Lessons from the Field

Control of scabies, skin sores and haematuria in children in the Solomon Islands: another role for ivermectin

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Objective To assess the effects of a 3-year programme aimed at controlling scabies on five small lagoon islands in the Solomon Islands by monitoring scabies, skin sores, streptococcal skin contamination, serology and haematuria in the island children.
Methods Control was achieved by treating almost all residents of each island once or twice within 2 weeks with ivermectin (160–250 μg/kg), except for children who weighed less than 15 kg and pregnant women, for whom 5% permethrin cream was used. Reintroduction of scabies was controlled by treating returning residents and visitors, whether or not they had evident scabies.
Findings Prevalence of scabies dropped from 25% to less than 1% ($P < 0.001$); prevalence of sores from 40% to 21% ($P < 0.001$); streptococcal contamination of the fingers in those with and without sores decreased significantly ($P = 0.02$ and 0.047, respectively) and anti-DNase B levels decreased ($P = 0.002$). Both the proportion of children with haematuria and its mean level fell ($P = 0.002$ and $P < 0.001$, respectively). No adverse effects of the treatments were seen.
Conclusion The results show that ivermectin is an effective and practical agent in the control of scabies and that control reduces the occurrence of streptococcal skin disease and possible signs of renal damage in children. Integrating community-based control of scabies and streptococcal skin disease with planned programmes for controlling filariasis and intestinal nematodes could be both practical and produce great health benefits.

Keywords Scabies/drug therapy/complications; Ivermectin/administration and dosage; Permethrin/therapeutic use; Pyoderma/microbiology; Skin ulcer/microbiology; Streptococcus pyogenes; Nephritis/etiology; Hematuria; Solomon Islands (*source: MeSH, NLM*).

Mots clés Gale/chimiothérapie/complication; Ivermectine/administration et posologie; Perméthrine/usage thérapeutique; Ulcère cutané/microbiologie; Pyodermite; Streptococcus pyogène; Néphrite/étiologie Hématurie; Iles Salomon (*source: MeSH, INSERM*).

Palabras clave Escabiosis/quimioterapia/complicaciones; Ivermectina/administración y dosificación; Permetrina/uso terapéutico; Pioderma/microbiología; Ulcera cutánea/microbiología; Streptococcus pyogenes; Nefritis/etiología; Hematuria; Islas Salomón (*fuente: DeCS, BIREME*).

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Voir page 40 le résumé en français. En la página 41 figura un resumen en español. يمكن الاطلاع على الملخص بالعربية في صفحة 41.

Introduction

Scabies and streptococcal skin disease are a burden in crowded communities and are among the most common presentations to health services (*1*). Costs to families and services are high and the diseases have long-term implications through post-streptococcal renal disease and possibly rheumatic heart disease (*2*, *3*).

In 1991 Taplin et al. reported excellent scabies control in a community where everyone, whether or not they had scabies, was very carefully treated with topical permethrin cream. With no other treatment, streptococcal pyoderma decreased markedly after scabies control. Treating returnees and visitors with permethrin maintained these benefits (*4*). However this methodology has not been widely adopted because it is messy, time-consuming, and intrusive.

Orally administered ivermectin is active against scabies. It is used in the mass annual treatment of millions of people

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for onchocerciasis (*5*) and filariasis. Treatment has been found to be safe except in people with loaiasis who have high microfilaraemia (*6*). Ivermectin is the usual treatment for scabies in domestic animals and has been used successfully for this purpose in humans (*7–9*). In cases of ordinary scabies, one dose of ivermectin is effective (*10–12*). One-dose treatment is crucial to practicality in community settings.

Acute nephritis following pyoderma is well-recognized. Subclinical renal damage from multiple skin infections in childhood might contribute to the pathogenesis of renal and cardiovascular disease in adult life. Recently, in a population where end-stage renal disease was extremely common, it was found that many factors including scabies and previous nephritis were independently associated with a raised urinary albumin-to-creatinine ratio (*13*). It is not clear how much of the haematuria found in children in developing countries is causally related to the many skin infections they experience, although they are correlated (*14*). Haematuria may be a sensitive indicator of low-level damage, as tubular reabsorption of protein after minor glomerular leakage of red cells and protein may leave haematuria as the only sign.

We predicted that scabies control would lead to reductions in sores, in haematuria, and in the group A streptococci (GAS) present in the communities involved.

Methods

Rationale

This was a trial of scabies control in a practical context, to assess the feasibility and effects of treating a whole population at once and then maintaining control over a period, with limited input, while people went about their normal lives. The islands selected were very crowded and scabies common. The island location helped define the area and the population to be managed as residents came and went. No continuing comparison of treated and untreated groups within the population was possible because of the underlying principle of the intervention: i.e. the need to treat everyone, thus removing all scabies mites and preventing reinfection. Orally administered ivermectin was the major agent used, because effective topical treatment of large numbers is so difficult as to be unacceptable and impracticable. We investigated the relationships between scabies, pyoderma, renal damage and GAS in sores and on the fingers of children in the community. We considered this strategy reasonable and likely to reflect the presence of scabies in the population as the prevalence in children is generally higher than that in adults. Also post-streptococcal disease is largely confined to children. In practice, children tend to be more easily available and tolerant of imposition than adults.

Setting and population

We studied the people of five small densely-populated islands (Sulufou, Foueda, Nuileni, Funafou and Addagege) in the Lau Lagoon, Malaita Province, Solomon Islands. Our census included 1558 people, about half of whom were on the islands at any one time. Many lived elsewhere and visited infrequently. The largest island, Sulufou, is about 120 metres in diameter and had around 500 people in residence. The other islands were similarly crowded. Information was given in the local language at public meetings as well as being distributed in print, and the communities were asked to consider taking part in the trial. Free informed consent was given by volunteers and/or their guardians. The study was approved by the Solomon Island Research Ethics Committee and by the Queensland Institute of Medical Research Human Research Ethics Committee. The study ran from July 1997 until June 2000 and reviews were conducted three times per year (Fig. 1). Two retired local female health workers who were respected in the community were trained and employed to implement the project.

Fig. 1. **Study timeline**

Visit number	Sulufou	Foueda	Funafou Addagege Nuileni
1/ July 1997	Diagnosis Culture and tests Mass treatment	Diagnosis Culture and tests No treatment	Nil
2/ November1997	Diagnosis Culture and tests Case treatment	Diagnosis Culture and tests Mass treatment	
3–9/ February 1998–June 2000	Diagnosis Culture and tests Case treatment		

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Baseline assessment and treatment

In July 1997, children on Sulufou and Foueda aged 12 years or under were examined for scabies and sores and specimens were collected from cooperating children. At that first visit the whole population of Sulufou was offered treatment, whereas no treatment was given to people on Foueda who acted as a control population. In November 1997 the children present on Foueda and the remaining islands were examined and medication offered to everyone (see timeline). Information on adverse events was sought.

As much of each child's skin as was accessible without embarrassment for children of each age was examined. The effects on the analysis of a few older children having lesions that were confined to their genitals was considered acceptable because about 90% of people with scabies have lesions on their hands and arms (*15*) and some of the other 10% would have visible lesions on the lower limbs and trunk. Scabies in children was diagnosed clinically by one investigator on the basis of the nature and distribution of lesions (*16*). These included findings such as pruritic papulonodular and vesicular lesions on the hands, arms, wrists, feet, thighs, trunk and buttocks. Also, a more generalized symmetrical papulonodular eruption contributed to some diagnoses, as did acropustulosis in some infants. Where findings were suggestive, but not definitive, a diagnosis of possible scabies was recorded. In children without apparent active pruritis but with superficial scarring and changes in pigmentation from recent scabies, healed scabies was recorded. The category of "possible scabies" was used in case our intervention had reduced the intensity of infestation in a substantial number of children who were actually infected, so that a confident diagnosis could not be made. Demonstration of mites for diagnosis was not attempted, but mites were recovered from lesions during protocol development. Unhealed sores (any

break in the skin), including those from burns and trauma, were recorded by site and number. The size and severity of sores was not recorded. The hands and arms of all adults were examined for scabies at the time of treatment and easily available adults were re-examined at the end of the study.

To ensure that coverage was as complete as possible, two treatments 2 weeks apart, were offered on each island except Addagege. On Addagege, because compliance was complete on the first day, only one treatment was given. Throughout the study, treatment was offered to returning residents and overnight visitors whether they had apparent scabies or not.

Medication

Orally administered ivermectin was given at a dose of 160–250 μg/kg, using 6 mg scored tablets (15–18 kg, 3 mg; 19–27 kg, 4.5 mg; 28–36 kg, 6 mg; 37–55 kg, 9 mg; 56–74 kg, 12 mg; 75–100 kg, 15 mg). Children who weighed less than 15 kg were treated topically with 5% permethrin cream as were women who, in response to queries from a health worker, volunteered the information that they were or might be pregnant. Ivermectin treatment was directly observed by a team member. For those treated with permethrin, a full tube was supplied by a health worker who demonstrated its use and gave instruction in the local language. The seven adults with severe generalized scabies were treated twice with both ivermectin and permethrin. No antibiotic treatment was provided or advised for pyoderma.

Follow-up

At reviews three times per year, children were examined and specimens collected as described below. Children were given small gifts such as balloons to encourage attendance. Those found to have scabies at review were treated, as were their household contacts.

Specimens

Swabs from sores and/or fingertips were taken using sterile swabs wetted with nutrient broth containing 10% glycerol. These were frozen and stored on dry ice within an hour. Blood samples were collected from cooperating children aged over about 4 years on all islands other than Addegage and the plasma frozen. All samples were indexed and stored at –70 °C until use. Urine was collected at the initial visit and then monthly on all islands except Addagege and Nuileni where the only testing after treatment was at reviews. In addition urine collections were made every 2 weeks for the first few months from children on Sulufou and Foueda to assess the normal pattern of findings. Testing was done within hours using commercially available urine testing strips. Results for haematuria were recorded as negative (0), trace (10), small (25), moderate (80) or large (200) cells per microlitre, approximately.

Microbiology and serology

Frozen swabs from sores and from the fingertips of children with and without sores were randomly selected from the relevant "stored cohorts" (stored cohorts is the term used to describe a particular group of samples, e.g. all the stored finger-swab samples from children who had no sores early in the study) to measure the proportion positive for GAS before and after scabies control. Swabs were thawed and plated on plain horse-blood agar (HBA) and HBA with gentamicin. After incubation at 36 °C with carbon dioxide, representative beta haemolytic catalase-negative colonies were plated on HBA with a bacitracin disc. Subsequent isolates were typed using a streptococcal typing kit and preserved by freezing.

Anti-streptolysin O titre (ASOT) and anti-DNase B levels were measured using commercial kits. Thirty pre-treatment serum samples were selected using a list of random numbers to compare the mean titre with thirty serum samples randomly selected from those collected in 2000. Also, all the pairs of samples in cases in which a sample had been collected at baseline and in January 2000 from the same child, were tested.

Statistical methods

Because many of the same children were seen on numerous occasions, a generalized estimating equations approach was used for all logistic regression models examining change in the proportion of children with scabies. Negative binomial regression analysis (with repeated measures) was used to test the association between number of sores per child and time after treatment, because number of sores was found to follow an approximately negative binomial distribution. The likelihood ratio statistic was used to test for statistical significance. Spearman's correlation coefficient was used for quantification. Fisher's exact test was used to compare the proportion of children with scabies and sores before and after treatment and the proportions of positive swab isolates from the earlier and later samples. Geometric means were used to compare serological titres. All analyses were conducted using SAS statistical software (release 8.0).

The association between proportion of children with haematuria ($\geq$ 25 and $\geq$ 10 cells per microlitre) as well as mean red cells per microlitre of urine and time since scabies treatment were analysed using weighted least squares linear regression to draw the lines of best fit. Ordinal logistic regression was used to assess the significance of the overall change in concentration of red cells per microlitre over time.

The relationship between sores and haematuria was examined by correlating the number of sores with the numbers of red blood cells/microlitre at the time of the sore review and also in urine collected a month later. Results from all visits were pooled for this analysis. Non-parametric methods (Spearman coefficient) were used to calculate correlations and logistic regression used to assess statistical significance. Results were analysed using both $\geq$ 25 red cells/microlitre and $\geq$ 10 red cells/microlitre to define haematuria.

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Results

Five hundred and forty-one different children were seen in the course of the study; 258 (48%) were seen four times or more (frequencies: 142 × 1, 75 × 2, 66 × 3, 67 × 4, 68 × 5, 59 × 6, 45 × 7 and 19 × 8 times). The estimated age distribution of the subjects stayed relatively constant because as older children dropped out infants and toddlers were being added.

Treatment efficiency

The prevalence of scabies fell dramatically on all the islands after treatment (Fig. 2), from a mean of 25%, 66 of 267 (95% CI, 20–30), to a steady level of less than 1%, 2 of 305 (0.7%; 95% CI, 0.1–2.2), $P < 0.001$. No adverse events were noted.

Over 95% of the people who were present on the islands during the treatment period were treated; just over half of them

twice. On Sulufou where the census population was 743, 228 were away, 494 were treated once or twice and 21 declined or avoided treatment. Ten per cent of the children said to have scabies or possible scabies at baseline were diagnosed as having scabies or possible scabies at the next review, 4 or 5 months later. Of these possible failures, half were among the 24% of children treated topically with permethrin. On Addagege a single treatment was similarly effective although half the population had scabies before the treatment was given. Here, all ten children with scabies who were treated with ivermectin and seen again 4 months later were cured.

Although not all the ivermectin distributed was actually swallowed (we found some partially dissolved tablets on the ground), few re-treatments were required. Most cases of scabies seen at reviews were in children who had returned from elsewhere and had not been treated in the interim.

Controls

On Foueda, two pre-treatment observations were made, in July and November 1997. At the time of the first observation, 23% (14/61) of the children seen had scabies or possible scabies; 14 had healed scabies. The proportion of children with scabies and those with sores did not change significantly between July and November (26%; 12/46).

Scabies in adults

At the time of treatment about 20% (81 of 374) of the adults for whom findings were recorded had scabies. At the last review when the hands and arms of about 250 adults from all islands were examined only two, neither of whom had been treated, were diagnosed as having scabies.

Sores

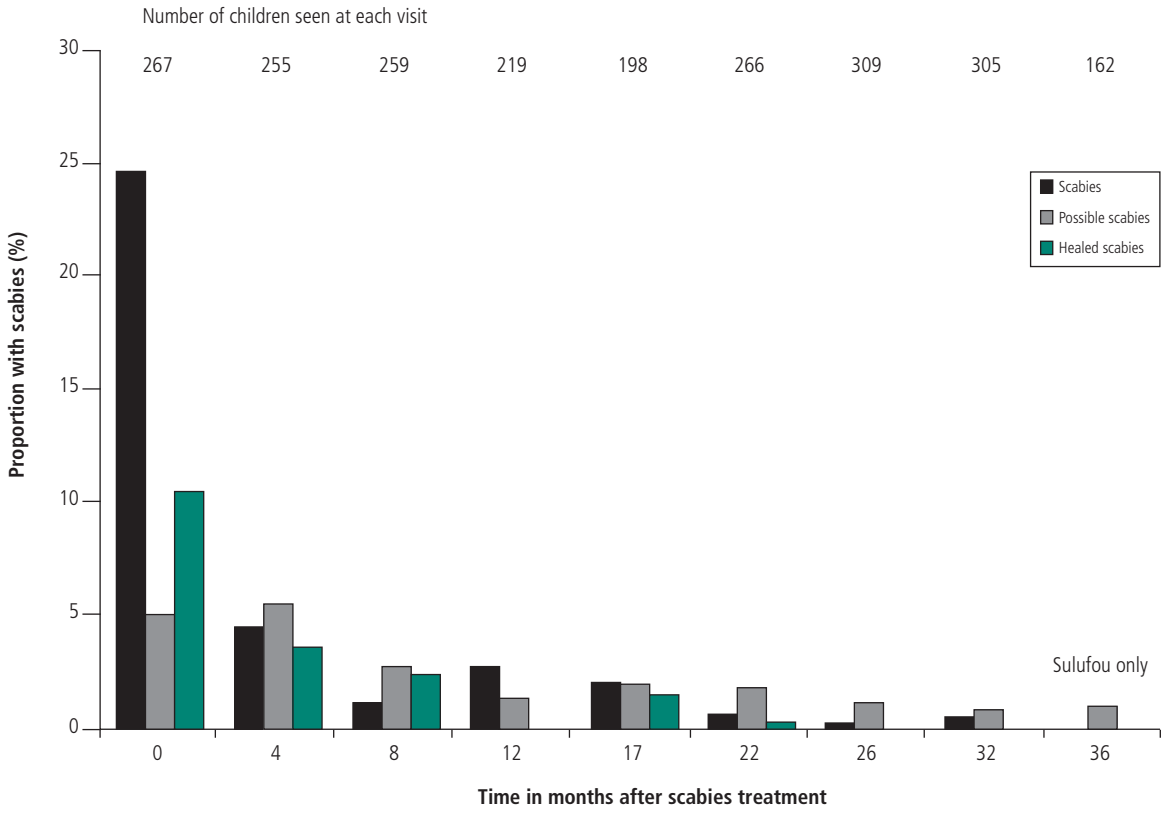
The proportion of children with sores decreased from 40%, 91 of 226 (95% CI, 34–47) to 22%, 35 of 162 (95% CI, 16–28; $P < 0.001$) and the mean number of sores per affected child decreased with time (Table 1). The fall was statistically significant, the correlation with time being –0.15 (P for trend < 0.0001). The proportion of children with sores on the more trauma-prone lower limbs stayed at about 20% (33 of 162). The number with sores on the upper body, including those with sores on both the upper and lower body, fell from 16%, 34 of 215 (95% CI, 11–21) to less than 5% by the end of the study (3.1%, 5 of 162 (95% CI, 1–7)) $P < 0.001$.

At the review in January 2000, many children had circular marks on their skin that were said to have followed recent superficial blisters: probably due to impetigo which, in these conditions, is usually streptococcal (*17*). No change in scabies was reported.

Microbiology and serology

In stored samples from sores, randomly selected from those collected in 1997, November 1998 and January 2000, GAS grew in 92%, 90% and 84%, respectively ($P = 0.52$). GAS were found in 61% of finger swabs taken from children with sores early in the study whereas, of the swabs taken later in the study, only 32% were positive ($P = 0.02$) (Table 2). Of the fingertip swabs taken from children without sores, 24% (9/38) of those taken

Fig. 2. **Number of children with scabies by approximate months after treatment**[a]



[a] The fall in the proportion of children with scabies is significant ($P < 0.001$). As treatment began 4 months earlier on Sulufou, the results at 36 months refer only to Sulufou children, about half the total.

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Table 1. **Percentage of children with sores at baseline and after scabies treatment, percentage with 1–4 and > 4 sores and mean number of sores per child**[a]

Time examined	Total number of children examined	> 4 sores (%)	1–4 sores (%)	Any sores (%)	Mean sores per child (standard error)
Baseline	230	5	35	40	1.03 (0.11)
4 months	236[b]	5	32	37	0.92 (0.12)
8 months	257	4	26	30	0.85 (0.15)
12 months	214[c]	3	31	34	0.78 (0.12)
16 months	196	4	31	35	0.72 (0.10)
21 months	264[c]	2	25	27	0.50 (0.07)
26 months	308	1	28	29	0.49 (0.06)
31 months	303	2	20	22	0.46 (0.07)
36 months	163	3	18	21	0.48 (0.11)

[a] Correlation of number of sores with approximate number of months after treatment= –0.15, *P*-value from Spearman correlation < 0.0001.
[b] Two of the 236 children had sores, but the number of sores was not counted.
[c] One child in this group had sores, but the number of sores was not counted.

early in the study contained GAS, whereas only 5% (2/38) of those taken later were positive ($P = 0.047$, all tested with Fisher's exact test) (Table 2). The total numbers of swabs from sores and fingers tested during the study were 153 and 321, respectively. Ninety-eight per cent (150) of all samples from sores tested grew streptococci, 92% (141) grew GAS; of the fingertip swabs 38% (122) grew streptococci and 30% (96) GAS.

The geometric means (GMs) of the ASOT and anti-DNase B titres in random serum samples collected before treatment and at the end of the study were not significantly different ($n = 30$ for each group). The means for ASOT titres from samples taken early and later in the study were 184 and 189; for anti-DNase B titres the means were 316 and 359, respectively. However, in the paired samples from the children who provided sera at the time of treatment and again at the end of the study ($n = 33$), there was a significant fall ($P = 0.002$) in the titre of anti-DNase B from 512 (95% CI, 404–650) to 346 (95% CI, 278–428). The GM for the ASOT titres in the same samples did not change significantly (178 in samples taken early in the study and 203 in those taken later). Unfortunately, for logistical reasons the events surrounding the possible impetigo outbreak in late 1999 could not be examined.

Haematuria

There was a significant decrease in the proportion of children with haematuria at both ⩾ 25 cells/microlitre ($P = 0.002$) and ⩾ 10 cells/microlitre ($P < 0.001$), despite wide variation from month to month. The mean levels of haematuria (Fig. 3) also fell with time ($P < 0.001$). There was however a sharp rise in the mean haematuria levels in the period prior to the January 2000 review when the marks left by the possible impetigo outbreak were noted.

Where a child in a household was found to have haematuria (⩾ 25 cells/microlitre) the odds ratio of another child in that household having haematuria at the same time was 2.04 compared with children overall (95% CI, 1.11–3.75, $P = 0.02$).

The number of sores per child was not significantly related to haematuria measured at the same review (1124 pairs of data examined; correlation 0.02; $P = 0.69$). However, the number of sores was related to haematuria a month later; correlation 0.09; $P = 0.03$ (573 pairs of pooled data). Of the 573 children in question only 20 had more than four sores, three of whom (15%) had ⩾ 25 cells per microlitre of urine, compared to 12% (66) in those with up to four sores, not a marked difference. However, 65% (13) of the children with more than four sores had ⩾ 10 cells/microlitre of urine, whereas in children with four sores or fewer only 19% (101) had haematuria at this level a month after the sores were diagnosed ($P = 0.0015$; Fisher's exact test).

Discussion

The precipitous fall in the prevalence of scabies among treated children on Sulufou, and the fact that infestation in children on Foueda remained unchanged until after their treatment later in the study, provide strong evidence that the control of scabies was a direct result of treatment. The effect was greater than that reported in Papua New Guinea following a dose of ivermectin (*18*), probably because the whole population was treated. Another study reported that 95% of cases of scabies among 1500 prisoners were cured when a single dose of ivermectin was given to the whole jail population (*10*). In our study, scabies was greatly reduced by the initial treatments and reinfection was largely prevented by treating returnees and visitors. In the late stage of the study, scabies was found only on untreated people showing that transmission within the population was minimal. On the smaller islands, treatment of returnees and visitors was less immediate and less thorough than on Sulufou where a treating staff member was resident. Nevertheless, scabies control was maintained on these islands despite the delay and movement of people. This raises the possibility that an annual treatment in situations when no active interim treatment can be provided might also be an effective strategy.

Ivermectin has major advantages over topical treatments. It is far more convenient to use and there is no problem with incomplete application or with the treatment being washed off. Also ivermectin has prolonged activity (a single dose made pigs resistant to applied *Sarcoptes* for a week and a human who had taken ivermectin was lethal to feeding mosquitoes for a longer period) (*19*, *20*), suggesting there may be considerable flexibility in the time available to complete community treatment. Because of the safety of ivermectin at a dose of 400 µg/kg (*11*) and because there was a lower rate of cure of scabies when

Table 2. **Streptococcal isolates from sores and fingertips, early and late in the study**

Time	Swabs tested	GAS[a] isolated (%)	Other streptococci isolated (%)	No streptococci isolated (%)
Swabs taken from sores before and after scabies control[b]				
1997	85	78 (92)	19 (22)	3 (4)
November 1998	30	27 (90)	18 (60)	0
January 2000	25	21 (84)[c]	11 (44)	1 (4)
Finger swabs taken from children with sores before and after scabies control[d]				
1997	36	22 (61)	7 (19)	12 (33)
1999; 2000	28	9 (32)[e]	8 (29)	15 (54)
Finger swabs taken from children without sores before and after scabies control[f]				
1997	38	9 (24)	3 (8)	26 (68)
2000	38	2 (5)[g]	2 (5)	34 (89)

[a] GAS, group A streptococci.
[b] There was no significant change in the proportion of sores containing GAS.
[c] $P = 0.52$ (January 2000 vs 1997).
[d] The proportion of children with sores who had GAS on their fingers declined.
[e] $P = 0.02$.
[f] The proportion of children without sores with GAS on their fingers fell.
[g] $P = 0.047$; all tests Fisher's exact test.

ivermectin was administered at 100 μg/kg (*21*), the dose of approximately 200 μg/kg employed in this study should not be reduced. Higher doses might be advantageous as they may lessen the chance of resistance emerging. The reliability, palatability and historical safety of oral ivermectin suggest that data on its safety in children below the present lower limit of 15 kg body weight should be collected. The present 3 mg tablet broken in half would be practical for administration to children with body weights down to 7.5 kg.

Drug safety is particularly important in situations where many unaffected people are treated. We are aware of no reports of idiosyncratic responses to ivermectin in humans, although there are reports of a genetic susceptibility in dogs (*22*). Although no problems were reported in a study of pregnant women in Africa (*5*), we did not use ivermectin in women known to be pregnant or who were possibly pregnant. No adverse events were noted in this study.

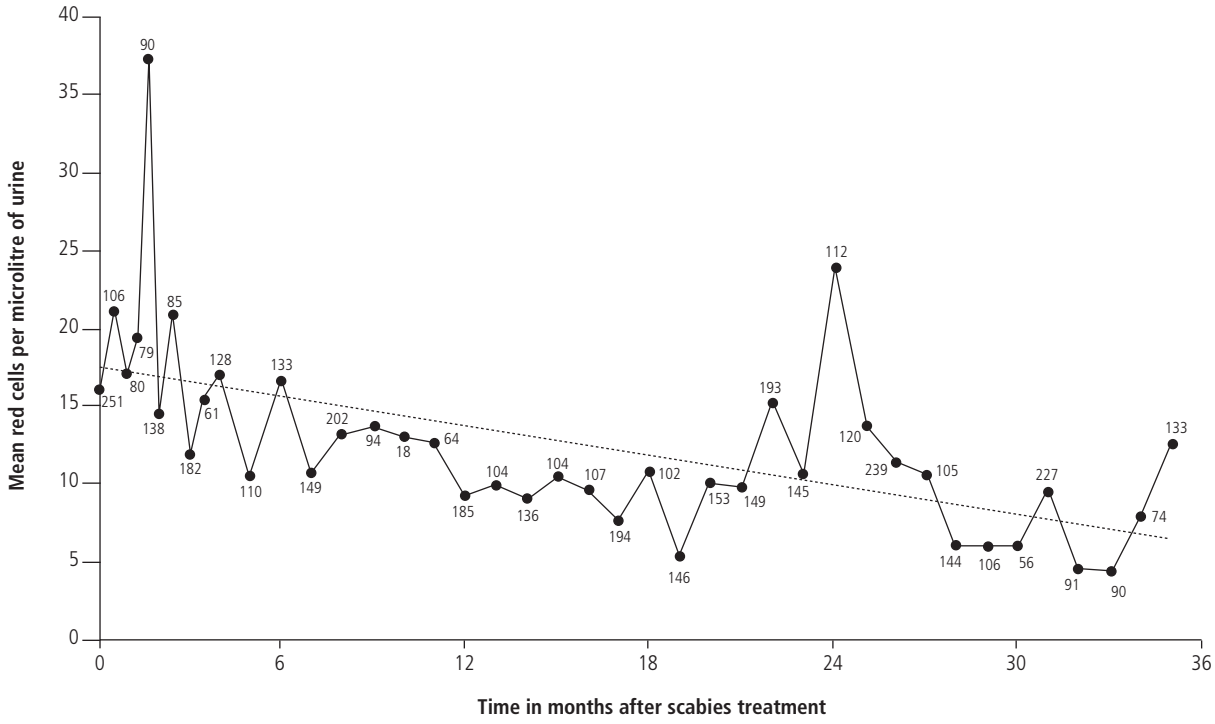
Although the children appeared to be clean and spent much time in the sea, almost one third of all the finger swabs tested contained GAS, emphasizing the high level of exposure of the children to this organism. Taplin found similar levels (25%) among children living with pyoderma in an earlier study (D. Taplin, personal communication, 2003). Hand contamination is likely to be central in the transfer of strains of GAS from child to child, and in the infection of skin injuries, slowing their healing. Sores and scratches are the likely reservoir of GAS in this situation, as normal skin is not usually a source (*23*), but scabies, because it leads to constant scratching and rubbing, must be important in spreading the organism and contaminating the fingers as well as damaging the skin. Evidence for this comes from the significant decrease in the number of sores and in contamination of fingertips with GAS that was observed in our study after scabies control in the absence of any specific treatment for sores. Similar findings relating to sores have been reported by others (*4*, *10*). However, in our study, because many sores infected with GAS remained, the effects of scabies control on the epidemiology of GAS might have been hastened and increased by treating children who had sores using penicillin.

The reduction in haematuria seen to occur in parallel with the decline in sores, the significant correlation between the presence of sores and haematuria a month later, the temporal clustering of children with haematuria in households and the peak in incidence of haematuria that followed a probable outbreak of impetigo, all provide support for a post-infectious cause for many of the cases of haematuria we found. The significant reduction in the proportion of children with haematuria may reflect a change in low levels of specific post-streptococcal damage.

The changes in incidence of scabies, sores and haematuria that followed scabies control on the five islands probably resulted directly from the intervention, although other factors may also have contributed. There were no changes in the clinical services available, or in access to them, over the study period to explain the observations. A concomitant fall in the average nephritogenicity of the GAS strains circulating in the communities is an unlikely explanation for the progressive fall in haematuria, as, in crowded circumstances such as these, many strains are circulating (*24*). The reduction in the prevalence of sores, in GAS on the hands and fingers, and in haematuria that we demonstrated following scabies control, might, if extended over the whole of childhood, make a substantial difference to the accumulation of renal damage.

The programme we used to demonstrate the effects of scabies control would not be practical in most of the countries in which scabies and streptococcal skin disease are important because treatments frequently fail without very careful supervision. Also, the expense of the drugs and of initiating a specific community-based programme for this disease complex would be competing with more pressing health needs. However, our

Fig. 3. **Mean level of red cells in the urine after scabies treatment**[a]



[a] A possible reason for the peak 2 years after treatment is given in the text. The decline in mean concentration of red cells represented by the regression line is significant ($P < 0.001$). The number of urine samples tested at each point has been superimposed on the graph.

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collaborators report that the prevalence of scabies remains very low on Sulufou in 2004 despite there having been no further input since our intervention. This suggests that the programmes proposed for control of filariasis, which deliver either ivermectin or diethylcarbamazepine (DEC) and albendazole annually (*25*), may well provide effective scabies control when ivermectin is used.

The ivermectin and albendazole combination given annually to whole communities may well control a number of significant health problems including: scabies, hookworm, strongyloides and other intestinal nematodes, as well as filariasis. The added impact on skin disease and post-streptococcal disease and on strongyloides and trichuris infection, would justify a preference for using ivermectin rather than DEC in these programmes. Also, the parallel health benefits may justify its use in areas in which filariasis is not a concern, and, if the drugs for this purpose were donated, their use could prove sustainable in countries with limited health budgets. Further studies are recommended. ■

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Résumé

Lutte contre la gale, les lésions cutanées et l'hématurie chez les enfants des Îles Salomon : un autre rôle pour l'ivermectine

Objectif Évaluer les effets d'un programme sur 3 ans de lutte contre la gale sur cinq petites îles lagunaires des Îles Salomon à travers la surveillance de la gale, des lésions cutanées, de la contamination de la peau par des streptocoques, de la sérologie et de l'hématurie chez les enfants de ces îles.

Méthodes Les responsables du programme sont venus à bout de la gale en traitant presque tous les habitants de chaque île une à deux fois en l'espace de deux semaines avec de l'ivermectine (160 à 250 μg/kg), à l'exception des enfants pesant moins de 15 kg et des femmes enceintes, chez lesquels ils ont utilisé de la crème à 5 % de perméthrine. Ils ont fait obstacle à la réintroduction de la gale en traitant les habitants revenant d'un déplacement et les visiteurs, qu'ils présentent ou non une gale de façon manifeste.

Résultats La prévalence de la gale est passée de 25 % à moins de 1 % ($p < 0,001$), celle des lésions de 40 % à 21 % ($p < 0,001$), la contamination des doigts par des streptocoques chez les personnes présentant ou non des lésions a diminué significativement ($p = 0,02$ et 0,047, respectivement) et les concentrations d'antiDnase-B ont baissé ($p = 0,002$). La proportion d'enfants souffrant d'hématurie et la valeur moyenne de cette proportion ont chuté ($p = 0,002$ et $p < 0,001$, respectivement). On n'a observé aucun effet secondaire des traitements.

Conclusion Les résultats montrent que l'ivermectine est un agent efficace et pratique dans la lutte contre la gale et que la prévention de cette maladie réduit la fréquence des infections cutanées streptococciques et des signes éventuels de lésion rénale chez les enfants. L'intégration aux programmes planifiés de lutte contre la filariose et les nématodes intestinaux de la lutte à l'échelle de la communauté contre la gale et les infections cutanées streptococciques pourrait constituer une option à la fois pratique et très bénéfique pour la santé.

Resumen

Control de la sarna, las lesiones cutáneas y la hematuria en los niños en las Islas Salomón: otra utilidad de la ivermectina

Objetivo Evaluar los efectos de un programa de 3 años encaminado a combatir la sarna en cinco pequeños atolones de las Islas Salomón, procediendo para ello a vigilar en la población infantil de las islas las manifestaciones de esa enfermedad, las lesiones cutáneas, la contaminación de la piel por estreptococos, la serología y los casos de hematuria.

Métodos Se logró controlar la enfermedad tratando a casi todos los residentes de cada atolón con ivermectina (160–250 μg/kg) una o dos veces en un periodo de dos semanas, salvo en el caso de los niños que pesaban menos de 15 kg y las mujeres embarazadas, a quienes se administró pomada de permetrina al 5%. Se evitó la reintroducción de la sarna tratando a los residentes que regresaban del exterior y a los visitantes, tuvieran o no signos evidentes de sarna.

Resultados La prevalencia de sarna se redujo de un 25% a menos del 1% ($P < 0,001$); la prevalencia de lesiones cutáneas lo hizo de un 40% a un 21% ($P < 0,001$); la contaminación estreptocócica de los dedos, entre personas con y sin lesiones, disminuyó de forma significativa ($P = 0,02$ y 0,047, respectivamente), y los niveles de anti-DNasa B se redujeron ($P = 0,002$). Descendieron también tanto la proporción como el nivel medio de niños con hematuria ($P = 0,002$ y $P < 0,001$, respectivamente). No se detectaron efectos adversos de los tratamientos.

Conclusión Los resultados indican que la ivermectina es un agente eficaz y práctico contra la sarna y que las medidas de control reducen la aparición de lesiones cutáneas estreptocócicas y los posibles signos de daño renal en los niños. La integración del control comunitario de la sarna y las lesiones cutáneas estreptocócicas junto con programas planificados de control de la filariasis y los nematodos intestinales podría ser una opción práctica y, al mismo tiempo, generar grandes beneficios sanitarios.

ملخص

مكافحة الجرب وقرحات الجلد والبيلة الدموية لدى الأطفال في جزر سليمان: دور آخر للإيفيرمكتين

الهدف: لتقييم تأثير برنامج امتد لثلاث سنوات وكان يهدف لمكافحة الجرب في خمس جزر صغيرة مليئة بالبحيرات الضحلة في جزر سليمان، وذلك برصد الجرب وقرحات الجلد وتلوث الجلد بالعقديات والدراسة السيرولوجية (المصلية) والبيلة الدموية لدى أطفال تلك الجزر.

الطريقة: لقد أمكن تحقيق المكافحة بمعالجة جميع السكان تقريباً في كل جزيرة بجرعة أو جرعتين خلال اسبوعين بمقدار (160 - 250) مكروغرام لكل كيلوغرام من الوزن من الإيفيرمكتين، وذلك باستثناء الأطفال الذين تقل اوزانهم عن 15 كيلوغرام وباستثناء الحوامل، إذ استخدم عند هؤلاء مرهم 5% بيرمثيرين. وتمت مكافحة عودة ظهور الجرب مرة أخرى بمعالجة السكان الذين عادوا إلى الجزر ومن يزورهم، سواءً ظهرت عليهم علامات الجرب أم لم تظهر.

الموجودات: لقد انخفضت معدلات انتشار الجرب من 25 % لأقل من 1 % (معامل الدقة يزيد على 0.001)، كما انخفض معدل انتشار القرحات من 40 % إلى 21 % معامل الدقة يزيد على 0.001). كما انخفض معدل التلوث بالعقديات في اصابع المصابين بالقرحات الجلدية بشكل ملحوظ (معامل الدقة يعادل 0.02) وفي أصابع غير المصابين بالقرحات الجلدية (معامل الدقة يعادل 0.047). كما ازداد مضاد إنزيم الدناز البائي (معامل الدقة يعادل 0.002). وقد انخفض كل من النسبة المئوية للأطفال المصابين بالبيلة الدموية (معامل الدقة يعادل 0.002)، والمستوى المتوسط للبيلة الدموية (معامل الدقة يقل عن 0.001). و لم تلاحظ أية تأثيرات ضائرة للمعالجة.

الاستنتاج: توضح النتائج أن الإيفيرميكتين دواء فعَّال وعملي في مكافحة كل من الجرب وأمراض الجلد الناجمة عن العقديات والعلامات المحتمل حدوثها نتيجة أذية الكلية لدى الأطفال. إن إدماج المكافحة المرتكزة على المجتمع للجرب ولأمراض الجلد الناجمة عن العقديات ضمن برامج مخطَّط لها لمكافحة داء الفيلاريات والمسودات المعوية، فذلك الإدماج سهل التطبيق عملياً ويؤدي للكثير من المنافع الصحية .

References

1. Mahe A. Bacterial skin infections in a tropical environment. *Current Opinion in Infectious Diseases* 2001;14:123-6.
2. Carapetis JR, Currie BJ, Kaplan EL. Epidemiology and prevention of group A streptococcal infections: acute respiratory tract infections, skin infections, and their sequelae at the close of the twentieth century. *Clinical Infectious Diseases* 1999;28:205-10.
3. Gibbs S. Scabies. *Tropical Doctor* 2000;30:232-5.
4. Taplin D, Porcelain SL, Meinking TL, Athey RL, Chen JA, Castillero PM, et al. Community control of scabies: a model based on use of permethrin cream. *Lancet* 1991;337:1016-8.
5. Pacque M, Munoz B, Greene BM, White AT, Dukuly Z, Taylor HR. Safety of and compliance with community-based ivermectin therapy. *Lancet* 1990;335:1377-80.

6. Gardon J, Gardon-Wendel N, Demanga N, Kamgno J, Chippaux JP, Boussinesq M. Serious reactions after mass treatment of onchocerciasis with ivermectin in an area endemic for Loa loa infection. *Lancet* 1997;350:18-22.
7. Meinking TL, Taplin D, Hermida JL, Pardo R, Kerdel FA. The treatment of scabies with ivermectin. *New England Journal of Medicine* 1995;333:26-30.
8. Sullivan JR, Watt G, Barker B. Successful use of ivermectin in the treatment of endemic scabies in a nursing home. *Australasian Journal of Dermatology* 1997;38:137-40.
9. Buffet M, Dupin N. Current treatments for scabies. *Fundamental & Clinical Pharmacology* 2003;17:217-25.
10. Leppard B, Naburi AE. The use of ivermectin in controlling an outbreak of scabies in a prison. *British Journal of Dermatology* 2000;143:520-3.
11. Kazura J, Greenberg J, Perry R, Weil G, Day K, Alpers M. Comparison of single-dose diethylcarbamazine and ivermectin for treatment of bancroftian filariasis in Papua New Guinea. *American Journal of Tropical Medicine and Hygiene* 1993;49:804-11.
12. Geurden T, Verelst A, Somers R, Dierickx N, Vercruysse J. Efficacy of ivermectin against *Sarcoptes scabiei* var suis in pigs. *Veterinary Record* 2003;153:272-3.
13. Hoy WE, Mathews JD, McCredie DA, Pugsley DJ, Hayhurst BG, Rees M, et al. The multidimensional nature of renal disease: rates and associations of albuminuria in an Australian Aboriginal community. *Kidney International* 1998;54:1296-304.
14. Perlman LV, Herdman RC, Kleinman H, Vernier RL. Poststreptococcal glomerulonephritis. A ten-year follow-up of an epidemic. *JAMA* 1965;194:63-70.
15. Mellanby K. *Scabies.* London: Oxford University Press; 1943.
16. Burgess I. *Sarcoptes scabiei* and scabies. *Advances in Parasitology* 1994;33:235-92.
17. Dajani AS, Ferrieri P, Wannamaker LW. Natural history of impetigo. II. Etiologic agents and bacterial interactions. *Journal of Clinical Investigation* 1972;51:2863-71.
18. Bockarie MJ, Alexander ND, Kazura JW, Bockarie F, Griffin L, Alpers MP. Treatment with ivermectin reduces the high prevalence of scabies in a village in Papua New Guinea. *Acta Tropica* 2000;75:127-30.
19. Arends JJ, Skogerboe TL, Ritzhaupt LK. Persistent efficacy of doramectin and ivermectin against experimental infestations of *Sarcoptes scabiei* var. suis in swine. *Veterinary Parasitology* 1999;82:71-9.
20. Foley DH, Bryan JH, Lawrence GW. The potential of ivermectin to control the malaria vector *Anopheles farauti. Transactions of the Royal Society of Tropical Medicine and Hygiene* 2000;94:625-8.
21. Glaziou P, Cartel JL, Alzieu P, Briot C, Moulia-Pelat JP, Martin PM. Comparison of ivermectin and benzyl benzoate for treatment of scabies. *Tropical Medicine and Parasitology* 1993;44:331-2.
22. Schinkel AH, Smit JJ, van Tellingen O, Beijnen JH, Wagenaar E, van Deemter L, et al. Disruption of the mouse mdr1a P-glycoprotein gene leads to a deficiency in the blood-brain barrier and to increased sensitivity to drugs. *Cell* 1994;77:491-502.
23. Taplin D, Lansdell L, Allen AM, Rodriguez R, Cortes A. Prevalence of streptococcal pyoderma in relation to climate and hygiene. *Lancet* 1973;1:501-3.
24. Carapetis J, Gardiner D, Currie B, Mathews JD. Multiple strains of *Streptococcus pyogenes* in skin sores of aboriginal Australians. *Journal of Clinical Microbiology* 1995;33:1471-2.
25. Cline BL, Savioli L, Neira M. Introduction: opportunities to work together: intestinal helminth control and programmes to eliminate lymphatic filariasis. *Parasitology* 2000; 121 Suppl:S3-4.