EXPERT REVIEWS

New insights in pediculosis and scabies

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Despite the use of powerful insecticides and the prodigious efforts of parents and health providers, successful control of head louse infestations remains unattainable in most countries. The main reasons for ineffective control of head lice are sale of ineffective pediculicides, incorrect use of pediculicides, use of alternative remedies and methods for which efficacy has not been clinically proven, development of resistance to insecticides, improper attention to possible fomite transmission, difficulty in diagnosing head lice infestations and embarrassment and social stigma that prevents reporting. Scabies is an intensely pruritic disorder induced by a delayed type hypersensitivity response (type IV immune reaction) to infestation of the skin by the mite *Sarcoptes scabiei*. This article reviews the biology of the mite, the clinical aspects and diagnosis of scabies infestations, as well as the treatment of choice with permethrin 5% dermal cream and the use of scabicides based on other chemical substances. Reports of scabies mites resistant to ivermectin and permethrin indicate that alternative treatment modalities should be sought and investigated.

Keywords: *Pediculus humanus capitis* • *Pediculus humanus humanus* • *Pthirus pubis* • *Sarcoptes scabiei*

Human louse and scabies infestations are an ancient, common and well known medical problem of mankind. These ectoparasitic infestations have been, and unfortunately still are, associated with a perception of uncleanliness and social stigma. Despite their relatively 'simple' and straightforward nature, these infestations continue to be a significant public-health problem. The number of cases of human louse infestations has increased worldwide since the mid-1960s [1], reaching hundreds of millions annually [2]. The worldwide occurrence of scabies, with epidemics during war, famine and overcrowding, is responsible for an estimated 300 million people currently infested [3].

The aim of this review is to provide an up-to-date summary of the biology, epidemiology, diagnosis, clinical aspects, prophylaxis and treatment of head lice and scabies. The discussion of body and pubic lice are beyond the scope of this review and accordingly they are mentioned only briefly.

In January 2009 we searched the Medline database for the years 2004–2009 for the keywords *Pediculus*, pediculosis, scabies, *Sarcoptes*, pubic louse, *phthiriasis* and *Pthirus*, each separately. Those publications that had a special clinical and/or scientific interest were included in this review.

Pediculosis capitis

Despite the use of powerful insecticides and the prodigious efforts of parents and health providers, successful control of louse infestation remains unattainable in most countries. In developed countries, the high prevalence of head lice is due to a variety of reasons (for recent reviews see [4–8,201,202]), including:

- Sale of ineffective pediculicides, potentially due to changes in formulation, manufacturing processes or ingredient sourcing over the years [9–11];
- Incorrect use of pediculicides, for example, a single application of lotion formulations, which are not 100% ovicidal; the high dilution of shampoo formulations; or applying pediculicidal crème rinse to hair that is too wet [9,12];
- Use of alternative remedies and methods for which efficacy has not been proven by *in vitro* and *in vivo* studies with human head lice;
- The development of lice resistance to insecticides such as dichlorodiphenyltrichloroethane (DDT), lindane, permethrin and D-phenothrin, malathion and carbaryl [13–16];
- Improper attention to possible fomite transmission [17,18];

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- Difficulty in diagnosing head lice infestations. Many health providers are not able to accurately diagnose an active infestation, owing to lack of experience, knowledge, time or equipment (i.e., good lighting, nit combs and magnifiers);
- Embarrassment and social stigma that prevents reporting.

Biology of the head louse

Head lice (*Pediculus humanus capitis*) (Figure 1) are insect parasites, spending their entire life on the host scalp and feeding exclusively on blood, four- to five-times daily. Man is the only known host of this parasite. Although any part of the scalp may be colonized, lice favor the nape of the neck and the area behind the ears, where the eggs are usually laid. During its lifespan of 4 weeks a female louse lays 50–150 eggs (Figure 2). From the egg hatches the first nymphal stage, which after three molts, develops to nymph two, nymph three and to either a male or female louse (Figure 3).

Epidemiology of head louse infestations

Normally, head lice infest a new host only through close contact between individuals. Social contacts among children and parent–child interactions are more likely routes of infestation than shared combs, brushes, towels, clothing, beds or closets. Head to head contact is by far the most common route of lice transmission.

Figure 1. Female of the head louse (*Pediculus humanus capitis*). Female lice are approximately 3 mm in length and slightly bigger than males. In this specimen, an egg is visible in the body of the louse.

Figure 2. Head louse egg. Living eggs are round, transparent and shiny, with a whitish-pink color.

The number of children per family, the sharing of beds and closets, hair washing habits, local customs and social contacts, health care in a particular area, for example, school and socioeconomic status were found to be significant factors in head louse infestation [23,24].

Girls are two- to four-times more frequently infested than boys. Children between 4 and 13 years of age are the most frequently infested group [25].

Approximately 6–12 million people, mainly children 3–12 years of age, are treated annually for head lice in the USA [26]. An increased rate of louse infestation was reported in recent years from a number of countries, including North and South America, Europe, Asia and Australia [17,22,27,28].

Clinical aspects of head louse infestations

The most characteristic symptom of infestation is pruritus on the head, which normally intensifies considerably 3–4 weeks after the initial infestation. The bite reaction is very mild and can rarely be seen between the hairs. Bites can be seen, especially on the nape of the neck of long-haired girls when hair is pushed aside (Figure 4). In rare cases, the itch–scratch cycle can lead to secondary infection with impetigo and pyoderma (Figure 5). Swelling of the local lymph nodes and fever sometimes occur, but allergic reactions to louse bites are very rare.

Diagnosis

The presence of nits (empty egg shells or dead eggs) alone (Figure 6) is not an accurate indicator of an active head louse infestation. Examination of over 16,000 children revealed that 11–19% of the them were infested with living lice and eggs (Figure 7), while another 22–30% had nits only [27].

In any case, if no living lice or eggs are detected on the hair, a person should be considered negative for head louse infestation and accordingly should not be treated for lice.

Since children with nits are usually at higher risk of a new infection than children without nits [29], they should be thoroughly examined for several days after identification of nits.

The diagnosis of head louse infestation is usually performed by direct visual examination by hand, and very often the diagnosis

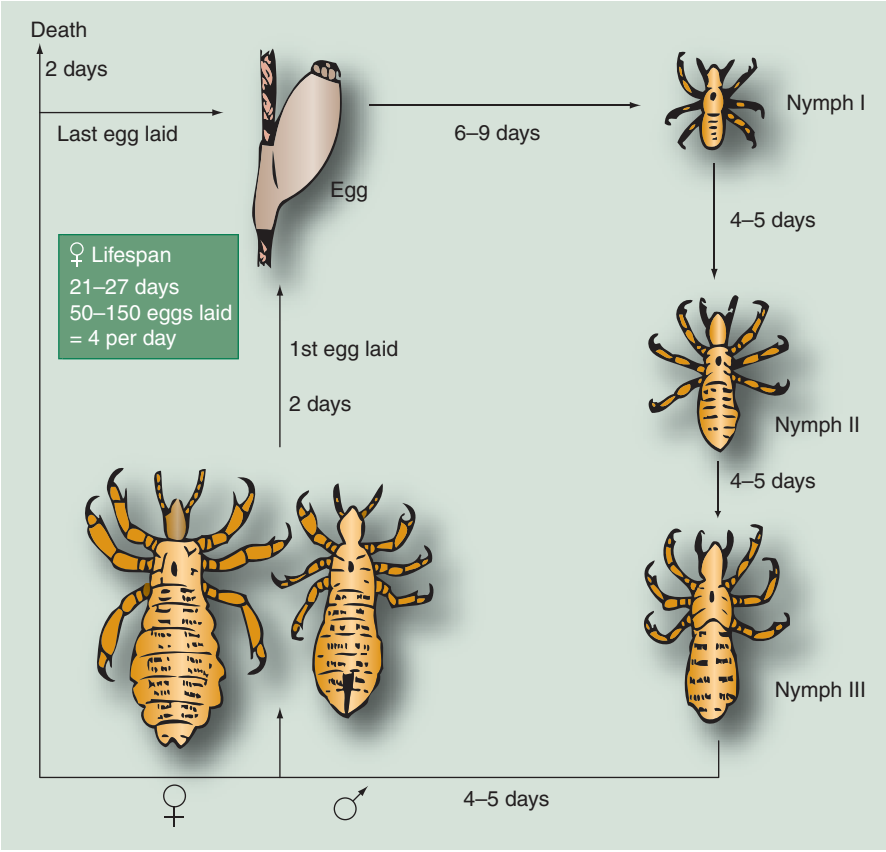

Figure 3. Life-cycle of the head louse. A female louse lays 50–150 eggs during her adult life. From the egg hatches the first nymphal stage, which after three molts, develop to nymph 2, nymph 3 and to either a male or female louse.

of louse infestation is based on the presence of nits. Combing the hair with a louse comb is four- to five-times more effective than visual examination [25,30,31]. Owing to the fact that nits may remain attached to the hair up to 6 months after a successful treatment, they only indicate a past, nonactive infestation, while living eggs indicate an active infestation.

It is difficult to diagnose a louse infestation by hand examination, since approximately 97% of infested children have 1–20 lice on their scalp [32], most of them being nymphs 1–2 mm in length [33], Owing to the fact that in direct visual examination the examiner spends more time looking at the hair, the chance of finding nits and, accordingly, diagnosing a false-positive infestation is increased.

However, in children with long and/or frizzy hair, examination with a comb is often very difficult and, in these instances, the inspection should be performed by direct visual examination, either by hand or with the help of a screening stick. Treating the hair with shampoo or conditioner could facilitate the combing, first with a regular comb or brush and thereafter with a louse comb. In any case, more time should be invested in the examination of the hair by visual examination.

All family members, especially those younger than 14 years old, should also be examined when a family member has been diagnosed with head lice.

Psychological aspects of louse infestation

Over the centuries, lice became a symbol of filth, poverty and shame. While recent epidemiological studies clearly demonstrate that lice infest children from all socioeconomic classes, the stigma still exists. The psychological effects of a louse infestation often exceed the physical ones: in the majority of cases a mild pruritus is the only sign of a louse infestation. Parents, teachers, kindergarten staff, social workers and even nurses and physicians are distressed by the presence of lice. They often blame the child and make him/her feel responsible for the infestation.

The examination of 140 drawings from 3–6-year-old children in Israel revealed that 43% used black crayon to draw a louse on part of the child's head. Used excessively, black suggests sadness and desperation [34]. Small black dots, as were often seen in these drawings, indicated anxiety. In addition, children drew sad faces and faces with tears, while disproportionally big lice were infesting their hair [35].

The immediate expulsion of a child from a camp, daycare, kindergarten or school according to a 'no-nit' policy must cause significant damage to the self-esteem of a young child and probably also to his/her parents. There are also negative effects on the parent–child relationship, especially when combing becomes painful and the parent and/or child becomes impatient. In this stressful situation parents sometimes use drastic methods for louse control, which include spraying the entire house with insecticides, use of food-grade oils, hair gels, Vaseline® and mayonnaise, as well as formulations that should be used only for parasitic and ectoparasitic infestations of pets or free-living insects in the household.

Treatment

Chemical pediculicides

Synergized pyrethrins, permethrin, lindane, malathion and oral ivermectin ('off label' use) are used to treat infested individuals in the USA [36]. In many other countries bio-allethrin, D-phenothrin and carbaryl are also used in the battle against head lice [37].

For the treatment of an infestation, products that have been specifically approved by the health authorities for the control of lice should be used. Instructions for use should be carefully read and all infested family members should be treated simultaneously.

A day after the last treatment the scalp should be re-examined for the presence of lice using a louse comb. If no living lice are found, the treatment was successful. If living lice are still present, a pediculicide with a different active ingredient should be used for the continuation of the treatment [38].

Figure 4. Bites of head lice. Bites are more often seen on the neck of long-haired girls, when the hair is pushed aside. The local reaction is due to the saliva that the louse injects during blood-sucking.

Pyrethroids are viewed as a relatively safe alternative, although evidence of worldwide resistance of head lice to this class of insecticide is emerging. In Israel, the pyrethroid permethrin was introduced in 1991 for the control of head lice and subsequently accounted for approximately 80% of pediculicides used between 1991 and 1995. First reports of permethrin control failure in Israel occurred in early 1993. Permethrin resistance was confirmed by bioassays on head lice collected from Israeli school children in mid-1994 [14,39].

Additionally, resistance of lice to pyrethroids, such as permethrin and phenothrin, as well as to malathion has also been documented in the USA, Argentina, Czech Republic, France and the UK [40–46].

Oral and topical formulations of ivermectin have been successfully used for the treatment of head and body lice [47–49]. Use of oral ivermectin 200 mg/kg repeated every 10 days has been shown to be effective against head lice. An ivermectin 0.8% lotion was successfully applied to a series of 25 patients [50]. Ivermectin is not currently approved by the US FDA as a pediculicide [51].

Natural pediculicides

Control efforts using chemical treatments are becoming increasingly ineffective, with insecticide resistance recorded in several countries. Essential oils have been widely used in traditional medicine for the eradication of lice, including head lice, but due to the variability of their constitution the effects may not be reliable, safe and reproducible.

Natural products tested clinically and found to be safe and effective could be very important in the control of head lice, as the complexity of the active ingredients may prevent the rapid development of resistance. In addition, they are generally more acceptable to the public.

Several botanical extracts and essential oils, such as aniseed, eucalyptus, peppermint, cinnamon, coconut, neem, monoterpenoids and tea tree oils, offer promise as new compounds to treat head lice infestation. However, the number of clinical studies on these products is very limited [52–61].

Physical treatment modalities

Treatment with a louse comb

Treatment of an infestation by combing alone (also known as 'bug busting' or wet combing) is possible if the hair is combed daily or every second day for a period of 12–14 days [62]. This technique is, however, only effective for children with short or medium-length and/or straight or wavy hair. Three studies have shown that combs remedy an infestation in 38–53% of the children treated in this way [63–66].

There are a large number of wooden, plastic and metal combs on the market. According to the texture, thickness and length of the hair, parents should find the comb that produces the best result and is easy to use. Wooden combs made by hand are not always smooth and the distance between the teeth can vary considerably. The static electricity generated during combing with a plastic comb may enable the lice to 'jump' off the comb. Some plastic combs were found to be less durable and break easily. Some metal combs are not suitable for dry hair and others are too pointed, causing damage to the skin and pain to the child. Damage can be caused by some combs due to the heat developed by the friction of the hair between the comb's teeth and, therefore, excessive combing should be avoided. Light-colored combs were found to be better for visualization of the nits than dark colored combs [10].

Combing is more painful and removal of lice and eggs less effective in children with long, curly or frizzy hair. In such cases, the examination should be made by parting the hair at 2-cm intervals

Figure 5. Impetigo and pyoderma seen on the head of an infested individual. Nowadays, these kind of infections are very rarely seen in children living in industrialized countries.

Figure 6. Nit of louse. Nits are dead eggs or empty egg shells, which remain attached to the hair for over 6 months. They are usually flattened, whitish, nontransparent and nonshiny.

and looking for lice moving near the scalp. An inspection by hand should last at least 10 min.

Louse combs can be cleaned with an old tooth-brush and then left outside for 2–3 days or soaked in an antilouse solution for 30 min.

The use of a louse comb should be an integral part of any antilouse control strategy. A fine-toothed louse comb can be used: for the diagnosis of louse infestation; for the prevention of louse infestation by suppressing the establishment of lice on the scalp after the initial infestation; as an accessory tool to any antilouse treatment method; for the treatment of a long-term head louse infestation; for verification that treatment with a pediculicide was successful; and for the removal of nits.

Heat

Several devices blowing hot air onto the scalp have been tested for their efficacy to kill lice and eggs. The most successful method, which uses a custom-built machine called the LouseBuster™, resulted in nearly 100% mortality of eggs and 80% mortality of hatched lice [67].

Silicon derivates

Dimethicone is a silicon derivate and works through a physical process that effectively covers and drowns or dehydrates the louse [68]. The lotion is safe to use in pregnancy. The lotion is applied to dry hair and allowed to dry naturally, the lotion being left on for at least 8 h, after which hair may be washed with normal shampoo [54,69–71].

Isopropyl myristate

Isopropyl myristate is a noninsecticide-based drug commonly used in cosmetics. A pediculocide rinse containing 50% isopropyl myristate was assessed in two Phase II trials conducted in North America and was found to be effective in the 'proof-of-concept' study and comparator trial using a positive control. Recently, it has been introduced in Canada, several European countries and in Israel as a pediculicide.

Its mode of action is a mechanical process that weakens the waxy shell of lice, resulting in internal fluid loss and dehydration [72,204], making development of lice resistance unlikely.

Electricity

A battery-operated louse comb (Robi Combi®) not only mechanically removes the lice but also electrocutes them on contact. The device's concept is based on an electronic circuit, charging the comb's teeth with a constant voltage, which is discharged when shorted by the lice body, killing the lice on contact. The circuit's low capacity and the insulation of the comb's teeth tips prevent the delivery of any current to the skin or discomfort for the user. The louse egg is not destroyed because it does not generate a short circuit, and it is recommended to repeat the treatment daily for 10 days, killing all hatched lice [Mumcuoglu K, Unpublished Data].

Treatments not recommended

Prophylactic treatments with pediculicides are not advised owing to possible side effects, as well as to diminish the chances of the development of resistant lice. Insecticides and any other chemicals that are not labeled for use on humans or for the treatment of head lice, should not be used. Gasoline or kerosene is toxic and flammable and, accordingly, it should never be used. Treatment of objects such as clothes, furniture and carpets is not necessary. The use of trimethoprim and sulfamethoxazole for control of head lice is not recommended. Owing to the psychological damage that could be caused to a child, shaving the head or even a short haircut for prevention or control is not advised.

Prevention

Louse combs

Examination of the child's head at regular intervals using a louse comb allows the diagnosis of louse infestation at an early stage. Early diagnosis makes treatment easier and reduces the possibility of others becoming infested. In times and areas when louse infestations are common, weekly examinations of children, especially those 4–13 years old, carried out by their parents will aid control.

Early diagnosis of louse infestation makes treatment easier and reduces the possibility of infesting other children. Combing the child's head with a louse comb every week or fortnight is one of the best means of preventing a louse infestation. In this way, the small numbers of lice that first infest the child's hair are easily removed and the establishment of a louse population prevented.

Figure 7. Nits on the hair of an infested child. Female lice usually lay their eggs close to the scalp, where the environmental conditions are favorable for the development of the embryo. Any egg/nit at a distance of more than 5 mm from the scalp is usually either dead or empty.

Repellents

Essential oils, such as rosemary, citronella and piperonal, have been tested for repellency to laboratory colonies of body lice [73]. One placebo-controlled clinical trial demonstrated the efficacy of a citronella formulation as a louse repellent [74].

A study by Canyon and Speare demonstrated that the transfer of head lice to treated hairs was limited by the slippery nature of the oils rather than their repellent qualities. Irritancy was not important because lice proceeded despite being highly irritated, except in the case of coconut oil. Tea tree and peppermint oil caused the most repellence, and tea tree and lavender oil prevented some blood feeding on treated skin [61].

Other preventive measures

Head-to-head contact is by far the most common route of transmission for head lice. Studies in Australian schools showed that classroom floors, brushes and hats are not risk factors for pediculosis. The chances of a live head louse or egg becoming reunited with a person would seem exceptionally remote. However, lice have now been shown in the laboratory to be readily dislodged by air movements such as blow-drying one's hair, combing and toweling. Moreover, passive transfer to adjoining fabric is also frequently observed. Louse transmission by fomites apparently occurs more frequently than has been commonly believed [75,76]. Nevertheless, not sharing brushes and combs with other family members or friends, keeping girls' hair tidy, being well informed on the biology and control of lice, and regular examinations are helpful in the prevention of infestations with head lice.

Away from the host, lice can only live for 1–2 days. Clothes, towels, bedding, combs and brushes that came into contact with the infested individual can be disinfected either by leaving them unused for 4–5 days or by washing them at 55–60°C for 30 min [9,77,78].

Nits & nit removal remedies

Female lice often lay their eggs at the base of the hair, attaching them to the hair with quick-hardening glue excreted from her body. The young lice hatch 6–10 days later, leaving the eggshell behind. Human hair grows at a rate of approximately 1 cm per month and the nits move away from the scalp as the hair grows. After 2–3 months, the nits are more visible, particularly on dark hair. The appearance of nits several months after the last treatment can lead to a false-positive diagnosis. In general, louse eggs found more than 0.5 cm from the scalp are unlikely to be viable except in warm countries, where live eggs have also been found further away from the scalp [12].

Biochemical analysis has revealed that the nit sheath is composed of four bands of protein, possibly crosslinked to aliphatic components with a tertiary structure of β-sheeting. Possible targets to destroy the nit sheath include proteases, denaturants, β-sheet breaker proteins and small protein inhibitors of sheath formation [79].

Removal of nits with a louse comb is easier when the hair is wet, or after shampooing or treatment with a conditioner. However, this method is not suitable for removing freshly laid eggs and should be repeated weekly for several weeks.

The 'no-nit' policy

The 'no-nit' policy requires the immediate dismissal of a child from a school, camp or childcare setting until all head lice, eggs and nits have been removed from the hair.

This policy is commonly adopted because it is assumed that health professionals cannot differentiate between live and dead eggs, or because the screeners refuse to use a louse comb for the examination of the child's head to find living lice. This involves long hours of nit removal, repeated treatments with pediculicides and absence from school for the child and possibly from work for at least one parent. The immediate expulsion of children from a camp, kindergarten or school must cause significant damage to their self-esteem and also upsets their parents. Moreover, even if the visible nits are removed from the scalp, it does not necessarily mean that the person is no longer infested with lice.

The efficacy of the 'no-nit' policy was questioned by other groups of scientists [80–85], as well as by the American Academy of Pediatrics and the National Association of School Nurses in the USA, and by the Canadian Pediatric Society [205].

There are no convincing data that demonstrate that enforced exclusion policies are effective in reducing the transmission of lice and, therefore, we believe that this policy is unjust, as it is based on intolerance and misinformation rather than on objective science.

Recommendations

In order to reduce the proportion of children infested with head lice and to slow down the emergence of strains of lice resistant to pediculicides, the following steps are recommended [84]:

- Health authorities should introduce more efficient methods for evaluating pediculicides and more stringent regulations for adoption of new antilouse products;
- Health providers, such as physicians and pharmacists, should be updated on new developments related to louse repellants and control. Pharmacists should only promote pediculicides that they know are effective. They should be able to recommend alternative pediculicides as a second-line treatment;
- Academic institutions should conduct baseline and efficacy studies on pediculicides and other treatment modalities, as well as research on the biology and epidemiology of lice;
- The pharmaceutical industry should aim to introduce pediculicides based on new chemical compounds, especially natural products. Companies should develop effective and safe repellents and nit-removal remedies;
- A committee, including physicians (e.g., pediatricians and dermatologists), epidemiologists, medical entomologists, public-health specialists, parents, nurses, social workers and representatives of the pharmaceutical industry, could support evidence-based louse control policies in each country. They could adopt prevention and control strategies, taking into account existing regulations, local customs and available treatments. The committee could also coordinate the activities of the different institutions that are involved in the control of louse infestations, disseminate information, conduct surveillance and adopt strategies to reduce development of resistance;
- An authoritative and balanced internet site should be available in each country, to provide maximum information about louse biology and control, existing treatment methods, pediculicides (instructions for use, efficacy level, side effects and price) and answers to the most commonly asked questions. The website should also include answers to the public's email queries;
- Parents should regularly inspect their children, treat as necessary and try to avoid creating stigma and emotional problems for the child. Sharing information on infestation with other parents would facilitate case finding. Feedback from parents to health providers in their area about louse infestations and treatment failures would help improve local control. Parents could also volunteer to examine children in their own or other children's kindergartens and schools after appropriate training;
- School nurses should address the head louse problem proactively by making information available to parents and investigating institutions with abnormally high incidence. In addition, the school nurse can support families who find it difficult to manage treatment;
- Children should be examined regularly by school nurses. A letter should be sent to the parents of all children examined. Parents of noninfested children should receive a letter encouraging them to examine their children's hair regularly for new infestations. Parents of children infested with nits should be urged to examine the child, as well as the other family members (especially siblings), as soon as possible with a louse comb and to treat all louse-infested individuals immediately. Letters should include information on how to examine, treat if necessary and check that the treatment was effective. However, excluding children from school because of the presence of lice or nits is not recommended;
- Parents should be given a pamphlet offering an informed choice of treatment methods, and notification of whom to ask if there are questions about which pediculicides or other treatment method(s) would give the best results;
- Parents could be requested to fill in a questionnaire about when the first treatment session was carried out, when consecutive sessions will be performed, if necessary, and which product was used;
- Children should be allowed to return to school immediately after the first treatment session. Ideally, the school nurse could check for lice on the tenth day after the letter was sent and conduct follow-up inspections until the treatment is successful;
- Infested children should be treated immediately but should not be prevented from attending school until the last nit is removed from the hair. Only children whose parents refuse to treat, either by physical methods, such as combing, or by pediculicides, should be excluded from the school;
- The school nurse should check the child with a louse comb 10 days after the letter was sent to the parents and contact the parents if lice are detected. Infested children should be followed up until the treatment is successful.

Figure 8. Female human scabies mite. *Sarcoptes scabiei* var. *humanus*. The mite is approximately 0.3 mm in size, has a roundish body and very short legs.

Lice throughout the ages

Lice evolution

The parasitic sucking lice of primates are known to have undergone at least 25 million years of co-evolution with their hosts. For example, chimpanzee lice and human head/body lice last shared a common ancestor roughly 6 million years ago, a divergence that is contemporaneous with their hosts. In an assemblage where lice are often highly host specific, humans host two different genera of lice, one that is shared with chimpanzees and another that is shared with gorillas. Phylogenetic and cophylogenetic analyses suggest that the louse genera *Pediculus* and *Pthirus* are each monophyletic, and are sister taxa to one another. The age of the most recent common ancestor of the two *Pediculus* species studied matches the age predicted by host divergence (~6 million years), whereas the age of the ancestor of *Pthirus* does not. The two species of *Pthirus* (*Pthirus gorillae* and *Pthirus pubis*) last shared a common ancestor approximately 3–4 million years ago, which is considerably more recent than the divergence between their hosts (gorillas and humans, respectively) of approximately 7 million years ago. Reconciliation analysis determines that there are two alternative explanations that account for the current distribution of anthropoid primate lice. The more parsimonious of the two solutions suggests that a *Pthirus* species switched from gorillas to humans [86,87].

Lice taxonomy

To assess the taxonomic status of head and body lice, Light *et al.* provided a synthesis of publicly available molecular data in Genbank®, and compared phylogenetic and population genetic methods using the most diverse geographic and molecular sampling presently available [88]. Their analyses found reticulated networks, gene flow and a lack of reciprocal monophyly, all of which indicated that head and body lice do not represent genetically distinct evolutionary units. Based on these findings, as well as inconsistencies of morphological, behavioral and ecological variability between head and body lice, they recommend head and body lice as morphotypes of a single species.

Human head lice are subdivided into three deeply divergent mitochondrial clades (Clades A, B and C), each having unique geographical distributions. Data suggest that lice belonging to mitochondrial Clade B may have originated in North America or Asia. It is likely that lice belonging to this mitochondrial clade recently migrated to other geographic localities, such as Europe and Australia, and, if not already present, may disperse further to occupy all geographic regions [89].

In contrast to the findings mentioned previously, Leo *et al.* used microsatellite DNA to study 11 double infestations, that is, hosts infested with head lice and body lice simultaneously [90]. Their study showed that: the head and body lice on these individual hosts were two genetically distinct populations; each host had their own populations of head and body lice that were genetically distinct to those on other hosts; and that lice had migrated from head to head and from body to body, but not between heads and bodies. Accordingly, they concluded that head and body lice are separate species.

Lice & archeology

Lice are mentioned in the Bible as the third plague visited on the Egyptians when the Pharaoh denied the request of Moses to let the Israelites go. From Sumerian, Akkadian, Egyptian and Biblical sources it is evident that the ancient inhabitants of the Middle East were well acquainted with head lice. In the Near East, head lice and eggs were found on the hair of Egyptian mummies, while 9000 year-old louse eggs were found from hair-samples of an individual who lived in Nahal Hemar Cave near the Dead Sea in Israel.

In Asia, large numbers of lice were recovered from a 3800-year-old Loulan-period female mummy. In Europe, ancient head lice are known to have existed from the Roman period onwards, and there are records from Iceland and Greenland.

In North America, head lice and their eggs were found on mummified remains of prehistoric Indians from the American Southwest. Lice have been found in hunter–gatherer and agricultural sites in the USA and from central Mexico. The prehistoric peoples in these areas appeared to control the lice by eating lice groomed from hair (a common method of louse control among tribal cultures, even today) as adult lice have been found deep in the matrix of coprolites.

In South America, lice were found on a mummy from an Inca prince, who lived approximately 500 years ago, as well as on mummified pre-Columbian Indians from Peru. Head louse eggs were recovered from human hair found in Brazil and carbon

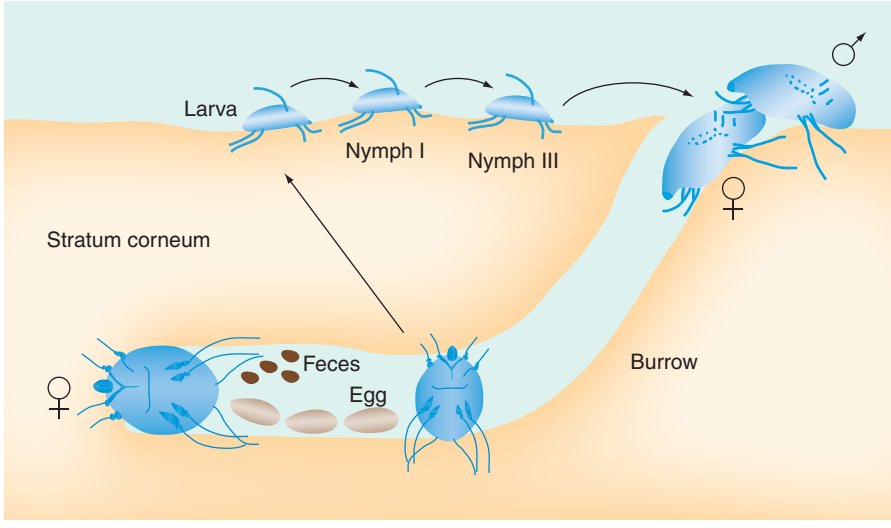

Figure 9. Life-cycle of the scabies mite. Only the female mite creates a burrow in the skin. Larvae hatch from the eggs, exit the burrows and continue their life on the skin surface. They develop to the nymph stages and then to adulthood. Male mites remain on the skin surface.

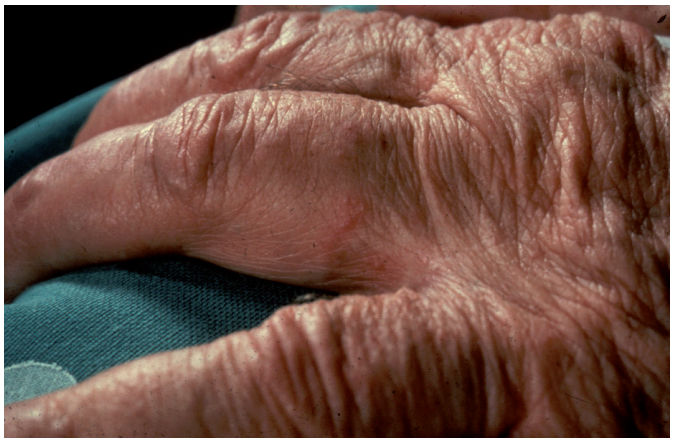

Figure 10. Scabies burrows between the fingers. The size of the burrow is usually approximately 1 cm. With the help of a magnifying glass, a stereo-microscope or a dermatoscope, the mite can be seen in one end of the burrow.

dated to approximately 10,000 years. Hair samples from seven mummies from Camarones (Chile), carbon-dated to approximately 1900–1500 BC, were examined and head lice eggs were found in six of them.

The oldest combs, which are similar to today's louse combs, are known from 1500 BC. Royal combs from Pharaonic times in Egypt were used for delousing. Head lice were recovered from the debris found between the fine teeth of a wooden comb excavated in Antionoe (Egypt) and dated between the fifth and sixth centuries AD. Head lice and their eggs were also found in combs recovered from archeological excavations in the Judean and Negev deserts of Israel, including from Masada and Qumran. Most of the combs were two-sided, while some were also single-sided. One side of the comb was used to open the knots while the second side with the fine teeth was used to remove lice and eggs. Most combs found in archeological excavations were made out of wood, some were made from bones and ivory, yet all bear a resemblance to modern-day combs. Lice were found in 12 out of 24 combs examined from the Judean and Negev deserts [91].

Lice played a key role in Napoleon Bonaparte's disastrous invasion of Russia. Napoleon marched into Russia in 1812, leading some half a million soldiers toward Moscow. By 6 months later, the army was reduced to 25,000 men and only 3000 survived the war. The dead were buried in mass graves. One such grave, containing approximately 3000 corpses, was discovered in 2001. Using PCR, Raoult *et al.* were able to demonstrate that louse-borne pathogens were a major factor in the French retreat from Russia [92]. The analysis of bone fragments and remnants of clothing revealed the presence of five body lice, three of which carried DNA from relapsing fever. The scientists then also analyzed dental pulp from teeth, taken from the remains of soldiers, and sequenced the DNA of *Bartonella quintana*. The team also detected the DNA of *Rickettsia prowazekii* in some soldiers, indicating that Napoleon's army also suffered from epidemic typhus. Overall, nearly a third of Napoleon's soldiers buried in the mass grave were affected by louse-borne infectious diseases, showing the impact of louse-borne diseases on troops during Napoleon's invasion in Russia.

In order to determine which louse type or types were found in the Americas before European colonization, Raoult *et al.* used the PCR technique to amplify DNA from two genes (*Cytb* and *Cox1*) belonging to 1000-year-old lice collected from Peruvian mummies [93]. Only the worldwide type (type A) was found and, accordingly, this phylotype was worldwide before European colonization, as type A lice were common in Europe, Africa and Asia.

Pediculosis corporis

The infestation with body lice (*Pediculus humanus humanus*), also known as pediculosis corporis, is a common worldwide problem that affects people of all races. Body lice are predominantly seen under conditions of poor sanitation and crowding in developing countries. Homelessness in developed countries is an increasing public health problem. Owing to poor living conditions and limited access to healthcare systems, homeless persons are exposed to many communicable infections, including body louse infestations [94]. The main clinical symptoms are pruritus and pyoderma of clothing-covered areas. A more general reaction of fever, headaches, a diffuse rash, fatigue and myalgias may appear a few weeks or months after the beginning of the parasitism [95,96].

Three pathogenic bacteria are transmitted by the body louse: *R. prowazekii*, the agent of epidemic typhus of which the most recent outbreak (and the largest since World War II) was observed during the civil war in Burundi; *Borrelia recurrentis*, the agent of relapsing fever, historically responsible for massive outbreaks in Eurasia and Africa, which currently prevails in Ethiopia and neighboring countries; and *B. quintana*, the agent of trench fever, bacillary angiomatosis, chronic bacteremia, endocarditis and lymphadenopathy. Recently, a forth human pathogen, *Acinetobacter baumannii*, has been associated with body lice [92,97,98].

The mainstays of treatment of body-louse infestation in humans in a community setting are insecticides and the removal of infested clothing. Foucault *et al.* recently reported the dramatic effect that three doses of oral ivermectin (12 mg each)

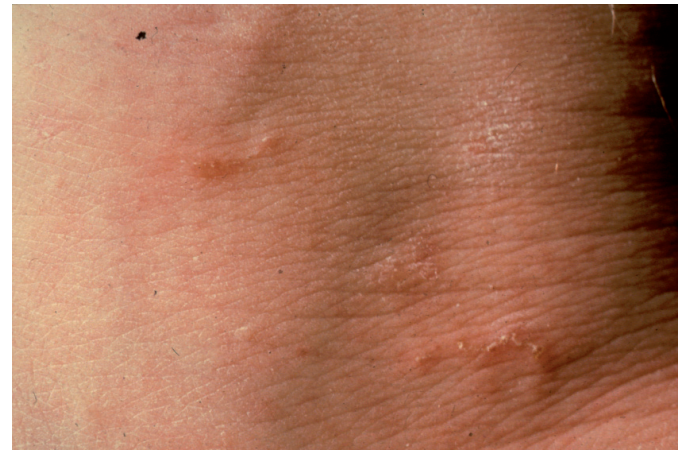

Figure 11. Scabies burrows on the flexural area of the wrist. Scabies burrows are more often seen on fingers and wrists of scabiotic patients.

administered at 7-day intervals have in reducing the total number of body lice in a cohort of homeless men from a shelter in Marseilles, France [99].

Phthiriasis

Pubic lice (*P. pubis*) are usually transmitted by sexual contact among adults and by close contact between parents and children. They are normally located on the pubic and perianal area. In male patients especially, pubic lice can also be found in hair on the abdomen and armpits, as well as the beard and moustache, while in children these lice can also be found in the eye-lashes. Infection in a young child or teenager may indicate sexual abuse. A pubic louse infestation (*phthiriasis*) is diagnosed by looking closely through pubic hair for nits, nymphs and adult lice. The main symptom is itching, usually in the pubic hair area, which results from hypersensitivity to louse saliva and becomes strong 2 or more weeks following initial infestation. In the majority of infestations a characteristic grey–blue or slate coloration appears (maculae corulae) at the feeding site, which may last for days and is also characteristic for the infestation (for recent reviews see [100,101]).

Recently, digital epiluminescence dermatoscopy has been applied for the diagnosis of pubic louse infestations [102].

Figure 12. Scabies burrows on the feet of an infant.

Pubic lice are probably susceptible to most pediculicides used for head lice. A second treatment 10 days after the first is recommended. Recently, treatment with albendazol and ivermectin has been proposed [103104].

All partners with whom the patient has had sexual contact within the previous 30 days should be evaluated and treated, and sexual contact should be avoided until all sexual partners have successfully completed treatment and are thought to be cured. Owing to the strong association between the presence of pubic lice and classic sexually transmitted diseases (STDs), patients diagnosed with pubic lice should undergo evaluation for other STDs [105].

Most recent publications on pubic lice are focused on eyelash infestations (*Phthiriasis palpebrarum*), which are often seen in young children. For the treatment of infested eyelashes, application of permethrin formulations with the help of an applicator, instead of mechanical removal with forceps, has been proposed [106–108].

There have been few epidemiologic studies of pubic lice in recent times, and the exact incidence is unknown. The trends of pubic lice infestation in a risk group of male and female prostitutes in an STD unit in Spain was investigated and it was found that infestation with pubic lice was frequently associated with STDs. Homosexual men were infested and reinfested more often than heterosexuals and, in general, reinfestations occurred more frequently in male than in females prostitutes [101]. Among soldiers of the Israeli Defense Forces, pubic louse infestations were more prevalent in the cooler months of the year. A significant negative association was found between both the number of years of formal education and a measure of socioeconomic status with infestation with both head and pubic lice [109–111]

Scabiosis

Scabies is an intensely pruritic disorder induced by a delayed type hypersensitivity response (type IV immune reaction) to infestation of the skin by the mite *Sarcoptes scabiei* (Figure 8). The female mite penetrates the skin and excavates a burrow in the stratum corneum/epidermal junction. During the next 2–3 weeks it lays 3–4 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 (Figure 9).

Generally, prolonged skin-to-skin contact is required for transmission (a quick handshake or hug will not usually spread infestation). Infestation is easily spread to sexual partners and household members and may also occur by sharing clothing, towels and bedding.

In many tropical and subtropical areas, such as Africa, Egypt, Central and South America, northern and central Australia, the Caribbean Islands, India and Southeast Asia, scabies is endemic. In industrialized countries, scabies is observed primarily in sporadic individual cases and institutional outbreaks. Epidemiological studies indicate that the prevalence of scabies is not affected by sex, race, age or socioeconomic status. The primary contributing factors in contracting scabies seem to be poverty and overcrowded living conditions [112].

The burrows of the female are found mainly on hyperkeratotic areas on the sides of hands and fingers (Figure 10), finger webs and flexural areas of wrists (Figure 11), but also on elbows, feet (mainly infants) (Figure 12), genitalia (Figure 13), buttocks, around the nipples and in axillae. The dermatosis related to the hypersensitivity 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 troublesome at night. Those who are infested more than once begin to show symptoms within a day or two.

A papular polymorphic rash may be visible in areas such as around the waist (Figure 14), inside the thighs, on the lower buttocks, lower legs, axilla (Figure 15), ankles and wrists. Secondary infections are common (Figure 16).

Nodular lesions develop in approximately 7% of scabietic patients (Figure 17). The lesions appear during active scabies and consist of itchy, round, reddish-brown smooth nodules, 5–8 mm in diameter. They characteristically persist after the rest of the eruption has cleared with treatment. Such nodules may develop on the front folds of the axillae, around the naval and, in males, also around the groin. Nodules have been regarded as a reaction of the reticuloendothelial system to mite antigens. Typical and atypical clinical presentations with pruritus as a hallmark of scabies occur in young, pregnant, immunocompromized and elderly patients and include bullous and crusted (Norwegian) manifestations, as well as those masked by steroid use (scabies incognito).

Crusted scabies is characterized by the involvement of all parts of the body, including head and neck. The nails are often affected, resembling onychomycosis (Figure 18). Crusted scabies may begin as ordinary scabies with burrows, papules and vesicles in the same places but later a keratotic reaction develops. The patient is usually suffering from Down's syndrome, mental deficiency, neurological disorders, immunosuppression due to corticosteroid treatment, radiation or AIDS. The burden of mites can reach several thousands in people who are severely immunocompromized [113,114].

The diagnosis of scabies is commonly made clinically by examining the burrows or rash. 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 scarping, by surface microscopy using a dermatoscope [115].

A negative result 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 have obscured the presentation.

Recently, *in vivo* reflectance confocal microscopy has been used for the diagnosis of scabies [116] (for reviews see [3,117–119]).

Scabicides

Permethrin, lindane, crotamiton, ivermectin, sulfur and benzyl benzoate are widely used for the treatment of scabies (for reviews see [119,120]).

Crotamiton

Crotamiton (10%) was effective after two applications over a 24-h period, but the success rate was less then 100% [121]. Poor results were obtained by several authors [122,123]. Crotamiton is odorless, nongreasy, nonirritating and has antipruritic properties and, accordingly, is a good medication for the persistent post-scabietic itch. It has been advocated for the treatment of children [124], but appears to require prolonged application. 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 10% sulfur ointment is an effective treatment for scabies [117]. 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 about the clinical efficacy of such a combination. The cream should be applied once daily for 3–5 days and 48 h after the last application the entire body should be washed in a warm bath. Local irritation, rash or inflammation were rarely observed.

Figure 13. Scabies burrows on the penis of an infested patient.

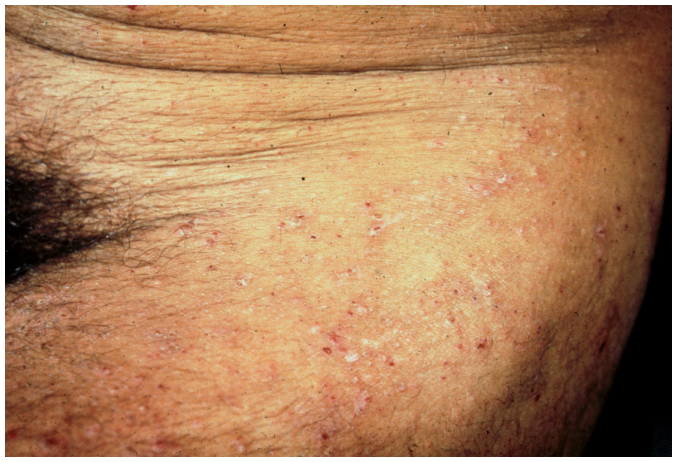

Figure 14. Scabies rash seen around the waist and thighs.
A common polymorphic rash may be seen practically everywhere on the skin. The abdomen, waist, inner thighs, lower buttocks, lower legs and armpits are usually affected.

Benzyl benzoate

It is generally accepted that 25% benzyl benzoate aqueous emulsion gives reliable results. The emulsion should be applied to the body after a bath or shower and left for 5–10 min to dry before dressing. Benzyl benzoate could cause scrotal irritation and should not be used if there is any broken surface on the skin. It is also a conjuctival irritant and should not be used in infants and young children [117].

Gamma benzene hexachloride (lindane)

Earlier clinical trials showed that three applications of lindane were 100% successful [125,126]. However, more recent studies showed that the cure rate was approximately 85% [127,128]. In total, 11 instances of aplastic anemia and two of leukemia suspected to have been caused by contact with lindane were reported [129]. Lee and Groth 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 [130]. Rasmussen reviewed the literature on lindane and came to the conclusion that its benefits probably outweighed its risks, taking into consideration that 30 million units were sold over a 5-year period [131]. It is recommended that lindane is applied to cool dry skin for 30 min–6 h [132,133]. It is not recommended for infants, small children or pregnant women and should not be used on inflamed, secondarily infected or heavily excoriated skin. Treatment should not be repeated within 8 days [134]. Resistance of scabies mites to lindane was reported [135].

Ivermectin

Ivermectin is a chemically modified avermectin. It has a broad spectrum of activity against numerous nematodes and arthropod parasites. It has been widely used for the treatment of sarcoptic mange in animals in topical, oral and parenteral preparations. In humans, oral ivermectin for scabies is increasingly used worldwide, particularly for crusted scabies [118,136] and was recently approved for treatment of ordinary scabies in France [137].

Efficacy of scabicides

In the Cochrane Database of Systematic Reviews, 20 small trials involving 2392 people were included [138]. One trial was placebo controlled, 16 compared two or more drug treatments, two compared treatment regimens and one compared different drug vehicles. Fewer treatment failures occurred by day seven with oral ivermectin in one small trial (55 participants). Topical permethrin appeared more effective than oral ivermectin (85 participants, one trial), topical crotamiton (194 participants, two trials) and topical lindane (753 participants, five trials). Permethrin also appeared more effective in reducing itch persistence than either crotamiton (94 participants, one trial) or lindane (490 participants, two trials). One small trial did not detect a difference between permethrin (a synthetic pyrethroid) and a natural pyrethrin-based topical treatment (40 participants). No significant difference was detected in the number of treatment failures between crotamiton and lindane (100 participants, one trial), lindane and sulfur (68 participants, one trial), benzyl benzoate and sulfur (158 participants, one trial) and benzyl benzoate and natural synergized pyrethrins (240 participants, one trial); all were topical treatments.

No serious adverse events were reported. A number of trials reported skin reactions in participants randomized to topical treatments. It was concluded that topical permethrin appears to

Figure 15. Skin rash on the axilla of a patient with scabies.

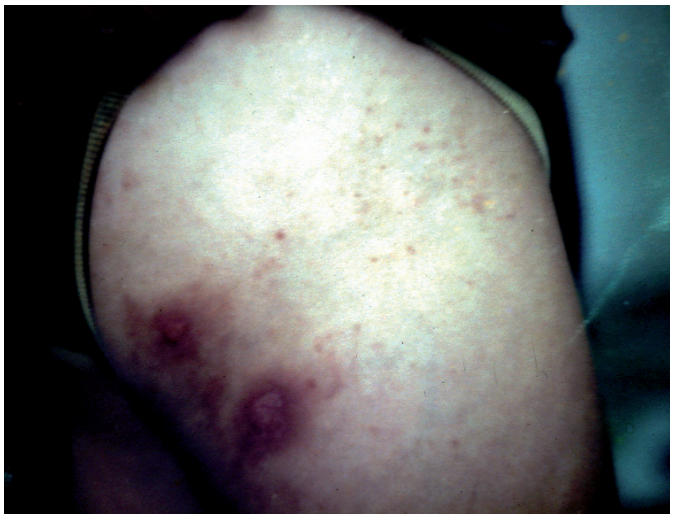

Figure 16. Secondary infection due to scabies infestation. Pruritus, which accompanies the skin rash, urges the patient to scratch themself persistently, leading to superinfections.

be the most effective treatment for scabies. Ivermectin appears to be an effective oral treatment.

Permethrin

In the last 10–15 years, permethrin 5% dermal cream has been the treatment of choice [127,135,139–143]. It is important to note the following points when treating the patient:

- 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 of the head to the soles of the feet;
- Remember to remove watches and rings;
- 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 h 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.

Limited effective treatments, coupled with recent observations of emerging drug resistance to oral ivermectin and permethrin 5% [144,145], raise concerns regarding the future control of scabies, especially in severe cases and in endemic areas where repeated community treatment programs are in place [146].

Further measures regarding the treatment

Permethrin 5% dermal cream is suitable for use by adults, including the elderly and children. However, children between 2 months and 2 years of age and pregnant women should be treated under medical supervision.

- 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, as very dry areas of skin absorb more cream;
- The itch may persist for a week or more after treatment. This does not necessarily imply a failure of treatment or reinfestation. However, if fresh spots appear or lesions still remain 4 weeks following 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 with allergy to chrysanthemum or permethrin;
- Clothing, towels and bed-clothes used by the infested person in the 48-h period prior to treatment should be laundered using the hot cycle or dry cleaned. Alternatively, items may be placed in a dry place for approximately 1 week before they are reused, as mites cannot survive lengthy periods away from the human body;
- Treatment in those with crusted scabies should also include their face, neck, scalp and ears;

Figure 17. Nodular scabies. Nodular lesions are seen in approximately 7% of patients with scabies. The lesions (5–8 mm in diameter) appear during active scabies infestation and can been seen weeks after a successful treatment.

Figure 18. Crusted scabies. Also known as Norwegian scabies, this form of scabies is characterized by the involvement of all parts of the body, intense hyperkeratosis and by the high number of mites found in the skin.

- For crusted scabies, treatment with an oral ivermectin may also be considered;
- Secondary infections should be treated with appropriate oral antibiotics.

S. scabiei of animal origin, such as dog, cow or goat, may penetrate human skin. However, it cannot develop there and dies within few days without reproducing itself. Accordingly, it is necessary to treat the animal with scabicides and the patient with antipruritic medication.

Recently, permethrin- and ivermectin-resistant strains of *Sarcoptes* mites have been reported in the literature [154,145,147,148].

Expert commentary

Head louse and scabies infestations will continue to be prevalent in all socioeconomic levels of our societies. The prolonged incubation times (4–8 weeks) before the appearance of pruritus accompanying head lice infestations and the development of delayed-type hypersensitivity reaction to scabies infestation make early diagnosis of these parasitosis difficult and, accordingly, contact persons will continue to be infested and reinfested with these ectoparasites. Owing to the fact that these parasites are able to develop resistance to chemicals, control and treatment will remain a continuous challenge to health providers and the pharmaceutical industries.

Five-year view

Lice will probably develop resistance to any old or new classical insecticide more quickly in the future. Alternative methods, such as silicon derivates, physical methods (heat) and natural products (which are usually a mixture of several complex molecules) will replace the classical pediculicides that are usually based on single molecules.

Limited effective treatments, coupled with recent observations of emerging drug resistance to oral ivermectin and permethrin 5%, raise concerns regarding the future control of scabies, especially in severe cases and in endemic areas. Therefore, new acaricides should be found to better control scabies infestations in the future. Owing to possible crossresistance, no other pyrethroids should be introduced as scabicides.

Furthermore, progress in molecular biology and cloning of relevant antigens could enable the development of new diagnostic methods and candidate vaccines.

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Key issues

- A louse comb should be used for the detection of lice where possible.
- The diagnosis and treatment of an active louse infestation should be based only on the detection of living lice.
- Children presumed to be infested with lice should not be immediately excluded from the school, camp or childcare setting.
- Children should not be made to feel responsible and should not be blamed for an infestation with lice.
- Head louse control can only be achieved by more involvement of the school nurse, increased awareness, better recognition of infestation and improved education of school staff, parents and health providers.
- Permethrin 5% is the treatment of choice for scabies.
- Ivermectin should be used for crusted scabies.
- Resistance of scabies mites to ivermectin and permethrin has been reported and alternative treatment modalities should be investigated.

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