Hyposensitisation to wasp venom in six hours

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Abstract

Eleven patients with a history of anaphylaxis, positive reactions to skin tests, and specific IgE antibody to wasp venom underwent hyposensitisation in a six hour procedure. No general reactions occurred. Complement activation and proteinuria could not be shown.

The patterns of specific IgE, IgG1, and IgG4 were as described in other procedures—namely, IgE increased sharply and then decreased; IgG1 and IgG4 increased steadily and then decreased—but increase and decrease came earlier.

Challenge by a stinging insect at least four weeks after treatment proved complete protection. The skin reactivity two years later showed an unpredictable pattern.

References

8. Davidson JN, Garry RK. The absorption of monosaccharides from the large intestine of the rat under urethane anaesthetic. J Physiol (Lond) 1939;96:172-5.

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Clinical and laboratory data of 11 patients with anaphylactic reactions to wasp venom who underwent hyposensitisation

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Skin threshold (µg venom)*</th>
<th>Specific IgE ( % binding)</th>
<th>General reactions</th>
<th>Challenge (inadvertent in two years)</th>
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<tr>
<td></td>
<td></td>
<td></td>
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*Amount of venom necessary to provoke a reaction.

- = No reaction. + = Positive reaction. 0 = No inadvertent challenge.

An intracutaneous skin test was considered to have given a positive reaction at a titre of 0-01 mg/l or less. Total IgE and specific IgE, IgG1, and IgG4 were estimated with a radioallergosorbent test. The titre of specific IgG1 and IgG4 was expressed in percentages of a C1q reference serum and specific IgE in % binding. Estimations of C1q, C3, and C4 were performed according to the Mancini procedure, and haemolytic component (CH50) was estimated with a haemolysis test.

The patients were admitted to the intensive care unit for 24 hours. An intravenous needle was inserted, and clemastine and adrenaline made ready for use. Pulse rate, blood pressure, and temperature were measured every half hour. The initial dose of venom was a factor of 10 measured every half hour. The threshold for the venom in the skin—that is, amount of venom that provoked a reaction—was estimated, and the initial dose of venom was a factor 10 below the threshold. The venom was injected subcutaneously in both upper legs. The amount of venom was increased 10-fold up to 1 µg. The next doses, of 5, 20, 30, 60, and 100 µg, were all given with a 30 minute interval. Blood samples were collected before and half an hour after the last injection for estimation of C1q, C3, C4, and CH50, and urine samples were taken for detection of proteinuria.

Booster injections were given in the outpatient department with a dose of 100 µg at seven, 14, and 28 days after hyposensitisation and then every four weeks. All patients were rechallenged by a wasp sting, at least four weeks after the start of the hyposensitisation. A living wasp was pressed on the underarm, and the sting was left in situ for at least 20 seconds. The same precautions were taken at the time of challenge as for the hyposensitisation procedure.

Results

There were no general reactions during hyposensitisation in spite of the fact that the total dose given in six hours was equivalent to nearly four stings. All the patients had a considerable local swelling with redness and pain at the site of injection; this reaction started two to six hours after the first dose and decreased after 24-36 hours. No fever developed. Neither booster injections nor the provocation induced general reactions. It was remarkable that most stings remained in the skin after removal of the insect, as the small barbed hooks present in the wasp sting are less pronounced than in the honeybee.

There was no change in the level of C1q, C3, C4, or CH50. Proteinuria was not detected. The specific IgE decreased after a quick initial rise. There was a fast rise of specific IgG1 and IgG4 (figs 1-3).

Skin tests were repeated two years later, while the booster injections were still continued every six weeks. Six patients had the same skin threshold, in four it lowered, and in one patient it increased sharply. We rechallenged this patient with a living wasp, but only a local reaction occurred. Five other patients received wasp stings inadvertently but again had only a local reaction.

![Graph 1](http://www.bmj.com)

**FIG 1**—Titre of specific IgG1 (as % of standard serum) against wasp venom at 0, 1, 2, 4, 16, and 28 weeks after hyposensitisation. (n=11.)

![Graph 2](http://www.bmj.com)

**FIG 2**—Titre of specific IgG1 (as % of standard serum) against wasp venom at 0, 1, 2, 4, 16, and 28 weeks after hyposensitisation. (n=11.)
We thank R C Aalberse and J C J Clemens for performing the tests for immunoglobulins, E J Hensen for commenting on the paper, and Ms S van Elst for typing the manuscript.

References
1 Parish HM. Deaths from bites and stings of venomous animals and insects in the United States. Archives of Internal Medicine 1959;104:198-207.

Discussion
Protection against a general reaction after a sting with wasp venom could be presumed from the titres of specific IgG1 and IgG4, which increased and then decreased after one to four weeks. IgE also increased and then decreased after one to two weeks. This pattern has been described before.2,13,14 The rise of antibody titres varied considerably between patients as has also been described.5,6 In this series no general reactions occurred. We have now treated 60 patients with anaphylaxis for both wasp and bee venom in the same way and only in three of them was a slight general reaction noted. It is difficult to explain how the procedure can be performed in six hours without provoking any serious general reaction. Because of the cross linking of the receptors at the surface of the mast cell when antigen (allergen) is bound by the fixed IgE, the dose of antigen could be the crucial point. When the dose is too low, cross linking is not possible nor can the mast cells be activated, resulting in tolerance.14 Alternatively, the production of IgG antibody may have a crucial role and antigen binding by IgG may block the access of antigen to IgE.14 From our results it can be seen that during treatment there is a steady increase of serum titre for both IgG1 and IgG4, with a decrease thereafter for both subclasses. The appearance of IgG antibodies is not the only responsible factor, however, because Urbanek et al showed the absence of correlation between IgG antibody titre to bee venom and the degree of clinical protection.7 Also, in patients who failed to respond to immunotherapy, a significant rise in their serum IgG antibody titre conferred no obvious protection.14 Another cause of the unresponsiveness of the immune system to the challenge antigen may be selective depletion of recirculating lymphocytes.15 Whether this mechanism enables hyposensitisation to be performed in six hours or less without general reactions is unknown. The pattern of the skin threshold during the hyposensitisation is unpredictable. That five of the 11 patients were stung again within two years gives an indication of the presumed risks. In conclusion, a fast hyposensitisation procedure in cases of anaphylaxis to wasp venom has proved effective without serious side effects.

ONE HUNDRED YEARS AGO Sir,—In order to be more secure, if possible, from contamination, I send my household dirty linen to a steam laundry (Battersea Park). A short time ago, my little boy, aged 6½, had a slight attack of German measles. His nurse, by my directions, saturated the whole of the linen, used by him, in “sanitas” before leaving the nursery, and made a remark in the washing-book as to the child’s aliment (German measles). A few days later, a regular letter from the manager of the establishment was written to my wife, for neglect in not sending for their special cart, etc. To my astonishment, a charge of 15s was then made for disinfecting the linen of the whole house. I laud the precaution as most praiseworthy; but if a charge of 15s is to be made for every time a child has German measles, is it the proper way to get parents to report cases of even small-pox or scarlet fever? On my remonstrance regarding the charge, I am to be allowed a deduction of one-half, because I am a medical man. In my opinion, the sooner this sort of extra charge is done away with, the sooner we shall get great the truth regarding infectious diseases. It would be, I think, of great importance if the BRITISH MEDICAL JOURNAL would lay down some plain rules for disinfecting clothing efficiently and at a cheap rate for all launderies, and also instructions for parents as to precautions regarding linen, etc, and so help to lessen the punishment on parents. —Yours faithfully, COSMO G LOGIE, MD, late Surgeon-Major, Royal Horse Guards. (BRITISH MEDICAL JOURNAL 1883 p.798.)