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FOOD ALLERGY IN THEORY AND PRACTICE

By

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In food allergy as in other branches of allergy many of the pioneers have themselves suffered from the disease, as for instance Doerr (22), Richet (22), Küstner (9), and Rowe (16), and therefore it is not surprising that they think a lot about it. But the difficulties in diagnosis have made many others doubt the aetiological significance, and psychiatrically trained doctors call food allergy patients typical psychosomatic cases.

It is, indeed, a difficult diagnosis as will be discussed later. In America interest is greater than here in Europe; this is probably due to the fact that food is more often the cause of allergic conditions there. There are no obvious reasons for this, but according to the work of Glaser (5) not only cow's milk allergy but also other allergic conditions are far more frequently produced in children fed with cow's milk from birth than in breast-fed children, and the frequency of breast feeding is essentially lower in U.S.A. than in the Scandinavian countries. Similarly the North American children will only exceptionally get the natural food which is used here, but are fed on industrially manufactured foods which have added various preparations of a chemical nature to make them attractive (Knight (8)). It has been proved experimentally (12, 17, 21) that the infantile mucosa of the intestine is more easily penetrated by even rather large protein molecules as

for instance undigested egg white. It is therefore possible that the early use of these compounded meals, which are even cooked in factories, exposes the infants to a greater variety of allergens than our more simple breast milk, oat-meal, mashed potatoes and so on. Adults of North America also eat far more chemicals, as the vastness of the country and the size of the towns make it difficult to transport fresh natural foods from the locality where they are produced to the consumers, and they must therefore add preservative agents more often. In the American literature it is also often mentioned that spices give allergy (4, 6, 14, 15, 18), but generally the foods most frequently eaten are by and large the allergens most frequently found guilty, although one can hardly mention any kind of food which has not been said to be the cause of allergic reactions, including beer, wine and whisky.

The symptoms may be localized to any organ of the body—apart from the bones—if the literature is correct. Allergy has been described in the nervous system, cerebrum as well as cerebellum, eyes and ears, in the respiratory tract from nose to lungs, in the mouth, the salivary glands, ventricle, small intestine, gall bladder, colon, in the urinary tract, in joints, in muscles, in the blood vessels and in the blood itself, besides the fact that ordinary fatigue and malaise have been ascribed to food allergy.

The difficulty in finding the relationship between the allergen and the symptoms is partly due to the fact that some of the foods have a long reaction time. There are some, as for instance fish and flour, which cause effect after inhalation and often quickly, and others which act by contact and especially produce symptoms from the skin or the oral mucosa, but the majority work after peroral intake. Nuts, for instance, give an immediate reaction while others, as meat, may react after 1–2 days. The explanation has been that the allergenic food does not react in its pure form, but the symptoms are produced by one or more of the digestion products,—the importance of the case history is thus reduced to a certain extent, but still everybody agrees that this is the most important

single factor in the investigation,—as a result, however, attempts have been made to exploit digestion products for the cutaneous tests. Cutaneous tests with foods are far less reliable than with inhalants. Scratch tests give a number of false negative reactions and intracutaneous tests often give false positive reactions (but both methods may result in the opposite). Actually the prick test method in my experience is the best, at least with children. As mentioned, attempts have been made to add digestion enzymes in various combinations to the allergenic food before the test is made, but the value of these experiments has never been equal to the labour, and cannot replace a thorough case history and food experiments which are nearly always indispensable (2, 3).

If there is an allergy towards a seasonal food or a rarely eaten dish the patient will often know in advance what he does not tolerate, but frequently the allergy is due to several foods, and if these are for instance milk, butter and cheese or anything else which is consumed daily, the history will not reveal which of the common foods the patient does not tolerate. Also a patient eats thoroughly cooked food without trouble, while he reacts to the same thing when it is raw. The opposite may also happen as with Küstner who was allergic to boiled fish but could eat raw fish without symptoms, and peculiarly enough some patients allergic to fish report that canned fish produces no symptoms; perhaps it is cooked more thoroughly in the factory than at home.

In food allergy it seems generally to be as in other allergies that the patient has no trouble when he meets the allergen for the first time, while a second intake some time later produces a reaction. Yet infants may react the first time they drink cow's milk. This is in accordance with Ratner's theory (10, 11) about sensitization in utero, as it is unlikely that a hereditary disposition for allergy can be so specific. The question about active or passive sensitization, i.e. whether a child itself has produced antibodies in utero or has received antibodies from the maternal blood—has given rise to a number of experiments and discussions. Both ways seem to be possible and although its

value cannot yet be said to be established, pregnant allergic women are recommended to have a varied diet during their pregnancy and not give way to one or another passion for a definite dish which is not unusual under these circumstances.

In allergic infants, negative cutaneous reactions are often found, but as they grow the chances of positive reactions increase. As mentioned above, both cutaneous and intracutaneous tests often fail, but—as Walzer (20) puts it—“no technique is better than the technician who uses it” and the estimation of the tests must be particularly critical with food allergens. Some investigators use group testing and this may be sufficient for instance with fish which frequently gives a multiple sensitivity, but except for this rare instance one must be very careful as the group reaction may be wrong as with inhalants. It is also an advantage to use different extracts for trial, as one manufacturer may make the best preparations for instance from meat and fish, another is best for vegetables.

It is not recommended to make too many intracutaneous tests at the same time, as very bad local and general reactions may be encountered. Death has been reported after intracutaneous tests (7) and it is claimed that even a previous negative scratch test does not exclude the possibility of a strong reaction to intracutaneous testing. The scratch and prick tests are not so dangerous. A possible reason for the greater reliability of cutaneous tests with inhalants is that they reach the blood more intact than the digested foods; therefore it may not be necessary for this reason to pay attention to the late reactions, whereas such late reactions with foods—according to my experience—seem to be of value in some cases.

It is most important—as mentioned above—to make a thorough case history in order to see if anything may suggest a suspicion of food allergy, and it is necessary to keep in mind the fact that many patients are allergic to inhalants and food at the same time. If the patient has a definite idea about his potential allergy to certain dishes, one must ask how this suspicion arose; with children it is sometimes worth while to investigate the reaction to the dishes they do not like, as they

cannot explain why they do not agree with them. It is probably always of advantage to make skin tests, as they may help to direct the mind to the daily eaten foods the patient reacts to; and thereafter there are two ways of further investigation. One is to eliminate for some days or weeks the foods that give rise to suspicion and or positive reactions, and watch the effect, and then expose the patient to one food at a time and see what happens. The second is to prescribe to all patients a special diet and follow the effect. Rowe (13), who used to employ the first method, now always prescribes one of two specific diets and reports that he gets the best results that way. Both diets eliminate milk, and all of its products and eggs; one excludes further all kinds of flour and cereal, the other all fruits and spices, but they may be combined. Andresen (1), on the other hand, gives at once a provoking diet which includes only the most frequent causes of food allergy. He claims that if this diet provokes symptoms it is easy, from the few foods in the diet, to find the guilty ones. It must be said, however, that a patient may be allergic to several, even many, different kinds of food, common as well as rare ones.

My patients have been put on an elimination diet which excludes all the foods which gave positive reactions, whether it be by prick or intracutaneous tests, and those foods which the patient suspects to be responsible even if they gave negative reactions. This diet must be maintained for at least 2 weeks, after which time it is supposed that every trace of earlier taken potential allergenic foods will have been broken down. The effect is noted by the patient and he can try eating the thing he misses most for three days, unless symptoms develop before. If this happens the guilty agent is eliminated at once from the diet and the former list of foods it used until the condition is as before the provocation test. This does not necessarily mean that the patient is free of symptoms, because he may also have an inhalation allergy (this is why it is not recommended to test a seasonal hay fever patient in the season). If no symptoms appear by the provocation test even when the patient eats large quantities of the test food for 3

days, he can keep this food in his diet and try the next thing for 3 days and so on. After these exposure tests, which may be time consuming and laborious, it may be possible, if the patient is co-operative, to gain an impression whether there is a food allergy and perhaps to what the patient is allergic. The difficulty is partly to maintain the diet and partly that this procedure involves several possibilities of influencing the patient psychologically which can distort the picture, but I shall relate presently that it may give good results. It may be easier and better, however, to work out certain elimination diets with definite information about the foods which are allowed *ad modum* Rowe (13).

One can also perform the Prausnitz-Küstner test (9), either in the usual way or by giving the food perorally after injecting the patient's serum intradermally. After the intake the sensitized part of the skin will react when the "noxious" food is digested and absorbed and transported by the blood.

Eosinophilia in the blood is frequently present and may reach high values, and if allergic phenomena are found in the intestines it is often possible to trace eosinophilia in the faeces. In these cases X-ray photographs with barium, with and without the allergen added, may give information as the barium with the reacting food will stay longer in the stomach (due to oedema of the pyloric part?) or provoke an altered—usually an increased—motility of the intestines. This is supposed to be the explanation of the colic-like pains, the vomiting and the diarrhoea which are caused by gastro-intestinal allergy. One must remember from X-rays and from provocation tests that the allergic state is not always only qualitative, but also quantitative; results may depend on the amount given, and the threshold amount changes with the condition of the patient as in inhalant allergy.

If the cause of the symptoms seems to have been found, generally it is easiest and simplest to tell the patient to avoid the foods or to tell him how he can find substitutes for them; but there are certain things which are difficult to avoid or to do without in an ordinary household, and then it may be worth

while trying to desensitize the patient in the ordinary way by subcutaneous injections with increasing doses or by giving increasing amounts perorally, starting with very small doses. The value of this treatment varies very much. The result may be very beneficial, however, and then, of course, everybody is happy, but it may be an economic burden for the patient to undergo long-lasting treatment with a doubtful outcome, so it must be considered carefully. If the patient must in any case have a desensitizing treatment with inhalants, the food allergens may be mixed with the inhalant extracts and given simultaneously.

TABLE 1
Allergic diseases caused by foods in different ages and sexes.

	Age: 0-3		4-16		over 30		totals		
	Sex: ♂	♀	♂	♀	♂	♀	♂	♀	♂ + ♀
Respiratory tract:									
Bronchial asthma	3		1			2	4	2	6
Allergic rhinitis	1		11		5	5	17	5	22
Gastro-intestinal allergy ...	3	3	4	1		1	7	5	12
Skin:									
Oedema Quincke, hives...	2		13	3	2	3	17	6	23
Besnier's prurigo, eczema	4	1	11		1		16	1	17
Purpura	1			2			1	2	3
Migraine						3		3	3
Menier's disease					1		1		1
	14	4	40	6	9	14	63	24	87

If elimination treatment has been chosen, the patient will ask when he may try the reacting food again. The answer is, that he may try about every third month for a couple of years, and if he cannot tolerate it after that, he will hardly ever be able to eat it without developing symptoms. One must be careful with these feeding experiments, whether the patient undergoes desensitization or not, to avoid strong reactions, and new cutaneous tests will hardly be of any help as they stay unchanged for a long time even when provocation tests are negative. They disappear especially in infants and children—who nearly always outgrow their food allergy although it may

last for a long time—and with elderly people whose skin reactivity diminishes.

Table I shows the allergic diseases I have found to be caused by foods. There were 63 patients of whom 44 were male and 19 female, but representing 87 allergic manifestations. This is not a complete survey of the patients with this kind of allergy, but represents cases from the children's department, the out-patient clinic and private office. The cases are selected and comprise only those in which it was definitely felt that the allergen revealed really did produce the specific allergic symptoms, that is: either a frequently seen relationship between cause and effect in the history or definitely positive results from elimination and provocation. Unfortunately it has not been possible in a number of cases to perform masked provocation tests, as nearly all the patients are investigated and treated as out-patients and some of them partly by correspondence. I have not included the results of the blood counts or the X-rays, but the leucocytes and thrombocytes have been counted in several cases together with provocation tests; but the methods of Vaughan (22) and Storck (19) have both failed so often that the results of these findings have been without influence upon our diagnostic considerations, even when the investigations are still going on for scientific reasons in the suitable cases.

As usual the boys outnumber the girls, whereas there are more women than men. I have also had patients between 16 and 30, although not very many, but just one of the patients most markedly allergic to food belongs to this group. It is easily seen that skin symptoms are the most frequent, nasal symptoms the next and also gastro-intestinal difficulties are quite common. As seen from the figures some of the patients have manifestations from more than one organ due to food allergy, but it does not appear from table 1 that many of them also had asthma caused by something else.

Table 2 shows the most common causes. Out of the 63 patients 38 had symptoms provoked by more than one allergen. It is readily seen that the most common foods like milk,

TABLE 2
Foods causing allergy.

Food	Total	Allergy in the family		Other allerg. manifestations		History		Elimination		Provocation	
		+	÷	+	÷	+	÷	+	÷	+	÷
Milk, butter, cheese	29	18	11	18	11	2	27	27	2	28	
Egg	23	20	3	19	4	14	8	16	1	17	
Fish	20	18	2	18	2	13	7	19		17	
Beef	8	5	3	6	2	2	6	8		8	
Pork	7	4	3	6	1		7	7		7	
Tomato	7	4	3	5	2	1	5	6		6	
Wheat	4	3	1	2	2		4	4		4	
Rye	3	2	1	3		1	2	3		3	
Peas	3	2	1	3			3	3		3	
Other things	12	7	5	10	2	6	5	10		10	
Total	116	83	33	90	26	39	74	103	3	103	

butter and cheese comprise the most frequently found group of causes, while the group named "Other things" includes shell-fish, nuts, apples, strawberries, grapes, bananas, cocoa, tea, horse-meat, all of them foods which are eaten seldom and therefore do not have the same chance of sensitizing the organism.

From the table it may also be seen that there is often found allergy in the family, and many have other allergic manifestations. Dairy products and meat and flour hardly ever give rise to suspicion or "+ history", while egg, especially raw egg, fish and rarely eaten dishes in "other things" cause suspicion much more often.

As the elimination diet and provocation tests were the basis for the diagnosis they have naturally given quite uniform results. That the figures are not always identical is due to the fact that not all the mothers wanted to carry out the provocation tests (when the history was convincing for the parents) or that the anamnestic informations were uncertain.

It may be added that the cutaneous reactions were as follows

(positive/negative): milk, butter, cheese: 20/9, egg: 18/5, fish: 19/1, tomato: 6/1, rye: 2/1, meat, wheat, peas, shellfish, nuts, cocoa: all positive, vegetables: not done.

Thus all milk proteins give a positive reaction in 2/3 of the cases, eggs in $\frac{3}{4}$, the others were nearly all positive when a combination of prick and intracutaneous tests were performed and compared with the diet tests.

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