

# STUDIES IN SENSITIZATION AS APPLIED TO SKIN TEST REACTIONS

## III. INFLUENCE OF AGE UPON SKIN REACTIVITY

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**I**N A previous communication,<sup>1</sup> we discussed the various factors which might influence skin test reactions. It was pointed out that positive reactions may increase, decrease, or remain stationary, depending upon such influences as avoidance, specific treatment, or various physiologic reasons. The latter included change in the reactivity of the skin with advancing age. Thus, as indicated by our questionnaire survey,<sup>1</sup> some allergists believe that older people have a lessened skin reactivity which accounts, perhaps, for the change in skin reactions upon retest. Clinical experience also has suggested that there is a lower incidence of positive skin test reactions in the aged, even to potent allergens, but these are opinions based solely upon clinical impressions rather than upon the results of investigative studies. This is supported by a review of the literature which did not reveal any confirmatory evidence to support these contentions. In an attempt to obtain more definite evidence, investigations were carried out, the results of which form the basis of the present report.

### METHOD OF STUDY

Two types of studies were undertaken. The first consisted of the determination of the incidence of positive skin test reactions at various decades of life; the second involved the determination of skin reactivity to varying concentrations of histamine at varying age periods.

To obtain the information comprising the first part of this study, we reviewed the skin test records of our private patients to determine the incidence of positive reactions to food allergens at various ages. Starting with the letter "A," we went through our files alphabetically, recording the age of the patient and the skin reaction, until we had obtained a total of 100 for each food and for each decade. The foods selected were those listed as "commonly eaten" and "uncommonly eaten" and utilized in a previously reported study<sup>2</sup> concerning the contact factor in skin sensitization. Listed as commonly eaten foods were banana, chicken, chocolate, corn meal, egg, flounder, lobster, milk, orange, oyster, green pea, peanut, strawberry, tomato, wheat; the uncommonly eaten ones were blackberry, chestnut, goose, green pepper, sweet potato, pumpkin, and rhubarb.

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All tests were done by the intracutaneous method, 0.02 ml. of the routine dilution of the food extract being injected. Only those positives were selected which had been retested at least once to be certain of their specificity. Reactions were classified either as negative or as slight, moderate, or marked positive; doubtful reactions were considered negative. The totals for each decade and for each grade of reaction are listed in percentages in the tables.

For the second part of this study, routine intracutaneous skin tests (0.02 ml.) were performed with four dilutions of histamine (1-1000, 1-10,000, 1-100,000, and 1-1,000,000) upon nonallergic persons at various age periods, selecting 100 persons for each decade of life. The results were recorded as negative, slight, moderate, or marked. All doubtful reactions were considered negative. An attempt was made to carry out similar tests upon allergic patients, both private and clinic, currently being studied. We were unable to obtain a number in the various decades comparable to that of the nonallergic group, so the evidence furnished by this portion of the study has been omitted from the present study.

#### RESULTS

A summary of the data comprising the results of the first part of the investigation is tabulated in Tables I and II and charted in graphic form in Figs. 1 and 2. It will be noted in Table I that we were able to obtain 100 records

TABLE I. COMMON FOODS. INCIDENCE OF POSITIVE REACTIONS ACCORDING TO AGE GROUP

| AGE GROUP   | TOTAL NUMBER TESTS | PER CENT NEGATIVE | PER CENT SLIGHT | PER CENT MODERATE AND MARKED | PER CENT TOTAL POSITIVE |
|-------------|--------------------|-------------------|-----------------|------------------------------|-------------------------|
| 0 to 10     | 1,500              | 75.3              | 22.1            | 2.6                          | 24.7                    |
| 11 to 20    | 1,500              | 78.5              | 19.9            | 1.6                          | 21.5                    |
| 21 to 30    | 1,500              | 81.0              | 17.3            | 1.7                          | 19.0                    |
| 31 to 40    | 1,500              | 79.3              | 19.3            | 1.4                          | 20.7                    |
| 41 to 50    | 1,500              | 80.9              | 18.2            | 0.9                          | 19.1                    |
| 51 to 60    | 1,500              | 86.2              | 13.1            | 0.7                          | 13.8                    |
| 61 to 70    | 817                | 86.8              | 12.7            | 0.5                          | 13.2                    |
| 71 and over | 172                | 87.2              | 12.2            | 0.6                          | 12.8                    |

TABLE II. UNCOMMON FOODS. INCIDENCE OF POSITIVE REACTIONS ACCORDING TO AGE GROUP

| AGE GROUP   | TOTAL NUMBER TESTS | PER CENT NEGATIVE | PER CENT SLIGHT | PER CENT MODERATE AND MARKED | PER CENT TOTAL POSITIVE |
|-------------|--------------------|-------------------|-----------------|------------------------------|-------------------------|
| 0 to 10     | 700                | 91.0              | 8.9             | 0.1                          | 9.0                     |
| 11 to 20    | 700                | 93.2              | 6.6             | 0.2                          | 6.8                     |
| 21 to 30    | 700                | 92.9              | 7.1             | 0                            | 7.1                     |
| 31 to 40    | 700                | 93.8              | 6.1             | 0.1                          | 6.2                     |
| 41 to 50    | 700                | 95.0              | 5.0             | 0                            | 5.0                     |
| 51 to 60    | 700                | 95.6              | 4.4             | 0                            | 4.4                     |
| 61 to 70    | 277                | 97.8              | 2.2             | 0                            | 2.2                     |
| 71 and over | 63                 | 96.8              | 3.2             | 0                            | 3.2                     |

for each of the fifteen common foods, giving a total of 1,500 tests for each decade up to the age of 60 years. After age 60, however, the total for each food was less because of the lack of patient material in that age period. This also was true for each of the seven uncommon foods; 100 records for each one were

obtained up to the age of 60, giving a total of 700 for each decade, but a smaller number was obtained in those after 60 (Table II). Because of the smaller number present in the groups aged 61 to 70 years and 71 years and over, the totals in these two age periods were combined when the graphs were made. These slight deviations, however, did not interfere with either the final results or their interpretation.

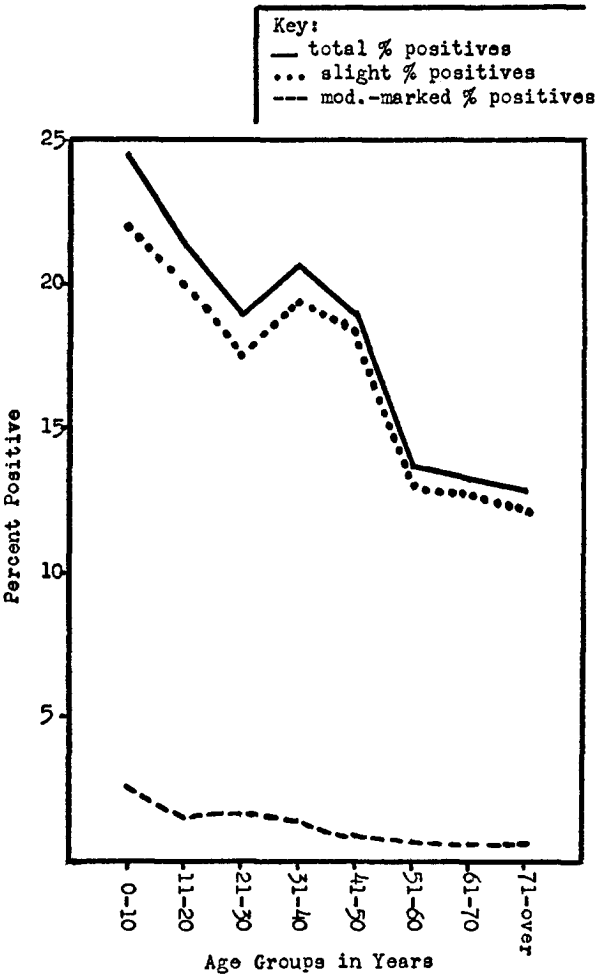


Fig. 1.—Incidence of positive reactions to common foods in allergic patients according to age group.

As seen from the tables, and more graphically in Figs. 1 and 2, the incidence of positive reactions is greatest in the first decade, with only slight reduction in the second decade. Little change then occurs between the ages of 21 and 50 years, but from 51 to 60, and especially after 60, there is a sharp drop in incidence, particularly when one compares it with the first decade. This is true not only of the composite curves (Fig. 1, solid line) but also of

the individual curves for slight positive reactions (dotted line). The percentage for the moderate-marked positive reactions (combined together, as there were so few marked positives) was too low for accurate interpretation, but even these curves show a diminishing tendency with advancing age (broken line). The diminishing incidence of positive reactions with advancing age is seen more strikingly in the curves of the commonly eaten foods

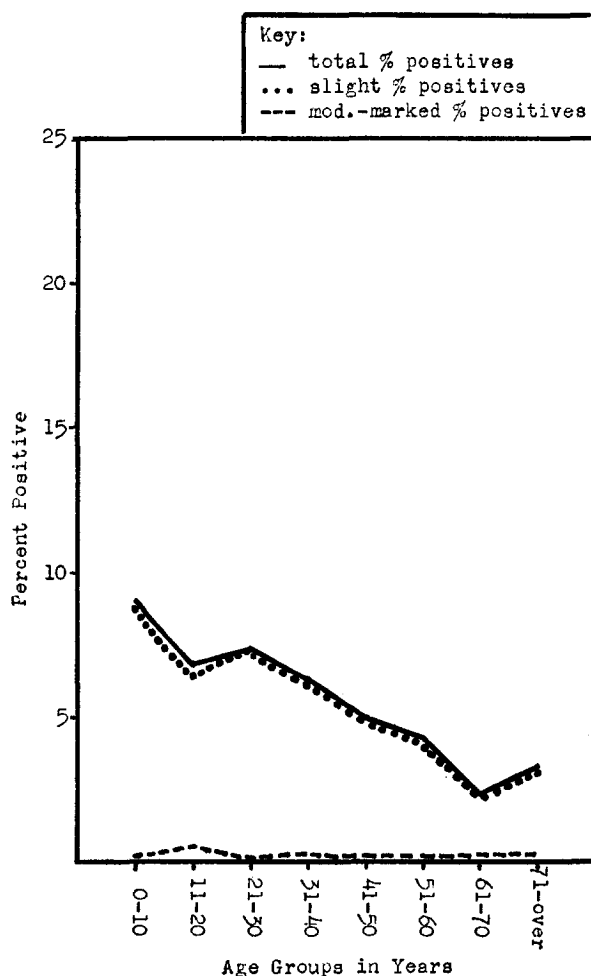


Fig. 2.—Incidence of positive reactions to uncommon foods in allergic patients according to age group.

(Fig. 1) than in those of the uncommonly eaten ones (Fig. 2), although the general contour of the curve is similar in both. However, as indicated in our previously reported study,<sup>1</sup> this is because the incidence of positives in the uncommonly eaten group ordinarily is low so that little change is to be expected. This is verified also by the extremely low and almost negligible number of moderate to marked positives in the uncommon group as compared

with the commonly eaten foods. On the whole, the results of this portion of the investigation serve to verify the clinical impression that skin reactivity is highest in the first two decades, and that a slight decrease then occurs in the third, fourth, and fifth decades, with definite diminution after the age of 50 years.

The results of the tests with histamine in nonallergic persons at various decades are shown in Table III and Fig. 3. Inspection of these shows at once that nearly all persons, regardless of age, reacted to histamine in the 1-1,000 concentration, in either moderate or marked degree. On the other hand, few reacted to the 1-1,000,000 concentration, even in slight degree. This renders the latter concentration unsuitable for use in interpretation for comparative purpose, as contrasted particularly with the results of the tests with the other three strengths. Likewise, since in the 100 tests with 1-100,000 concentrations there were only eight moderately positive and no marked positive reactions, these results are included for purposes of comparison with the slight reactions as "positive" without regard to degree. Similarly the four marked positive reactions to the 1-10,000 strength are included with the moderates, whereas the eight negatives are grouped with the slights and the slights with the moderates in the 1-1,000 strength, both for purposes of comparison and for charting the curves.

TABLE III. INCIDENCE OF SKIN TEST REACTIONS TO HISTAMINE IN NONALLERGIC PERSONS\*

| CONCENTRA-<br>TION OF<br>HISTAMINE | REACTION | AGE GROUPS |             |             |             |             |             |             |                |
|------------------------------------|----------|------------|-------------|-------------|-------------|-------------|-------------|-------------|----------------|
|                                    |          | 0 TO<br>10 | 11 TO<br>20 | 21 TO<br>30 | 31 TO<br>40 | 41 TO<br>50 | 51 TO<br>60 | 61 TO<br>70 | 71 AND<br>OVER |
| 1-1,000,000                        | Negative | 88         | 98          | 100         | 99          | 97          | 100         | 100         | 100            |
|                                    | Slight   | 12         | 2           | 0           | 1           | 3           | 0           | 0           | 0              |
|                                    | Moderate | 0          | 0           | 0           | 0           | 0           | 0           | 0           | 0              |
|                                    | Marked   | 0          | 0           | 0           | 0           | 0           | 0           | 0           | 0              |
| 1-100,000                          | Negative | 6          | 22          | 11          | 16          | 16          | 10          | 38          | 39             |
|                                    | Slight   | 87         | 78          | 88          | 84          | 84          | 90          | 62          | 61             |
|                                    | Moderate | 7          | 0           | 1           | 0           | 0           | 0           | 0           | 0              |
|                                    | Marked   | 0          | 0           | 0           | 0           | 0           | 0           | 0           | 0              |
| 1-10,000                           | Negative | 0          | 0           | 1           | 2           | 0           | 0           | 0           | 5              |
|                                    | Slight   | 15         | 42          | 25          | 28          | 40          | 34          | 61          | 61             |
|                                    | Moderate | 85         | 58          | 74          | 70          | 59          | 63          | 39          | 34             |
|                                    | Marked   | 0          | 0           | 0           | 0           | 1           | 3           | 0           | 0              |
| 1-1,000                            | Negative | 0          | 0           | 0           | 0           | 0           | 0           | 0           | 0              |
|                                    | Slight   | 0          | 2           | 2           | 6           | 3           | 6           | 10          | 15             |
|                                    | Moderate | 25         | 37          | 52          | 36          | 64          | 64          | 69          | 73             |
|                                    | Marked   | 75         | 61          | 46          | 58          | 33          | 30          | 21          | 12             |

\*One hundred tests for each decade with each concentration.

In making an interpretation of the results, it will be seen from inspection of Table III that in the 1-100,000 concentration, there is a progressive increase in negative reactions from the first decade on, compared with a progressive decrease in slight positive reactions. Thus, the reactivity is highest in the first decade (94.0 per cent positive) and lowest both in the sixth decade (62 per cent) and after age 71 (61 per cent). Incidentally, it is to be noted as verification of the high reactivity of the first decade that practically all the moderate reactions (seven) to the 1-100,000 strength occurred in this age

period. This progressive reduction of reactivity, as indicated by the slight positives, is illustrated in the broken line shown in Fig. 3. Similar findings were obtained with the results of the tests with the 1-10,000 concentration. Thus, there is a progressive increase in the slight positive reactions from the first decade (15 per cent) to those after age 60 (61 per cent) and, conversely, a progressive decrease for the moderate positive reactions from 85 per cent

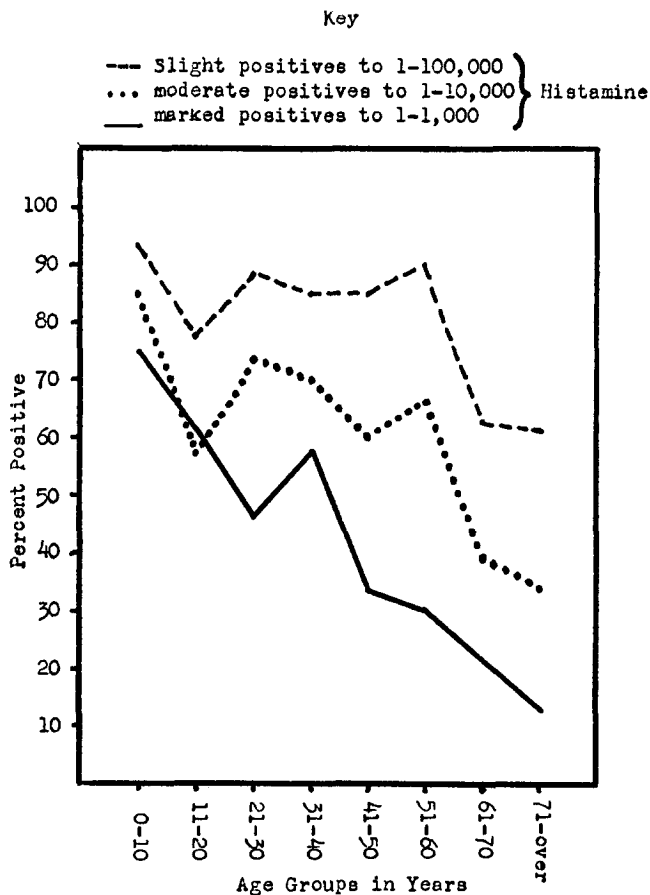


Fig. 3.—Incidence of skin test reactions to histamine in nonallergic patients.

in the first decade to 34 per cent in the group past 70 years of age, which also showed the largest number of negative reactions (5 per cent). This decrease in reactivity is shown in Fig. 3 by the dotted line representing the moderately positive reactors. Finally, these findings also are verified by the results with the tests to the 1-1,000 concentration which show an increase in moderate reactions and a corresponding decrease in marked positive reactions from the first decade to the period after 70 years of age. The latter is represented by the solid line in Fig. 3.

Regardless, therefore, of which concentration is utilized, the results as shown graphically in the curves in the chart indicate that, at least in non-

allergic persons, the reactivity of the skin in relation to histamine is highest in the first decade. It diminishes thereafter, slightly and not altogether uniformly, from the second to the fifth decades, inclusive, with little tendency to any consistent or striking diminution. But after age 60, there is a definite and marked reduction in reactivity, the curve falling rather precipitously from ages 61 to 70, with little reduction after age 71. The results of these histamine tests roughly parallel those obtained from the analysis of the incidence of positive allergic skin test reactions according to age as shown in Fig. 1. The only point of difference is that in the latter a sharp drop in incidence as seen in the curve occurs after age 50, whereas in the histamine group it does not appear until after age 60. Whether this is the result of statistical variation, perhaps ascribable to the inclusion in the older age group of patients likely to have few or no positive reactions (as, for example, those with the nonallergic or "intrinsic" forms of asthma) or whether it represents an actual difference in the reactivity of the skin of the allergic patient, as contrasted with the nonallergic person, awaits further elucidation.

#### COMMENT

The demonstration of a reduction in skin reactivity with advancing age provides an additional reason, as indicated in our first report,<sup>1</sup> for changes in skin test reactions, especially when patients are retested at long intervals. The actual reason for this decrease is not known, but for the present it must be regarded as physiologic and normal.

Realization of this loss of reactivity in the skin of older people may be important clinically, because until now we have assumed that failure to obtain positive reactions with routine tests, especially in persons past 50 years of age, indicated an absence of sensitization to specific allergens. As a result, such persons often are classified as being nonsensitive or nonallergic. The results of the present study suggest that failure to react may be due to a low threshold of skin reactivity rather than to an absence of specific sensitivity. Since patients usually are tested with that concentration of the allergenic extract which has been considered from experience to be the proper testing strength, older persons with lessened reactivity might show a negative reaction with that concentration but a positive one when tested with the next higher strength. We see this not infrequently in hay fever patients, some of whom may react only to higher concentrations (0.01 or 0.1 mg. of N per milliliter) and others to lower ones (0.0001 or 0.001 N). Unless this variation in skin reactivity is realized, a positive test may be missed. Since most people react to histamine in a 1-10,000 or 1-100,000 concentration, routine skin tests with these concentrations might provide a clue as to the patient's skin reactivity. Thus, if patients have a slight reaction to the 1-100,000 and a slight to moderate reaction to the 1-10,000 strength, their reactivity can be considered average or normal. If, however, they react negatively to the former and doubtfully or only slightly to the latter, their reactivity should be considered relatively low. This should be taken into account in the interpretation

of their skin tests. We are now utilizing these tests in our allergy patients for the estimation of their skin reactivity in the hope that this experience might determine its clinical usefulness.

#### SUMMARY AND CONCLUSIONS

1. The incidence of positive skin reactions to food allergens is highest in the first decade of life and decreases slightly up to age 50, but after 50 (and especially after 60) there is a sharp decrease, especially when compared with the first decade.

2. Skin tests with histamine in varying concentrations done on nonallergic persons at different decades of life show that skin reactivity is highest in the first decade and diminishes slightly from the second to the fifth decades, with definite and marked reduction after the age of 60 years.

3. Failure to demonstrate positive reactions in older persons may be due to loss in skin reactivity rather than to a lack of specific sensitivity.

4. The possibility of utilizing histamine skin tests (1-10,000 and 1-100,000) for determining skin reactivity is discussed.

#### REFERENCES

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