Scabies in the developing world—its prevalence, complications, and management

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Abstract

Scabies remains one of the commonest of skin diseases seen in developing countries. Although its distribution is subject to a cycle of infection, with peaks and troughs of disease prevalence, this periodicity is often less obvious in poor communities. Scabies is a condition that affects families, particularly the most vulnerable; it also has the greatest impact on young children. Largely through the association with secondary bacterial infection caused by group A streptococci and *Staphylococcus aureus*, the burden of disease is compounded by nephritis, rheumatic fever and sepsis in developing countries. However, with a few notable exceptions, it remains largely neglected as an important public health problem. The purpose of this review is to provide an update on the current position of scabies with regard to its complications and control in resource-poor countries.

Keywords: Developing countries, glomerulonephritis, neglected tropical diseases, rheumatic fever, scabies

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Epidemiology

The prevalence and complications of scabies make it a significant public health problem in the developing world, with a disproportionate burden in children living in poor, overcrowded tropical areas [1,2]. The exact number of infected cases worldwide is not known, but is estimated to be up to 300 million [3].

Exhaustive and complete data are not available from many countries, but such data as can be utilized suggest that scabies is endemic in tropical regions, with an average prevalence of 5–10% in children. A WHO review collated data from 18 prevalence studies between 1971 and 2001, and reported a scabies prevalence ranging between 0.2% and 24% [4]. Selected prevalence studies since 2001 are shown in Table 1. It is notable that particularly high prevalence figures have been reported in India, the South Pacific, and northern Australia. For example, in a study of young people in a rural Indian village, the prevalence of scabies was 70% [5] In Australian Aboriginal communities, prevalence figures of up to 50% have been reported, and studies in Fiji, Vanuatu and the Solomon Islands have found the prevalence of scabies in children to be 18.5%, 24%, and 25%, respectively, with the prevalence being as high as 42% in one Fijian village [6,7]. In all regions, the burden of scabies is associated with increased rates of pyoderma and complications of secondary bacterial infection with group A streptococci and *Staphylococcus aureus* [8]. For example, in Fiji, children with scabies were 2.4 times more likely than children without scabies to have active impetigo lesions [9].

A number of epidemiological factors have been proposed as influencing the distribution of scabies infestation in populations, including: age, gender, ethnicity, overcrowding, hygiene, and season. Scabies prevalence was previously thought to be cyclical, but studies of long-term incidence suggest that epidemics and other observed fluctuations are multifactorial,

TABLE 1. Prevalence studies of scabies in developing areas since 2004

Year	Country	Environment	Ages	Study area	Diagnosis	No of people seen	Scabies (%)	References
2005	Turkey	Urban	4–6 years	Preschool	Clinical and scrapings	1134	0.4	[102]
2005	Nigeria	Rural	4–15 years	School	Clinical	1066	4.7	[103]
2005	Brazil	Urban	All ages	Slum	Clinical	1185	8.8	[20]
				Village		548	3.8	
2007	Timor-Leste	Rural	All ages	Four districts	Clinical	1535 (245)[a]	17.3 (39.1)[a]	[16]
2008	Nepal	Rural	All ages	Village	Clinical	878	4.7	[104]
2009	Malaysia	Urban	13–17 years	Boarding schools	Clinical	944	8.1	[105]
2009	Brazil	Rural	All ages	Village	Clinical	1014	9.8	[106]
2009	Fiji	Rural/urban	5–14 years	Schools	Clinical	3462	18.5	[9]
2010	Malaysia	Urban	Children	Welfare home	Clinical	120	31	[22]

[a]In brackets - children < 10 years.

being related to social and environmental changes such as wartime, overcrowding, and climatic changes [10–14]. Endemic rates in many tropical countries, without the significant fluctuations reported elsewhere, suggest that the role of herd immunity is likely to be more limited than previously thought [15].

Whereas in developed nations the rates of infestation are similar across age ranges [12], the highest rates in developing countries are among preschool children to adolescents; rates significantly decrease in mid-adulthood, and increase in the elderly [13,16]. The attack rate is probably equal between the sexes, and the differences in prevalence reported in some studies are probably attributable to confounding factors [17]. Differences among racial groups have also been described, and are probably attributable to socio-economic and behavioural factors [10,17].

Overcrowding is an important factor in the spread of scabies. Studies from Mali, India, Brazil and northern Australia all show an association with overcrowding, especially sleeping quarters [7,18–20]. Closed communities and institutional environments experience high endemic rates and epidemic outbreaks in tropical and developing countries. For example, 86% of children in a Sierra Leone displacement camp [21], 31% of children in a Malaysian welfare home [22] and 87% of children in a Thai orphanage had scabies [23]. The role of hygiene is controversial [24]; although poor hygiene has been associated with high impetigo prevalence, and the use of soap and water has been shown to reduce the prevalence of impetigo [8,25], the available data suggest that hygiene is not a significant factor for scabies infestation [26].

Overwhelmingly, the highest global rates of scabies are seen in countries with hot, tropical climates [24]. However, scabies is not limited to these regions. For example, studies from Scotland and Israel demonstrated higher rates during cooler seasons [11,27]; it has been suggested that this may be related to increased human personal contact and overcrowding, as well as increased mite survival and fertility in cold weather [28,29], possibly because of microenvironmental conditions at the skin surface.

Crusted scabies is usually seen in immunocompromised patients, especially in those with human immunodeficiency virus infection, human T-lymphocytic virus I infection, or medical immunosuppression, as well as in those with leprosy and developmental disability, including Down syndrome. However, there are reports of crusted scabies in those with no identifiable immunodeficiency, especially Aboriginal Australians [15,30,31].

Transmission

The transmission of scabies occurs with the burrowing of *Sarcoptes scabiei* into the epidermis of the skin. Fertilized adult female mites burrow into the stratum corneum, laying 0–4 eggs per day for up to 6 weeks before dying. The entire developmental life cycle, from egg to adult, involving three active intermediate stages or instars, takes c. 2 weeks. However, classic transmission studies have documented the first observation of an adult female 3 weeks after initial colonization [32]. In primary infestations, an increase in *S. scabiei* numbers for up to 4 weeks has been reported, with a gradual reduction to c. 10–12 mites as host immunity develops. In contrast, the severe form of the disease, crusted scabies, is characterized by extremely high mite burdens and severe crusting of the skin [33].

The most common source of transmission is prolonged skin-to-skin contact with an infected individual (hand-holding, sexual contact, etc.). It takes c. 15–20 min of close contact for successful direct transmission, and for this reason scabies is also considered to be a sexually transmitted disease. Intrafamilial transmission is frequently reported, and genotyping results confirm long-held beliefs that transmission events for *S. scabiei* tend to be localized in time or space, and that the family/household is the focus of transmission [34,35]. However, cultural changes, such as the increasing use of institution-

alized care for the elderly and day care for the very young, establish susceptible populations, and increasing institutional outbreaks of scabies are now being reported in the literature.

Early classic studies proposed that it is the newly fertilized adult female that is primarily responsible for transmission, as up to 90% of immature mites die before reaching the adult life stage [32,36]. An individual with a low parasite burden can be cured by removal of only the adult females [37], and Mellanby [36] was unable to establish an infestation by using immature mites only. However, as the adult female rarely leaves the burrow, the active, more immature, forms may be responsible for transmission [38]. Infestations with high parasite rates (>100 adult females) will have a proportionally much greater number of developmental instars than adult females, supporting the contention that the immature life-cycle stage may be capable of transmission.

Blankets and clothing do not appear to be important in transmission, and there is no conclusive evidence to suggest that washing of clothing and blankets is necessary for the prevention of spread. Live mites have been recovered from the homes of scabetic patients [39]. The mite is an obligate parasite and is highly susceptible to dehydration when off the host. At temperatures below 20°C, mites are almost immobile. Significantly, in tropical conditions (30°C and 75% relative humidity), female mites have been shown to survive for 55–67 h off the host [40], suggesting that, in these regions, fomites may be a potential source of transmission. It is of note that eggs can remain viable at low temperatures for up to 10 days off the host, indicating that shed skin harbouring eggs is a potential source of infestation. This is particularly pertinent in cases of crusted scabies, where the patient's surroundings are contaminated with shed epithelial debris containing all life stages. Animal scabies mites can sometimes infect humans, but these infestations are self-limiting, and most cases and outbreaks of scabies are caused by the human strain [35].

Pathogenesis

The pathogenesis of scabies involves many complex immunological and inflammatory pathways, some of which we are only just beginning to understand. Skin inflammation, papules and pruritus result from an immune-mediated antigen-specific delayed hypersensitivity reaction. The initial 3–4 weeks after the primary infestation are usually symptomless. In subsequent infestations, however, symptoms reappear much more rapidly, in approximately 1–2 days. Mellanby, in an attempt to re-infest patients who had been previously infected, was successful with only 40% of his subjects, indicating the development of protective immunity [35].

Two major forms of disease are recognized, ordinary and severe crusted scabies, and are associated with protective and pathological host responses, respectively. The different clinical manifestations result from the type and magnitude of the innate, cellular and humoral responses to mite proteins. Some of the possible allergens potentially causing this immune response have now been identified as a result of the scabies gene discovery project [41]. Reports have now documented that patients with both crusted scabies and ordinary scabies have strong cellular and humoral responses to multiple *S. scabiei* homologues of house dust mite allergens [42]. Current data indicate that the protective immune response in ordinary scabies is dominated by a Th1-type cytokine profile associated with CD4^{+} T-lymphocytes, whereas the severe form of crusted scabies is dominated by a nonprotective Th2 cytokine profile, and there is evidence that the predominant effector cells in the skin may be CD8^{+} lymphocytes [43]. Analysis of cytokine levels showed that the interferon-γ/interleukin (IL)-4 ratio was significantly higher in *S. scabiei*-stimulated peripheral blood mononuclear cells (PBMCs) from ordinary scabies patients than in PBMCs from crusted scabies patients, and increased levels of IL-5 and IL-13 were observed in stimulated PBMCs from crusted scabies as compared with PBMCs from ordinary scabies patients [44]. Interestingly, PBMCs stimulated with scabies mite extracts in healthy subjects showed increased production of the regulatory cytokine IL-10. Accumulation of eosinophils and production of total and specific IgE can be seen in both forms, but are highly elevated in crusted scabies [45]. Mechanisms of tissue damage in crusted scabies include direct cytotoxicity against keratinocytes, mostly mediated by CD8^{+} T-cells, and release of cytokines, which amplify the inflammatory response by targeting resident skin cells. The roles of skin keratinocytes, eosinophils and basophils are not well understood, but are likely to be critical to understanding the evolution of the immune response in scabies.

Tissue-feeding parasites face significant dangers to their early survival, owing to host innate immune responses. Scabies mites feed on epidermal protein and host plasma, and are exposed both internally and externally to host defence mechanisms. Studies have found that uncharacterized mite proteins have immunomodulatory properties that favour invasion of the host by the parasite via downregulation or depression of inflammatory processes of resident cells in the skin, and possibly by influencing a delayed immune reaction [46]. Experiments on human skin equivalents have demonstrated that scabies mites can downregulate the expression of many cytokines and adhesion molecules of skin epidermal keratinocytes, dermal fibroblasts, and dermal microvascular endothelial cells [47–49]. Complement has been shown to be an important

component in host innate defence against ectoparasites, as shown in blood-feeding ticks [50,51]. A scabies mite-binding protein of gut origin (peritrophin) has been recently identified within the mite gut as potentially binding to mannan-binding lectin, and thus activating the lectin pathway of human complement activation [52]. Interestingly, with the identification of a family of inactive multiple scabies mite homologues of the group 3 serine protease allergens, a novel host immune evasion strategy has been proposed for the scabies mite [41,53]. Two of these scabies mite-inactivated protease paralogues were recombinantly expressed and shown to inhibit all three pathways of the human complement system [54].

Another major subset of T-cells conprises the Th17 cells, which are recognized as stimulating many cells of the innate immune system; in particular, they recruit to and activate neutrophils at sites of inflammation, and stimulate endothelial and epithelial cells to synthesize the inflammatory cytokines IL-1, IL-6, and tumour necrosis factor-α. Impairment of the IL-17 pathway is associated with hyper-IgE syndrome [55], whereas increased proliferation of Th17 cells is observed in psoriatic plaques [56]. Preliminary findings of elevated IL-17 and IL-23 in crusted scabies are the first to indicate a contribution of Th17-associated cytokines to a dysregulated immune response in crusted scabies pathology (K. Mounsey, personal communication).

Finally, the host-specific behaviour and transient nature of cross-infestation on an unnatural host by scabies mites also points towards possible factors beyond immunity in host protection and pathology. Physiological compatibility becomes critical once a parasite makes intimate contact with a potential host. Physiological compatibility is defined by the availability of appropriate and sufficient nutrients and suitable physical, chemical and immunological conditions for the parasite to develop and reproduce. As well as digesting host proteins as a food source, scabies mite proteases would facilitate the invasion of host tissues, assisting in skin penetration and tissue migration. Characterization of parasite excretory/secretory products is vital for further understanding of host–parasite relationships [57]. Emerging *S. scabiei* resistance to available treatments and concerns about the effects of drug residues on consumer health emphasize the need to develop effective antiparasite therapies. Improved understanding of scabies pathogenesis will aid the development of vaccines or new therapeutic treatments for susceptible populations.

Clinical Manifestations

Scabies remains one of the commonest of all skin diseases of all ages in many regions in resource-poor societies, whereas in industrialized societies its manifestations are different, and the infection is most prevalent in specific groups, e.g. the elderly living in institutions, such as nursing homes, or young adults. The problem of scabies in resource-poor environments is compounded by the frequency of secondary infection by group A streptococci and staphylococci [58,59].

The clinical features of scabies follow the invasion of the adult mite into the skin [60]. Itching, which may be very severe and worse at night, is the predominant symptom. The length of the incubation period after initial infection and before symptoms first appear is variable, but it may take 14 days or more before itching is noticed. Classically, scabies affects several skin sites, predominantly the hands between the fingers, wrists, elbows, shoulders, genital area, including the penis, lower legs, particularly the ankles, the scrotum in males, and the breasts in women. Scratch marks are often more widely distributed. The clinical signs are small (<5 mm) papules or pustules, and small raised or flattened burrows, which mark the course of the mite within the epidermis. These are curved linear lesions that often end in a tiny papule or pustule, the site of the adult mite. These are often difficult to find, as they are often excoriated, but they are easiest to see on the hands, fingers, wrists, and ankles. There are often papules without obvious burrows on the external genitalia. In light infestations, the best sites to examine for lesions are the hands, fingers, and external genitalia. Usually, the head is not affected, although it may be involved in infants and babies, and, once again, itchy papules can be seen. The other important clue to infection is the presence of itching with or without a rash in other household members. Usually, in tropical areas, several members of the family or household are affected, often to strikingly different degrees, with some patients showing fewer than four or five itchy papules, and others being covered with papules and excoriations.

Secondary infections are also common in the tropics, with pustular lesions and crusted scales in the main affected areas or over the face in children. These lesions may resemble impetigo, and they are usually infected with group A streptococci or *Staphylococcus aureus*.

Late in some infections, larger, very itchy, papules or small nodules, known as post-scabetic nodules, can be seen, and are the result of a developing immune reaction to mite antigens. Lesions are common in the genital area, and they may also occur after treatment. In such cases, it is important to screen for burrows, as these are the best sign that the infection remains active.

Other clinical variants include the crusted form of scabies, also known as Norwegian scabies, which is seen in the severely ill or immunocompromised. It has also been

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reported in Down's syndrome. However, Human Immunodeficiency Virus-infected adults and children may show a similar appearance. Here, the same areas are affected as in common scabies, although there is less itching; other family members are affected with the normal disease pattern. The clinical features of crusted scabies are the appearance of dry scales and crusts that are most marked over prominences such as the dorsum of the fingers, wrists, and ears. The face may be involved, and one or more nails show hyperkeratosis and thickening. These crusted infections are caused by a superinfection with thousands of mites, and such patients are very contagious.

Diagnosis

Clinical diagnosis remains the main method of disease ascertainment in poor countries. It relies on identifying the presence of burrows in the skin, coupled with clinical features such as the presence of itching in other members of the family, itching that is worse at night, and the anatomical distribution of lesions. [61]. In communities in the tropics, normal scabies may be hard to diagnose in every patient, as it has to be distinguished from other causes of itching and papule formation; in areas endemic for onchocerciasis, it is not easy to separate acute papular onchodermatitis from scabies [62]. A further diagnostic difficulty is that, often within a single family, there is a range of disease severity, with lesions clustering in older children in a few sites, perhaps just the hands, whereas infants often have very widespread papular lesions, including those affecting the scalp.

Confirmation of the diagnosis by direct tests, including the demonstration of adult or immature scabies mites, ova or even faeces in scrapings taken from a skin burrow, requires both skill and perseverance. The technique uses direct microscopy of material mounted in potassium hydroxide. It remains a cheap but time-consuming option with a large margin of diagnostic error. The use of the dermatoscope [63] or PCR for diagnosis [64], or serodiagnosis [45], has not been assessed in a tropical environment.

In most tropical areas, diagnosis depends on clinical recognition, but for community-level diagnosis, simple clinically based diagnostic algorithms have been advocated. The first of these, developed in Mali, provides a degree of diagnostic accuracy [65] This approach is based on a simple combination of symptoms and signs, and could be delivered after a single day of training. A second algorithm, used in Fiji [66], has also been shown to be useful in field settings. Both were designed to aid the diagnosis of common skin diseases seen in the local areas.

Complications

Whereas in many countries the main disabilities associated with scabies, such as sleep loss, are caused by itching, the disease in resource-poor settings is different, in that secondary infection brings a series of additional complications.

The best documented of these is the result of secondary infection by group A streptococci [67]. For some time, it has been recognized that infection with streptococci may result in the development of glomerulonephritis [58]. This can be detected with screening tests in a varying proportion of those affected, mainly children. For instance, symptomatic acute glomerulonephritis was reported in 10% of children in a survey in northern Australia, but, in addition, 24% had microscopic haematuria [68]. Thus, asymptomatic renal damage can also occur. The infection was closely linked to skin sores, and scabies was identified as the principal cause. Infection with streptococci can also occur in the absence of scabies [69]. Acute post-streptococcal glomerulonephritis is different in the tropics, as the skin, rather than the pharynx, appears to be the main source of infection. It has also been noted that persistent proteinuria can be detected for up to 16 years after the initial infection in 13% of those with recognized post-streptococcal glomerulonephritis vs. 4% of controls in an area endemic for scabies-associated infection [70]. The real possibility exists that the renal damage that occurs after a primary attack of scabies with secondary infection may persist for years afterwards, with the potential to cause long-term glomerular damage. A further study has shown that control of scabies with ivermectin is also associated with a significant reduction in both haematuria and isolation of streptococci from skin lesions [71]. More information on the frequency, geographical spread and chronic impact of these renal complications, based on long-term scientific research, is clearly needed.

A relationship between streptococcal infections secondary to scabies and acute rheumatic fever has also been proposed [2]. This is based on the observation that, in many areas where rheumatic fever remains a significant problem in children, the incidence of group A streptococcal throat infection, the traditional source of infection linked to rheumatic fever, is low. By contrast, infection of the skin with group A strains is common. There is, however, a paucity of group C and group G streptococci linked to rheumatic fever, although such strains may be identified in the throat in tropical areas. It is therefore possible that the throat strains may exchange virulence determinants with the more prevalent skin bacteria and lead to rheumatic fever. Therefore, although the definitive proof remains to be established, rheumatic fever remains

a possible association with scabies-associated streptococcal infections.

A further area where there is a possible link between scabies and bacterial sepsis is in infant septicaemia caused by *Staphylococcus aureus* [72]. The evidence is limited at present, but an association between potentially fatal infant septicaemia caused by *Staphylococcus aureus* and the presence of a skin rash, possibly scabies, has been reported in the Gambia.

Not all of the complications of scabies are related to infection, and household economic loss is also a problem in resource-poor communities. A study in rural Mexico indicated that families were spending a significant part of their household income on ineffective treatment of scabies ($24) over a 3-month period [73]. This had an impact on the family's ability to purchase other commodities, including food for their families. Scabies in poor environments is therefore both a potential cause of morbidity and a source of financial burden, which compounds the impact of disease resulting from this simple infection in poor communities.

Treatment

The incidence of scabies varies in a cyclical pattern with time, although, in some communities, it is relatively static. The reasons for this variation are unclear, but in resource-poor settings any fall in incidence is inevitably followed by a subsequent increase; in Guerrero state, Mexico [73], the incidence of scabies cases has been through a trough, but is beginning to rise once more. Treatment is therefore important in all cases. Likewise, treatment should be given to all household contacts, in order to prevent or contain spread. The options for the treatment of scabies are summarized in Table 2. Topical agents are considered to constitute first-line treatment, with oral ivermectin generally being reserved for recurrent, difficult-to-treat cases, or for patients with crusted scabies; however, there is increasing interest in ivermectin for the treatment of simple scabies.

Topical agents

A number of topical agents are highly effective. Patients should be given specific instructions about the use of topical agents. The agent should be applied to the entire skin surface, avoiding the eyes, mouth, and areas of non-intact skin, for the period specified, and then completely washed off. Application to the head is particularly important in children and the elderly, who more commonly have lesions in the scalp. Absorption is higher in infants and children, and the agent should not be applied to warm or wet skin after a bath [74,75]. Appropriate treatment for secondary bacterial infection should also be given. There are no published data on the efficacy of concurrent treatment of secondary bacterial infection and scabies, but usually this is the most practical approach to treatment in resource-poor communities. There have been reports of serious adverse events (Table 2) with lindane, permethrin, and crotamiton, but the causality is unclear, and they appear to be confined to cases where there is improper use of the products [4]. In developing countries, the cheaper medications, such as sulphur preparations and benzyl benzoate, are often used. Sulphur-containing preparations can also be used in infants and young children.

The rash and itch may persist for up to 2 weeks after a successful treatment [76] Antihistamines can assist with itching. Causes of apparent treatment failure with an effective regimen include incorrect diagnosis, dermatitis secondary to the mite or topical agent, incorrect application of the topical agent, poor penetration of hyperkeratotic skin or nails, re-infestation from close contacts (especially those with crusted lesions), and potential drug resistance [15].

Novel treatments, based on herbal compounds, have been proposed, but comparisons with currently accepted treatments are lacking [77]. Tea tree oil, eugenol compounds, toto soap and lippie oil all show potential [78–81].

Oral agents

Ivermectin is the main oral agent used in scabies, although there are other emerging agents, such as moxidectin, which have shown success in the treatment of other parasitic infections. Oral ivermectin has shown great promise in scabies treatment, particularly for crusted scabies, institutional outbreaks, and mass administration in highly endemic communities.

Efficacy

A review of randomized controlled trials by the Cochrane Collaboration concluded that permethrin was the most effective agent for the treatment of scabies when treatment failure was used as the outcome measure [82]. The superiority of permethrin includes comparison with ivermectin, although, in one study, cure rates between ivermectin and permethrin were similar when two doses of ivermectin were given 2 weeks apart (95% vs. 97.8%, respectively) [82]. Oral ivermectin has been found to be equally or more effective than benzyl benzoate in four trials [83–87], although, in one recent trial in Senegal, the study had to be stopped prematurely because of higher efficacy in the benzyl benzoate group (68.8% cure) than in the ivermectin group (24.6%) [88]; however, the trial has been criticized for a number of reasons, including the dose of ivermectin used. Overall, there has been considerable heterogeneity in the methods and outcome measurements among treatment trials, and there is

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TABLE 2. Options for treatment of scabies

Drug	Instructions for use [107]	Notes
Topical[a]		
Permethrin 5%	Apply overnight (8–14 h), and then wash off	In use since the 1980s.
		The most expensive topical agent (up to ten times the cost of benzyl benzoate in some regions), but the most widely used agent in developed countries
		Generally well tolerated with few side effects
		Treatment failures described with use of the 1% formulation (which should be used for head lice, not scabies). There is increasing concern about potential resistance of the scabies mite to permethrin [107]
		Permethrin is generally considered to be safe for younger children, but, owing to the theoretical risk of neurological complications, some advocate a shorter application time in infants aged <2 months. In the USA, oermethrin is only approved for infants aged >2 months
		Permethrin is safe for use in pregnancy and lactation
Benzyl benzoate 10–25%	Leave on skin for 24 h	In use since the 1930s
	Dilute for use in children and infants	Availability and cost vary, but it is the most widely used agent in developing countries
		Transient skin irritation and burning, immediately after application, is relatively common with the 25% lotion. Neurological complications are possible with misuse
		To reduce irritation, benzyl benzoate should be diluted to 12.5% for children and to 6.25% for infants, but this reduces efficacy
Crotamiton 10%	Apply for 24 h, and then wash and reapply. Repeat applications for 3–5 days	In use since the 1970s
		It is a safe alternative for infants, but is less practical, as requires multiple treatments
		Crotamiton is safe in pregnancy and lactation
Gamma benzene hexachloride (Lindane) 1%	Apply for 8 h, and then wash off	In use since the 1940s
		Lindane has been withdrawn from many countries, and is now a second-line treatment in developed countries. It continues to be used in many tropical and developing countries, as it is cheap and effective
		Systemic absorption is greater than for permethrin or crotamiton. There are several reports of aplastic anaemia and neurological complications, including convulsions, which are more likely in cases of misuse [108]. The greatest risks are for infants, pregnant women, and those with neurological disorders
		There is evidence of resistance and treatment failures with lindane [109]
		Lindane should be avoided in infants, pregnant women, and lactating women
Malathion 0.5%	Apply for 24 h	In use since the 1970s
		Has been used in the UK, but is infrequently used in other parts of the world
Sulphur ointment 6% (2–10%)	Apply for 24 h, and then wash and reapply	Sulphur compounds have been used for centuries
	Repeat applications for 3 days	The ointments are not recommended first-line agents, but are the only products available in some regions. They been shown to be effective in outbreaks in regions without available alternatives
		Precipitated ointments are often poorly accepted, as they are messy, malodorous, and cause skin irritation
Oral		
Ivermectin	200 µg/kg orally	In use for mass treatment of onchocerciasis and filariasis since the late 1980s
	Repeat after 1–2 weeks	Ivermectin is not approved for treatment of uncomplicated scabies in most countries (France and Brazil are two notable exceptions)
		Ivermectin has the additional benefit of treating multiple parasitic infections of the skin and digestive tract [110]
		A report of increased risk of death among elderly patients taking ivermectin during an institutional outbreak of scabies has not been replicated in other settings, and the causation of these results has been questioned[111]
		Ivermectin is a substrate for the cytochrome P450 3A4 pathway, and so caution should be exercised in people taking medications that induce or inhibit this pathway
		Ivermectin has limited ovicidal activity, so repeat treatment is recommended
		Further data are required regarding the use of ivermectin children of <15 kg and pregnant women; until these data are available, ivermectin is not recommended for use in these groups

[a]All treatments applied as a single application are likely to be more effective if repeated at 7–14 days, owing to the life cycle of the mite. Overtreatment should be avoided, because of increased toxicity and local effects.

a need to standardize protocols for future trials, and, particular, to standardize the clinical assessment of scabies infestation.

Crusted scabies
No randomized controlled trials have compared treatment regimens for patients with crusted scabies. Removal of the crust is particularly important. Experience in northern Australia suggests a regimen of multiple doses of oral ivermectin with repeated topical permethrin and keratolytic therapy [30,89].

Control of transmission, including environmental decontamination
Treatment of close contacts, including recent sexual partners, is recommended to prevent spread and re-infestation.

This is particularly important for mothers of infected infants. Identification and treatment of 'core transmitters' with crusted scabies is also important, because these patients have extreme loads of parasites [90].

Living mites have been found in environmental dust samples on floors and furniture [91], particularly from patients with crusted scabies [92]. However, early research by Mellanby [36] demonstrated that transmission through bedding, furniture and fomites is uncommon.

In resource-poor environments, treatment of bedding is seldom practical.

Scabies can affect many mammals, including domestic dogs and pigs, but the mites are genetically distinct, and cross-infectivity is limited [35]. Successful control programmes, without treatment of animals, suggest that resources should be directed towards human control [6,93].

Community control

In many developing countries, the Integrated Management of Childhood Illness programme provides the backbone of clinical care for primary healthcare workers by providing clinical guidelines for the management of common childhood illnesses.

Although the strategy of treating clinical cases and their contacts undoubtedly provides relief for individuals with scabies, there are few data that support its success in reducing population prevalence in the longer term. Mass drug administration, however, offers an alternative approach to population control of scabies. Studies in scabies-endemic locations, such as Panama and northern Australia, have shown that mass treatment of highly endemic communities with topical permethrin can substantially reduce scabies prevalence [5,6,94–97]. Treatment of scabies alone also resulted in a significant decrease in impetigo [98].

Oral ivermectin was used for mass treatment in the Solomon Islands [71]. There was a considerable reduction in scabies prevalence from 25% to 1%, with concomitant reductions in impetigo and haematuria. A study from Papua New Guinea also demonstrated decreased scabies prevalence after mass administration of ivermectin [99].

Factors in successful control include community involvement and motivation, education, close follow-up, regular re-screening, and prompt treatment of new cases [100]. Difficulties in sustaining a low prevalence have resulted from low levels of treatment uptake of topical permethrin among household contacts, and low motivation in some communities [101].

Conclusions

Scabies is a common disease that often dominates the pattern of skin infection in developing countries, where it causes both distress and discomfort to children and families. Largely through poor management, families are forced to spend much of their scarce money in trying to treat this infection. Secondary bacterial infection is almost universal in this environment, with potentially serious consequences for the individual's health. In recognition of its profound impact in the poorest communities, it is now listed as a neglected tropical disease by the PLoS Neglected Tropical Diseases Journal (http://www.plosntds.org/static/scope.action). Action to control scabies in those countries where it has a significant impact on public health should now be a priority. One of the recurrent problems of this disease is that, in many parts of the world, including Latin America and Ethiopia, there is a close association between human louse infestations and scabies, and control of both may be strategically linked with ivermectin [20]. Further action aimed at achieving realistic control targets should involve further research topics, such as the long-term health consequences of scabies infection or the explanation for cyclical incidence, as well as refining and trialling appropriate regimens for community-based scabies control using ivermectin and topical agents. In addition, we need to establish an international alliance of partners, bringing different skills, as well as influence, in order to make control a realistic and achievable goal.

Transparency Declaration

The authors report no conflicts of interest.

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