Skin infections in developing countries

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Purpose of review

In developing countries, where the majority of people have a low income and live in resource-poor settings, skin infections are prevalent. Data from recent studies provide insight into the most common skin infections and their management.

Recent findings

Several studies confirm that skin infections account for the majority of pediatric mortality and morbidity in developing countries. They are prevalent in resource-poor settings and rural areas in certain parts of the world. Also, hot, humid climates and overcrowding predispose to skin infections. Most of the skin infections are curable with effective medication.

Summary

Skin infections are of particular importance in developing countries. This review focuses on the most common skin infections and summarizes the most recent knowledge on the epidemiology, morbidity, and treatment in resource-poor settings.

Keywords

children, infection, skin

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Introduction

The incidence of skin diseases is especially affected by geographic and socioeconomic factors in developing countries [1]. Various skin disease surveys conducted in developing countries have concluded that skin diseases are very common in children and adolescents, infections being high on the list [2–4]. The higher frequency of skin infections in developing countries is due to large rural populations with low socioeconomic status [2]. This review concentrates on the most common primary skin infections and infestations in developing countries, those potentially serious if not diagnosed and treated.

Pyoderma

Pyoderma is the general name, often applied loosely, for bacterial infections of the skin. It therefore includes the main bacterial infections such as impetigo, ecthyma, folliculitis, furuncle, and carbuncle, but extends to the rarer conditions such as necrotizing fasciitis [5••,6••]. Pyodermas are found more often in children from families with low socioeconomic status who live in overcrowded conditions and are undernourished. In endemic areas the incidence of pyoderma seems to vary during the year, with the peak occurring in the hot and humid season [7].

Although pyoderma can be caused by group A *Streptococcus pyogenes* (GAS) and *Staphylococcus aureus*, boils, furuncles, and carbuncles are usually caused by *S. aureus* infections [6••].

The commonest of the diseases among the spectrum of pyoderma is impetigo, which is a bacterial infection of the superficial layers of the epidermis. Children normally become infected through contact with other children, but fomites are another source of infection.

Impetigo contagiosa is the most prevalent type of impetigo [8]. Previously *S. pyogenes* was the bacterium most often associated with impetigo contagiosa; however, *S. aureus* has been implicated in this disorder more frequently [9]. The typical presentation of impetigo contagiosa starts with a single 2–4 mm erythematous macule, which soon becomes vesicular or pustular. The vesicles are delicate and easily ruptured, leaving an exudate characteristic 'honey-colored' yellow crust over the superficial erosion (Fig. 1). Direct extension rapidly follows, causing several individual or coalesced macules and patches to erupt, which may be eroded or crusted [8].

Poststreptococcal glomerulonephritis is a relatively unusual but occasionally serious complication of pyoderma, which is related to infection with nephritogenic strains of β-hemolytic group A streptococci [10]. Appropriate treatment with antimicrobials generally does not have any effect on the risk of poststreptococcal glomerulonephritis [11].

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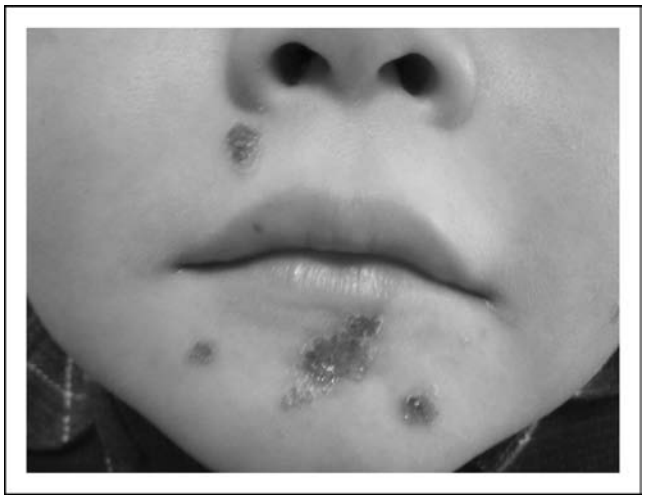
Figure 1 Characteristic impetigo lesions with crusts on the perioral area of a boy



Differential diagnosis of impetigo contagiosa includes herpes simplex, varicella, atopic dermatitis, contact dermatitis, dermatophytosis, candidiasis, scabies, pediculosis, and childhood discoid lupus erythematosus [8].

Common impetigo, also known as secondary impetigo, can complicate herpes simplex, acute vesicular dermatitis, pediculosis, scabies, and insect bites which cause breaks in the skin. The clinical presentation is similar to impetigo contagiosa. The course of the underlying disease is often improved with treatment of impetigo [8].

Bullous impetigo most commonly affects neonates. *S. aureus* can be isolated from the skin lesions. Initially, large, superficial, fragile bullae can develop on the trunk and extremities. Frequently, only remnants of the bullae are seen, which are annular or oval superficial erosions with a typical collarette of scale at the periphery of the bullae [8]. There is epidermal separation caused by a staphylococcal exotoxin, usually made by phage group 2 [12]. The most common systemic symptoms of bullous impetigo include weakness, fever, and diarrhea. Meningitis and pneumonia are much rarer, but they are the most severe complications, which may lead to death. Differential diagnosis of bullous impetigo includes pemphigus vulgaris, bullous pemphigoid, thermal burns, Stevens–Johnson syndrome, bullous erythema multiforme, and necrotizing fasciitis [8].

The identity of a skin pathogen causing pyoderma may be confirmed through culture of a specimen collected from the moist areas below the crusty surface of the lesion. In many cases a microbiologic diagnosis is not necessary, although it may be indicated in severe infection or infection not responding to standard therapy [6••].

Topical antibiotic therapy with sodium fucidate, mupirocin, or retapamulin is appropriate for settings where pyoderma occurs sporadically but not in endemic or epidemic situations. In the settings with high prevalence of pyoderma, oral antibiotics should be used [6••,13]. A range of oral antibiotics are effective in eradicating bacterial skin infections. Group A streptococci are still sensitive to penicillin, with alternatives for staphylococcal infections being cloxacillin, flucloxacillin, and erythromycin [5••].

Anthrax

Anthrax is a zoonosis that essentially affects grazing herbivorous animals. Humans are incidental hosts, and are infected through direct or indirect contact with animals or contaminated products [14]. The causative agent, *Bacillus anthracis*, is a Gram-positive aerobic or facultatively anaerobic, nonmotile, spore-forming bacterium [14,15]. Although the incidence of anthrax is diminishing in developed countries, it remains as a considerable public health problem in developing countries, especially those whose main source of income is farming [16••].

The clue to the diagnosis of anthrax is the history and rapid development of a painless ulcer surrounded by extensive nonpitting edema. The lesion results in a necrotic eschar. Patients with cutaneous anthrax may have fever, extensive edema, and other systemic signs [16••,17••]. The differential diagnosis of cutaneous anthrax includes spider bite, ecthyma, accidental vaccinia, ulceroglandular tularemia, and necrotic herpes simplex [16••].

The diagnosis is confirmed by bacteriological examination of infected tissue (Gram staining and culture) or isolation of the bacillus from blood cultures in systemic infections [18].

Penicillin G is still the drug of choice in the treatment of anthrax, but ciprofloxacillin and doxycycline have also been recommended as first-line therapies [16••].

Cutaneous diphtheria

Chronic carriage of *Corynebacterium diphtheriae* on skin remains common in developing countries [19]. The disease is characterized by shallow skin ulcers, which can occur anywhere on the body and are usually chronic [20].

Any break on the skin can become colonized with *C. diphtheriae*, leading to cutaneous ulceration [19]. They are often associated with infected insect bites, frequently coinfected with pathogens such as *S. aureus* and *S. pyogenes* [20]. Common sites for diphtheric lesions include the lower limbs, feet, and hands [19].

Systemic toxic manifestations are uncommon among immunized persons. The lesions of cutaneous diphtheria are an important reservoir of infection and can cause respiratory and cutaneous infections in contacts as well as outbreaks [21]. Severe nonrespiratory disease, including septicemia, septic arthritis, and endocarditis has also been reported after infection with nontoxigenic strains [22].

Cutaneous diphtheria is less likely to be diagnosed than respiratory infection, because the clinical appearance is nonspecific, and other pathogens often coinfect the lesions. In case of chronic nonhealing skin lesions, wound swab samples should be examined for *C. diphtheriae*, especially in disease endemic areas [20].

Erythromycin or clindamycin is recommended for the treatment of cutaneous diphtheria, but penicillin has also been reported to be effective. It is also recommended that erythromycin is given to close contacts of patients with toxigenic diphtheria to eliminate symptomless carriage [19].

Cutaneous tuberculosis

Despite prevention programs, tuberculosis is still progressing endemically in developing countries [23]. Tuberculosis of the skin is caused predominantly by *Mycobacterium tuberculosis* but can also be produced by *Mycobacterium bovis*, and, under certain conditions, by the bacillus Calmette-Guérin, an attenuated strain of the former [24]. Although the portal of entry is often the respiratory tract, skin also may be primarily involved [25].

Inoculation from an external source causes a primary complex similar to that seen in the lung, with histology showing granulomatous inflammation and caseating necrosis. The skin lesion starts as a reddish-brown, painless nodule, which ulcerates. Regional lymphadenopathy develops and may drain through a sinus tract. Warty tuberculosis occurs with skin inoculation, usually on the hands or arms in previously sensitized individuals. BCG vaccination causes local lymphadenitis and ulceration in up to 10% of recipients if injected too deeply [26].

Spread from an underlying focus such as lymph node or bone causes an abscess which forms by continuity or fistula formation from an underlying nidus with subsequent induration of surrounding areas resulting in an ulcer surrounded by keloid tissue. It is known as scrofuloderma, and the most commonly affected areas are the neck, axillae, chest wall, and groin [27].

Orificial tuberculosis occurs by autoinoculation from pathogens in the respiratory or gastrointestinal tract. This causes poorly healing ulceration around the nose, mouth, and perineum, and is usually a sign of overwhelming infection [26].

Miliary tuberculosis is the form usually seen in the context of advanced pulmonary disseminated tuberculosis arising from hematogenous source. The trunk is the most common location, with small erythematous macules or papules that become necrotic [27].

Lupus vulgaris, the most common form of cutaneous tuberculosis, is due to hematogenous spread. It presents as a slowly enlarging plaque with a slightly elevated verrucose border and central atrophy. The consistency is soft, and the color is reddish brown, having a classic 'apple jelly' appearance on diascopy. Lupus vulgaris of the face produces scarring and facial deformity [27].

The Mantoux intradermal test, histopathologic examination, chest X-ray, and polymerase chain reaction (PCR) may be helpful when cutaneous tuberculosis is suspected. The demonstration of acid-fast bacilli by Ziehl–Neelsen staining is the absolute criterion for the diagnosis, although culture is usually negative [23,26,28].

Standard therapy regimens involving 2 months of quadruple therapy (isoniazid, rifampicin, pyrazinamide, and ethambutol) followed by a further 4 months of isoniazid plus rifampicin are adopted in most centers [27]. Failure to respond to therapy raises the possibility of drug resistance [29].

Buruli ulcer

Buruli ulcer, caused by *Mycobacterium ulcerans*, is endemic in rural wetlands of Africa, the Americas, Asia, and Australia. The disease can afflict all age groups, but children younger than 15 years old represent the largest part of the Buruli ulcer disease burden. Humans become infected by traumatic introduction of *M. ulcerans* into skin from the overlying *M. ulcerans* contaminated surface. Contamination of the skin could result from direct exposure to stagnant water, aerosols arising from ponds and swamp surfaces, or fomites [30••]. Aquatic insects have been suspected to be involved in transmission but this mode of transmission remains unproven [31]. Initial infection is primarily related to two properties of *M. ulcerans*: optimal growth at 30–33°C and elaboration of the toxin, myolactone [32].

The lesion appears as a small painless nodule. After a few weeks the lesion begins to fluctuate. This eventually breaks down and forms an indolent ulcer which is painless and has a necrotic base with an undermined rim. The base later assumes the aspect of red granulation tissue [17••]. Healing leads to fibrosis and scarring and can severely limit movement. The scar may form keloids

and often causes major contraction deformities. Differential diagnosis includes stasis, diabetic, or tropical phagedenic ulcers, leishmaniasis, deep fungal or atypical mycobacterial infections, cutaneous tuberculosis, other bacterial infections, arthropod bites, pyoderma gangrenosum, and autoimmune disease [32].

For laboratory diagnosis, direct smear examination by Ziehl–Neelsen or auramine stain, culture, PCR, and histopathologic examination are available [30••,32].

There is no specific vaccine against Buruli ulcer. Excisional surgery with primary closure or skin grafting remains the recommended therapy [30••]. Also, the use of rifampicin plus streptomycin is recommended for small and uncomplicated lesions [33].

Leprosy

Leprosy is a chronic granulomatous infection, principally affecting the skin and peripheral nerves, caused by the obligate intracellular organism *Mycobacterium leprae* [34]. Transmission of *M. leprae* is from untreated lepromatous patients [35].

The clinical features are determined by the host response to *M. leprae*. Patients commonly present with skin lesions, numbness or weakness caused by peripheral nerve involvement, or, more rarely, a painless burn or ulcer in an anesthetic hand or foot. Tuberculoid disease is characterized by a single or a few lesions. These are macules or plaques with well defined edges. In dark skin, hypopigmentation predominates over the erythema, or copper color, more easily seen in lighter skin. Acid-fast bacilli are not seen histopathologically. In lepromatous disease, the early skin changes are widely and symmetrically distributed macules with mild hypopigmentation and erythema. Flesh-colored and occasionally erythematous papules and nodules may be present. The skin thickens because of dermal infiltration, giving rise to the 'leonine facies'. Hair loss, notably from eyelashes and eyebrows (madarosis) is seen. Abundant acid-fast bacilli are seen histopathologically. Borderline leprosy is the intermediate form between the two polar forms [35].

Nerve involvement in leprosy affects sensory, motor, and autonomic function of peripheral nerves. Sensory loss is the earliest and most frequently affected modality, but a predominantly motor loss can also occur. Involvement of autonomic fibers causes a reduction in sweating in skin patches, and a glove and stocking hypohydrosis also occurs [35].

The most severe complication of leprosy, known as leprosy reaction, is extremely common in borderline patients. Type 1 reaction usually develops abruptly as exacerbations of preexisting skin and nerve lesions. Type 2 reactions, also known as erythema nodosumleprosum, occur only in lepromatous and borderline patients and are characterized by abrupt development of crops of red, tender nodules on various part of the body, and histologic evidence of acute inflammation [36•].

Differential diagnosis is dependent on the clinical form of leprosy and the stage of the disease. Vitiligo, pityriasis alba, pityriasis versicolor, and postinflammatory hypopigmentation can mimic leprosy [35]. Borderline lesions can be similar to granuloma annulare and sarcoidosis [28]. Amyloid can cause nerve thickening, and nerve enlargement due to neurofibromatosis can also mimic leprosy [37].

The diagnosis is usually made clinically, but is supported by slit-skin smears and skin biopsy. *M. leprae* cannot be cultured *in vitro* [35].

Leprosy is treated with a multidrug therapy regimen with dapsone, clofazimine, and rifampicin [38]. Reactions are common during treatment and may be managed with corticosteroids, thalidomide, or clofazimine [38,39].

Scabies

Scabies is an ectoparasitic infection caused by the mite *Sarcoptes scabei* [5••]. It is spread by close physical contact and particularly common among the poor and when there is overcrowding. The organisms can survive in bed linen, clothing or other fomites [17••,40••].

Scabies in the typical patient is characterized by itching that is most prominent in the evening. It produces a diagnostic rash with burrows most observed between the fingers, along the sides of the palms, on the heel of the hand, or on the flexor surface of the wrists and ankles (Fig. 2). They are accompanied by small, often excoriated, papules on the wrists, forearms, axillary folds, breasts, hips, penis, and ankles. The presentation of scabies is different in infants and babies. They have eczematous patches over much of the body, including the face. Pustules on the palms and soles are diagnostic for scabies in babies. Crusted scabies occurs when there are thousands or millions of mites on the body. There are psoriasiform or eczematous patches in the scalp, face, trunk, hands, and feet [40••].

The lesions of scabies become easily infected, often with streptococci, which can cause heart and kidney problems. Differential diagnosis includes acropustulosis infantum for scabies in infants, and erythrodermic psoriasis and eczema for crusted scabies [17••].

Scabies is usually a presumptive diagnosis based on the clinical features with the finding of classical skin burows.

Figure 2 Typical burrows and papules on the trunk and upper arm of an infant with scabies

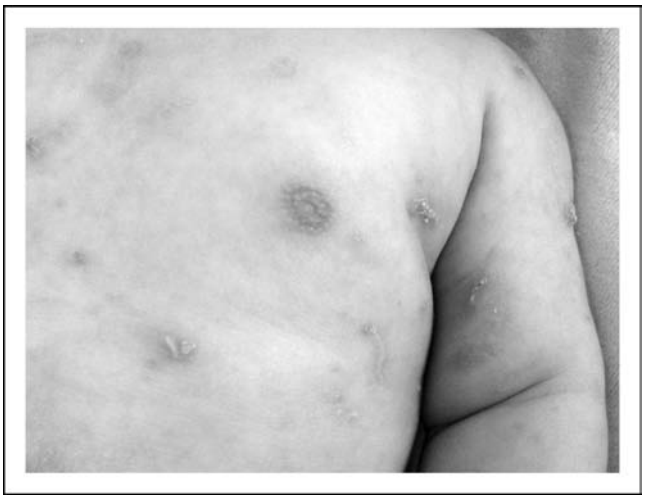
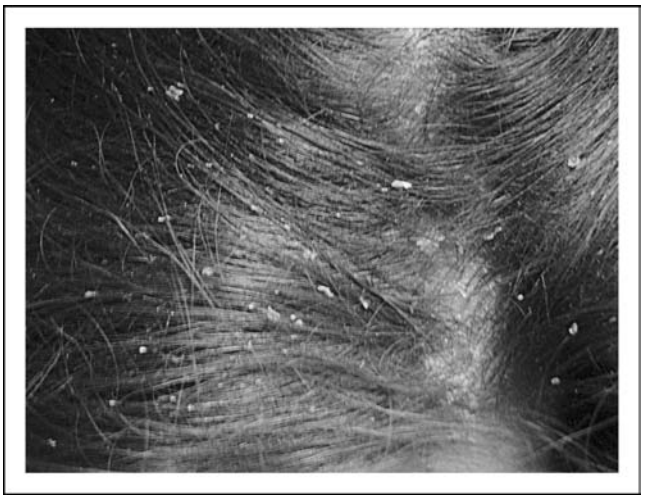


Figure 3 Head lice infestation with nits on the occipital area of a girl



Parasitological diagnosis requires the mineral oil scrape technique to collect skin scrapings for microscopic analysis [6••].

The effective management of the disease requires isolation, careful decontamination of clothing and bed-linens, and treatment of all family contacts. Local treatment has to be extended to the entire tegument, including nails and scalp. The most used topical scabicides are lindane 1%, permethrin 5%, monosulfiram, crotamiton, malathion, precipitated sulfur (6–10%), and benzyl benzoate. Ivermectin, which is approved for use in patients older than 5 years, is the effective oral treatment [41].

Pediculosis capitis

Head lice infestation with *Pediculus humanus capitis* is a worldwide problem during childhood [42]. The incidence is highest (2–15%) in primary school-aged children and is influenced by fashion and population density [43,44]. Close physical contact is necessary for the infestation through adult lice, nymphs, or eggs. Fomite transmission by headwear, helmets, brushes, combs, earphones, bedding, upholstered furniture, and rugs could be significant under certain circumstances [41,42].

Lice are visible only in heavy infestations. Nits are often seen in the occipital and retroauricular regions (Fig. 3) [45,46]. The majority of patients present with pruritus; however, hypersensitivity reactions, erosions, and signs of secondary bacterial infection complicate the actual diagnosis [45,47].

Treatment is recommended for all family members and close contacts, in addition to disinfections of potential fomites. Pharmacological treatment agents are formulated as lotion, shampoo, and cream rinse. Lindane, permethrin 1%, pyrethrins 0.33%, and malathion are the agents used for head lice. Oral ivermectin is suggested as a good option for mass infestations [41].

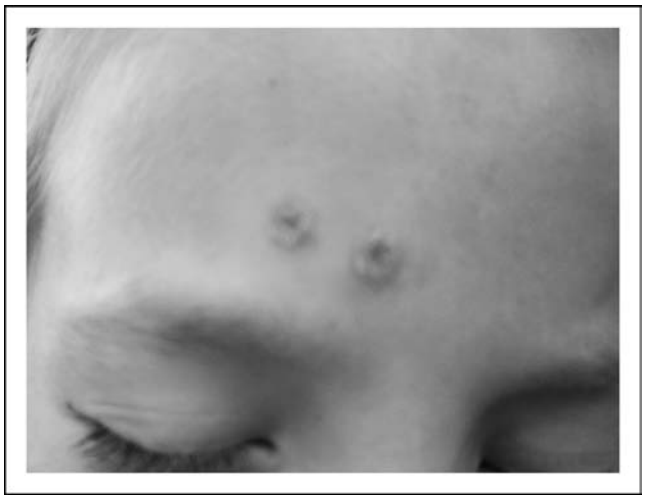
Cutaneous leishmaniasis

Cutaneous leishmaniasis is a health and social problem caused by various species of *Leishmania* protozoa, which are usually transmitted by the bite of infected sandflies [48,49]. There are a great number of *Leishmania* spp., some of which are known to be significant in humans: *Leishmania tropica*, *L. major*, and *L. aethiopica* in the Old World, and the *L. braziliensis* and the *L. mexicana* complex in the New World [50].

In the Old World, the initial presentation is an erythematous papule or nodule that develops at the site of insect feeding, usually on exposed regions such as the face, neck, and arms (Fig. 4) [51]. The papule slowly enlarges in several weeks forming an ulcer with a violaceous border [52]. The lesion heals spontaneously after several weeks to months, leaving a depressed and disfiguring scar [51]. When lesions tend to be more chronic, they develop into recidivans leishmaniasis, a long-lasting, destructive, and difficult-to-treat form [53].

In the New World, the typical and more common lesion is a round ulcer with a much infiltrated border that occurs in exposed areas. Atypical lesions may present in immunocompromised patients as round, nonulcerated nodules. The lesion heals leading to a typical scar characterized by thin and pale skin over the site surrounded by a hyperpigmented halo [54••].

Figure 4 Erythematous nodules of cutaneous leishmaniasis on the forehead of a girl



Diffuse leishmaniasis affects only the skin but with generalized skin lesions. It is seen mainly in Africa, transmitted by *L. aethiopica*. In mucosal leishmaniasis the parasite may spread to the mucous membranes, especially those of the nose, mouth, and throat, and cause extensive destruction. It is seen mainly in South America, but it can also be caused by species from the Old World [48].

Differential diagnosis includes cutaneous tuberculosis, anthrax, actinomycetoma, Buruli ulcer, tropical ulcer, pyoderma gangrenosum, cutaneous lymphoma, and fungal causes such as eumycetoma and paracoccidiodomycosis. Hyperkeratotic lesions may resemble impetigo and psoriasis, diffuse lesions may resemble lepromatous leprosy, and lymphatic involvement may resemble sporotrichosis or *Mycobacterium marinum* infection [49].

The diagnosis of cutaneous leishmaniasis has to be suspected in children presenting with chronic, nodular, or ulcerated lesions. Diagnosis should be confirmed with Giemsa-stained smears looking for amastigotes, histology looking for granulomas +/− amastigotes, culture in NNN medium to grow promastigotes, and PCR with Old World primers [55].

Localized ulcers are treated with electrosurgery, simple excision, or cryosurgery. Topical treatment with paramomycin has been effective in some areas. Intralesional injections with trivalent or pentavalent antimony are of great value. *L. tropica* and *L. major* are sensitive to ketaconazole or itraconazole. For the South American species and some of the Old World species sodium stibogluconate or pentamidine injections have to be given. In severe cases, liposomal amphotericin B may be used. Miltefosine is a new agent that seems effective against a number of species [17••].

Cutaneous larva migrans

Hookworm-related cutaneous larva migrans (CLM) is endemic in resource-poor communities in the developing world, particularly in Brazil, India, and the West Indies. The condition is caused by cat and dog hookworms, most commonly *Ancylostoma braziliense*, *Ancylostoma caninum*, and *Uncinaria stenocephala* [56]. It is acquired by skin contact with the infective larvae that reside in the sand or soil [57]. In humans the larvae are capable of penetrating to epidermis and dermis but cannot progress into mature worms. Thus, larva migrans, typically, is a self-limiting disease [40••].

A reddish papule appears at the penetration site. In most cases, 1–5 days after penetration the elevated track appears. Larvae usually migrate in the epidermis for 2–8 weeks to several months. The itching is intense and pain can also be present [56]. The cutaneous tracks can be single or multiple. Less classic presentations of CLM are folliculitis and eczematous-like eruption [58,59]. Lesions tend to become superinfected with pathogenic bacteria as a result of scratching, particularly in developing countries. The differential diagnosis includes scabies, tinea, cellulitis, contact dermatitis, erythema chronicum migrans, migratory myiasis, and jellyfish stings [56].

The diagnosis of CLM is easily made clinically and is supported by history. Biopsies of the skin are routinely negative for organisms and show only an inflammatory reaction [40••]. Epiluminescence microscopy has been used to visualize migrating larvae [60].

The first recommended treatment for CLM is oral ivermectin in a single dose. The second suggested treatment is topical thiabendazole solution or ointment at 10–15%. Alternative treatments include oral thiabendazole and oral albendazole [57]. Since ivermectin and albendazole perform better and cause fewer adverse events, the use of oral thiabendazole is not recommended [56].

Conclusion

Infections of the skin form a large proportion of skin problems in children in developing countries. In many instances, skin infections can be treated if diagnosed properly. Epidemiological, clinical, and therapeutical aspects of the most common skin infections due to resource-poor settings are summarized in this review offering insight into the disease burden in developing countries.

References and recommended reading

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- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 553).

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