

educational messages which were essential to successful implementation of net use. Follow-up identified that a specific strategy is needed to ensure that families with first children born after implementation, obtain and use nets.

After confirming the beneficial effect of net implementation in this small cluster of villages, the project team identified additional target villages with severe malaria problems and continued to implement net use on a village-by-village basis. During implementation of the project on a broader scale we realized that we needed more manpower to help with the administrative aspects of the programme on a village level. Village Health Committees (VHCs) were established in each village to oversee the coordination of educational activities, net distribution and payment. Since initiating the pilot study, the net project has expanded into an ongoing malaria prevention programme, now part of a community-based health promotion programme (Loloma Integrated Health Promotion Program) that focuses on malaria, HIV/AIDS and tuberculosis. The mandate of the VHCs has expanded beyond malaria activities to include many different aspects of health on the village level. Every village in the catchment area of Loloma Mission Hospital has now been included in the programme and we are receiving requests from adjacent villages outside the catchment area to participate in the programme. Awareness and demand for nets has increased rapidly.

Although we were able to demonstrate a beneficial effect of net use, there are a number of limitations inherent in our project. This project was not conducted as a formal clinical trial, and while this may enhance its generalizability, the reliability of data is not as strong. Our post-intervention survey was incomplete compared to the pre-intervention survey due to the unexpected absence of a number of families. While we used Field stain to assess parasitaemia (the standard stain for malaria diagnosis in the hospital at the time of the project), Giemsa staining is recognized to be more sensitive for the identification of malarial parasites. Although this may have underestimated the incidence of parasitaemia, it should have affected both pre- and post-intervention data equally. Although we did not evaluate climatic data for both seasons in order to confirm lack of significant difference, there was no obvious difference in the rainfall or temperature for the 2 years. Also, there were no dramatic differences in the diagnosis of malaria or admission rates in the general population. Although periodic follow-up visits to the pilot project villages have continued, we have not been able to formally reassess net use, integrity, or effects on malarial disease since the 1-year point. Data on longer-term efficacy are thus lacking.

The use of subclinical parasitaemia rates, spleen rates and haemoglobins were easily measurable markers for the burden of malarial disease but we were not able to prospectively follow clinical episodes of malaria due to personnel constraints. Data regarding transfusions were found to be unreliable as many 'under 5 cards' were incomplete.

Despite these limitations we feel that net introduction using a village-by-village strategy with targeted educational interventions has proven highly successful in this setting with very limited personnel and financial resources. Awareness and acceptance of nets quickly increased and the cost of nets is now at a sustainable level allowing us to continually expand the project. The elimination of taxes and tariffs would significantly reduce costs of nets and facilitate a more rapid uptake of nets. However, the main

limitations to rapid expansion of the project are insufficient personnel and limited availability of nets.

## References

- 1 Alonso PL, Lindsay SW, Armstrong JRM, *et al.* The effect of insecticide treated bed nets on the mortality of Gambian children. *Lancet* 1991;i:1499–502
- 2 Greenwood BM, Greenwood AM, Bradley AK, *et al.* Comparison of two drug strategies for control of malaria within a primary health care programme in The Gambia, West Africa. *Lancet* 1988;i:1121–7
- 3 Menon A, Snow RW, Byass P, Greenwood BM, Hayes RJ, N'Jie ABH. Sustained protection against mortality and morbidity from malaria in rural Gambian children by chemoprophylaxis given by village health workers. *Trans R Soc Trop Med Hyg* 1990;84:768–72
- 4 Snow RW, Rowan KM, Greenwood BM. A trial of permethrin-treated bed nets in the prevention of malaria in Gambian children. *Trans R Soc Trop Med Hyg* 1987;81:563–7
- 5 Appropriate Health Resources and Technologies Action Group. *Insecticide Treated Nets for Malaria Control: a directory of suppliers of insecticides and mosquito nets for sub-Saharan Africa*. London: AHRTAG, 1997
- 6 *Community Based Malaria Prevention Control Programme in Zambia, Funding Proposal*. Zambia: Central Board of Health, Ministry of Health, 2000

## Oral desensitization in papular urticaria in children

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TROPICAL DOCTOR, 2002, 32, 142–145

**SUMMARY** Papular urticaria (PU) is among the commonest skin ailments in children. Induced specific desensitization to insect bites is theoretically an effective means of prevention of PU. In this double blind placebo controlled study, an oral vaccine prepared from insect saliva was compared with placebo (stable vaccine solvent). Vaccine and placebo effectiveness were tested by counting active PU lesions, serum eosinophils, and IgE, before and after 4 months of treatment. Statistically significant differences between oral vaccine and placebo were not found in the clinical or the immunological variables tested. We conclude that, although a lack of oral vaccine efficacy was suspected, larger study samples are needed to strengthen our conclusion.

## Introduction

Papular urticaria (PU) is a common dermatosis in children of tropical countries. It is defined as a reaction of delayed hypersensitivity to bites by dipterous (mosquitoes), siphonapterous (fleas) and ixodideous (ticks) insects<sup>1-5</sup>. Hot and humid weather favour insect development<sup>6</sup>.

Geographical and environmental factors determine the species to which children will be exposed<sup>7</sup>. One to 7-year-olds are affected<sup>8,9</sup>. Younger children are less exposed, older children develop spontaneous desensitization after recurrent insect bites<sup>2,9-11</sup>. In Mexico City, PU represents 28% of dermatological diagnoses in paediatric outpatients. It is the most frequent skin disease in childhood<sup>8</sup>.

As the insect bites, its saliva containing antigens, anticoagulants and toxic substances with irritating and lytic materials<sup>1,9,11,12-15</sup>, elicits a hypersensitivity reaction<sup>12,14,16</sup>. There is a wide spectrum of poison concentration and antigenicity in the mosquitoes' saliva<sup>17</sup>. In human serum, a spectrum of antigens with great molecular weight variations have been identified.

Hypersensitivity to insect bites requires previous sensitization to insect antigens<sup>16</sup>. After the insect bites an IgE and IgG immediate acute urticarial inflammatory reaction lasting around 1 hour takes place<sup>12,17-20</sup>. After 24-48 hours, a T-cell mediated reaction is manifested clinically by skin coloured, firm, and extremely itching papules<sup>2,12,20-23</sup>. The severity of the reaction depends on individual sensitivity and number of bites<sup>9,10,12,15,24,25</sup>. Eosinophil increase in blood and tissue were found in 26% of 69 patients with PU<sup>8</sup>.

There are a few published studies about the use of oral vaccination in PU and their results have been controversial.

A double-blind, crossover, parallel, prospective study in PU patients was designed to compare an oral vaccine with placebo, in terms of IgE serum levels, percentage of eosinophils in peripheral blood and number of skin lesions, both before and after treatment.

## Patients and methods

The present study was performed in the National Institute of Pediatrics (NIP), in Mexico City. Eighteen patients with ages between 2 and 6 years, from both sexes with active lesions of PU were studied. Sample size was determined by the amount of available vaccine.

Patients with atopic history (asthma, rhinitis and atopic dermatitis), with immunodepression due to illness or medications, and those presenting parasites in stools were excluded.

In all patients, an intradermal test with 0.1 mL antigens of lyophilized and sterile insect saliva components of insect saliva, lyophilized and sterile (donated by Alerbrás Laboratory<sup>1</sup>) was performed in the left forearm and read 24 hours later. All patients who presented with a positive reaction that consisted in 10 mm or larger a papule.

The patients' parents answered a questionnaire about personal data, living conditions, medications, time of evolution of PU and frequency of episodes of PU. Informed consent was duly obtained and signed by all patients' parents.

All patients were randomly allocated to vaccine or placebo. Both vials had the same physical characteristics so that its content could not be identified, either by the parents or physicians. Parents were instructed to administer the antigens in increasing concentrations from

1/10000 to 1/10, by means of three sublingual drops, twice a day: morning and afternoon, during 4 months.

The active oral vaccine was manufactured from the rostrum of insects where the salivary glands are located and diluted in a stable solution. Vials with placebo contained stable solution (only sodium chloride, sorbitol, sodium and potassium phosphate and parabens) (Alerbrás Laboratory<sup>®</sup>).

In accordance with the Ethics Committee instructions, all patients received as insect repellent 150 mg of vitamin B1 daily, during 4 months; for skin lesions, iodochloride-hydroxyquinolein was recommended as the sole medication. The use of oral antihistamines or corticosteroids was not permitted.

Before and after 4 months of treatment, physical examinations and blood laboratory tests were performed. The number of active PU lesions were counted. Blood (3 mL) was collected from a dorsal vein in the hand and serum obtained by centrifugation at 3,000 g during 5 minutes and stored in sterile propylene tubes (Nalgene) at  $-20^{\circ}\text{C}$ .

IgE serum levels were measured by immunoenzymatic test (Enzygnost IgE Micro, Behring<sup>®</sup>) and analysed in Behring ELISA Processor II<sup>®</sup>. Normal values were between 60 and 90 IU/mL for ages between 1 and 9 years. For eosinophils counts 1 drop of blood was placed in a glass slide, and stained with Wright, and observed under a microscope.

Biomedical Computer Programs (BMDP) version 7 was used for statistical analysis, performed with the following rationale: the comparability between the two groups (vaccine versus placebo) was determined in terms of the initial data. In the next step the end results between both groups were compared, and then, the difference between initial and final values within each group, for the most important variables. When we used as explicative variable the assignment to vaccine or to placebo, Fisher exact test was performed when the response variable was categorical; when continuous, Mann-Whitney test; Wilcoxon paired test, for the comparison between two dependent samples with continuous variables. All tests were two-tailed with an  $\alpha = 0.05$ .

## Results

Eighteen patients completed the therapeutic scheme and returned for clinical and laboratory evaluation. Eight patients received vaccine and 10, placebo.

Six patients in the vaccine group and nine in the placebo group were male. The group receiving vaccine had the following characteristics: in five cases there was contact with plants; in six contact with animals, two of whom received topical steroids; four received oral antihistamines, one thiamin and one vioform.

In the placebo group seven cases had contact with plants and eight had contact with animals, three had used topical steroids, two oral antihistamines, and one vioform. When each of the above mentioned variables was compared with Fisher exact test, no significant differences were detected ( $P > 0.05$ ).

As shown in Tables 1 and 2, when both groups were compared, no significant differences were detected, neither regarding their initial values, nor their final values. The only significant differences found were within the placebo group: final versus initial values, in number of lesions in upper versus lower limbs ( $P = 0.04$  and  $P = 0.03$ , respectively), and initial versus final total number of lesions ( $P = 0.02$  and  $P = 0.008$ ).

## Discussion

Treatment of PU represents a challenge. Management consists in prevention with insect repellents and treatment with antihistamines to decrease itching. The natural evolution of the disease is toward spontaneous healing. As the child grows up, episodes of PU become less frequent and less severe until they disappear. Repeated exposure to bites leads to a state of natural desensitization with initial disappearance of the late papular reaction, followed by the disappearance of the immediate (wheal) reaction.

Treatment of PU with specific hyposensitizing antigen from insects has the objective of transforming delayed reaction into an immediate one. Specific hyposensitization through subcutaneous injections has given contradictory results<sup>1,4,14,15</sup>.

Some believe that oral vaccine does not have the same antigenic properties as that of parenterally administered vaccine. However, Pires *et al.*<sup>3</sup> found good results (lack of skin lesions) in 87% of 23 patients after an oral vaccine,

compared with only 12% of 17 patients in the placebo group.

Studies based in the number of skin lesions in patients with PU are few<sup>14,19</sup>. In our patients a decrease in the number of lesions at the end of treatment was observed. Nevertheless, statistically significant differences were detected in the placebo group. The presence of eosinophilia seems to be common in patients with PU. In the series of 300 cases of Ruiz-Maldonado *et al.* PU was detected in 20% of the children. In our cases a high dispersion of values was observed in both groups of study, before and after treatment. Proença *et al.*<sup>26</sup> found an increase of total IgE levels in 33% of children with PU and concluded that there was no relation between presence of lesions and IgE levels. In our study, no significant statistical differences in IgE levels were detected when the two groups of study were compared.

Statistically significant differences between oral vaccine and placebo groups were not found in the clinical or immunological variables in our patients. Due to the many variables involved, therapeutic or preventive trials in PU

**Table 1** Oral desensitization in papular urticaria

	Vaccine (n=8)			Placebo (n=10)			Mann-Whitney test (P)
	Median	Minimum	Maximum	Median	Minimum	Maximum	
Age (months)	36	17	64	24.5	11	64	0.2
Evolution (months)*	0.25	0.001	1.7	0.0124	0.001	0.6	0.49
Serum IgE IU/mL (i)	355	30	750	122.5	24	560	0.2
Serum IgE IU/mL (f)	240	13	550	35	13	460	0.2
Difference <sup>†</sup> (P= )	0.08			0.17			
Blood eosinophils (%) (i)	7	0	16	4	1	12	0.47
Blood eosinophils % (f)	4.5	0	20	3	0	8	0.72
Difference <sup>†</sup> (P= )	0.56			0.59			

\*Only seven cases in the vaccine group

<sup>†</sup>P value with Wilcoxon test (within group comparison)

Values: (i)=initial; (f)=final

**Table 2** Oral desensitization in papular urticaria

	Vaccine (n=8)			Placebo (n=10)			Mann-Whitney test (P)
	Median	Minimum	Maximum	Median	Minimum	Maximum	
Total lesions in:							
Face (i)	2	0	50	0	0	50	0.59
Face (f)	0	0	3	0	0	4	0.68
Difference <sup>†</sup> (P= )	0.12			0.47			
Neck (i) (FV=0)	0	0	1	0	0	11	0.58
Upper limbs (i)	5.5	2	100	7.5	0	80	0.66
Upper limbs (f)	0	0	17	0	0	14	0.52
Difference <sup>†</sup> (P= )	0.09			0.04*			
Lower limbs (i)	11	1	42	4.5	2	20	0.4
Lower limbs (f)	0.5	0	23	0	0	4	0.66
Difference <sup>†</sup> (P= )	0.14			0.03*			
Thorax (i)	2	0	20	0	0	16	0.39
Thorax (f)	0	0	2	0	0	4	0.93
Difference <sup>†</sup> (P= )	0.12			0.37			
Abdomen (i)	0	0	4	0.5	0	5	0.46
Abdomen (f)	0	0	3	0	0	3	0.87
Difference <sup>†</sup> (P= )	0.62			0.19			
Buttocks (FV=0)	0	0	20	0	0	0	–
Total (before study)	41	9	192	14	3	173	0.25
Total (end of the study)	1.5	0	45	2	0	16	0.82
Difference <sup>†</sup> (P= )	0.008*			0.02*			

\*Statistically significant

<sup>†</sup>P value with Wilcoxon test (within group comparison)

Values: (i)=initial; (f)=final; (FV=0), final value=0

need to be double blind controlled. Drop-outs are frequent due to the inherent irregular evolution and lack of an effective therapy. Our group of carefully studied patients, even though small, sheds some light on this controversial issue.

## References

- 1 Reunala T, Brummer-Korvenkontio H, Lappalainen P, Räsänen L, Palosuo T. Immunology and treatment of mosquito bites. *Clin Exp Allergy* 1990;20(suppl 4):19–24
- 2 Ruiz-Maldonado R, Tamayo L. Treatment of 100 children with papular urticaria with thiamine chloride. *Int J Dermatol* 1973;12:258–60
- 3 Pires MC, Bojadsen IA, Martin MGL, et al. *Hipossensibilização Sublingual Para o Estrófulo. Estudo Duplo-cego*. São Paulo: Trabalho da Faculdade de Medicina de Jundiaí, 1989:1–21
- 4 Najjar HCF, Pradez de Faria GMP. Tratamiento inmunológico del prurigo estrófulo con antígenos de insectos precipitados en aluminio. *Alergia* 1977;24:23–7
- 5 Martins ER, Ouricuri A, Chigres B, et al. Prurigo estrófulo. *Alergia Pediátrica* 1989;3:5–8
- 6 Perlman F. Insect allergens: their interrelationship and differences. *J Allergy* 1961;32:93–101
- 7 Rook A. Papular urticaria. *Pediatr Clin N Am* 1961;8:817–33
- 8 Ruiz-Maldonado R, Sandrez LT. Prurigo infantil por insectos. Estudio de 300 casos. *Rev Mex Ped* 1973;42:743–59
- 9 McKiel JA, West AS. Nature and causation of insect bite reactions. *Pediatr Clin N Am* 1961;8:795–16
- 10 Mroczkowski TF, Millikan LE. Pruritis and prurigo. In: Ruiz-Maldonado R, Parish LC, Beare JM, eds. *Textbook of Pediatric Dermatology*. Philadelphia: WB Saunders, 1989:611–15
- 11 Hudson A, Bowman L, Orr CWM. Effects of absence of saliva on blood feeding by mosquitoes. *Science* 1960;131:1730–1
- 12 McKiel JA. Sensitization to mosquito bites. *Canad J Zool* 1959;37:341–51
- 13 Brown SJ, Shapiro SZ, Askenase PW. Characterization of tick antigens inducing host immune resistance. I. Immunization of guinea pigs with *Amblyomma americanum*-derived salivary gland extracts and identification of an important salivary gland protein antigen with guinea pig anti-tick antibodies. *J Immunol* 1984;133:3319–25
- 14 Benson RL. Diagnosis and treatment of sensitization to mosquitoes. *J Allergy* 1936;8:47–59
- 15 Allington HV, Allington RR. Insect bites. *JAMA* 1954;155:240–7
- 16 Benjamini E, Feingold BF, Kartman L. Antigenic property of the oral secretion of fleas. *Nature* 1960;188:959–60
- 17 Millikan LE. Papular urticaria. *Semin Dermatol* 1993;12:53–6
- 18 Penneys NS, Nayar JK, Bernstein H, Knight JW, Leonardi C. Mosquito salivary gland antigens identified by circulating human anti-bodies. *Arch Dermatol* 1989;125:219–22
- 19 Reunala T, Lappalainen P, Brummer-Korvenkontio H, Coulie H, Palosuo T. Cutaneous reactivity to mosquito bites: effect of cetirizine and development of anti-mosquito antibodies. *Clin Exp Allergy* 1991;21:617–22
- 20 Fergus JOR, Murnaghan MF. The cutaneous reaction to the bite of the mosquito *Aedes aegypti* (L.) and its alleviation by the topical application of an antihistaminic cream (Pyribenzamine). *J Allergy* 1953;24:120–5
- 21 Frew AJ, Kay AB. Eosinophils and T-lymphocytes in late-phase allergic reactions. *J Allergy Clin Immunol* 1990;85:533–9
- 22 Diven DG, Newton RC, Ramsey KM. Heightened cutaneous reactions to mosquito bites in patients with acquired immunodeficiency syndrome receiving zidovudine. *Arch Intern Med* 1988;148:2296
- 23 Shibasaki M, Sumazaki R, Takita H. Hypersensitive reactions to mosquito bites in congenital agammaglobulinemia. *Ann Allergy* 1986;56:81–4
- 24 Killby VA, Silverman PH. Hypersensitive reactions in man to specific mosquito bites. *Am J Trop Med Hyg* 1967;16:374–80
- 25 Brummer-Korvenkontio H, Lappalainen P, Reunala T, Palosuo T. Clinical aspects of allergic disease. Detection of mosquito saliva-specific IgE and IgG4 antibodies by immunoblotting. *J Allergy Clin Immunol* 1994;93:551–5
- 26 Proença NG, Morales LML, Grotti A. Prurigo estrófulo e IgE. *An Bras Dermatol* 1989;64:257–60

## Ability of mothers to assess the presence of fever in their children without using a thermometer

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TROPICAL DOCTOR, 2002, 32, 145–146

**SUMMARY** Fever is a common complaint in paediatrics and the ability of mothers to identify high temperatures in their children when there is no thermometer available needs to be assessed. A total of 169 mothers from a low social and economic background were studied to assess the accuracy of fever diagnosis in their children by palpation. In 137 children with axillary temperatures  $\geq 38^{\circ}\text{C}$  as measured by a mercury glass thermometer, mothers were able to detect fever by palpation in 104 cases (sensitivity of 75.9%). In another 32 children without fever, 29 were correctly identified (specificity of 90.6%). Only 21% of mothers in the study had a thermometer in their home and only 44% of these knew how to use it properly. Results show that mothers use palpation to assess the presence of fever in their children and are able to do it correctly in most cases.

## Introduction

Fever is a common complaint in paediatric practice and one of the most frequent problems presenting as an emergency<sup>1</sup>. In a large number of cases it represents a benign and self-limiting condition. However, children under 2 years with temperatures of  $38.9^{\circ}\text{C}$  or higher have an increased risk of bacteraemia. In addition, a fever lasting longer than 72 hours is a source of increased concern<sup>2</sup>. Furthermore, the Integrated Management of Childhood Illnesses (IMCI) strategy of the World Health Organization assumes mothers are able to identify fever and its management protocols rely on this information<sup>3</sup>.

A parent who is unable to assess the presence of fever may, in theory, delay appropriate care. There are unanswered questions about parental ability to evaluate