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FOOD ALLERGY IN CHRONIC DISEASES OF THE DIGESTIVE TRACT

By

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Because of the wide distribution of allergic diseases, interest in their discovery has recently been growing. This particularly relates to food allergy which is one of the important of all the allergic diseases (1, 2, 3, 10). However the lack of the characteristic clinical symptoms and reliability of laboratory methods of investigation make it difficult to diagnose this disease, especially when food allergy is secondary to chronic disorders of the gastrointestinal tract (4, 8).

Food allergy is infrequently known to be demonstrated only with symptoms in the gastrointestinal tract. On the other hand a chronic inflammatory process in the gastrointestinal tract, suggests the possibility of food allergy. The aim of this work is to study the comparative value of different tests for the diagnosis of food allergy and find out its frequency in chronic diseases of the alimentary tract.

METHODS

We observed 670 patients with different chronic diseases of the digestive tract. As criteria for diagnosis were taken clinical symptoms, laboratory data (gastric secretion, intestinal ferments, duodenal intubation, coprogram etc), X-ray investigations; aspiration biopsies of stomach and colon and liver biopsy with Menghini's needle if necessary.

Besides such routine examinations of the patients, we used some additional methods of diagnosis:

1. *Studying the history* of allergic manifestations.

2. *Skin tests* with the food allergens. Allergens of cow's milk, eggs, fish, meat, tomatoes, melons, strawberries and honey were tested by methods reported previously (1, 6, 7). The results of the tests were appraised as positive by the presence of stable hyperaemia and papules at the site of injection, and also by any general allergic reaction such as urticaria, Quincke's oedema and so on. Both immediate and late skin reactions were taken into consideration.

3. *Elimination-provocation tests*

After 1-2 days hunger the menu would include some product (only for one day), suspected as intolerant, in sufficient quantity to produce an allergic reaction. In case of good tolerance to this product, another product was included in the diet of the patient and so on. After finding out the reaction to a definite kind of food, the latter was excluded from the diet for 4-5 days and then as a provocation test, was given again. In some cases when there was a suspicion that the reaction was produced by some psychogenic factor, the provocation test was performed by the blind method of *Vaughan* (14).

4. *X-ray studies* of food intolerance were made with the use of one of the modifications of *Wiedemann's* method (15). First the motor activity of the gastrointestinal tract was investigated with the usual contrast media. In the subsequent investigation the contrast media consisted of barium mixed with food allergens. Motor activity of stomach and intestine were studied for six hours.

5. *Investigation of food intolerance with the help of electrogastrography*

We suggested this method in 1968 (8). Biocurrents of the stomach (electrogastrogram) were recorded first at the picture of standard breakfast with the help of Soviet apparatus EGG-3 (*Sobakin* 13). On the following day electrogastrography was performed after eating the food allergen. (Glass

of milk or tomatoe juice, 100 g meat or fish and so on). The rhythm of variation and the size of electric biopotentials of the stomach were compared.

6. *Demonstration of antibodies to the food products* was performed by the method of passive transmission of antibodies according to *Prausnitz & Küstner* (10) and by the method of indirect degranulation of basophiles (12).

7. *Biopsy of gastric mucosa*

The mucous membrane of the stomach taken by an aspiration biopsy on an empty stomach and 24 hours after the provocation food exertion was studied. Special attention was made of the cellular content of the stroma (eosinophilic, plasmocytic, lymphoid infiltration) and to the condition of the vascular component (oedema, stasis).

Biopsy taken as late as 24 hours after the provocation was made because it is usually the time of late allergic reaction.

Biopsy of gastric mucosa was obtained by means of "blind" aspiration and it was difficult to determine the exact part of the stomach where the excision was made.

RESULTS

418 patients from 670 observed (62.3 per cent) complained of intolerance to one or several food products. The frequency of food intolerance in different diseases of the digestive tract is given in Table 1.

Most often these complaints occurred in patients with chronic involvement of small and, somewhat rare, large intestine. The symptoms of food intolerance were particularly expressed in the period of exacerbation of the main disease.

Intracutaneous tests with some food allergens were made in 418 patients complaining of food intolerance. There was a positive result in 134 patients (32 per cent), negative in 284 patients (68 per cent). Skin tests in all 252 patients without complaints of food intolerance, were found to be negative. The great majority of the patients had positive skin reactions of immediate type, in 7— of delayed type, in 4— the positive

TABLE 1

Frequency of Food Intolerance by Anamnestic Data in Chronic Diseases of Digestive Tract.

Nosologic forms	Number of investigated patients	Number of patients with complaints of food intolerance*	Food intolerance to								
			Milk	Eggs	Fish	Meat	Tomatoes	Melons	Water melons	Strawberry	Honey
Number of patients											
Gastric and duodenal ulcer	63	31 (49.2 %)	14	14	6	5	3	3	—	—	1
Chronic gastritis with secretory function untouched	86	39 (45.3 %)	15	12	14	9	2	3	—	—	1
Chronic gastritis with secretory insufficiency	152	95 (62.5 %)	61	26	26	11	8	8	4	3	2
Condition after gastric resection	25	14 (56 %)	8	3	6	1	2	2	—	—	—
Chronic gastroenterocolitis	39	36 (92 %)	27	8	7	2	4	9	4	—	—
Chronic colitis	126	88 (70 %)	68	20	29	8	6	14	4	2	—
Chronic cholecystitis	137	95 (69 %)	31	52	33	24	14	19	4	—	1
Chronic hepatitis and liver cirrhosis	42	20 (47 %)	9	7	2	3	5	5	—	—	—
Total	670	418* (62 %)	233	132	123	63	44	63	16	5	5

* This number shows a number of the patients with intolerance to one or more products.

skin tests were accompanied by general reactions such as generalized urticaria, paroxysms of bronchial asthma, Quincke's oedema. Food allergy, according to the skin tests, is more often seen in patients with chronic gastro-enterocolitis, chronic colitis and after gastrectomy (Table 2). Elimination-provocation tests were made in 147 patients with food intolerance according to the data of anamnesis and skin tests. After ingestion of intolerant food products in 120 of 147 patients either local (abdominal pain, nausea, vomiting, diarrhoea etc.) or common (urticaria, oedema, skin pruritis etc.) allergic symptoms were observed. In 29 patients intolerance occurred to two or more products. Provocational tests were noticed to be positive after intake of fish (in 47 patients), of eggs (in 43 patients); milk (25 patients); tomatoes (15 patients), melons (13 patients), strawberry (4 patients) and honey (1 patient).

For the objective registration of an irritated stomach symptoms, occurring on ingestion of intolerable food products, we together with *Shubina* (1968) used for the first time the method of electrogastrography. At first the electrogastrograms were obtained after a standard breakfast (50 g of white bread and 400 g of water).

After a good tolerant food intake, electrogastrograms were changed little. Electric activity of stomach was usually noticed to be even reduced by intake of fat food, milk and juice. More detailed description of method of electrogastrography was been given before (8, 13). The use of "allergic" breakfast (milk, eggs, fish, vegetables) produced the changes, characteristic of food intolerance, in 38 of 51 patients. In this in comparison with the standard breakfast the wave voltage was raised, there appeared disturbances of the electrogastrogram rhythm and atypical waves.

All the patients showed dyspeptic and pain symptoms.

The following observation may serve as an example:

The patient M. 49, has suffered from chronic gastritis for 10 years, and the last 2 years from bronchial asthma in addition. Since childhood the use of products containing eggs, fancy, sturgeon, caviare, even in small quantities,

TABLE 2
The Results of Skin Tests with Food Allergens.

Nosologic forms	Number of investigated patients	Number of patients with positive skin tests*	Positive skin tests					
			Milk	Eggs	Fish	Water-melons	Melons	Strawberry
								Honey
			Number of patients					
Gastric and duodenal ulcer	31	9	1	5	4	3	—	—
Chronic gastritis with secretory function untouched	39	7	1	4	4	—	—	—
Chronic gastritis with secretory insufficiency	95	27	8	11	10	3	1	1
Condition after gastric resection	14	6	1	1	2	2	1	—
Chronic gastroenterocolitis	36	17	7	2	5	3	2	—
Chronic colitis	88	37	14	7	17	1	6	2
Chronic cholecystitis	95	24	2	10	12	2	5	1
Chronic hepatitis and liver cirrhosis	20	7	—	4	2	1	1	—
Total	418	134	34	44	56	15	16	4
								1

* Many patients had positive skin tests simultaneously to different food products.

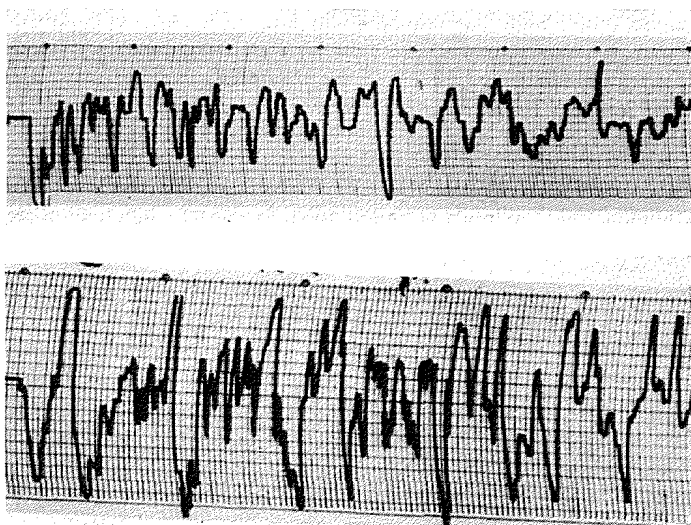


Fig. 1.

Electrogastrogram of the patient M. Clinical diagnosis: chronic gastritis with secretory insufficiency. a) after standard breakfast. b) after using eggs ("allergic meal").

produces in 10–15 minutes nausea, pains in the epigastric region and around the umbilicus, acute weakness, dizziness, cyanosis of nails. Skin tests with egg antigen was extremely positive. Provocational test with egg, performed according to Vaughan's method (mixture with semolina) confirmed the above mentioned symptoms of intolerance. Electrogastrographic investigation with bread breakfast showed the evidence of normo-kinetic curve (0.4 mv). In 30 minutes after the ingestion of one egg mixture with semolina, the symptoms of an irritated stomach occurred: hyperkinetic curve with the voltage of the waves to 1.4 mv and disturbances of peristaltic rhythm. Electrogastrographic signs of nutritive intolerance were accompanied with unpleasant sensations in the mouth, pains in the epigastric area, and nausea. In an hour and a half there was vomiting and in 2 hours a watery stool (Fig. 1).

A significant correlation of the results of the provocation tests and electrogastrographic studies ($r = 0.62$) gives the evidence that the electrogastrographic method may serve as a true index of food intolerance of various origins.

The X-ray method of studying food intolerance was used in 15 patients. It is known that using products containing fat (meat, eggs, milk) by healthy persons slows the motor evacuating activity of the stomach and ingestion of carbohydrate products accelerates it.

Quite another X-ray picture of motor-evacuating activity of the stomach was seen in 11 of 15 patients, who took barium sulphate mixed with milk, eggs, fish, or tomatoes. All these patients some minutes after ingestion of allergenic products had sharp acceleration of peristalsis, short or long spasm of the pylorus, static outbalancing of the stomach and antiperistaltic waves. Evacuating activity of the stomach contents into the duodenum was either stopped or considerably accelerated. In all the 11 patients there was a quick passage of the test mixture in small intestine with formation of spastic outbalancing and abundance of air was noted. In 6 of 11 patients the contrast mass was noted in the large intestine in 30-40 minutes. Along with the roentgenologic signs of accelerated peristalsis all the 11 patients had clinical signs of food intolerance (nausea, vomiting, sensations in the umbilical area, collywobes, transfusion, watery stool).

Passive transmission of antibody (Prausnitz & Küstner) was made in 86 patients, 34 of them (40 per cent) being positive. In patients with food allergy accompanied by gastrointestinal disturbances and positive skin allergic tests, the Prausnitz & Küstner reaction was positive somewhat more often (56.5 per cent).

Indirect reaction of basophil degranulation (Shelley), performed with the serum in 79 patients, suffering from food intolerance, was positive in 26 (33 per cent). When the provocational food load in patients was accompanied not only by digestive disturbances, but skin allergic symptoms as well Shelley's reaction was positive more often (in 47.2 per cent). The reaction of basophil degranulation was found to be positive only in those patients, whose complaints of food allergy were confirmed by the positive provocational and skin tests. In all the patients with the negative provocational and skin

tests Shelley's reaction was also negative. This fact shows the specificity of the test in diagnosing food allergy (Table 3).

TABLE 3
Frequency of Discovery of Antibodies to Different Food Products with the Prausnitz & Küstner Test and Shelley's Reaction.

Food	Prausnitz & Küstner test			Shelley's reaction		
	Positive	Negative	Total	Positive	Negative	Total
Number of the patients						
Milk	—	14	14	1	12	13
Eggs	13	13	26	11	16	27
Fish	8	15	23	2	18	20
Tomatoes	6	7	13	5	5	10
Melon	4	1	5	4	—	4
Total	34	52	86	26	53	79

Among 42 patients examined by gastrobiopsy normal gastric mucosa was found in 2 patients; superficial gastritis in 6; atrophic gastritis in 29 and intestinal metaplasia in 5.

In gastrobiopsy made after provocation, the changes, peculiar to the allergic process in the stroma of the gastric mucosa, were found in 19 of 42 patients, i.e. vascular stasis, oedema and eosinophilic infiltration. In the other 23 patients the morphological picture of the gastric mucosa after provocation with foods underwent insignificant changes of a non-specific character.

The following case may be an example of intolerance to fish with a tissue allergic reaction of the gastric mucosa. The patient E. 51, suffers from chronic gastroenterocolitis for 15 years. Thirty minutes after ingestion of boiled fish (sazan) there occurred nausea, weakness, headache, watery stool and urticaria on the following day. A skin test with antigen from sazan and the leucopenic test were positive, both Prausnitz & Küstner test and Shelley's reaction were negative. Aspiration biopsy of gastric mucosa before (Fig. 2 a) and after (Fig. 2 b) fish load was performed. Plasma and eosinophilic cells in large amounts with oedema of the stroma were seen after provocation.

In all 19 patients with the peculiar morphological allergic changes of the gastric mucosa and skin, provocation tests were positive and in half of them there were positive Prausnitz-Küstner and Shelley test. Thus the histological method of gastric mucosae study, may be used in the diagnostic of food allergy, especially in the cases when the antigen-antibody reaction is localized in the given organ.

DISCUSSION

The results of our investigations are given in Table 4. According to these data the conclusion of clinical value of different tests cannot be made as these investigations were not made in all cases of the disease. More complex investigations were made only in special groups of patients with pronounced food allergy. Not all patients with complaints to food intolerance suffer from true food allergy. Bad tolerance to food may also depend on involvement of the digestive organs themselves, enzymic insufficiency, fermentative and putrefactive processes, dyskinetic disorders, psychogenic factors and so on

TABLE 4
Summary Results of Different Tests in Diagnosis of Food Allergy.

Methods of investigation	Number of patients investigated	Positive results	
		Number of patients	Per cent
History of allergic manifestations	670	418	62.3
Skin tests	418	134	32.0
Electrogastrography	51	38	74.5
Elimination-provocation test	147	119	81.5
X-ray studies	15	11	73.3
Prausnitz & Küstner's reaction	86	34	40.0
Shelley's reaction	79	26	32.9
Gastrobiopsy	42	19	45.2

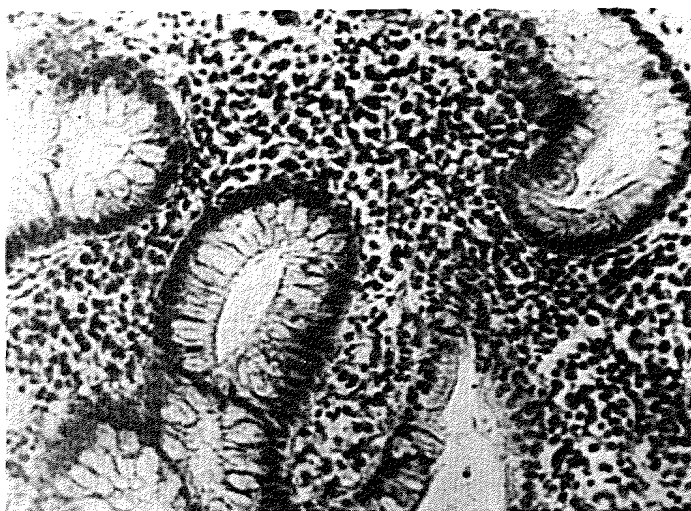
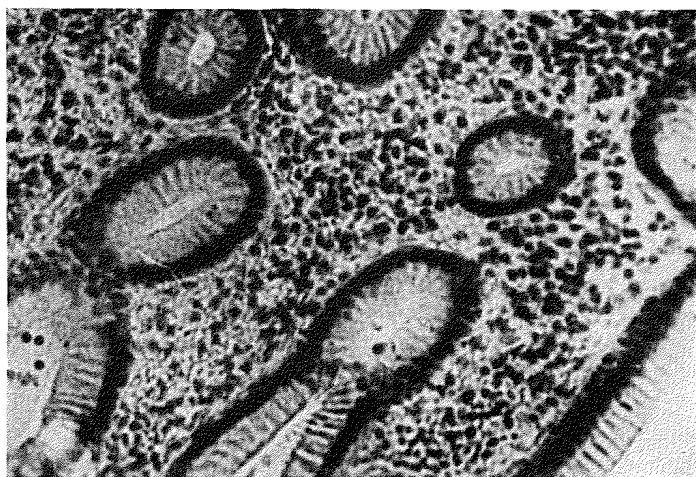


Fig. 2.

The sample of gastric mucosa of patient E. before (a) and after (b) fish ingestion.

(5, 6, 7). In the cases when the ingestion of food results to common symptoms (urticaria, skin putritis, chilliness, dizziness, eczema etc.) the allergic nature of the illness is not in doubt. We suppose that the most specific method for diagnosis of true food allergy is elimination-provocation testing. There was good correlation ($r = 0.53 \pm 0.03$) between provocation and skin tests. Only in 17 patients skin tests seemed to be pseudopositive. There is also good correlation between provocation tests, on one hand, and electrogastrography and X-ray tests, on the other ($r = 0.62 \pm 0.05$). We suggest that it is advisable to use the electrogastrographic method in cases of food intolerance from the part of the stomach. In this case the chance of radiation of the patient is absent and the antigenic properties of food in mixing it with barium sulphate are not changed. If clinical symptoms of food intolerance appear mostly in the intestine, it is advisable to make an X-ray control with the passage in the small and large intestines.

Our investigations made it possible to consider that the test of passive transmission of antibodies (Prausnitz & Küstner reaction) is positive only in the patients with food allergy, proved clinically and by positive provocation and skin tests. A positive Prausnitz & Küstner reaction is proved to be specific and reliable. As to negative results they do not exclude the possibility of a true food allergy, proved by other methods of investigations. The same picture gives a reaction of the basophil degranulation test of Shelley.

The Prausnitz & Küstner test and Shelley's reaction give more possibilities to discover antibodies to plant products rather than to animal ones. In discovering antibodies to fish the Prausnitz & Küstner test had a real predominance over Shelley's reaction. Nevertheless, in spite of the specificity and diagnostic value of Shelley's test it is somewhat relative, as in more than 50 per cent of cases, it is negative in food allergy proved by some other methods. It may be supposed, that it depends on an insufficient concentration of specific antibodies in the blood.

Aspiration gastrobiopsy may be useful for diagnosis of food allergy with clinical symptoms in the stomach.

The most practical value is attached to clinical symptoms of food allergy in elimination-provocation tests, especially using X-ray and electrogastrographic investigations. The discovery of specific antibodies with the help of Prautnitz & Küstner and Shelley's reactions is the proof of food allergy. Only the complex study of patients by tests, showing different sides of allergic process, may give an exact diagnosis of food allergy. By complex investigations of the patients with chronic digestive diseases by means of different tests, food allergy was marked in 14.7 per cent.

More often food allergy was diagnosed in patients with chronic diseases of the intestine. It may be explained by the absorption of insufficiently decomposed protein substances of the food, preserved their antigenic properties. Animal products possess the largest antigenic ability.

SUMMARY

Food allergy often occurs in pathology of the digestive tract. To get an accurate diagnosis complex investigations with relation to anamnesis, elimination-provocation tests, intradermal tests with food antigens, electrogastrographic and X-ray investigations, tests for antibodies in the blood serum by Shelley and Prausnitz-Küstner reactions were performed. Aspiration gastrobiopsy after provocation may be of some value in the diagnosis of gastric trouble in food allergy. Clinico-laboratory signs of true food allergy were found in 99 of 670 (14.7 per cent) patients investigated with chronic diseases of the digestive tract.

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