a bath 8–10 hours after the last application. Benzyl benzoate is an irritant to the eyes and mucous membranes and in certain cases may be irritating to the skin. Hypersensitivity reactions have been observed.

### Gamma benzene hexachloride (lindane)

Earlier clinical trials showed that three applications of lindane were 100% successful [24,25]. More recent studies, however, showed that the cure rate was around 85% [2,26]. Eleven instances of aplastic anemia and two of leukemia caused by contact with lindane were reported [27]. Lee and Groth [28] reported nine instances of systemic toxic effects in humans caused by lindane, seven of which resulted from its therapeutic application to the

skin, some of them after a single application. Rasmussen [29] reviewed the literature on lindane and reached the conclusion that its benefits probably outweigh its risks, taking into consideration that 30 million units were sold over a 5 year period. It is recommended that it be applied to a cool dry skin for 30 minutes to 6 hours [30,31]. It is not recommended for infants, small children and in pregnancy. It should not be used on inflamed, secondarily infected or heavily excoriated skin and the treatment should not be repeated within 8 days [32]. Resistance of scabies mites to lindane has been reported [3]. In Israel, Bicide® cream formulation (1% lindane) (Fischer Pharmaceuticals, Israel) should be applied once for 8 hours.

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- Correspondence:** Dr. K.Y. Mumcuoglu, Dept. of Parasitology, Hebrew University-Hadassah Medical School, P.O. Box 12272, Jerusalem 91120, Israel.  
Phone: (972-2) 675-8093  
Fax: (972-2) 67507425  
email: kostam@cc.huji.ac.il