

STUDIES IN SENSITIZATION AS APPLIED TO SKIN TESTING PROCEDURES

II. INFLUENCE OF ALLERGEN CONTACT

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ALLERGISTS long have recognized the important role which contact with allergens plays in the mechanism and production of clinical sensitization. Adequate discussion of this subject, particularly as related to hereditary predisposition, is to be found in all monographs or books on allergy.¹ Grove probably was the first to demonstrate this in some unpublished observations reported in 1931 by Coca.² She tested thirty-six timothy hay fever subjects residing in Berlin, where there is no ragweed, with a strong ragweed pollen extract. All reactions were negative except in one person who had spent some time in the United States and was the only one to have had contact with ragweed pollen. These observations subsequently were substantiated by others and serve to explain the common finding of the "nonclinical" positive skin test reactions. Despite the general acceptance of the role of contact in sensitization, little is known about the amount of contact required to induce sensitization, which on the one hand may be limited to the skin and indicated only by a positive skin test reaction, or may involve other tissues as well and be responsible for associated clinical symptoms. Many believe that it depends largely upon the sensitizing ability of the offending allergen as well as upon the degree of maturity of the sensitized cells, the latter being influenced perhaps by hereditary predisposition. As a consequence of these influences, when sufficient antigenic stimulation is provided by adequate contact with the specific excitant, evidence of hypersensitiveness will appear. The development of this sensitivity may be hastened either by contact with an excessive amount of the allergens or by nonspecific influences.

Adequate clinical and experimental proof of these ideas already has been offered by various investigators, who have shown, for example, that sensitization can be induced artificially in any person (atopic or nonatopic) by many agents if the contact is adequate and sufficiently prolonged. Thus, horse serum will sensitize all individuals if injected in sufficient amounts and especially if given intravenously.³ Poison ivy also will sensitize all individuals if the contact is adequate. On the other hand, as shown by Brunner,⁵ atopic individuals could not be sensitized by known powerful atopens (for example, egg white, rabbit epithelium, or orris root), nor do nonatopic individuals exposed to large amounts of pollen or injected with its extract develop hay fever.

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²Read in part before The American Academy of Allergy, Feb. 26, 1953, at Boston, Mass.
³Received for publication, March 29, 1954.

Although allergen contact admittedly is of paramount importance in the development of clinical sensitization, the attending allergist, nevertheless, usually is more concerned with determining the clinical or nonclinical nature of the positive skin test reaction than with attempts at determining the manner in which the sensitization developed, especially in its initial phase or pre-clinical period. In order to bridge this gap, the present series of studies has been undertaken. These studies have as their purpose the investigation of the following criteria of sensitization: the susceptibility of the individual; the nature of the sensitizing substances, as well as the mode and duration of contact; and, finally, whether the process resulting in a positive skin test reaction differs from that bringing about clinical symptoms. In our first article,⁷ we reported the results of investigations seeking to answer the question as to whether or not positive skin tests change under the influence of such factors as avoidance or specific treatment. The present report concerns itself with our studies of the role and importance of contact in relation to sensitization. The first portion of the report concerns itself with studies done in patients allergic to horse serum; the second portion with studies into sensitization with foods eaten often or infrequently.

A difficult problem for the allergist is the correct interpretation of "non-clinical" positive skin test reactions, those provoked by prior contact with antigens which sensitize the skin but without concomitant clinical symptoms. A striking example of this is seen in patients with clinical ragweed hay fever who have positive skin test reactions to grass pollens but no clinical evidence of grass pollinosis. While such nonclinical positive skin reactions are the result of previous contact with grass pollens, the extent of contact necessary to induce this skin sensitization is unknown, as well as that required to induce clinical sensitization. This process of sensitization applies not only to pollens, but also to foods with which the patient comes in contact early in life and which likewise could account for either clinical or nonclinical positive skin test reactions. Thus, Schloss⁸ in 1920 showed that the ingestion of egg white by marantic infants induced sensitization indicated both by a positive skin test and circulating antibodies, but without associated clinical manifestations of allergy. Subsequent clinical experience has shown that food contact, especially in young children, may provoke temporary clinical symptoms; later they seem to acquire a tolerance and can eat the food again with impunity. If tested during the latter period, such patients still have a positive skin reaction, which now is the only evidence of their previous antigenic contact. Such a reaction may persist for long periods, even throughout the patient's life. This is true, for example, of children clinically allergic to milk or egg in infancy who later take these foods without difficulty, but in whom the positive skin reactions are proof of their former sensitizing contacts. Unless the allergist tries to obtain a detailed history of their clinical reactions to these foods in infancy or childhood, such nonclinical positives may be regarded as "nonspecific" or "irritating," with no attempt being made to investigate the reasons for their occurrence.

It seemed to us that the subject could be clarified if additional evidence was provided showing that contact with specific allergens may induce specific skin sensitization, regardless of the presence of clinical sensitization. Food and pollen allergens would seem to offer the logical approach to this problem; but, unfortunately, these allergens are so ubiquitous and varied as to raise valid objections. For example, it would be difficult to obtain a reliable history from such a patient as to the extent of contact which was responsible for the production of his positive skin test reaction. Even if this obstacle could be surmounted, it would be hard to overcome another objection, namely, that the sensitization was induced by exposure to homologous food antigens present in other foods. For example, a positive reaction to lobster could be explained by sensitization with a similar antigen present in shrimp or crab;⁹ similarly with pollens, exposure to one type of ragweed would cause sensitization to other related types.

The same objection, it seemed to us, did not apply similarly to exposure to an antigen like horse serum. Except for patients who are sensitive to horse dander or who might have ingested horse meat, a patient's only possible exposure to horse serum is that which results from the injection of an immune agent or mixture containing horse serum. If sensitization ensues, it would be indicated by a positive skin test reaction to horse serum, but not all patients receiving horse serum are sensitized. Hooker¹⁰ in 1924 and Tuft¹¹ in 1932 both showed that about 25 per cent of children who had received, at weekly intervals, the usual three immunizing injections of diphtheria toxin-antitoxin containing extremely minute amounts of horse serum later showed positive skin test reactions as indications of active sensitization. That this sensitization was not necessarily clinically important was substantiated first by Park¹² and subsequently by clinical experience which indicated that horse serum could be reinjected into some skin test positive patients without inducing a reaction. However, as shown by Tuft,¹¹ the incidence of serum reactions was greater in patients previously sensitized by toxin-antitoxin. Therefore, a positive skin test reaction to horse serum in a patient not sensitive to horse dander or horse meat is an indication of previous contact with horse serum, regardless of whether the sensitization is limited to the skin or involves other tissues as well. This should provide additional and incontrovertible evidence of the importance of allergen contact in sensitization, since such sensitization, with the rare exceptions already mentioned, could have resulted only from previous injection.

In an attempt to provide such evidence,* we reviewed the case histories of 528 clinic and private patients (most of whom were being looked over for other investigative purposes⁷) to determine the incidence of horse serum sensitization as indicated by a positive skin test reaction to our routine testing strength of horse serum (1:100). At the same time, the reaction to horse epithelium in our routine testing strength (0.001 mg. N per milliliter) likewise

*As described in our previous article,⁷ all skin tests were done intracutaneously in the routine dilutions used in all our allergic patients. Every positive test, regardless of degree, was checked by a repeat test done later in order to determine the constancy of the reaction. Whenever comparisons were made, we were careful to compare the tests in the same concentrations. This was true not only for horse serum but also for foods, pollens, or other inhalants.

was recorded to see whether there might be an antigenic relationship. In all instances, and especially in those patients with positive reactions to horse serum, the history was reviewed for evidence of previous injection of horse serum or of clinical sensitivity to horse epithelium in an effort to substantiate the positive reactions. Patients usually do not offer information about previous injections unless specifically requested, since it has no particular bearing upon their allergic complaint. Consequently, many of our histories did not contain this information when the patient was first seen. However, after completion of the allergic studies, when the skin test results of all private patients were reviewed with the patient or, in the case of a child, with the parents, a special effort was made to get a history of previous injection of agents containing horse serum whenever a positive reaction to horse serum was obtained. In this way we often obtained in retrospect more definite information about previous injections of horse serum than was supplied by the original history.

TABLE I. RESULTS OF HORSE SERUM REACTIONS IN 528 CASES

	NUMBER	PER CENT	TOTAL NUMBER
<i>Negative skin reactions to horse serum</i>			458 (86.7%)
1. Negative history of previous injection			
a. Negative horse serum, negative horse epithelium	384	83.8	
b. Negative horse serum, positive horse epithelium	11	2.4	
2. Positive history of previous injection			
a. Negative horse serum, negative horse epithelium	60	13.1	
b. Negative horse serum, positive horse epithelium	3	0.7	
<i>Positive skin reactions to horse serum</i>			70 (13.3%)
1. Positive history of previous injection			
a. Positive horse serum, negative horse epithelium	40	57.1	
b. Positive horse serum, positive horse epithelium	17	24.3	
2. Negative history of previous injection			
a. Positive horse serum, positive horse epithelium	6	8.6	
b. Positive horse serum, negative horse epithelium	7	10.0	

The results of this investigation are summarized in Table I. It will be observed that of the total number of records reviewed, 458, or 86.7 per cent, had a negative test to horse serum. Of this negative-reacting group, most (384, or 83.8 per cent) gave a negative history of previous serum injection, whereas 60, or 13.1 per cent, had a positive history of previous injection and a negative skin test, indicating an absence of sensitization despite previous contact, which is in accordance with the previously mentioned experiences of Hooker¹⁰ and of Tuft.¹¹ It is of interest in this connection that a small number (11, or 2.4 per cent) of the group with negative histories of previous injection had positive tests to horse epithelium but negative tests to horse serum; also, there were three additional patients with positive tests to horse epithelium who had negative reactions to horse serum, despite a positive history of previous horse serum injection. These findings indicate that, while patients sensitive to horse epithelium often also are sensitive to horse serum because of the presence of a common antigen,¹² this is not always true; therefore, patients may be sensitive to horse epithelium alone without being sensitive to horse serum, and on occasion even may be given a horse serum injection without resultant reaction.

Of more interest in relation to the present investigation was the review of the seventy patients showing positive reactions to horse serum (Table I). Of the seventy, forty-seven were positive to horse serum alone and twenty-three to both horse serum and horse epithelium. In the latter group, the positive reaction could be accounted for either by a previous serum injection (in seventeen) or by homologous antigenic relationship in the absence of a history of previous injection. The latter was true in six patients, five of whom had definite clinical evidence of sensitivity to horse epithelium (asthma or coryza, or both, after contact with horses). However, of the entire group of seventy with positive reactions to horse serum, only seven patients (10 per cent) with concomitant negative tests to horse epithelium failed to give a history of previous horse serum injection or at least were uncertain as to whether they ever had received a previous injection. It is possible, of course, that some of these might be ascribed to technical error in performing the skin test, but a more plausible explanation probably is the failure to get a complete history of previous serum injections. Since most of these patients were adults, they might have received toxin-antitoxin injections when they were young but did not remember it. That failure to obtain such a history does not exclude a possible previous horse serum injection was emphasized frequently when we reviewed the history either with the patient or with the parent (if the patient was a child) after a positive skin reaction to horse serum had been obtained. Often, when asked specifically about previous injections, they then would remember having received some type of serum injection, even though they did not consider it important enough to mention or had forgotten it when asked at the initial visit. This is nicely exemplified in the following two brief case reports:

CASE 1.—A 10-year-old boy had a positive reaction to horse serum. Upon asking the patient's mother whether he had ever received an injection, she immediately denied it. But at her next visit she stated that after thinking about it more she recalled that the patient was bitten by a dog some years previously and at that time was given "a serum injection against lockjaw," with no particular reaction. Obviously, had we taken the initial word of the mother, we would have considered the history of previous injection negative and thus would be unable to explain the positive horse serum reaction.

CASE 2.—A boy, 12 years of age, seen for hay fever, had a positive skin reaction to horse serum. When asked about it at his next clinic visit, he denied having received any previous serum injection. We instructed him to ask his parents when he got home. Upon his return he told us that his mother recalled that at the age of $3\frac{1}{2}$ he had an accident to his thumb for which he received a "lockjaw injection."

In both these instances, as in others, if we had relied solely upon the initial history we could not have determined the reason for the horse serum sensitization indicated by the positive skin test. This perhaps also was true of the small number of patients in the group who had positive skin tests to horse serum but who were not too certain as to a previous serum injection. Nevertheless, despite these exceptions, the evidence obtained from a survey of this group of patients clearly indicates that a positive skin test to horse serum constitutes definite indication of previous sensitization by horse serum which could not be acquired in any other way except by previous antigen contact,

usually artificially induced. This is true regardless of whether the patient has a clinical sensitization and would develop symptoms upon serum reinjection (a clinical positive) or whether the sensitization is limited solely to the skin (nonclinical positive). Once the sensitization has been acquired, it may persist as a positive skin test reaction for varying lengths of time, either unchanged or in lesser degree. In one patient with a positive test to horse serum, there was an interval of twenty-five years between the time of injection and the positive skin test, indicating that such sensitization can persist for long periods.

If this evidence of previous contact as the primary factor in the production of sensitization is true for horse serum, it should apply also to sensitization provoked by food and pollen antigens. Unfortunately, as previously mentioned, in the latter instances it is much more difficult to obtain adequate proof of previous allergenic contact or its extent, except at times from clinical history or experience. Thus, for example, it is not unusual in older children to obtain positive skin reactions to such foods as milk or orange which they can eat without provoking any clinical symptoms. However, detailed inquiry into the past histories of such patients often reveals that during infancy or early childhood, they experienced considerable difficulty when taking milk or orange; but, later, either after abstinence or at times after continued ingestion, they apparently were able to overcome the clinical sensitivity and could eat the food in question again without untoward effects. Nevertheless, such patients still had a positive skin test reaction long afterward as concrete evidence of their previous clinical sensitization. If this is true of milk or orange, it also must apply to other foods but, since one must depend entirely upon clinical findings in these instances, it is difficult to secure good objective evidence in support of the contact factor. During the course of our investigations into changes in retest reactions, already reported in a previous article,⁷ we obtained additional evidence of the influence of allergenic contact which we are now reporting. In our first study we were concerned primarily with comparing the retest results with that of the original test after the lapse of varying time intervals. It was soon evident that certain patients showed newly acquired sensitivities, as indicated by positive skin reactions to foods* to which they formerly were skin test negative. Thus, of forty-eight patients in whom the retest results were compared and in whom the food histories were reliable, fifteen patients had a total of thirty-three newly acquired, but definite, positive skin reactions to various foods, some patients having positive reactions to more than one food. Upon reviewing the histories of these patients, it was found that in twenty-eight instances out of the total of thirty-three, the sensitization was to foods frequently eaten by the patient, whereas in the remaining five the sensitization existed to foods which were uncommonly eaten. Furthermore, in thirty of the thirty-three instances of newly acquired positive reactions, we elicited the history that this was a new contact with these foods, since the patient did not recall having eaten them previously. In addition, further review of our data indicated that the longer the duration of

*See previous footnote.

contact with the food, the greater was the chance of sensitization, since a larger number of patients showed positive reactions when retested five or more years after the original than if retested before five years. In certain patients, too, after review of their food histories, we showed that excessive antigenic contact with certain foods seemed to induce sensitization at least as indicated by a positive skin test reaction.

This evidence strongly suggested that both the type and the duration of allergenic contact were important factors in the acquisition of sensitization to foods so that the greater the extent of contact, the more likely was sensitization to result; also that sensitization is more likely with foods eaten often than with those which were not eaten so frequently. The latter evidence seemed contrary to the commonly held viewpoint that food sensitization depended largely upon the antigenic nature of the food. Therefore, in order to obtain more definite evidence, we attempted to determine from the review of a substantial number of our skin test records the relative incidence of positive reactions to such commonly eaten foods as banana, chicken, chocolate, cornmeal, egg, flounder, lobster, milk, orange, oyster, green pea, peanut, strawberry, tomato, and wheat in comparison with the incidence of positive reactions to such uncommonly eaten foods as blackberry, chestnut, goose, green pepper, sweet potato, pumpkin, and rhubarb. In all instances we included only those positive reactions which were slight to marked in degree and which had been rechecked by repeated tests in the same concentrations as the original test. Whenever new positive reactions were obtained, we reviewed the history with the patient to ascertain whether these foods were eaten frequently, only occasionally, or not at all during the period between the original or initial test and the retest.

The data obtained in this review are summarized in Table II. Inspection of the latter reveals at once a significantly higher incidence* of positive reac-

TABLE II. POSITIVE REACTIONS TO COMMONLY AND UNCOMMONLY EATEN FOODS

FOOD ALLERGEN (COMMON FOODS)	TOTAL NUMBER OF PATIENTS	PER CENT TOTAL* POSITIVES	FOOD ALLERGEN (UNCOMMON FOODS)	TOTAL NUMBER OF PATIENTS	PER CENT TOTAL* POSITIVES
Banana	670	21.6	Blackberry	657	7.5
Chicken	663	6.2	Chestnut	647	4.5
Chocolate	673	36.5	Goose	640	2.9
Corn meal	672	20.2	Pepper (green)	641	6.2
Egg	673	7.6	Potato (sweet)	661	7.3
Flounder	670	4.6	Pumpkin	644	7.3
Lobster	646	13.0	Rhubarb	651	7.4
Milk	673	10.5			
Orange	671	14.9			
Oyster	652	9.0			
Pea (green)	672	41.4			
Peanut	657	12.4			
Strawberry	652	13.8			
Tomato	675	60.7			
Wheat	670	13.4			

*P = <.0001 (highly significant).

*The figures in this table were subjected to statistical analysis by the X^2 formula. We are indebted for this and subsequent analyses to Dr. Hugh Hamilton, Professor of Psychology, Temple University, Philadelphia, Pennsylvania.

tions to most of the foods commonly eaten (left-hand column) than to those uncommonly eaten (right-hand column). Some percentages seemed unusually high, such as those for tomato, green pea, and chocolate, three very commonly eaten foods. But this is true for most of the commonly eaten foods which individually showed significantly higher figures statistically ($P = <.0001$) than the foods eaten infrequently. At first glance one might attempt to explain this difference upon the basis that the commonly eaten foods contained larger amounts of active allergens which are more easily capable of inducing sensitization. It seemed hard to believe, however, that substances like goose or chestnut which are relatively high in protein would be less allergenic than chicken or peanut, or that strawberry is more allergenic than blackberry. When the percentages for these particular foods are compared, as in Table III, it immediately is apparent that this is not a valid explanation for this difference, since there was a definite and statistically significant difference between the incidence of positive reactions to chicken as compared with goose, to peanut as contrasted with chestnut, or to strawberry compared with blackberry. While the amount of allergen present in a food undoubtedly is a factor, it becomes important only if the contact factor also is present. This accounts for the difference between the incidence in the two groups.

TABLE III. COMPARISON BETWEEN COMMON AND UNCOMMON FOODS

FOOD ALLERGEN	TOTAL NUMBER PATIENTS AND/OR TESTS	TOTAL POSITIVES (PER CENT)
Chicken	663	6.2*
Goose	640	2.9
Peanut	657	12.4*
Chestnut	647	4.5
Strawberry	652	13.8*
Blackberry	657	7.5

*All statistically significant ($P = <.01$).

It might be said in objection to the figures obtained in Table II, especially in relation to the high percentages of positive reactions to such foods as tomato, green pea, or chocolate, that we were dealing with extracts which gave nonspecific positive reactions because of either faulty preparations or the presence of irritating materials. If this was true of these extracts, then one would expect high percentages in similar tests conducted in a control non-allergic group. To determine this, we tested a group of 100 nonatopic individuals, all students between the ages of 21 and 30, in whom we could get no history of past or present atopic disease (asthma, hay fever, migraine, or eczema). All were tested with extracts of those foods (common and uncommon) which we had used to test the allergic patients. Furthermore, in order to make the comparison more accurate, we selected at random a group of 100 allergic patients whose ages also were between 21 and 30. We then determined the incidence of positive skin tests* in these two comparable groups for both groups of foods. The results are shown in Table IV.

*All done intracutaneously in the same comparable dilutions used routinely in testing our allergic patients.

TABLE IV. FOOD TESTS IN ALLERGICS AND CONTROLS*

FOOD ALLERGEN† (COMMON FOODS)	CONTROL (NONATOPIC)	ALLERGIC	FOOD ALLERGEN‡ (UNCOMMON FOODS)	CONTROL (NONATOPIC)	ALLERGIC
Banana	4	21	Blackberry	5	10
Chicken	2	4	Chestnut	2	5
Chocolate	13	33	Goose	2	4
Corn meal	12	22	Pepper (green)	0	6
Egg	2	6	Potato (sweet)	3	9
Flounder	2	3	Pumpkin	4	9
Lobster	11	15	Rhubarb	7	7
Milk	1	10			
Orange	3	17			
Oyster	4	11			
Pea (green)	5	44			
Peanut	1	11			
Strawberry	14	14			
Tomato	7	60			
Wheat	10	14			

*Done on 100 patients in each group, all aged 21 to 30 years.

†For comparison between common foods in allergics and controls. $P = <.001$ (highly significant).

‡For comparison between uncommon foods in allergics and controls. $P = <.53$ (not significant).

Inspection of this table at once shows rather strikingly that the incidence of positive reactions to the commonly eaten foods is definitely and significantly higher in the allergic than in the control group. This is especially true of those foods showing a high incidence of positives, notably tomato, green pea, and chocolate. For example, the incidence for tomato in the allergic group was 60 per cent, compared with 7 per cent for the control group; for green pea it was 44 per cent, compared with 5 per cent; and for chocolate it was 33 per cent, compared with 13 per cent in the control group. This striking difference indicates that the high incidence could not be due to the presence of nonspecific or irritating material, but that allergic individuals apparently are more readily sensitized by foods which they eat commonly than are non-allergic persons.

On the other hand, when we compare the incidence of positive skin test reactions in allergic patients to foods uncommonly eaten with that of the control group, it is immediately apparent that, while the incidence in the former is somewhat higher than in the control, the difference between the two is not sufficient to be statistically significant ($P = <.53$); or to put it another way, foods infrequently eaten are not likely to induce any greater incidence of skin sensitization (as indicated by a positive skin test reaction) in the allergic patient than in the nonallergic or control group. The inference to be drawn from these observations is that all individuals, especially allergics, are sensitized more readily by foods which they eat often and in large amounts than by those which they eat infrequently.

While this has no particular bearing upon the question of allergen contact, which is the subject of the present report, an interesting sidelight of our results is the relatively low incidence of positive reactions to most of the food allergens in the control group. This at first would seem contrary to the older

observations, particularly those of Grow and Herman,¹⁵ who in 1935 reported much higher percentages in a group of 150 normal persons tested with thirteen common allergens. However, if the doubtful positive reactions were not included in their estimation of percentages and if the inhalants were excluded from consideration, their figures would be lower and would compare favorably with our figures as to the incidence of specific positive reactions to food allergens in normal persons.

COMMENT

While the results of these reported studies verify the clinical observation that contact with allergenic agents is extremely important in the induction of sensitization, they also show that this is more true of allergic or atopic individuals than of normal or nonallergic control groups. Thus, sensitization more frequently followed exposure to food allergens which are eaten frequently and in larger amounts than exposure to those eaten only occasionally and in small amounts. This was substantiated by our finding that there was a higher incidence of positive skin test reactions to foods frequently eaten (tomatoes, chocolate, or peas) than to those which are infrequently eaten (goose, chestnut, green pepper, and the like). The factor of allergenic contact in these instances probably is not the sole one. Undoubtedly, the amount of active allergen present in a particular food also must be important but, as we showed in our studies, it required a combination of the two factors, namely, a potent sensitizing active principle as well as extensive allergenic contact, perhaps aided by hereditary predisposition to bring about definite sensitization. The latter may be limited to the skin only and manifest itself only as a positive skin test (a nonclinical positive) or it may involve other tissues as well and give rise to clinical reactions. While nonclinical positives may indicate past or future (potential) clinical sensitization, additional proof that they indicate past sensitization was furnished by our studies of patients with positive reactions to horse serum, in which we showed that such reactions almost always resulted from previous exposure to horse serum regardless of the route. Since the skin is such an excellent memory organ, it retains this evidence for years, perhaps for the remainder of the patient's life. Thus, in one of the patients, the positive reaction to horse serum remained for twenty-five years after the initial sensitization, despite the lack of continued antigenic contact.

Just what it is that converts a nonclinical positive into a clinical one, associated with clinical symptoms, still remains to be determined. Unusual or excessive antigenic stimulation undoubtedly is a factor. This was true, for example, in some of our patients who were sensitized by the ingestion of larger amounts of certain foods (for instance, milk) than they previously had taken. Under those circumstances, it is not unlikely that excessive antigenic exposure may convert a previously existing nonclinical sensitization, localized primarily to the skin, into one which also affects other tissues and manifests itself in clinical symptoms.

From a practical clinical standpoint, a significant lesson to be learned from these observations, and one which may be important in prophylactic

treatment, is that allergic patients, especially children, with significant positive reactions to commonly eaten foods should be warned against eating such foods in large amounts as a preventive measure against possible future clinical sensitization.

Finally, the results of these studies also suggest another point which might be applied profitably in clinical practice. Since the incidence of positive reactions to foods uncommonly eaten has been shown to be rather low and not much different from that found in the nonallergic controls, it would seem unwise to continue testing patients with foods which they eat infrequently and/or in small amounts, since the chance of discovering the existence of such sensitization, at least in our experience, seems to be remote. Elimination of tests to foods uncommonly eaten would shorten our testing procedures and serve to streamline our test lists. This, according to information obtained from our questionnaire data,⁷ is something desired by allergists, for it would serve to increase the value of and respect for our testing methods.

CONCLUSIONS

From the results of our observations and studies, the following conclusions seem warranted:

1. Allergenic contact is extremely important in the induction of sensitization, more so in atopic persons than in normal persons.
2. Sensitization, at least as indicated by positive skin reactions, is more frequent after exposure to foods eaten frequently and in large amounts than to those infrequently ingested.
3. Sensitization, once induced, may persist for extremely long periods of time as exemplified by sensitization to horse serum. Since we have demonstrated that a positive skin test reaction to horse serum constitutes definite and incontrovertible evidence of previous contact with horse serum, it should apply equally to other allergens, inhalant or food, and thus explain the existence of many positive reactions which appear to have little clinical significance (nonclinical positives).
4. Allergic patients, especially children, with positive tests to commonly eaten foods should be advised against eating these in large amounts, since excessive antigen contact may convert a nonclinical sensitization into a clinical one.
5. Since the incidence of positive skin test reactions to foods infrequently eaten is quite low, their elimination from the routine skin test lists would seem advisable, as it would shorten the testing procedure materially.

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