

THE RELATIVE AND ABSOLUTE VALUE OF SKIN- REACTIONS FOR THE DIAGNOSIS OF FOOD ALLERGY*

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Since long skinreactions with foodextracts have been performed by allergists in order to detect hypersensitivity to foods. Already in 1922 Nils P. Larsen, Royce Paddock and H. L. Alexander (1) and also Aaron Brown (2) and in 1926 A. H. Fineman (3) gave convincing proof in elaborate studies over a great number of allergic patients, who were clinically hypersensitive to certain allergens, that the intracutaneous method of skintesting was highly preferable to the scratch-method.

They, and others after them proved, that the first method is nearly 100 times more sensitive and that it gives much more accurate results than the scarification method. The latter many times fails to bring to light an undoubtedly clinically existing hypersensitivity whereas the intracutaneous method gives much more trustworthy results. The difference in sensitivity of the two methods enables us to use 50 to 100-times more diluted solutions in the intracutaneous test. This higher dilution of the testfluids is a warrant against general reactions.

Though, up to the present time, intracutaneous skinreactions are the easiest and quickest method for detecting food allergy and though they are valued highly by many allergists in their daily routine-practice and also fit for experimental

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studies, others and especially those physicians, who have but little experience in allergy may have doubts about the merits of intracutaneous and other skintesting for the diagnosis of food allergy. Indeed, if we realise that sometimes the skin-reaction on a certain food may be negative whereas *after some time* an undoubtable clinical hypersensitivity to it may be stated, then the adversaries of the method have seemingly a strong weapon against the defenders; moreover positive skinreactions may change in the course of some time.

The following description of clinical evidence and of my experiments on the matter will, as I trust, overbridge this controverse, so that the doubt will be removed.

The first case that drew my attention to the possible cause of the variability of skinreactions with foodextracts was that of a nurse. She was suffering from asthma since youth. Since she was working in our clinic her asthma had disappeared nearly totally. The allergenfree air, with which the rooms of that clinic are ventilated, and a diet in which milk, milkproducts and potatoes had been eliminated (as she showed clinically as well as by intracutaneous skintest a marked hypersensitivity for these foods),—both measures against inhalants and foodallergens were undoubtedly the principal reasons for her well-being.

When on Sundays she visited her parents she always returned with asthma (inhalants), from which she recovered in the course of the following Monday, to stay well further, if not again visits in surroundings, with less allergenfree air than that of the clinic, interfered.

In her first weeks of working in our clinic the intracutaneous reaction on milk was + + +, after a month of milk-abstinence + +, after 3 months + and after nearly a year the reaction had turned negative. Then we permitted her to take milk again, 3 to 4 glasses daily. The first day all went well. The second day she started sneezing and got a violent vasomotor rhinitis and on the 4th day asthmatic symptoms appeared and grew gradually worse. On the 7th day we tested intracutaneously with milk. The reaction had now

turned over to $++\pm$. Then milk and its products were omitted totally. Within 2 days all the symptoms of asthma and rhinitis disappeared and did not return.

After six months, the skin reaction on milk having in the meantime changed to negative, we repeated the experiment with nearly exactly the same results. From this case we concluded that the hypersensitivity may disappear by long lasting avoidance of the food and return soon after again taking that same food. Parallel with this the skinreactions will change from positive to negative to get positive again as a result of retaking the food.

Another illustrative case was that of a woman, Mrs. M., old 45 years, who had a slight asthma and a severe colica mucosa. We regulated her diet by forbidding her those foods, which by intracutaneous skintests showed positive reactions. She was greatly benefitted by that diet as, during more than 7 months, she was perfectly well. After that she gradually again got more and more symptoms of colica mucosa and asthma. We retested the whole set (nearly 80) of foodextracts and experienced that many of them, which formerly had reacted positively, now had turned negative whereas others showed the reverse.

Her diet was changed accordingly, which, within some days, was followed by complete clinical recovery. Only after the passing by of 7 to 8 months some symptoms of her illnesses returned, which induced her to bid us to retest her. Again we stated that many of the foods which she had avoided accurately, now reacted negatively whereas others, of which she had eaten in the past period, now reacted positively. Now we changed the diet accordingly, which again had a very good clinical result.

After 4 months she returned again with slight symptoms. Everything repeated itself as on the two former occasions. And so, we experienced again and again in the following 5 years, intermittently with periods of half a year to a year the qualitative changing of hypersensitiveness, as well revealed clinically as by skinreactions. After these elaborate

descriptions there may follow still some cases from which I only mention the principal facts:

3. G. L., m, aged 33, asthma.

In 1943 ++ skinreaction on milk. By avoiding milk and milkproduct and some other foods, he was well during nearly one year. Then asthma began again. New tests revealed that milk now reacted —. Moreover he could very well clinically tolerate it now. But his skintest reacted + on potatoes. Now he avoided potatoes but took again milk, whereafter he felt well during a long time.

4. P. N., m, aged 40, asthma.

Skinreaction: 1941, potatoes +, milk +; then avoidance of both. Asthma cured.

10.11.1944. Consults me again. No asthma, but since 3 months he eats potatoes and drinks milk as he felt himself weak. Intracut. reactions: milk —, potato —.

Conclusion: After a 3 years-lasting avoidance of milk and potatoes the hypersensitivity disappeared; three months of retaking these foods did not reactivate the hypersensitivity to them.

5. Mr. A. A. B., 21 years, asthma.

1. Nov. 1943. Allergic to egg, potatoes, milk. Avoidance of the three. Good health. Consults me again on 10.11.1944. Had had no asthma. Intracut. reactions: egg and potatoes still +, but milk now —. Permitted to drink milk.

Conclusion: By avoidance automatically hypersensitiveness for milk disappeared.

Such cases I had in many variations. More similar experiments taught me also, that we may have:

1. The reaction on a certain food may be — and after eating that food repeatedly during some time the reaction may gradually get more and more + and at the same time we state clinically the new acquired sensitiveness, as eating

of that food causes asthma or other allergic symptoms. Such a "negativeness" we might call a "*passagère*" or *transient negativeness*. On the other hand a positiveness of skinreaction may gradually disappear by strict avoidance of the food. Such a positiveness we might call a "*passagère*" or *transient hypersensitiveness*.

2. The reaction on a certain food may be +; strict avoidance during a very long time causes only a slight diminution of the intracut. skinreaction. This we might call a *manifest positiveness s. hypersensitiveness*. The same may occur with negativeness of a food reaction: even eating the food during a long time may not cause development of hypersensitiveness. This we might call a *manifest negativeness*.—

I stated further that "passagère" or "manifest" did not depend on *the sort of food*, but most probably on particularities of the patient himself but I could not solve the question, how and why. Only this was found, that in patients with repeated disturbances of the digestion and disturbances in the intestines such as diarrhoea and especially in patients suffering from gastric ulcer and ulcers in the duodenum or other parts of the intestine, the negativeness was highly *passagère* whereas the positiveness might be either *passagère* or *manifest*.

EXPERIMENTS

Miss L. M., aged 24, ekzema and asthma.

Since 3 weeks hospitalized. We have but very little success with treatment. As 7 months ago she reacted: potatoe —, milk —, meat (beef) —, she was permitted to eat every day of these foods during these 3 weeks.

On Febr. 4, 1944 we, however, state: potatoe —, milk +, meat (beef) —. We stop milk and milkproducts. From that day on marked gradual improvement of asthma as well as of ekzema. She stays in the clinic until March 21. Asthma and ekzema nearly wholly cured.

We controlled in the meantime how skinreactions did change.

	Potatoe	Milk	Meat (beef)
	The positiveness of reaction on the 4th of Febr. now had turned negative, most probably by abstinence.		
Febr. 28	—	—	—
29	—	—	—
March 1	—	—	—
2	—	—	—
7	—	—	—
9	—	—	—
10	—	—	— Today we add milk to the diet.—
11	—	+	— More ekzema, more itching, we stop milk.
13	±	—	— Egg ±, tomato —

She has still some ekzema and after dinner also asthma. This is most probably the result of the false diet, given on March 10. (all other circumstances were kept unchanged). As well as milk on the 11th we now stop potatoes and eggs too, but continue with meat.

	Potatoe	Milk	Meat	Egg	
15	±	±	—	±	
16	—	—	—	—	ekzema and asthma much better
17	—	—	—	—	
18	—	—	±	—	
20	—	—	±	—	
21	—	±	+	—	

It seems that, as from March 18–21, the reaction on meat goes gradually more and more in the direction of positiveness, the milkreaction also seems to have the same tendency. As both are products of cow there may be in this case a relation between milk and meat hypersensitiveness, f.i. both may contain an identical protein on which the patient starts to react. By that way the eating of beef may be also a cause for a new development of milk hypersensitiveness.

From this very instructive case, which showed a rather great variability, we learn:

1. Negativeness of reaction on meat seemed nearly manifest negative. Nevertheless hypersensitiveness developed on March 18.

2. Milk hypersensitiveness was highly "passagère" as well as milk negativeness.

3. Negativeness of reaction on potatoe seemed nearly "manifest-negative". Nevertheless slight hypersensitiveness developed on March 13. This hypersensitiveness was "passagère" as it had already disappeared on March 16, after avoidance during 2 days.

4. Egg positiveness was "passagère".

Practical conclusion for the therapy: Foods which are eaten daily have a greater chance to sensitize the patient than foods, which are taken more seldom.

Therefore the first require a more frequent control by repeated skinreactions. Another instructive case and experiment was the following:

Mr. West . . . asthma since 1940.

Compelled in 1944 to work in Germany. There urticaria add to his asthma. He had, before his leaving for Germany, been tested on January 28.: milk +, potatoes +, meat +, so that I had advised him not to eat these things. On his return to Holland on March 1, he however admitted that, against my prescription, he had eaten every day some milk-soup and on Sundays some potatoes. Meat had been very scarce in Germany, but when he could get some, he had token it. As he had more asthma now and urticaria, he was hospitalized. We now avoided strictly those three foods, and made daily skintests:

		Milk	Potato	Meat (beef)	
March	3	+	±	+	
	6	+	±	+	
	9	+	—	+	
	10	±	—	+	
		Today we permit to eat again potatoes			
	11	±	+ ±	±	egg ±
	somewhat asthma we stop potatoes				
	15	± —	+	—	± stop egg
	16	—	—	—	—
	17	dismissed from clinical observation.			

From this experiment we learn that in this case:

1. milk-, potato- and meathypersensitiveness were maintained by eating small quantities daily or weekly (in Germany). Strict avoidance made them disappear. Eating potatoes only for one day, did revive the skinreaction and gave a slight general reaction. (March 11).

Conclusion: milk-, potato- and meathypersensitiveness, were in this case "passagère". Also potato-negativeness of skinreaction was in this case "passagère".

The conclusion of my experiences and experiments is clear: changing of skinreactions may occur in allergic patients. This is not in conflict with the reliability of intracutaneous skinreactions, as they change only according to and parallel with variable and varying clinical allergy. As I learned later, my results with reappearance of food allergy are only a special case of a more general rule as may be seen by quoting A. Rich. He writes in his "Pathogenesis of tuberculosis", 2nd printing, p. 400:

"When a specific antibody has once been produced as a result of contact of the tissues with a foreign antigen, the amount of antibody demonstrable in the circulation gradually decreases with the passing of time if there is no further contact with the same antigen, until, at length, none at all can be detected. If now the antigen enters the tissues again, antibody will reappear in the circulation and will reach a given level in much shorter time than was required following the first contact with the antigen".

So far as to allergy in men. It is interesting that much earlier in anaphylaxis related facts have been stated.

In "Die Serumkrankheit", Frantz Deuticke, Wien 1905, C. v. Pirquet and B. Shick describe the same coming and going of specific antibody in serumsickness, parallel with the varying activation by antigen.

For the allergic practice our experiments teach us that:

1. When a food reaction is negative, we are not sure, that indeed the food in question will be inoffensive for the patient. If after prescription of an allergenfree diet, in which that

food is permitted ("allergenfree" according to results of skin reactions) a patient does *not* go well, test him after some days of taking that food daily. Many times we will learn then that some reactions, which were negative, have changed into positive as the negativeness was "passagère" and now we can institute a really right "allergenfree" diet.

2. When a food reaction is + and refers to a food which either we or the patient himself think important (such as milk, meat, egg, potatoes, rice, e.g.) forbid it, but if the patient goes well for a reasonable long time, try then the skin reaction again. It may occur that the skinreaction then has turned to negative. We may then permit that food again, but under control of the patients clinical well-being and by controlling as well, if necessary, by skintests from time to time.

3. As long as a patient goes well, there is no great need for changing his diet, but in gradual redeveloping of illness, retest his whole diet.

4. If a skin reaction is only slightly positive, so that there may arise doubt how to interpret it: either to avoid that food or to permit it, we should be conducted by the consideration that such a reaction either may indicate a passagère hypersensitiveness going in the direction of a more outspoken hypersensitivity or in the reverse direction.

SUMMARY

Intracutaneous skintests for the detecting of food-allergy are highly important and accurate.

Elimination, during some months or longer, of a certain food in cases of hypersensitivity many times may lead to a better tolerance and even to complete disappearance of the hypersensitiveness for that food, whereas repeatedly eating of a certain food may result in a gradual sensitization.

Intracutaneous skintests at the same time will gradually turn from positive to negative, resp. in the second case; from negative to positive.

For the right interpretation of skintests in cases of food allergy these facts should be well considered.—

LITERATURE

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