Can skin prick tests provoke severe allergic reactions?

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Abstract. – Background. Studies have reported adverse reactions during skin prick tests (SPTs), however such reactions are almost non existent in children. On the contrary, there are controversial data on the effectiveness and reliability of diagnostic tools. SPTs are considered as the more rapid and effective tool for the diagnosis of pediatric allergies. SPTs, when employed either correctly or with standardized extracts, are rapid, safe, sensitive, inexpensive on a per test basis and the results are reliable, since they are largely experimented.

Observations. SPT is the more employed method for the diagnosis of atopic disease elicited by type I immune reactions, where sensitizing antibodies are present. However, we discuss a study surprisingly reporting six generalized allergic reactions after prick tests with fresh foods in infants less than 6 months of age out of 1,152 tested during three years (0.17% for each year).

Conclusions. In this study, all reactions were treated with epinephrine and/or antihistamines, plus steroids in three cases. Purpose of the present study was to assess whether the practice of performing SPTs, either in the usual manner, or in duplicate could be a risk factor in infants with extensive eczema. Moreover, excluding young babies from SPTs or even applying only one SPT each visit delays an early diagnosis. In the same period of three years, we have done SPTs in at least 10,000 children, without seeing any generalized allergic reaction.

Key Words: Skin prick tests, Rapidity, Safety, Sensitivity, Prick + prick tests, Adverse reactions, Duplicate tests, Infants, Extensive eczema, Early diagnosis.

Introduction

SPTs consist in allergen percutaneous administration. If correctly done and with standardized extracts the pros are: an excellent safety record, minimal skin trauma inflicted, cost results, simple to perform, high sensitivity and thus reliable and reproducible, because largely experimented, as a consequence SPTs are the more used method for the diagnosis of IgE-mediated allergic disease where are present skin sensitizing antibodies. When skin mast cells have surface IgEs for intruding allergens, mast cells degranulate releasing their mediators, so producing a cutaneous wheal-and-flare reaction, a type I immune reaction.

Although SPTs are more sensible and specific in respiratory allergies, representing the first choice investigation when an IgE-mediated allergic disease elicited by aeroallergens is suspected and in asthma epidemiologic studies, in food allergy (FA) diagnosis, SPTs might be less reliable, due to different factors. These include the lability of some allergens, crossreactivity between allergens belonging to different plant species or to the same species, antigenicity loss during extraction and inadequacy of allergenic extracts.

Untoward reactions to SPTs

In a recent paper, we read that 6 infants aged less than 6 months suffered from generalized allergic reactions after prick tests with fresh foods. This kind of skin testing is usually referred to as prick by prick (P+P) tests, and we use it for labile allergens. P+P tests were first performed at our Division in 1989-1990, and never elicited severe reactions. The technique is very simple. One pricks a normal lancet into the fresh or frozen fruit or vegetable, and immediately thereafter into the skin. Otherwise, the skin can be pricked first, and a piece of fruit/vegetable is firmly taped to this place, or rubbed on this place, or viceversa: the skin is rubbed first and pricked immediately thereafter.
We have prospectively P+P tested 118 children, using cow milk (CM), emulsioned whole raw egg, and a mixture of flour and boiled water, registering only mild reactions. Our Division started to work in 1969-1970, since then we have performed countless SPTs in children, according to fixed rules\textsuperscript{9,10} but have never seen severe reactions. Several adverse reactions occurred, but only in intradermally tested children\textsuperscript{5}, never practiced or seen by us.

Instead, in a retrospective study, the authors\textsuperscript{4} have found during three years (1996-1998) six infants aged less than six months, with active eczema and positive reactions to food items, who were positive to P+P tests to fresh food specimen, and suffered from generalized reactions. Each infant was tested with several foods (from 2 to 4 foods) (Tables 1 and 2)\textsuperscript{4}, without performing the negative controls. Not only the infants were tested with numerous foods (Table 1), but the same food was tested in duplicate in the same baby (Table 2): accordingly, we do not know which particular food elicited the reactions. We have documented that CM is so a potent allergen that one drop posed on the lower lip of an infant during a CM challenge may trigger anaphylaxis\textsuperscript{11}. Personal data show that in the first year of life CM allergy (CMA) starts in 72\%, and egg allergy in 68\% of cases\textsuperscript{12}. In addition, the babies were tested with fish (No. 2) and hydrolysates (HFs) (No. 4), however there are no details regarding such foods in the pertinent section. We use a mixture of 5 grams of fish and for HFs the recommended ready to eat concentration which is further diluted with water to one part per hundred.

As regards the reactions, there were four cases of generalized erythema, in one case with crepitations, and two cases of generalized urticaria, in one case accompanied with rhonchi, and in the other with hoarseness and cough. All babies received immediate treatment with epinephrine (three cases) and/or antihistamines (three cases) administered by the nurse. Without delay, a pediatrician added steroids to the treatment in three cases. Since in our Division SPTs are always performed by physicians, in case of whatever problem they immediately visit the child, and prescribe medications if necessary.

In our Division, SPTs are done by a qualified and trained doctor assisted by a qualified nurse, and with epinephrine and antihistamines at hand with appropriate emergency equipment available on site. We propose to increase the current recommendations\textsuperscript{5} adding a detailed family and personal history, and in children with convincing history of more or less severe clinical manifestations, P+Ps should be performed with diluted doses of the allergen. In addition to possible breast milk allergens\textsuperscript{4,5}, we mention that SPTs for CM could act as a booster dose in babies fed CM in maternity hospitals\textsuperscript{11}. Unfortunately, we cannot explore this matter further, since it was not elucidated whether eczema exacerbations in the four breast babies might correspond with the maternal diet, or if the mother was on a definite elimination diet.

**Discussion**

One limitation of the study\textsuperscript{4} is the practical impossibility of recognizing which food elicited the reported reactions. We have discussed the practical repercussions, and we do not

<table>
<thead>
<tr>
<th>Child</th>
<th>Sex</th>
<th>Age at test</th>
<th>Heredity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female</td>
<td>5 months</td>
<td>2 siblings</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>2.5 months</td>
<td>Mother + Father</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>3 months</td>
<td>Mother</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>3 months</td>
<td>Mother + Father + Sister</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>5 months</td>
<td>Sister</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>5 months</td>
<td>Father</td>
</tr>
</tbody>
</table>

Modified from reference 4.

A II babies had active eczema of varied severity when the tests were performed. Five out of six babies were breastfed, one was given also formula.
know whether the babies were already sensitized to any of the food items (in four breast-fed children no sensitivity to foods had been identified previously), otherwise it was inappropriate to test the babies. Among the employed foods, CM and egg are highly allergenic in the first year of life, and fish has triggered a 9% of reactions in children aged 0.1-15 years. HFs have provoked a number of severe, also generalized until to shock and anaphylaxis in a number of infants and young children. However, it is impractical to expand the findings of this article to other fresh or commercial foods.

During three years, the authors tested 1152 children, which gives a figure of 0.52%. In 30 years we have SPT-tested thousands of children each year, but both the nurse and one of us (AC) are regularly present in the Division since 1988 and have never seen severe reactions, therefore it is unachievable a pertinent comparison.

A more crucial limitation, when not a risk factor, is the practice of performing tests in duplicate in young infants with extensive eczema: this was the case of 4/6 infants, which certainly caused an extra allergenic load on the surface of the small arm, which is greatly limited in babies with extensive eczema. The authors correctly recognize that duplicate tests may increase the risk of summation of the reactions, and consequently the risk of generalized reaction. Hence it would be better to recur to the determination of specific IgE. Although the parallel use of SPT, CM-specific IgE, patch test and serum eosinophil cationic protein detected 85% of infants with CM allergy, the specificity was as low as 0.23.

Finally, we would stress that severe adverse reactions to skin testing were provoked by the intradermal method, nowadays largely replaced by SPTs. There were cases of death after injection of several proteins, including a 5-month-old baby (ovomucoid), a 4-year-old girl (foreign proteins), two asthmatic boys aged 10 and 11 years (food extracts), and a 9-year-old child with asymptomatic asthma (penicillin). No lethal reaction has been reported after SPTs in three large series.

In conclusion it is largely known that children tolerate epinephrine better than adults. Retrospective studies deprive doctors of their decision making. In comparable cases, a doctor considering the extensive eczema, the young age, and the possible risk of generalized reactions would have preferred an in vitro test.

In our Division, we test several children each day, and have never excluded children aged less than six months or recognized that SPTs are less reliable in infants less than one ear of age. Application of only one allergen at each visit, is a time-consuming methodology for physicians, nurses, and families. This is also a procedure procrastinating both the investigation and an early diagnosis, thus subjecting the child to unnecessary suffering from his allergic disease.

In conclusion, SPTs, when correctly employed or with standardized extracts, are rapid, safe, sensitive, inexpensive on a per test basis and the results are reliable, since they are largely experimented: consequently SPT is the more employed method for the diagnosis of atopic disease elicited by type I immune reactions, where sensitizing antibodies are present. SPTs are defined as fairly reliable in FA, but Sampson has demonstrated that SPTs elicit a greater number of positivities in comparison with double-blind, placebo-controlled food challenges.

### Table II. Summarized informations about SPT applied and SPT results.

<table>
<thead>
<tr>
<th>Child</th>
<th>SPT applied</th>
<th>Positive SPT results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Egg, CM, Fish, Casein hydrolysate</td>
<td>Egg 2, CM 2, Fish 2</td>
</tr>
<tr>
<td>2</td>
<td>Egg, CM</td>
<td>Not readable</td>
</tr>
<tr>
<td>3</td>
<td>Egg, CM</td>
<td>Egg 2, CM 2</td>
</tr>
<tr>
<td>4</td>
<td>Egg, CM, Fish, Casein hydrolysate</td>
<td>CM</td>
</tr>
<tr>
<td>5</td>
<td>Egg, CM</td>
<td>Egg 2, CM 2</td>
</tr>
<tr>
<td>6</td>
<td>Egg, CM, Casein hydrolysate, Whey hydrolysate</td>
<td>Egg, CM</td>
</tr>
</tbody>
</table>

All SPTs were done in duplicate. Results (5 babies) histamine wheal between 5 and 20 mm (mean = 9 mm), SPTs between 3 and 10 mm (mean = 6.7 mm).
References


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