

## Hypersensitivity to mosquito starting in winter.

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### Summary

Here are reported five cases of hypersensitivity to mosquito arisen for the first time in winter when mosquitoes are not biologically active. Notwithstanding, the history, the distribution of lesions and the prolonged observation of the clinical course confirmed the diagnosis of cutaneous hypersensitivity to mosquito. We hypothesize that antigenic residua of saliva persist for a more or less long period of time in the sites of sting and can be responsible for hypersensitivity reactions several months after the sting, when sensitization against these antigens occurs for the first time.

### Key words

Hypersensitivity to mosquito, persistent antigen.

The hypersensitivity to saliva of mosquito is suspected thanks to the history, distribution of lesions and observation of the environment surrounding the patient. On the other hand, allergological tests aimed at showing immediate or delayed reactions, both in the skin and blood, are not easily available (6).

The history can unveil factors favoring the sting of mosquito, both familial -history of hypersensitivity to mosquito or atopy in the relatives- and personal -history of atopy or previous infections, which can favor hypersensitivity to mosquito-. The history can also unveil environmental factors such as stagnant water, seasonal period -late spring and summer-, etc..

Characteristically, the cutaneous lesions prevail on exposed areas, bilaterally and asymmetrically, mainly affecting the face and hands, the upper limbs more than the lower limbs and their distal region more than the proximal one. This distribution of lesions is influenced by the greater or lesser exposure of the above mentioned sites and by the concentration of carbon dioxide in the breathed out air (2). The latter attracts significantly mosquitoes.

Finally, the reconnaissance of the environment surrounding the patient, especially when performed by a parent with personal history of hypersensitivity to mosquito, is important to confirm the presence of mosquitoes that already had their blood meal.

With regard to the seasonal clinical course, confusion may arise when lesions suspected for mosquito hypersensitivity, due to their distribution and their history, occur for the first time in autumn or even in winter, when the biological cycle of mosquitoes is by now ended.

We report five children with hypersensitivity to mosquito arisen in our northern hemisphere from October to February and propose a hypothesis in order to explain this apparent clinical inconsistency.

### Case report

We are dealing with five children, examined between 2000 and 2003, 4 males, aged 6 to 42 months at the moment of the first examination (see table 1). In all cases their parents reported a

history started a few weeks to 2 months before, when the children were aged 5 to 42 months, precisely in October in 1 case, November in 1 case, December in 2 cases and finally February in 1 case. The family history was positive in 1 case for recurrent acute urticaria and in 1 case for hypersensitivity to mosquito. The personal history was positive in 1 case for allergic asthma.

In 2 children total IgE had been investigated. The first child aged 6 months had increased IgE levels -515 u/ml- and marked peripheral eosinophilia (14%). The second child had increased IgE and transaminases.

In all cases the dermatological examination showed papules and weals distributed on the face and limbs, mainly upper limbs, with prevalent distal involvement (Fig. 1, 2). In the fifth case there were excoriated lesions and his parents showed still evident signs of persistent onychophagy.

The subsequent clinical course of the five patients showed a progressive decrease of the

cutaneous lesions till the months of April-May, when the lesions reappeared in the same sites and went on during summertime to decrease again significantly or completely during winter-time. In all cases the parents, once skilled, confirmed the role played by mosquito stings.

### Discussion

Physicians are aware that mosquito stings do not cause any evident reaction in the first months of age. Rarely a small hemorrhagic, asymptomatic macule, clinically devoid of any sign of inflammation, can be seen in sites of sting (2). The child may develop a hypersensitivity reaction usually after the age of two years, only after repeated contacts with the allergens of saliva of mosquitoes.

Experimental studies (3) showed that, after an initial phase devoid of any allergic reaction, first a delayed reaction appears; subsequently an immediate reaction associates with the latter;



Fig. 1



Fig. 2

Fig. 1, 2: In hypersensitivity to saliva of mosquitoes the lesions are distributed on exposed areas, that is face and limbs, mainly upper limbs and distally. On the hand in Fig. 2 you can see old small papules and new weals.

TABLE 1

<i>N</i> <sup>o</sup>	<i>S.N.</i>	<i>Sex</i>	<i>Ist</i> <sup>*</sup> <i>examin.</i>	<i>Onset of</i> <sup>*</sup> <i>sensitiz.</i>	<i>Month of onset</i> <i>sensitiz.</i>	<i>Family</i> <i>history</i>	<i>Personal</i> <i>history</i>	<i>Other</i>
1	T.R.	M	6	5	October	urticaria in mother	/	IgE 515, Eo 14%
2	C.M.	M	23	19	December	/	Asthma	IgE>, GOT>
3	S.T.	F	32	30	November	/	/	/
4	D.F.	M	43	43	February	hypers. mosquito mother	/	/
5	L.F.	M.	42	41	December	onychophagy	/	excoriation

LEGENDA:  
\* *age in months; N*<sup>o</sup> *number; S.N. surname name; M male; F female.*

later on in a further phase the delayed reaction disappears whereas only the immediate one still persists and finally a phase of tolerance is established, during which no reaction can be detected.

However, from a clinical point of view, this series of events is hardly seen. Particularly in children the third phase, which is characterized by the concurrent existence of the delayed and immediate reaction (Fig. 2), is usually observed. These reactions are usually directed against allergens of the saliva (1). The immediate type reactions are due to IgE, IgG<sub>4</sub> and IgG<sub>1</sub> (4) so that they can be transferred with serum to non hypersensitive recipients (7). At the end of summertime these antibodies increase in hypersensitive subjects (4). Experimental studies also showed with tests of lymphocyte proliferation delayed type reactions against the same allergens (5).

In our cases the clinical features and the distribution of the lesions got oneself strongly suspected a delayed type and sometimes even an immediate hypersensitivity reaction to mosquito saliva, even though the parents reported their children never presented similar lesions in the past. In two cases the parents, when faced the clinical suspicion of hypersensitivity to mosquito saliva, reported that in the previous summer they had seen mosquitoes stinging their children. However, they also stated that they had not

seen any evident cutaneous reaction in that summertime.

The subsequent clinical observation confirmed in all cases the typical seasonal clinical course of mosquito hypersensitivity from the end of April to the end of September. Mosquito hypersensitivity is the most common type of hypersensitivity to insects in our climate.

Once confirmed with the subsequent clinical observation the diagnosis of hypersensitivity to saliva of mosquito, one should explain how is that the lesions appeared first time in a period, that is from October to February, during which mosquitoes as well as most insects in our climate are not biologically active.

According to the history of their parents, we hypothesize that children did not present any hypersensitivity reaction, although they had been regularly stung by mosquitoes and therefore they had got in contact with their saliva allergens, throughout the summer preceding the appearance of the clinical features. After a more or less prolonged latent period, which varied from one other, children got sensitized to saliva allergens of mosquito, some in October, some in December and some in February. Once the children got sensitized, their specific antibodies and lymphocytes recognized the allergens present in the residua of saliva, which had remained in the sites of stings occurred in the previous summer and therefore in those same sites they gave rise

to a hypersensitivity reaction. Thus we hypothesize that allergens of saliva can persist for a more or less prolonged period of time in sites of sting and be responsible for hypersensitivity reactions even several months later.

This hypothesis is supported by some clinical and experimental data. From a clinical point of view physicians know that the mite of human scabies is responsible, mainly in children, for a chronic granulomatous reaction, that is nodular scabies, even when mites are not anymore present and probably in presence of their allergenic residua. These nodules persist for several months. To remain in the field of mosquito hypersensitivity, in some subjects gross papular lesions can persist and get again active even during wintertime. Even more frequently, mothers of children with mosquito hypersensitivity report that a single mosquito sting is enough

to light again sites of previous stings, which had subsided for a long time. From an experimental point of view, physicians know the flare up occurring during the first sensitization with strongly sensitizing allergens such as dibutyl ester of squaric acid. This flare up occurs 7-10 days after the first percutaneous application of the allergen in the precise site of its application, in which evidently allergen residua do persist.

In conclusion we reported five cases of mosquito hypersensitivity occurred for the first time in a period of time in which mosquitoes are not biologically active. This event could be explained with the persistence in the sites of summer stings of allergen residua able to react with circulating immunological factors, once a sensitization occurs and reaches for the first time during wintertime levels able to cause clinically evident reactions.

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### References

- 1) Asahi M., Nishinoh J. – Insect bite allergens in the mosquito saliva. *J. Dermatol.* 49, 246-51, 1987.
- 2) Maunder J.W. – Papular urticaria. In: Harper J., Oranje A., Prose N. eds. – *Textbook of Pediatric Dermatology*, 2000 Blackwell Science Ltd., p. 549-54.
- 3) Oka K., Ohtaki N. – Clinical observations of mosquito bite reaction in man: a survey of the relationship between age and bite reaction. *J. Dermatol.* 16, 212-9, 1989.
- 4) Palosuo K., Brummer-Korvenkontio H., Mikkola J., et Al. – Seasonal increase in human IgE and IgG4 antisaliva antibodies to *Aedes* mosquito bites. *Int. Arch. Allergy Immunol.* 114, 367-72, 1997.
- 5) Peng Z., Yang M., Simons F.E. – Immunologic mechanisms in mosquito allergy: correlation of skin reactions with specific IgE and IgG antibodies and lymphocyte proliferation response to mosquito antigens. *Ann. Allergy Asthma Immunol.* 77, 238-44, 1996.
- 6) Peng Z., Simons F.E. – Mosquito allergy: immune mechanisms and recombinant salivary allergens. *Int. Arch. Allergy Immunol.* 133, 198-209, 2004.
- 7) Reunala T., Brummer-Korvenkontio H., Räsänen L., et Al. – Passive transfer of cutaneous mosquito-bite hypersensitivity by IgE anti-saliva antibodies. *J. Allergy Clin. Immunol.* 94, 902-6, 1994.