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Vegan Regimen with Reduced Medication in the Treatment of Bronchial Asthma

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INTRODUCTION

Bronchial asthma has often been regarded as a disease of mainly psychogenic origin. With the development of allergology it was possible to obtain a somatic explanation to the disease. The mechanism was regarded to be sensitisation to specific allergens which, at a renewed exposure, release an allergic reaction localized to the bronchi. Previously metabolites such as histamine have been regarded as essential for this reaction. Later research instead points to leucotrienes and similar substances.

In patients with clinical asthma it has not always been possible to prove the presence of allergens as a reason for the disease. Additionally, the term endogenous asthma is used which is somewhat different from "real" allergy. The cases in which the asthma is released by substances which are said to lack allergic capacity form an intermediate position. The diagnosis will then be nonspecific irritation (for example, from certain substances in exhaust gas from cars) or hyperreactive bronchi.

Allergy against food is regarded as the cause of local symptoms from the intestines, but so far it has been difficult to study these mechanisms by direct observation.

Special attention has been paid to food containing milk which has also been assumed to cause symptoms outside the intestines, for example, in the joints. It is well known that the skin is a common target organ for food-induced allergy.

The normal opinion is, however, that allergy against foodstuffs plays no important part in the origin of the majority of cases with bronchial asthma.

In Sweden there is an active health movement that claims that a radically altered diet, such as a vegan diet, can improve or cure bronchial asthma.

The ability of the intestines to prevent resorbtion of allergenic substances is probably due to a great extent to the normal function of the mucous membrane. In the event of

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chronic irritation or the presence of unsuitable bacteria in the bowels, it is possible for allergenic substances to reach the blood to a much greater degree. We have experienced that, through a complete change of food, the bacterial composition in the bowel changes and different types of irritation can decrease.

In order to normalize the body's immune system, a complete diet is also of the utmost importance. Nowadays one talks about "good" and "bad" prostaglandins, especially concerning effects on thrombocytes and vessels. From the original substance, arachidonic acid, which mainly comes from animal food, among other things, leucotrienes are formed.

"Good" prostaglandins (for example, PGE_1) come from *cis*-linoleic acid which is found in vegetables. The transformation into prostaglandine E_1 covers at least four steps in which the gamma-linolenic acid is at an important level that the body might find difficult to pass. Among other things heating and processing of linoleic acid changes the natural *cis*-form of the acid into a *trans*-form. This *trans*-form cannot be transformed into PGE_1 and it also inhibits the synthesis of gamma-linolenic acid from *cis*-linoleic acid. The addition of a mainly *raw* vegetarian food would in this way be able to affect the balance between good and bad prostaglandines and help to normalize the immune defense.

A high intake of vitamin C intervenes positively with the immunological process and could be a further factor that positively affects allergic diseases.

In order to test these ideas and the effect of a vegan diet in bronchial asthma, we have followed a series of patients who were treated with a vegan regimen for 1 yr.

EXPERIMENTAL

Subjects

Thirty-five patients with long-established hospital-verified bronchial asthma were admitted to a health center for two 12-day periods 4 months apart and again after 1 yr. The following were the criteria for participation in the study: (i) age 25–70 yr; (ii) willingness to change completely to a vegan regimen, without milk or eggs for 1 yr and ability to finance the care and necessary travel; (iii) a disease duration of at least 1 yr with unchanged or perhaps even worsened symptoms; and (iv) existence of verified bronchial asthma.

The composition of the sample with regard to sex and age is shown in Tables 1 and 2.

It can be said, of course, that this is a selected group not representative of Swedish patients with bronchial asthma in general. This is, to some extent, true for most patients with bronchial asthma who are used for testing different therapies. However, in the patient group studied here, there was a further selection in that the patients were especially motivated to undertake individual initiatives in order to improve their health, they were more than usually dissatisfied with earlier treatment, and they had sufficient financial resources to pay for the therapy, which was not subsidized by the government.

The duration of the disease was on average 11.9 yr (range 2–33 yr). In about half the cases testing had been done for different allergens (skin test, provocation test, RAST test). Independent of the results of the tests there were usually no certain conclusions as

Table 1. Age and Sex Distribution of Asthma Patients Who Underwent Vegan Diet Therapy

AGE (yr)	<40	40–49	50–59	60–69	TOTAL
Men	0	3	5	2	10
Women	4	2	7	1	14
Total	4	5	12	3	24

Table 2. Age and Sex Distribution of Drop-Outs

AGE (yr)	<40	40–49	50–59	60–69	TOTAL
Men	2	0	2	0	4
Women	4	1	2	0	7
Total	6	1	4	0	11

to whether the asthma was really allergic or not in the case record. In many cases the diagnosis was, at times, endogenous asthma.

Some patients had been told that they were allergic to certain kinds of food; they had, however, not been given any special food restrictions. One patient was according to his case record, allergic against 35 out of 53 tested food substances. His doctor had, however, not suggested any change of food habits. The patient himself stopped eating butter as this produced asthma attacks.

Of the 35 patients, 20 had been admitted to hospital for acute asthmatic attacks during the last 2 years. Of these, one patient had received acute infusion therapy a total of 23 times during this period and another patient stated that he had been to hospital 100 times during his disease and on every occasion he had required infusion treatment. One patient had a cardiac arrest during an attack and had been brought back to life after heart massage, tracheostomy, and respiratory treatment.

All patients used medicines for their asthma at admission. The number of medicaments was on average 4.5 (range 1–8). Twenty of the 35 patients were constantly using cortisone at the admission to the vegan treatment and another seven had previously received this medicine. Only eight patients had not used cortisone. Thirty-one patients did not smoke. Of these, eight had smoked previously but had given it up 2–30 years ago without any improvement of the asthma. Four smoked 0–1, 0–1, 3–4, and 15 cigarettes a day.

These patients represented a fairly advanced type of asthmatic disease and would normally have been too difficult and too staff demanding to be taken care of at a health center.

METHODS

Methods of Treatment

The food that the patients received at the health center and was recommended, as much as possible, in their own homes was a vegetarian diet without meat, fish, and eggs and also without any kind of milk product. Their drinking water should have been spring water and not chlorinated tap water. Coffee, ordinary tea, chocolate, sugar, and ordinary salt are excluded, while on the other hand certain spices, especially herbal spices, were allowed, with large individual variations. Water or herbal teas up to 1½ L every 24 hr was recommended. The vegetables and other vegetable products that were used should preferably have been grown pesticide free. Vegetarian hot dishes, mainly soups, were also included in the therapy but could not dominate over the raw food.

The following vegetables were used freely: lettuce, carrots, beetroot, white and red onions, celery, cabbage, cauliflower, broccoli, nettles, weeds, cucumber, radishes, black radishes, Jerusalem artichoke, schorznoera, and all kinds of beans except soya and green peas. Potatoes were allowed in moderate amounts.

The following berries were used freely: blueberries, cloudberries, raspberries, strawberries, black currant, gooseberries, plums, and pears. Apples and citrus fruits were not allowed.

Cereals were very restricted or not allowed, but buckwheat was accepted as well as millet and lentils.

The food used has been analyzed for composition of nutrients as well as vitamins and certain mineral substances (1).

The food therapy now contains all nutritious substances recommended by nutritionists. The amounts of mineral substances, trace elements, and vitamins were usually higher than recommended. The only exceptions were vitamins D and B_{12} which could be supplemented. This has, however, not been done in this investigation.

During their stay at the health center the patients were given lessons and practical training in the recommended food. They were given lectures on how the food should look at different meals. In connection with the treatment at the health center, at least

the first time, a juice fasting of usually 7 days was included and also a number of different herbal remedies were given on an individual basis during the entire treatment. For example, the following herbs were used: *Lichen islandicus, Folium farfare, Radix glycurrhizae,* and *Radix althae*. They were given as tea or decoctions.

In the home, various food additives were recommended such as vitamin C, garlic drink, horse radish drink, and nettle juice.

These additives were also individualized according to special needs (such as anemia and tendency for infectious diseases).

The patients were encouraged to spend as much time as possible in fresh unpolluted air and every day undertake some kind of physical activity, for example, walking. They had, however, not been encouraged to train their physical capacity through regular running, etc. Clearing their environment from allergens was not recommended and was not done.

With the exception of a few essential preparations (for example, insulin), the patients were encouraged to give up most of their medicine when they no longer seemed to be needed.

There had been no psychotherapy and we did not try to solve the patients' possible personal problems or conflicts. However, their anxiety over their disease as well as anxiety for various troublesome symptoms and for side-effects of their medicine have been discussed. A positive view of the possibilities of becoming symptom-free and "well" had been related to the patients provided they adhered to the diet.

Statistical Methods

For clinical variables such as pulse at rest, vital capacity, and for laboratory tests, the initial values were compared with the values obtained at the 4- and 12-month follow-up. Student's t test was used to evaluate the statistical significances of the difference.

In order to determine the connection between subjective improvement and compliance variance analysis was done.

In order to evaluate the patients' subjective symptoms, the so-called longitudinal superiority test (2) has also been used in which the patients' overall opinion of their condition of health has been registered on a scale from 0 to 4 (0 = no symptoms at all; 4 = very severe symptoms). This registration was undertaken at weekly intervals up to 6 months before introduction of the treatment and then for another 4 months during the actual treatment. The time for commencement of the treatment was selected at random which means that it was possible to estimate whether the change of symptoms that occurred during treatment significantly differed from the "spontaneous" variation of the disease which existed during the control period prior to the introduction of the treatment.

Clinical Examinations

The patients' case-books were obtained from the relevant doctors and hospitals. A conventional case report was given and the patients were examined clinically in the usual way in order to verify the diagnosis and to form a general opinion about the patients' various diseases. The consumption of medicine was surveyed.

The following clinical examinations were performed: Systolic and diastolic blood pressure measured with the patient lying with a mercury manometer after 15 min rest; pulse at rest measured lying after 15 min rest; body weight; length; condition measured by Monarch's bicycle ergometer. This value has been estimated according to standard tables. The level of the pulse after 6 min cycling has been the parameter used to compare the patients' physical fitness. The load has not varied. Vital capacity was measured with a Vitallograph. $FEV_{1.0}$ (forced expiratory volume at 1 sec) was measured with a Vitallograph.

Laboratory Investigations

The chemical analyses were performed at the Department of Clinical Chemistry, Lund

University Hospital and a control of the analyses was performed before every series of investigations. The patients were examined before treatment, after 4 months, and after 1 yr. The analyses can be seen from Tables 5–9.

Further Investigations

At the 1-yr follow-up, the patients were questioned as to the extent they followed the given food directions. Because of the confidence established between patient and health center, we believe they have answered this question quite honestly. This was confirmed by the fact that they had thoroughly accounted for their difficulties and temptations and, for example, admitted that they had sometimes had coffee, used milk products, or other items which were not allowed. Fish has often been regarded by the patients as a less dangerous divergence than meat and has been "misused" more frequently. The assessment that the compliance is somewhere between 50% and 100% (perhaps less) is of course subjective

Table 3. Subjective Results after 4 Months and after 1 yr

	COMPLETELY RECOVERED	MUCH BETTER	BETTER	UNCHANGED	WORSE	TOTAL
4 months	0	7	14	3	0	24
1 yr	1	16	5	2	0	24
4 months			71%			
1 yr			92%			

Table 4. Clinical Variables before and after 1 yr of Vegan Diet Therapy in Asthma Patients

	(MEAN VALUES AND STANDARD DEVIATIONS) BEFORE THERAPY MEAN	SD	AFTER THERAPY MEAN	SD	STATISTICAL SIGNIFICANCE OF THE DIFFERENCE
Weight (kg):					
0–4 months	73.5	17.8	61.5	13.6	***[a]
0–12 months	73.5	17.8	65.2	13.6	***[a]
Physical work cap (pulse/min and constant load):					
0–4 months	136	14.7	125	8.5	***[a]
0–12 months	136	14.5	120	11.5	***[a]
Pulse at rest (pulse/min):					
0–4 months	75	9.8	67	9.8	**[b]
0–12 months	75	9.8	70	10.4	NS[d]
Systolic blood pressure (mm Hg):					
0–4 months	128	20.5	119	9.6	*[c]
0–12 months	128	20.5	120	15.4	*[c]
Diastolic blood pressure (mm Hg):					
0–4 months	77	11.0	69	6.7	***[a]
0–12 months	77	11.0	72	10.0	*[c]
FEV (L/sec):					
0–12 months	2.0	0.5	2.5	0.4	***[c]
Vital capacity (L):					
0–12 months	3.4	0.3	4.0	0.3	***[a]

[a] $p < 0.001$.
[b] $p < 0.01$.
[c] $p < 0.05$.
[d] NS denotes not significant.

but still gives an approximate picture.

In order to get an idea about the financial consequences of the patients' reduced sickness and medications their sick-leave during the year prior to the first intake and the following year have been compared. The same comparison has been made for their medication. The costs for medicine for the last 2 years has been estimated with the aid of the official price list of the Swedish pharmacies without the reduction that the official medication discount produces.

RESULTS

Drop-outs

Of the initial 35 patients one did not have asthma but only eczema of an allergic nature. He had had asthma as a child. He was, therefore, not included in the investigation. One patient died after 6 weeks in his home from a myocardial infarction, in connection with penicillin treated bronchitis. His asthma had improved prior to this development. Nine patients gave up the food therapy within 2 months after starting. Age and sex differences of the drop-outs can be seen from Table 2. They hardly differed from the rest of the group concerning age, sex, severeness of the disease, or medication. The patients said that the main reason for their drop-out was that they had not improved during the first 2 months but continued to have repeated attacks. They were often exposed to negative influence by their environment including their house physician. They were tired and had nervous problems. Two developed gastritis because of the raw food and could not get in touch with the health center for fur-

Table 5. Blood values before and after 1 yr of Vegan Therapy in Asthma Patients

	(MEAN VALUES AND STANDARD DEVIATIONS)				
	BEFORE		AFTER		STATISTICAL SIGNIFICANCE
	MEAN	SD	MEAN	SD	OF THE DIFFERENCE
ESR[a] (mm):					
0–4 months	17	20	5	4	*[b]
0–12 months	17	20	10	11	*[b]
Hb (g/L):					
0–4 months	146	13.4	149	12.9	NS[d]
0–12 months	146	13.4	138	10.5	**[c]
Red cells (10^{12}/L):					
0–4 months	4.8	0.4	4.8	0.4	NS[d]
0–12 months	4.8	0.5	4.6	0.3	NS[d]
EVF (%):					
0–4 months	44	4.1	45	3.8	NS[d]
0–12 months	44	4.1	41	2.9	*[b]
TIBC[e] (mmol/L):					
0–4 months	63.3	13.5	60.3	8.0	NS[d]
0–12 months	63.5	15.0	65.3	12.0	NS[d]
Iron (mmol/L):					
0–4 months	19.8	6.9	16.1	3.5	*[b]
0–12 months	19.4	7.4	18.7	4.3	NS[d]
Leucocytes (10^9/L):					
0–4 months	11.86	19.4	5.08	1.2	NS[d]
0–12 months	11.86	19.4	6.30	1.7	NS[d]

[a]ESR denotes erythrocyte sedimentation rate.
[b]$p < 0.05$.
[c]$p < 0.01$.
[d]NS denotes not significant.
[e]TIBC denotes total iron binding capacity.

ther advice. One patient was pregnant and did not feel well and one could not give up smoking (15 cigarettes a day), etc.

Only the patients who completed the treatment are included in the results.

Subjective Variables

A significant improvement was detected after the treatment, with the aid of the longitudinal superiority test for subjective

Table 6. Serum Metabolites in Serum before and after 1 yr of Vegan Diet Therapy in Asthma Patients

	(MEAN VALUES AND STANDARD DEVIATIONS) BEFORE		AFTER		STATISTICAL SIGNIFICANCE OF THE DIFFERENCE
	MEAN	SD	MEAN	SD	
Urate (mmol/L):					
0–4 months	322	102	435	140	***[a]
0–12 months	321	101	365	83	**[b]
Bilirubin (mmol/L):					
0–4 months	14.8	5.8	11.9	5.2	*[c]
0–12 months	15.5	6.4	7.6	2.9	***[a]
Cholesterol (mmol/L):					
0–4 months	5.9	1.3	5.1	1.3	**[b]
0–12 months	5.7	1.3	5.2	1.0	NS[d]
Triglycerides (mmol/L):					
0–4 months	1.2	0.6	0.9	0.3	*[c]
0–12 months	1.3	0.7	1.1	0.4	NS
Urea (mmol/L):					
0–4 months	4.3	1.5	2.2	0.9	***[a]
0–12 months	4.2	1.1	2.9	1.1	***[a]

[a] $p < 0.001$.
[b] $p < 0.01$.
[c] $p < 0.05$.
[d] NS denotes not significant.

Table 7. Serum Electrolytes before and after 1 yr of Vegan Diet Therapy in Asthma Patients

	(MEAN VALUES AND STANDARD DEVIATIONS) BEFORE		AFTER		STATISTICAL SIGNIFICANCE OF THE DIFFERENCE
	MEAN	SD	MEAN	SD	
Sodium (mmol/L):					
0–4 months	322	5.8	149	6.8	*[b]
0–12 months	145	5.9	142	4.4	*[b]
Potassium (mmol/L):					
0–4 months	4.4	0.4	4.5	0.5	NS[c]
0–12 months	4.4	0.4	4.1	0.4	*[b]
Calcium (mmol/L):					
0–4 months	2.5	0.1	2.6	0.2	*[b]
0–12 months	2.5	0.1	2.4	0.1	**[a]
Phosphate (mmol/L):					
0–4 months	0.9	0.2	1.1	0.1	**[a]
0–12 months	0.9	0.3	0.9	0.2	NS[c]

[a] $p < 0.01$.
[b] $p < 0.05$.
[c] NS denotes not significant.

symptoms that had been estimated on a 0–4 scale (from none to very severe). The values for the 20 weeks preceding the start of the regimen were compared with those during the second and 21st weeks of treatment (4 months). On both occasions the difference was highly significant ($p<0.001$), at 0.95 and 1.17 scale units, respectively.

The results of subjective evaluation of the patients was improvement or freedom from symptoms in 71% after 4 months and 92% after 1 yr (Table 3).

There was a reduction in both the number of asthmatic attacks and a reduction of their severity. Those patients who had no direct attacks found it easier to breathe and had improved physical capacity.

Many patients said that their improvement was so considerable that they, for example, felt like "they had a new life." One nurse had special difficulties at her work because most of her co-workers were inveterate smokers. After 1 yr she could withstand passive exposition to smoke without receiving asthmatic attacks as well as tolerating exhaust gas, flowers, animals, and dust which had always previously released an asthma attack.

Table 8. Proteins in Blood before and after 1 yr of Vegan Diet Therapy in Asthma Patients

	(MEAN VALUES AND STANDARD DEVIATIONS)				
	BEFORE		AFTER		STATISTICAL SIGNIFICANCE
	MEAN	SD	MEAN	SD	OF THE DIFFERENCE
Albumin (g/L):					
0–4 months	44.8	4.9	44.0	3.0	NS[d]
0–12 months	44.4	4.9	40.1	3.5	*[c]
Haptoglobin (g/L):					
0–4 months	1.6	0.6	1.1	0.5	***[a]
0–12 months	1.6	0.5	1.4	0.6	NS[d]
IgA (g/L):					
0–4 months	1.7	0.7	1.7	0.7	NS[d]
0–12 months	1.8	0.8	1.6	0.7	NS[d]
IgE (mg/L):					
0–4 months	263	191	337	532	NS[d]
0–12 months	241	110	174	130	**[b]
IgG (g/L):					
0–4 months	11.8	3.3	11.3	2.9	NS[d]
0–12 months	12.0	3.6	11.4	3.9	NS[d]
IgM (g/L):					
0–4 months	1.1	0.4	0.9	0.4	**[b]
0–12 months	1.1	0.4	0.9	0.4	**[b]
ALP[e] (μkat/L):					
0–4 months	2.55	0.6	2.96	0.9	**[b]
0–12 months	2.54	0.7	3.90	1.7	***[a]
ASAT[f] (μkat/L):					
0–4 months	0.5	0.2	0.4	0.5	NS[d]
0–12 months	0.5	0.3	0.3	0.3	*[c]
ALAT[g] (μkat/L):					
0–4 months	0.3	0.1	0.2	0.2	*[c]
0–12 months	0.3	0.2	0.2	0.2	***[a]

[a] $p < 0.001$.
[b] $p < 0.01$.
[c] $p < 0.05$.
[d] NS denotes not significant.
[e] Alcaline phosphatase.
[f] Aspartataminotransferase.
[g] Alaminaminotransferase.

Many patients had associated diseases especially of the rheumatic type. These had usually disappeared or diminished. Many patients previously had increased frequency of infectious diseases. They were greatly improved in this respect.

Objective Variables

The clinical variables examined at 4-month and 1-yr follow-ups are shown in Table 4. After 1 yr there was a significant decrease in blood pressure, pulse after constant load (physical working capacity), and body weight. Vital capacity and $FEV_{1.0}$ also showed significant improvements.

Concurrently with this improvement, the patients greatly reduced their consumption of medicine. At 1 yr, four patients had completely given up their medication. The majority had reduced their medication to 10%–50% of the original level and only two had an unchanged medicine consumption.

The number of medicines which initially had been on average of 4.5 with a variation from 1 to 8 was, after 1 yr, 1.2 with a variation from 0 to 4. Seven patients had completely given up their previous cortisone medication. These belonged to the group "no troubles" or "greatly improved."

Biochemical indices are summarized in Tables 5–9. Most of them showed significant improvements and of special interest from an allergologic point of view is the reduction of ESR, haptoglobin, IgM, and IgE.

The patients' self-assessment of their compliance with the diet was on the average 83%.

The correlation between the degree of subjective improvement and compliance to the food was significant ($p<0.001$).

The cost of the hospital care during the year before the stay at the health center was 609,000 SEK ($n=24$) and for the year after was 66,750 SEK, a savings of 22,594 SEK/patient during the year. The corresponding values for medicines were 2672 and 1012 SEK, which was equivalent to a cost-savings of 1660 SEK/patient during the year.

DISCUSSION

It is, of course, impossible to attribute the objective and subjective findings to part or parts of this multifactorial treatment with any degree of specificity. For the time being the regimen must be considered as a whole, and the results as an effect of the total treatment. In discussions of the results

Table 9. Urine Tests before and after 1 yr of Vegan Diet Therapy in Asthma Patients

	(MEAN VALUES AND STANDARD DEVIATIONS) BEFORE		AFTER		STATISTICAL SIGNIFICANCE OF THE DIFFERENCE
	MEAN	SD	MEAN	SD	
Osmolality (mOsm/kg):					
0–4 months	285	122	225	149	NS[d]
0–12 months	286	136	383	184	*[c]
Chloride (mmol/L):					
0–4 months	36.9	18.6	25.0	25.7	*[c]
0–12 months	34.8	17.3	72.5	44.3	***[a]
Chloride (mmol/day):					
0–4 months	81.1	49.5	41.3	41.4	***[a]
0–12 months	75.2	47.4	101.4	50.7	**[b]
pH					
0–4 months	6.14	0.6	6.30		NS[d]
0–12 months	6.14		6.31		NS[d]

[a] $p < 0.001$.
[b] $p < 0.01$.
[c] $p < 0.05$.
[d] NS denotes not significant.

which has already begun to some extent, it has been hinted that the elimination of tobacco is a plausible explanation of the improvement. When one considers the fact that only a few patients were moderate smokers, one can reject this explanation. Naturally tobacco is one etiological factor that must be eliminated when it exists.

Another explanation has been the good climate in the northern part of Sweden. Since the patients only spent 24 days out of 1 yr in this climate and the rest of the time in their ordinary environment, we also reject this explanation.

One patient who both gave up smoking and spent a month in a hotel in the same village did not improve until he received the special food that was served at the health center.

A common observation has been that the patient after diet therapy could be exposed to factors which previously regularly provoked an asthma attack, for example, dust, smoke, flowers, and animals. Where they previously could only live in a clean environment and then felt more or less isolated in their homes, they could now stay in various milieus without getting asthmatic attacks.

It was also frequently observed that the patients reacted against food additives found in common industrial products. They tolerated "biologically" grown vegetables, but developed problems with vegetables grown in the normal way (especially springed) even if the National Food Administration had declared that this food contained only harmless amounts of pesticides. This observation does not seem unreasonable since there is a large difference between concentration exerting poisonous effects and those causing allergic reactions.

A common objection has been that the results may be explained by suggestion to the patients (placebo effect). We cannot reject such an explanation since the investigation is not blind. The significant changes which occur in the "immune proteins" in the blood oppose the theory of suggestion. In one case, however, suggestion is important, namely, when persuading the patients to carry on with this difficult way of living.

The fact that the vital capacity, the $FEV_{1.0}$, the pulse at rest, and the physical working capacity, as well as the various laboratory variables have significantly improved also indicates that the effect rests on a somatic base.

The improvement can be partially explained by the patients' reduced tendency to infectious diseases. We cannot express this in figures but we can point to the clear empirical experience both from these patients and from other patients who have been given a similar food therapy.

The reduced costs for medical care and medicine which this therapy has brought with it can probably be ascribed mainly to the treatment itself and the patients' changed attitude towards increased responsibility for their health. Our opinion is then that the food therapy described has a pronounced favorable effect on asthma, that this effect has many reasons but that the placebo effect is probably the least important explanation.

SUMMARY

1. Thirty-five patients who had suffered from bronchial asthma for an average of 12 yr, all receiving long-term medication, 20 including cortisone, were subject to therapy with vegan food for 1 yr. In almost all cases, medication was withdrawn or drastically reduced. There was a significant decrease in asthma symptoms.
2. Twenty-four patients (69%) fulfilled the treatment. Of these, 71% reported improvement at 4 months and 92% at 1 yr.
3. There was a significant improvement in a number of clinical variables; for example, vital capacity, forced expiratory volume at one sec and physical working capacity, as well as a significant change in various biochemical indices as haptoglobin, IgM, IgE, cholesterol, and triglycerides in blood.

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EDITORIAL

Food Hypersensitivity and Asthma

For the practitioner of allergy therapy, the problem of food hypersensitivity and asthma may be viewed from two vantage points. First is the general question, how prevalent is asthma as a symptom induced by food ingestion? Second, and perhaps more pertinent to the clinician, does this person across my desk who has asthma wheeze due to ingestion of certain foods?

Before attempting to answer these questions, it is important to define the terms used in this field for which there is not universal agreement. I favor three terms. First, is food hypersensitivity. This which means that ingestion of food resulted in symptoms and that an immune mechanism is probable; in other words, IgE is detected or some other laboratory test of the immune system can be correlated with the positive challenge (this is symptomatic hypersensitivity, whereas immune sensitization in the absence of objectively confirmed symptoms is asymptomatic hypersensitivity). The term hypersensitivity is preferred to allergy or sensitivity (used earlier by us, but too generic to stand the vagaries of time). Food intolerances should, in my opinion, be reserved for problems of carbohydrate malabsorption (e.g., lactose intolerance). When food ingestion is reported to induce symptoms but the observation is not proven or the mechanism cannot be determined even when the observation is confirmed, then the term I favor is adverse reaction. This is the best generic term to use in order to avoid confusion. I avoid using the term idiosyncratic as being too vague and imprecise. Toxicologic, pharmacologic, and psychologic are three other terms which may be useful or applicable in certain circumstances.

Now to return to the questions. The answer to the first question is incomplete and is, of necessity, based on controlled studies using double-blind placebo-controlled food challenges (DBPCFC). Although a growing number of studies are beginning to answer this question, in the context of the general population, we cannot state a precise figure that accurately identifies the prevalence of food hypersensitivity-induced asthma. If we confine ourselves to the studies using objectively confirmed observations, namely those using DBPCFC, then at least certain points can be made. One of the few studies to broach the problem in adults was published by Onorato and colleagues in 1986 (1). They found that of 20 subjects with the complaint of food hypersensitivity-induced asthma, the symptoms were reproducible during DBPCFC in 6 patients. Studies using blinded challenges by Bernstein et al. (2), Novembre et al. (3), and Pastorello et al. (4) have also reproduced wheezing during DBPCFC. The

study by Atkins et al. (5), which used open challenges administered to highly atopic patients in a controlled setting, also reproduced significant wheezing symptoms in some patients.

In children, the group evaluated at National Jewish Hospital has included mostly (but not totally) children referred with asthma as their primary problem (6). Despite this selection bias, only 4 of 1014 food challenges (in 480 children) have produced asthma as the *sole* symptom elicited during DBPCFC while 36 of 1014 challenges have had asthma as one of the symptoms produced. Sampson's observations have been interesting because his patient selection has been biased toward patients referred with atopic dermatitis as the major manifestation. However, in some of his patients, wheezing has also been reproduced during DBPCFC (7).

From these studies one may conclude that asthma is certainly produced by food ingestion in food hypersensitive patients, probably (but not solely) by a mechanism involving IgE. Additionally, one may conclude that this is by no means a universal phenomenon and, in fact, occurs only in the minority of asthmatic patients seen by any allergist.

How do these data and the conclusions drawn therefrom help the practitioner of allergy? It suggests an approach that research and experience have shown may be applied to the daily practice situations. Careful perusal of the data suggests some predictable patterns which, although not absolute, may be helpful. The first is that a few foods are likely to cause most of the symptoms. These include egg, peanut, milk, wheat, soy, tree nuts, fish, and shellfish. The second observation is that despite histories to the contrary, the timing between ingestion and the onset of wheezing is almost invariably brief, minutes to a couple of hours. Third, in the vast majority of cases, the amount of food required to provoke the symptoms is small and reasonably easy to administer blindly.

These three points and the data from the studies suggest the following aproach. Take a thorough history maintaining a healthy degree of objectivity. Direct the history to ascertain the timing between ingestion and onset of wheezing, associated symptoms (skin, gastrointestinal) accompanying the wheezing, the quantity of food required to produce symptoms, the most recent occurrence of the food-induced wheezing, and the period over which the observations have been made. Not mentioned above but also very important are the studies showing the high negative predictive accuracy of food skin tests, suggesting that in most situations, positive histories (not anaphylaxis and not strongly held beliefs), accompanied by a negative skin test may be evaluated by an open challenge often at home but preferably under observation in the allergist's office. Positive histories accompanied by a strongly held belief or a positive skin test should be evaluated under observation using a single-blind or preferably double-blind food challenge. Using this approach most clinicians should find themselves replicating the studies already published which show that in well over half the patients (especially in an unselected group) most food challenges will refute the history and thus make the patient's life easier. In those patients in whom the challenge is equivocal or positive, challenges at regular intervals should be used to continue to evaluate the problem over time in order to determine whether or not the problem is going to disappear. Of course, these suggestions do not apply to food induced anaphylaxis.

Thus, using observations garnered from studies, one may develop and then refine an approach that will enable practitioners to help patients complaining of asthma induced by food ingestion (8). This approach can be tailored to fit most practices much as we each tailor other aspects of our clinical approach (skin tests, pulmonary function measurement, allergy injection treatment) to fit our individual practice styles and requirements. The approach is helpful to patients because it is a cost-effective method of determining what foods must be avoided and which foods may be eaten, thus improving the quality of life of the people who seek our help.

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REVIEW ARTICLE

Food Sensitivity in Asthma: Perception and Reality

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The institution of the double-blind, placebo-controlled food challenge (DBPCFC) provides evidence that foods and food additives cause asthma in some patients. There is still confusion, however, as to the mechanisms and prevalence of food-induced asthma, and a tendency among many patients and certain physicians to exaggerate food's contribution to asthma.

Most reports in the medical literature indicate that food provokes wheezing in only a small percentage of patients with asthma. In one of the earliest studies to employ the DBPCFC, Charles May of the National Jewish Hospital and Research Center tested 38 children with severe chronic asthma and a history of suspected food-induced bronchoconstriction (1). While 11 of the 38 children had positive challenges, their symptoms were primarily gastrointestinal; none of the children had respiratory reactions, nor did May observe any late asthmatic reactions during a 24-h observation period.

Two years later, however, at the same institution, Bock et al. carried out DBPCFCs on a population of 68 children (2). Twelve children (18%) exhibited wheezing within 2 h of the challenge, all but one in conjunction with cutaneous and gastrointestinal symptoms. The authors speculated that in some of the children, the wheezing may not have been caused by the food itself, but by other symptoms such as vomiting.

More recently, Onorato et al. (3) screened 300 consecutive patients with asthma entering a respiratory clinic in Montpellier, France. Only 25 patients had suspected food allergy established through history, prick test, or RAST. Of these, only 6 (2%) of the total screened population had a positive

asthmatic reaction upon DBPCFC. In a study of 140 asthmatic children in Florence, Italy, Novembre et al. (4) found that 8 (5.7%) had asthma symptoms in response to a double-blind food challenge.

Bock has performed more than 1,000 DBPCFCs at the National Jewish Center for Immunology and Respiratory Medicine in Denver. He reports that, "Asthma as the sole symptom of an adverse reaction to food has been distinctly unusual despite the fact that a major portion of the population undergoing DBPCFC are children with severe asthma (5). He reports that only 4 of 480, or 1%, of the children he has tested have exhibited asthma as the sole positive response to the double-blind challenge (6), but that asthma in combination with skin or gastrointestinal symptoms is more common, occurring in 36 of 1014 food challenges (3.5%). Bock also reports that the only late-onset reactions to food observed in the National Jewish Hospital Program have involved gastrointestinal and cutaneous symptoms.

In the above-mentioned studies, it is interesting to note how often a suspected history of food-induced asthma has not been confirmed by DBPCFC. The field of "food allergy" has traditionally been considered one of the thorniest in all of medicine, and a large measure of the controversy is rooted in this disparity, that more people believe they have food allergy than actually have it. In a 1989 Good Housekeeping Institute survey of 300 American mothers, 17% said their children suffered adverse reactions to foods or additives. An earlier *Good Housekeeping* study devoted specifically to food allergy surveyed 200 women: 27.5% said that someone in their household had an allergy to a food product. The U.S. Department of Agriculture has estimated that "some 15 percent of the population may be allergic to some food ingredient or ingredients. This amounts to 34 million people with an ingredient sensitivity" (7). By contrast, estimates in the medical literature of pediatric food sensitivity range from below 1% to 7.5% (8). The prevalance of food allergy in adults is thought to be lower still, but the true prevalence in both groups in unknown.

Why is there such a discrepancy between the perceptions of patients and clinicians? Part of the answer lies in the natural—and often valid—tendency to relate the foods we eat to the way we feel. Patients today are more health conscious in general, and more aware of the link between diet and diseases such as cancer, heart disease, and hypertension. Viewed in this context, food allergy may seem a plausible culprit in a broad range of disorders, from common allergic symptoms such as wheezing, to vague complaints of tension and fatigue.

Past generations of allergists were far too prepared to reinforce this perception. Throughout the earlier decades of this century, prominent allergists subscribed to an inflated and subjective assessment of food's role in immunologically mediated disease (9). While recent decades have seen a more rigorous and scientific approach to food hypersensitivity, early mistakes still cloud the field's reputation. Moreover, a minority of allergists, including some who maintain a very high public profile, persist in reinforcing patient beliefs instead of testing these beliefs with objective diagnostic tools. Many of these "alternative physicians" employ unproven tests and treatments, including cytotoxic testing, sublingual drops, severe dietary restrictions, and other practices deemed ineffective and/or harmful by the American Academy of Allergy and Immunology (10).

The problem is that many patients with food allergy complaints are evaluated and treated by such physicians—and nonphysicians—because more reputable practitioners are reluctant to treat them. Allerx, a biotech company involved in food allergy, surveyed a group of 173 physicians composed primarily of allergists. Eighty-one percent of these doctors said they were reluctant to handle food allergy complaints; 92% said they preferred to send such patients elsewhere (11). Avoidance, it would seem, is not only the preferred therapy for dealing with identified food allergens, but it is also the most common way of treating food allergy patients.

To rectify this situation, physicians, nutritionists, and other professionals involved in

the care of patients with food allergy complaints need to reach agreement on basic approaches to diagnosis and treatment. One might start with the term food allergy itself: it is used so indiscriminately to describe both immunologic and nonimmunologic reactions that some leaders in the field say its use should be abandoned, and the term food sensitivity, or hypersensitivity, used to describe immunologically based reactions. For the purpose of this discussion and others, definitions are offered in Table 1.

More standardized and accurate diagnostic procedures are also essential to verifying food allergy complaints. The most common technique now in use is the puncture or prick test. Radioallergosorbent testing (RAST) is usually less sensitive and far more expensive than skin testing; its usefulness in clinical situations is limited to occasions when skin testing would be difficult (e.g., patients with pervasive dermatitis) or dangerous (patients with a history of anaphylactic reactions).

Skin testing using appropriate antigenic extracts is believed to be very sensitive with a negative predictive value estimated at 95% (6). The positive predictive value, however, is considerably lower: a positive skin test to peanuts does not necessarily mean that a patient cannot tolerate peanuts. In fact, positive skin tests may be associated with mild allergic symptoms of little or no clinical significance, or even asymptomatic sensitivity. Positive results may also be false due to improper technique or to impurities or irritants in the extract used. It is estimated that only one in three patients with both a positive history and a positive skin test to a given food will exhibit symptoms after ingesting the food in a DBPCFC (6). For this reason, the DBPCFC has been proposed as a diagnostic "Gold Standard" in food allergy (12).

It may be more accurate, however, to refer to the DBPCFC as the "Silver Standard" in acknowledgment of the procedure's limitations. While DBPCFC can confirm specific food sensitivity or intolerance with a high degree of certainty, it cannot, with equal certainty, rule out the risk of specific adverse reactions. False negative food challenges result if the amount of food ingested is smaller than the patient would normally consume (13). Additionally, there is suspicion that in some asthmatic patients, foods might increase nonspecific bronchial hyperreactivity as measured by methacholine challenges without producing an actual episode (14).

Given the high negative predictive value of well-performed skin tests, it has been suggested that DBPCFC be limited to foods which produce a positive skin test, while negative skin tests may be confirmed by open challenges to rule out the possibility of a non-IgE-mediated intolerance. The rule is

Table 1.

Food intolerance: An abnormal reaction to a food or food additive not proven to have an immunological basis; includes idiosyncratic, metabolic, pharmacological, and toxic reactions.

Food hypersensitivity: Adverse reactions to food that are immunologically mediated.

Food allergy: In strict use, the same as food hypersensitivity, i.e., immunological reactions. In common use, food allergy has come to mean almost any adverse reaction to food, creating such confusion that the term has lost its scientific usefulness.

Food toxicity: A nonimmunologic reaction to a food/food additive, or food contaminant including microorganisms.

Sensitivity: The ability of a test to detect abnormal members of a population. Expressed by the equation

$$\frac{\text{True positives}}{\text{True positives} + \text{False negatives}}$$

Selectivity: The ability of a test to detect normal members of a population. Expressed by the equation

$$\frac{\text{True negatives}}{\text{True negatives} + \text{False positives}}$$

Prevalence: The total number of people in a group who have a disease as a percentage of the total group.

Incidence: The number of new cases of a disease occurring during a given period.

Positive predictive value: The probability that a patient with an abnormal (positive) result to a given test actually has the disease.

Negative predictive value (of a test): The probability that a patient with a normal (negative) result to a given test is actually free of the disease.

generally a good one, but there are significant exceptions, particularly in the area of food additives. Sulfiting agents, which are still commonly used as food preservatives and antioxidants, are believed to provoke bronchoconstriction in 5–10% of asthmatics (15). The role of the immune system in sulfite intolerance is unclear. While some evidence has been presented of skin test reactivity in sulfite-sensitive patients (15), negative skin tests have been reported in patients with near fatal reactions to sulfites (17). Skin tests are insufficient, therefore, to rule out a diagnosis of sulfite-induced asthma; the DBPCFC is required.

Asthmatic reactions have been reported as the result of MSG ingestion (the agent responsible for so-called Chinese restaurant syndrome) (18,19). Tartrazine, also known as FD&C yellow No. 5, causes symptoms in approximately 4% of asthmatics. Since neither of these additives (20) is believed to provoke symptoms through an immunological response, DBPCFC is the only accurate diagnostic test.

Bock estimates that the negative predictive accuracy of the DBPCFC is approximately 99% (6). A negative test, however, does not prove that the patient can safely eat the tested food in any dose or under any circumstance. It is therefore recommended that, following a negative DBPCFC, the patient should be openly challenged in the physician's office. A positive reaction may indicate that the dose used in the DBPCFC was insufficient, in which case the procedure can be repeated. It may also indicate a psychological reaction: if a patient truly believes he will react, the belief becomes a self-fulfilling prophecy.

Another concern involves the ability of the DBPCFC to detect delayed reactions, particularly those involving asthma. The importance of such reactions is debatable. Pelikan (21) tested 107 asthmatic patients and reported that nearly 60% showed positive bronchial responses as measured by spirometry. Moreover, nearly half of all patients tested showed evidence of a late bronchial response. Approximately 80% of the challenges were open, however, and the results are in conflict with other studies. More well-controlled studies are needed to address lingering concerns about late-phase asthmatic reactions to foods. In the meanwhile, patient claims of such reactions can be addressed by lengthening the periods between challenges.

In general, however, the advantages of the DBPCFC outweigh any limitations, and the technique is now being recommended for broader use. Procedures for performing office-based DBPCFC have now been endorsed in principle by the AAAI (22). Most clinicians are reluctant to start using it. In the Allerx survey cited above, 91% of physicians said they were not prepared to do office-based DBPCFCs. Their reasons included a lack of experience (92%), potential risk to the patient (71%), a low volume of food allergy patients (71%), the time involved (58%), and a lack of proper food challenge materials (51%) and trained personnel (41%).

Concerns about the safety of DBPCFC are more a problem of perception than reality. Many thousands of DBPCFCs have now been performed with no reported deaths or near-fatal reactions. The key to safety in the procedure is the taking of a careful patient history. It there's any reason to suspect that a severe reaction might occur, minute initial challenge doses can mitigate the risks. With sulfites, for example, the Bronchoprovocation Committee of the AAAI recommends an initial dose of 0.1 mg of sulfite in solution masked in Minute Maid Lemonade Crystals dissolved in water (23). Physicians must also be prepared to promptly treat severe reactions regardless of the apparent risk involved.

The other reservations expressed in the Allerx survey are essentially a matter of patient volume. The investment in time, training, and materials may only be justified by making food allergy complaints a significant part of one's practice. For this reason, the DBPCFC will most likely become a specialty test performed by a small percentage of physicians who have gained sufficient experience in the procedure—and a sufficient number of patients—by accepting referrals from other physicians. Dedicated centers have been developed to provide the diagnostic and

therapeutic services necessary to care for food allergy patients and their families, incorporating nutritional counseling and psychological support. In addition to providing patient services, these centers will generate a database of information which can be accessed by contributing researchers and clinicians worldwide.

As the DBPCFC becomes a more common procedure, the test may help to clarify the true prevalence of food-induced asthma in the larger asthmatic population. There is something of a catch-22 that impedes the pursuit of accurate prevalence data. To ascertain the prevalence of a disease, one needs to have accurate diagnostic tests. To assess the accuracy of such tests, one needs to know the prevalence of disease in the population of patients being tested.

Pooled data from epidemiologic studies employing DBPCFC will help to confirm or refine current estimates of the prevalence of food-induced asthma. Once firm estimates are established, practitioners will be able to better assess the role of foods in exacerbating asthma, and to educate patients as to the odds that their symptoms are actually food induced. When patients have respected and responsive doctors to turn to, they will be less inclined to consult the unscientific practitioners now profiting from the confusion surrounding food allergy. That should help both patients and physicians to breathe easier.

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