

CONTENTS

Scabies: New Opportunities for Management and Population Control

EDITORIAL BOARD

Editor: Delane Shingadia

Board Members

David Burgner (Melbourne, Australia)  
Kow-Tong Chen (Tainan, Taiwan)  
Luisa Galli (Florence, Italy)  
Steve Graham (Melbourne, Australia)

Cristiana Nascimento-Carvalho (Bahia, Brazil)  
Ville Peltola (Turku, Finland)  
Emmanuel Roilides (Thessaloniki, Greece)  
Ira Shah (Mumbai, India)

George Syrogiannopoulos (Larissa, Greece)  
Tobias Tenenbaum (Mannheim, Germany)  
Marc Tebruegge (Southampton, UK)  
Marceline Tutu van Furth (Amsterdam, The Netherlands)



# Scabies

## New Opportunities for Management and Population Control

Li Jun Thean, MB BS, BMedSci, DCH,\*† Daniel Engelman, FRACP, PhD, MPHTM,\*†‡  
John Kaldor, PhD, MA, BA,§ and Andrew C. Steer, FRACP, PhD, MPH\*†‡

Scabies is a skin condition caused by infestation with the microscopic mite *Sarcoptes scabiei* var *hominis*. Common scabies causes severe itch, mite burrows and secondary skin lesions. Scabies has a strong causal relationship with impetigo<sup>1</sup> which can lead to more severe skin and soft tissue infections, invasive bacterial infections and post-streptococcal sequelae.<sup>2</sup> Crusted scabies is a rare form, usually affecting people with immunosuppression and characterized by hyperkeratotic skin containing thousands to millions of mites.

The World Health Organization (WHO) adopted scabies as a neglected tropical disease (NTD) in 2017.<sup>3</sup> This recognition has led to increasing global awareness and efforts toward scabies control and even elimination as a public health problem. The

Accepted for publication October 2, 2018.

From the \*Tropical Diseases Research Group, Murdoch Children's Research Institute, Melbourne, Victoria, Australia; †Department of Paediatrics, University of Melbourne, Melbourne, Victoria, Australia; ‡Department of General Medicine, Royal Children's Hospital, Melbourne, Victoria, Australia; and §Kirby Institute, University of New South Wales, Sydney, Australia.

The authors have no funding or conflicts of interest to disclose.

Address for correspondence: Andrew C. Steer, FRACP, PhD, MPH, MB BS, BMedSci, Murdoch Children's Research Institute, Royal Children's Hospital, 50 Flemington Road, Parkville, VIC 3052, Australia. E-mail: andrew.steer@rch.org.au. Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0891-3668/19/3802-0211

DOI: 10.1097/INF.0000000000002211

2018 meeting of the WHO NTD Strategic Technical Advisory Group Working Group on Monitoring and Evaluation noted "strong initial evidence for ivermectin-based mass drug administration (MDA) for control of scabies in endemic populations and that simplified clinical case definitions for field surveys are available; however, there is currently no global strategy for scabies control."<sup>4</sup> With an increasing global focus on scabies, it is timely to review recent advances in the understanding of scabies epidemiology, diagnosis, treatment and public health control.

### EPIDEMIOLOGY OF SCABIES

Two recent studies have advanced the understanding of global epidemiology, while also highlighting several gaps and issues. The Global Burden of Disease Study estimated the global prevalence of scabies in 2015 to be approximately 200 million, and that scabies causes 71 disability-adjusted life-years (DALYs) per 100,000 people, ranking 101 of the 246 conditions studied, and contributing to 0.21% of global DALYs.<sup>5</sup> This burden is comparable with that caused by *Haemophilus influenzae* type b meningitis (ranking 100) and acute lymphoid leukemia (ranking 103). A systematic review in 2015 described available global data on prevalence and distribution of scabies.<sup>1</sup> Scabies prevalence ranged from 0.2% to 71.4%, was significantly higher in children than in adolescents and adults and was highest in the Latin American and Pacific regions. Most studies included were

conducted in countries with either a low or medium human development index.

These studies were unable to illuminate the distribution of scabies within countries and within populations, particularly in disadvantaged populations where overcrowding is more common. The high prevalence in indigenous communities within Australia,<sup>1</sup> and within refugee and displaced person populations, including new arrivals to Europe,<sup>6</sup> highlights the highly inequitable distribution of scabies.

While the direct burden of scabies estimated by the Global Burden of Disease Study is high, this may be the "tip of the iceberg" of the burden mediated through secondary bacterial infection. In studies in the Pacific, the population attributable risk of impetigo because of scabies ranges from 41% to 93%.<sup>7,8</sup> Complications resulting from impetigo include focal and systemic bacterial infections, post-streptococcal glomerulonephritis and possibly rheumatic fever although the attributable risk from scabies is not currently known. Furthermore, the considerable morbidity and mortality of crusted scabies were not factored into DALY calculations.

The quality of many studies included in these reviews was low, with variation in sampling and diagnosis. More rigorous studies in a range of settings, and targeting disadvantaged populations, are needed to describe the global burden and distribution of scabies. In addition, standardized methods of population sampling and diagnostic criteria are required.

The ESPID Reports and Reviews of *Pediatric Infectious Disease Journal* series topics, authors and contents are chosen and approved independently by the Editorial Board of ESPID.

## DIAGNOSTIC METHODS

The clinical signs of scabies are papules, vesicles and linear burrows with associated pruritus and scratch marks. In children and adolescents, lesions are most commonly seen in the finger web spaces and volar wrists. Lesions are also found frequently in the axilla, belt line, legs, feet and buttocks. In infants, lesions are commonly seen on palms, soles and ankles but can be widespread, including involvement of the head and face.

The reference standard for diagnosis is a demonstration of the scabies mite, eggs or fecal material through microscopic examination of skin scrapings. As scabies infestation typically involves only 10–15 mites, this method is highly operator dependent, with low sensitivity and is not feasible for most resource-limited clinical settings or field studies. Direct, low-power visualization of burrows in the skin using dermoscopy can be a useful aid for clinical examination.<sup>9</sup> Advances in high-power, noninvasive methods including videomicroscopy, videodermoscopy and reflectance confocal microscopy allow diagnostic confirmation through direct visualization of the mite.<sup>9</sup> These methods, although sensitive, require considerable time for a complete examination and are reliant on costly specialized equipment and personnel; they are therefore more appropriate for use in highly-resourced clinical or research settings. Serologic and molecular techniques are under development but are not yet at a stage where they can be recommended for clinical or public health use. In most settings, diagnosis is therefore reliant on clinical assessment of suggestive lesions in typical body distributions, supported by the presence of itch and affected close contacts.

A systematic review of diagnostic methods in therapeutic trials revealed wide variation with no predominant method.<sup>10</sup> Most studies did not have well-defined diagnostic criteria. This variation complicates the interpretation and comparison of findings from epidemiologic and therapeutic studies.

A standardized diagnostic approach is needed to better elicit the burden of disease and determine effectiveness of clinical therapies and public health interventions. An improved diagnostic approach will need to consider feasibility in resource poor settings while maintaining good sensitivity and specificity. A recent consensus study led by the International Alliance for the Control of Scabies using the Delphi method has yielded a set of diagnostic criteria for scabies, summarized in Table 1.<sup>11</sup> The criteria are organized into 3 levels according to the degree of diagnostic certainty. This approach allows for versatility in the standards to be applied, taking into account the specific aims and

**TABLE 1.** Summary of 2018 IACS Criteria for the Diagnosis of Scabies<sup>11</sup>

A. Confirmed scabies	At least one of: A1: Mites, eggs or feces on light microscopy of skin samples A2: Mites, eggs or feces visualized on individual using high-powered imaging device A3: Mite visualized on individual using dermoscopy
B. Clinical scabies	At least one of: B1: Scabies burrows B2: Typical lesions affecting male genitalia B3: Typical lesions in a typical distribution and 2 history features
C. Suspected scabies	One of: C1: Typical lesions in a typical distribution and 1 history feature C2: Atypical lesions or atypical distribution and 2 history features
History features	H1: Itch H2: Close contact with an individual who has itch or typical lesions in a typical distribution

Diagnosis can be made at 1 of the 3 levels (A, B or C). A diagnosis of clinical or suspected scabies should only be made if differential diagnoses are considered less likely than scabies.

IACS indicates International Alliance for the Control of Scabies.

practicalities of research and mapping projects. While validation of these criteria in varied research settings is required to determine the diagnostic accuracy and legitimize implementation, they represent a useful starting point to better describe scabies epidemiology.

## TREATMENTS

For all scabies medications, treatment of all the household contacts of an index case is recommended. There are several topical treatment options for scabies including permethrin (the most effective but also most expensive topical agent), benzyl benzoate, crotamiton, lindane, sulfur compounds and malathion. Although these treatments are efficacious, adherence is compromised by skin irritation and inconvenience (they need to be applied to the whole body for 8 hours or more). In poorly resourced countries, cost and drug supply limitations contribute to inadequate treatment of affected individuals and their household members. Inadequate application or adherence is the main reason for treatment failure and ongoing mite transmission. Resistance to permethrin has not been confirmed for human scabies but has been observed in animal scabies and other ectoparasites.<sup>12</sup>

Ivermectin is the only effective oral treatment available. Ivermectin does not have ovicidal activity, so a second dose after 7–14 days is recommended to kill new hatchlings. It has been approved for clinical use for scabies in several countries including France, the Netherlands, Germany, Australia and New Zealand and used off-label in many other settings. In addition to increased adherence for individual treatment, oral ivermectin has major advantages as a treatment for household contacts and for community control using a MDA approach.<sup>12</sup> Ivermectin is not recommended for pregnant women and children weighing less than 15 kg because of a lack of safety data. However, inadvertent use in pregnant women, and use in younger

children for other indications, has not shown any additional risk in these populations.<sup>13,14</sup>

A 2018 Cochrane review compared oral ivermectin, topical ivermectin and topical permethrin for scabies.<sup>15</sup> There was little difference between oral ivermectin and topical permethrin in achieving complete clearance of infestation by the second week after treatment. The authors also found no difference in efficacy when comparing oral ivermectin with topical permethrin, topical ivermectin with topical permethrin or topical ivermectin with oral ivermectin. There was also no significant difference in cure when comparing 1 versus 2 doses of ivermectin. However, the methodologies of the studies included limit the confidence in these conclusions, and more studies are needed.

Moxidectin is an oral agent, recently approved for onchocerciasis, which shows promise as an oral therapy for scabies. It is related to ivermectin, but with potential advantages because of its substantially longer plasma half-life (up to 43 days, compared with less than 1 day for ivermectin) and higher lipophilicity enabling higher bioavailability in skin.<sup>12,16,17</sup> These properties could eliminate the need for a second treatment dose, and confer protection against reinfestation. A study in pigs compared a single dose of moxidectin with 2 doses of ivermectin<sup>16</sup> and found 100% efficacy versus 62%, respectively, when measured 47 days after treatment. Further bioavailability and safety studies especially in young children will be important to establish moxidectin as a recognized treatment for scabies.

## PUBLIC HEALTH CONTROL

Although available topical and oral medications provide effective individual treatment, individuals living in resource-limited settings with high prevalence are rapidly reinfested from household and community contacts. An alternative strategy is to reduce

community prevalence and thereby minimize transmission by using MDA as demonstrated in the following trials. A series of single-arm studies in Panama, northern Australia and the Solomon Islands provided initial evidence to support this approach. A more recent comparative trial in Fiji demonstrated that ivermectin-based MDA had greater efficacy than both standard treatment (permethrin for affected individuals and household members) and permethrin-based MDA.<sup>18</sup> The island group that was allocated ivermectin-based MDA experienced a 94% relative reduction in scabies 12 months after MDA, with prevalence falling from 32% to 1.9%. The standard care and permethrin-based MDA groups experienced a reduction in scabies prevalence of 49% and 62%, respectively. Impetigo prevalence also fell with the greatest reduction in impetigo prevalence (67%) in the ivermectin group compared with standard care and permethrin-based MDA groups (32% and 54%, respectively).

Another study investigated ivermectin-based MDA in a remote Australian Aboriginal community using a before-and-after study design of 2 rounds of ivermectin-based MDA, 12 months apart.<sup>19</sup> Prevalence decreased 6 months after each treatment but rebounded quickly. There are several factors that may have led to contrasting results to the Fiji study. First, administration took place over 4 months, which may have allowed for reinfestation, although acquisition rates were noted to be low at 1%–2% per 6-month interval. Second, there was considerable mobility of the population, with 34% of participants at the 12-month follow-up not present in the community at baseline. A wider distribution of MDA may be required to account for population movement. Third, the increase in prevalence at 12 months was in a group of people linked to a person with crusted scabies, a condition which may serve as a source of ongoing transmission because of the very high mite counts.

A recent study in the Netherlands evaluated ivermectin-based MDA to control scabies in newly arrived asylum seekers. The program actively screened arrivals from Ethiopia and Eritrea, and 65% of the 897 individuals were diagnosed with clinical scabies. All individuals screened received ivermectin (apart from pregnant women and infants) and symptomatic individuals received a second dose after 2 weeks. Evaluation of the program demonstrated a reduction of recurrent

scabies episodes from 42% to 27% following the program and a reduction in scabies complications from 12% to 5%.<sup>6</sup>

## GLOBAL RESPONSES TO THE NEED FOR SCABIES CONTROL

The recognition of scabies as a NTD by the WHO and recommendations to establish guidelines and standards for public health interventions demonstrate motivation toward scabies control driven by multinational requests for guidance. The development of a global strategy for scabies control will require standardized diagnostic, mapping and surveillance strategies, as well as guidance on public health management for scabies. Important operational research to evaluate the viability of MDA as a disease control option includes proof of scalability, assessment of cost-effectiveness, evaluation of program acceptability and investigation of whether MDA for scabies can translate into reductions in the serious bacterial and autoimmune complications of scabies. Establishing a viable and sustainable drug supply for scabies control will also be crucial. The current indications for ivermectin on the WHO Model List of Essential Medicines are for treatment of filarial disease and intestinal helminths; addition of scabies as an indication will be a crucial step for any program implementation. Finally, global partnerships and meaningful collaboration, such as those fostered by the International Alliance for the Control of Scabies,<sup>2</sup> will be critical for progress toward control and potentially even elimination of scabies.

## REFERENCES

- Romani L, Steer AC, Whitfield MJ, et al. Prevalence of scabies and impetigo worldwide: a systematic review. *Lancet Infect Dis*. 2015;15:960–967.
- Engelman D, Kiang K, Chosidow O, et al; Members Of The International Alliance For The Control Of Scabies. Toward the global control of human scabies: introducing the International Alliance for the Control of Scabies. *PLoS Negl Trop Dis*. 2013;7:e2167.
- World Health Organization. Report of the Tenth Meeting of the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases. WHO Publications; 2017.
- World Health Organization. 9th NTD-STAG Global Working Group Meeting on Monitoring and Evaluation of Neglected Tropical Diseases. In: Zoerhoff K, Ramzy R, eds. World Health Organisation; 2018.
- Karimkhani C, Colombara DV, Drucker AM, et al. The global burden of scabies: a cross-sectional analysis from the Global Burden of Disease Study 2015. *Lancet Infect Dis*. 2017;17:1247–1254.
- Beerens DT, Ravensbergen SJ, Heidema A, et al. Efficacy of ivermectin mass-drug administration to control scabies in asylum seekers in the Netherlands: a retrospective cohort study between January 2014–March 2016. *PLoS Negl Trop Dis*. 2018;12:e0006401.
- Mason DS, Marks M, Sokana O, et al. The prevalence of scabies and impetigo in the Solomon Islands: a population-based survey. *PLoS Negl Trop Dis*. 2016;10:e0004803.
- Romani L, Koroiueta J, Steer AC, et al. Scabies and impetigo prevalence and risk factors in Fiji: a national survey. *PLoS Negl Trop Dis*. 2015;9:e0003452.
- Micali G, Lacarrubba F, Verzi AE, et al. Scabies: advances in noninvasive diagnosis. *PLoS Negl Trop Dis*. 2016;10:e0004691.
- Thompson MJ, Engelman D, Gholam K, et al. Systematic review of the diagnosis of scabies in therapeutic trials. *Clin Exp Dermatol*. 2017;42:481–487.
- Engelman D, Fuller LC, Steer AC; International Alliance for the Control of Scabies Delphi panel. Consensus criteria for the diagnosis of scabies: a Delphi study of international experts. *PLoS Negl Trop Dis*. 2018;12:e0006549.
- Mounsey KE, Bernigaud C, Chosidow O, et al. Prospects for moxidectin as a new oral treatment for human scabies. *PLoS Negl Trop Dis*. 2016;10:e0004389.
- Wilkins AL, Steer AC, Cranswick N, et al. Question 1: Is it safe to use ivermectin in children less than five years of age and weighing less than 15 kg? *Arch Dis Child*. 2018;103:514–519.
- Gyapong JO, Chinbuah MA, Gyapong M. Inadvertent exposure of pregnant women to ivermectin and albendazole during mass drug administration for lymphatic filariasis. *Trop Med Int Health*. 2003;8:1093–1101.
- Rosumeck S, Nast A, Dressler C. Ivermectin and permethrin for treating scabies. *Cochrane Database Syst Rev*. 2018;4:CD012994.
- Bernigaud C, Fang F, Fischer K, et al. Preclinical study of single-dose moxidectin, a new oral treatment for scabies: efficacy, safety, and pharmacokinetics compared to two-dose ivermectin in a porcine model. *PLoS Negl Trop Dis*. 2016;10:e0005030.
- Opoku NO, Bakajika DK, Howard H, et al. Single dose moxidectin versus ivermectin for *Onchocerca volvulus* infection in Ghana, Liberia, and the Democratic Republic of the Congo: a randomised, controlled, double-blind phase 3 trial. *Lancet*. 2018;392:1167–1278.
- Romani L, Whitfield MJ, Koroiueta J, et al. Mass drug administration for scabies control in a population with endemic disease. *N Engl J Med*. 2015;373:2305–2313.
- Kearns TM, Speare R, Cheng AC, et al. Impact of an ivermectin mass drug administration on scabies prevalence in a remote Australian aboriginal community. *PLoS Negl Trop Dis*. 2015;9:e0004151.