Strengths of this study include the use of a nationally representative outpatient cohort over 21 years. Limitations include lack of information on severity or complications of haemangiomas, access to health records, or longitudinal data on individual patients. As this is a real-world study, IH was classified by physician diagnosis without requirement to meet formal criteria. Future studies are needed to address these limitations.

P. Singh,[1] S. Chamlin,[2] E. Hignett[1] and J.I. Silverberg[3]

[1]*Department of Dermatology;* [2]*Department of Pediatrics and* [3]*Department of Dermatology, Preventive Medicine and Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, IL, U.S.A.*

Correspondence: Jonathan Silverberg.

E-mail: JonathanISilverberg@gmail.com

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In vitro ovicidal activity of current and under-development scabicides: which treatments kill scabies eggs?

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Dear Editor, Scabies is highly prevalent worldwide, affecting 100–200 million people annually.[1] It has a significant global burden in disability-adjusted life-years. In hyperendemic tropical regions, the link with secondary bacterial infections is increasingly recognized. Group A streptococcal and staphylococcal pyoderma can cause bacteraemia,[2] glomerulonephritis and acute rheumatic fever, potentially leading to rheumatic heart disease. Current scabies treatments are few in number and suboptimal. As neuroinhibitors they are expected to kill mites in motile stages but could be poorly ovicidal. Emerging drug resistances in the parasites are a further concern. New candidate drugs of the macrocyclic lactone and isoxazoline families are under investigation for scabies treatment,[3,4] but nothing is known about their ovicidal properties. If scabies eggs are not susceptible to a drug that has a shorter skin half-life than the time it takes for eggs to hatch, only well-timed and precisely dosed repeat treatments will eliminate hatching larvae and terminate the infestation. This presents a significant obstacle for scabies treatment management, in particular in public health approaches to scabies control in hyperendemic areas.

Aiming to survey systematically the *in vitro* scabicidal efficacies of available and experimental treatments, we performed mite survival and egg hatching *ex vivo* assays. Over 10 000 individual *Sarcoptes scabiei* var. *suis* eggs at early stages of development and adult female mites were exposed to five drugs currently available for human scabies treatment (permethrin, benzyl benzoate, ivermectin, crotamiton and lindane) and six drugs under development or in veterinary use (moxidectin, doramectin, selamectin, eprinomectin, afoxolaner and sarolaner).

All tested pure compounds and formulations were effective against motile mites (Fig. 1a, b). Eggs kept in medium alone hatched (Fig. 1c, d). In the presence of pure permethrin or pure ivermectin and in commercial ivermectin formulation most eggs hatched (Fig. 1c). Similarly, eggs hatched when exposed to pure or commercially formulated moxidectin, doramectin, selamectin, eprinomectin, afoxolaner and sarolaner (Fig. 1d). By contrast, commercial permethrin formulations prevented hatching (Fig. 1c); however, 12-h exposure (as recommended in clinical practice) resulted in a 10–12% increase of egg hatchability (full data available on request). Pure permethrin sourced from five independent manufacturers showed no ovicidal activity, with around 80% of hatched larvae surviving for 2 days (full data available on request). Benzyl benzoate, crotamiton and lindane were found to kill eggs (Fig. 1c); however, their tolerability, side-effects and clinical efficacies remain controversial.[5]

Our findings, that most of the drugs used to treat scabies are not ovicidal, can be explained by the neurologically immature, nonmotile eggs not being susceptible to these neuroinhibitors. Similar observations are reported from other arthropod studies. For example, ivermectin failed to kill the eggs of head lice,[6] and permethrin had limited ovicidal activities against the tick *Ixodes ricinus* at concentrations that eliminated motile larvae.[7] Only ivermectin has previously been proposed to have limited ovicidal activity on *S. scabiei* eggs. While also nonovicidal (Fig. 1d), moxidectin and afoxolaner have longer skin half-lives than ivermectin,[3,4] potentially making them more effective. Notably, five different pure permethrin preparations were not ovicidal, in contrast to the two commercial formulations. While we could not provide data from eggs treated only with the vehicles of the commercial products, this finding could be explained by an excipient being present in the commercial formulations that either is ovicidal or modulates permethrin activity.

Sarcoptes scabiei parasites are difficult to sample in large numbers from human patients, and an *in vitro* culture system has not been established. No phenotypic differences and much serological compatibility have been observed between *S. scabiei* biovars sourced from human and porcine hosts, and recent genome sequencing data suggest that some may be genetically

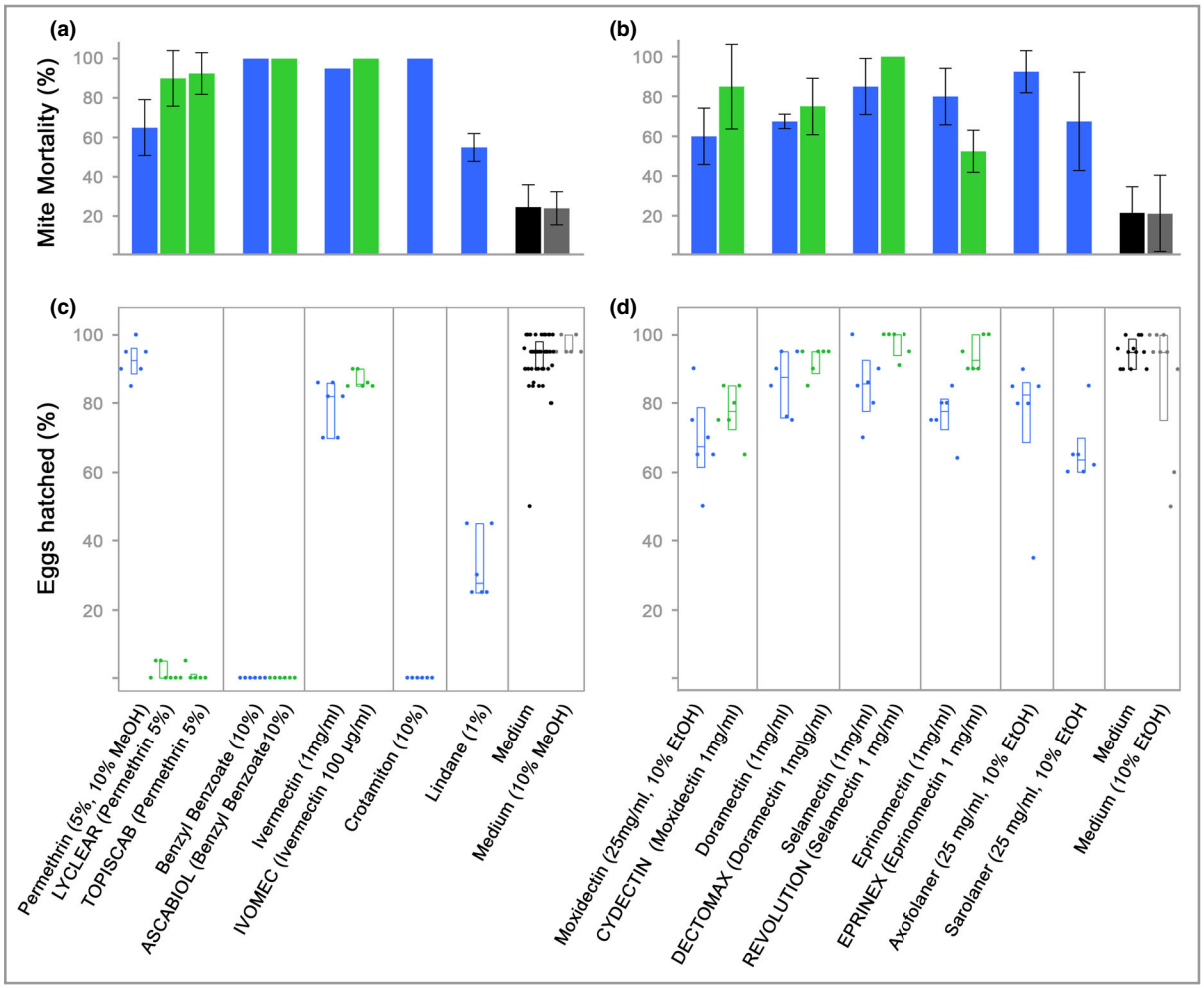

Fig 1. Mortality of mites and eggs hatching under *in vitro* drug exposure. Mite mortality (a, b) and egg hatchability (c, d) were monitored daily for 2 and 5 days, respectively. (a, c) Results for the currently most used drugs on the market for scabies treatment. (b, d) Results for treatments that are under development or in veterinary use. For each test the data of at least two independent experiments with three replicates each are shown. Twenty eggs per assay are represented by one dot. Blue colour represents pure compounds, green commercial drug formulations, grey medium plus 10% methanol or 10% ethanol, and black medium. Data were analysed using Dunnett's multiple comparisons test as part of one-way ANOVA (P-values $< 0{\cdot}05$ considered significant, error bars indicate mean ± SD) using GraphPad Prism 7 (a, b) and JMP Pro 14·2 (c, d). The details of all formulations are available on request.

very close. Furthermore, pigs and humans share outstanding resemblances in skin physiology. Using the abundant parasite numbers that can be sourced from our porcine model,[8] we provide a systematic *ex vivo* drug screen focusing on ovicidal properties. As half-lives will differ in live skin, *in vivo* validation will be required. While this is difficult to realize in human patients, the porcine model may be the ideal system for a future preclinical study.

Noncompliance to strict repeat-treatment regimens when using nonovicidal drugs is a real challenge in scabies management[5] and is likely a main cause of treatment failure, emphasizing the unmet need for novel drugs that target eggs in addition to motile stages. Surprisingly, *S. scabiei* eggs have been disregarded as a drug target despite being the most abundant stage in the scabies life cycle, with each gravid mite amplifying the parasite population by 60–180 times. We propose that a new generation of acaricides with both ovicidal and miticidal activities would improve future management strategies and make treatment in the long term more cost- and time-effective.

C. Bernigaud,[1,2,3] D.D. Fernando,[1,4] H. Lu,[1] S. Taylor,[1] G. Hartel,[5] J. Guillot,[3] O. Chosidow[2] and K. Fischer[1]

[1]*Cellular and Molecular Biology Department,Infectious Diseases Program and* [5]*Statistics Unit, QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia;* [2]*Dermatology Department, AP-HP, Hôpital Henri Mondor, Université Paris-Est, Créteil, France;* [3]*Research Group Dynamyc, EA7380, Faculté de Médecine de Créteil, Université Paris-Est, Créteil, France; and* [4]*Faculty of Veterinary Medicine and Animal Science, University of Peradeniya, Peradeniya, Sri Lanka*

Correspondence: Katja Fischer.

E-mail: Katja.Fischer@qimrberghofer.edu.au

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Role of the partner/spouse in melanoma discovery and related health behaviours and practices

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Dear Editor, Spouses and partners play a key role in early melanoma detection. We surveyed newly diagnosed patients with primary invasive cutaneous melanoma[1] and their spouses/partners regarding melanoma-related health behaviours in order to investigate the partners' role in earlier detection of melanoma.

Institutional board approval was obtained at Stanford University Medical Center, the Veterans Affairs Palo Alto Health Care System and the University of Michigan. Eligible, consecutive patients with melanoma, who were aged 18 years and older, and their cohabitating spouse/partner (for at least the previous 12 months) were surveyed from 2006 to 2009, within 3 months of diagnostic biopsy, as previously described.[1] The χ^2-test and t-test analyses were used to evaluate differences in demographics between the study participants and excluded patients without a qualifying spouse/partner, hereafter referred to as 'partner'. Logistic regression models were used to assess the relationship between a partner's reported health behaviours and patient sex, adjusted for patient age, and between the person who first detected melanoma (patient, practitioner vs. partner) and Breslow thickness at diagnosis, adjusted for patient sex and age. A type I error of 0·05 with a two-sided test was considered statistically significant. Analyses were performed using SAS 9·3 (SAS Institute Inc., Cary, NC, U.S.A.) and Stata 12·0 (StataCorp, College Station, TX, U.S.A.).

Of 566 patients surveyed overall (see reference for complete demographic information),[1] 433 patients (76·5%) had a cohabitating partner. A total of 313 patient–partner pairs completed the survey (312 male–female couples, one male–male couple). Of this group, 306 patients (98%) were white, and 208 (67%) were male, with a mean age of 57 years [95% confidence interval (CI) 55·7–58·9] for patients and 56 years (95% CI 54·3–57·4) for partners. Patients with partners did not differ from those without (n = 118) by age, sex or mean tumour thickness ($P > 0·05$ for all comparisons).[1] There was no statistically significant difference in the frequency of personal or family history of melanoma between patients and participating partners ($P > 0·05$ for both comparisons).

Female partners reported playing an active role in their spouse's health more frequently than male partners did (data available on request). Nearly half of surveyed partners (49·8%) reported knowledge of the ABCD rule for melanoma