5-1-1941

Food allergy

Jacob J. Krieg
University of Nebraska Medical Center

FOOD ALLERGY

By
Jacob Krieg Jr.

SENIOR THESIS

Presented To The College Of Medicine,

University Of Nebraska, Omaha, 1941.

Table of Contents

INTRODUCTION

During the past year, in the process of taking histories, I frequently asked the patient if there were any foods he could not eat, and if so, why not. Surprising were the number of affirmative answers, as were the reasons sometimes given. One gentleman from Greece told how he could not eat fresh meat while residing there because it always produced a severe reaction of hives. Since arriving in this country, he can eat meat to his hearts content without any noticeable after effects. This indeed was very puzzling and contributed in bringing to mind questions such as: Are these real food idiosyncrasies? What are the common foods causing idiosyncrasies and what are the manifestations produced? Would a careful investigation in this field be of value in later practice? Being of the opinion that the answer to the last question would be in the affirmative, a search is made in the literature to answer some of the questions which have arisen.

DEFINITION

Allergy, meaning altered reactivity, was coined by Von Pirquet in 1906 to indicate certain changes of reaction observed in children to second and subsequent small pox vaccinations and injections of horse serum (68). Since then allergy has been adopted to denote the sensitization reaction of man, and is synomymous with hyperssensitiveness, sensitization, idiosyncrasy, anaphylaxis and atopy.

Belgrade (9) defines allergy as an altered reactivity of the body cells to an existing substance which is harmless in similar amounts for the majority of members of the same species.

Brown (13) states that allergy is a chemical disease, due to the presence of whole or incompletely digested protein in the tissues in sufficient quantities to produce peculiar toxic reactions.

Williamson (68) explains it as a state of altered reactivity caused by contact with a substance and is demonstrated by a different reaction on subsequent contact with the same substance.

The present concept is that non-protein substances also may cause sensitization(9), and Cooke (15) defines the allergic state as one of potential specific reactivity due to the existence in certain cell of a mechanism (antibody) which mediates the linkage of the cell to the

to the specific substance (antigen).

Food allergy would include all of the allergic manifestations due to foods.

HISTORY

The present-day knowledge of allergy, though still vague and incomplete, is a by-product of the general use and anaphylactic reactions which followed subsequent injections of diphtheria antitoxin, which was discovered by Von Behring in 1890 (15). Thus it is a relatively new field in medicine, the most vigorous work and study has taken place in the last thirty years.

Various idiosyncrasies to foods have been noted and occasionally written about for a number of centuries. Hippocrates wrote: "It is bad to give milk to persons having headache" (15). Burton, in 1600, wrote: "The diet which is most propitious to one is often perniceous to another" (54). This has probably lead to the saying: "One mans meat is another mans poison", a quotation encountered any number of times in the literature. In 1794, Fothergill stated that foods were a cause of sick headaches. Bateman, in 1817, recorded internal causes of eczema(11). In 1860, Salter reported asthma following ingestion of milk and coffee (68). In 1884, Hutchinson spoke of idiosyncrasies, diatheses and inheritance. Ortan, in 1886, found egg sensitiveness in three generations of a family(54) (11). In 1910, Meltzer suggested that asthma

was related to anaphylaxis (62). In 1911, Von Pirquet suggested the term allergy (54). Since then Cooke, Duke, Coca, Piness, Vaughan, Rowe, Ratner, Brown, Eyermann, Alvarez and a great number of others have added many valuable contributions to the field of food allergy.

MANIFESTATIONS

The conditions described in the literature as being allergic by at least one author for each, includes well over a hundred sumptoms and diseases(13). How can so many manifestations occur? What is the mechanism and what is the pathology produced?

Allergic reactions to foods are produced in the same manner as allergic reactions due to any exciting substance. The exciting substance or allergen, also designated as antigen is usually absorbed into the blood stream by way of the gastro-intestinal tract. However, occasionally skin contact or inhalation of dusts of foods may lead to allergic manifestations. After absorption, the antigen is distributed by the blood. The other factor in producing an allergic reaction is the antibody or reagin, which is present in the blood or tissues. The antibody is produced by previous contact with the allergen.

Brown (11) explains the allergic manifestations are due to a histamine-like reaction of the bodies (antigen and antibody), which may occur in any tissue or organ in the body. In another later article (13), he expresses the belief that the reaction probably is a direct result of destruction of incompletely digested protein by the

affected or shock organs. Lippard and Schmidt (37) are of the opinion that antibodies protect against allergic reactions and the reactions occur only when there are insufficient antibodies to neutralize the absorbed antigen before it reaches the tissue.

Laroche, Richet and Saint Girons, as quoted by Tuft (62) explain their conception of the mechanism as follows: "Food anaphylaxis is an intoxication. Substances not sufficiently modified (insufficiency of the digestive juice) pass through the intestinal barrier and the liver does not stop them sufficiently (insufficiency of the liver). They provoke an intoxication of the organism (especially of the blood) and they modify the internal secretions and vagosympathetic tonus. The more marked the symptoms the greater the vagosympathetic instability."

May it suffice to say that manifestations of food allergy establish themselves almost always, through ingestion of specific foods to which the individual has become sensitized. Contact or inhalation of foods may also produce reactions. It must be admitted that it is not known definitely how a sensitization starts, what determines the allergen or the clinical manifestations.

The pathological reaction consists of edema and infiltration of the edematous area with leucocytes, a high percentage of which are eosinophils. Muscle fibers in the affected areas may be thrown into spasm (13).

Dzsinich and Paul state that in allergic diseases the lesion is an edema wherin water enters tissues and is bound there (58).

Cooke (15) describes the simplest pathology as edema or hyperemia occurring singly but as a rule together. There may be an inflammatory lesion which is exudative as in eczema, productive as in hyperplastic rhinitis, or it may be hemorrhagic.

There seems to be no organ or tissue which may not be sensitized and reacts with one of the pathological types. This would tend to explain the numerous symptoms and diseases which are described as due to tood allergy.

In general, most students of food allergy list quite similar manifestations. Brown (11) recognizes rhinitis, common cold, asthma, coated tongue, canker sores, nausea, vomiting, heartburn, diarrhea, pain, colic, mucous colitis, pylorospasm in infants, gall bladder-like symptoms,eczema, urticaria, angioneurotic edema, psoriasis, pruritis, purpura, migraine, epilepsy, Menieres syndrome, chorea, dysmenorrhea, glomerulo-nephritis,

rheumatism, cystitis, eye disturbances, fever and hypertension as allergic manifestions of food. Rowe(49) has a similar group but also include hypotension, high and low grade fevers and toxemia. Tuft (62) adds vertigo, neuralgia, functional paralysis, amblyopia, amaurosis, hypersomnia, insomnia, lethargy and even changes in personality. Acne and angina pectoris are other contributions (68) (69).

Multiple or associated manifestations were frequently encountered. The explanation of the mechanism and the description of the pathology produced problably also explains the multiple reactions of food allergy. Multiplicity has undoubtedly played an important role in the advancement of the knowledge of allergy. Liveing, in 1873, pointed out the frequent association of migraine, epilepsy, spasmodic croup, asthma, gastralgia and angina, and called attention to the interchangability of these diseases (69). In the various articles reviewed, the authors mentioning multiplicity found more than one manifestation in seven to eighty percent of the cases. Wirley(69) in his study of 135 cases of angina, found food disagreements in 47%, migraine in 35%, urticaria in 17%, hay fever in 12% and asthma in 9% of these patients. Rowe (52) has similar findings. In 270 of gastro-intestinal

allergy, 36% had migraine, 34% exhibited urticaria or eczema, 33% complained of nasal symptoms, 18% showed evidence of bronchial involvement. In 66 cases of perennial hay fever, 37% had bronchial, 31% cutaneous, and 30% had abdominal conditions. In 61 cases of urticaria, associated manifestations were bronchial 26%, nasal 21%, cutaneous 25%, headaches 15%, and abdominal 21%. In 48 cases of eczema, the accompanying complaints were 29% abdominal, 29% cutaneous, and 40% respiratory. In another series (49) of 175 cases, he found single manifestations in 51% of the cases and one or more associated conditions in the remaining. In 20 cases of urticaria, it was the only finding in 75%. In the survey of migraine, he found frequent skin manifestations.

Waters (66) detected that manifestations of the respiratory system were rarely present without gastro-intestinal or cutaneous complaints. Piness and Miller (46) report that gastro intestinal sumptoms are seldom a sole allergic condition. Sheldon and Randolph (57), in 127 cases of allergic migraine, discovered other manifestations in 34% of patients. Urticaria and hay fever comprised a large portion of this group. Fries and Zizmor (27) found only 7% respiratory and 7% constitutional disorders in 30 cases of gastro-intestinal allergy in

children. This would seem to indicate that manifestations are more likely to be single in infants and children than in adults.

Along with multiple reactions of sensitivity, several authors believe they have noted a general course which the allergic disorders follow throughout the life of the allergic individual. Brown (11) is of the conviction that a large percent of allergics have two or more forms of manifestation during their life. Cooke (15) writes that the allergic group represent an ingrained constitutional defect and that such individuals are likely to have not only recurrences, but different clinical varieties of allergy reappearing at any time through life. Ratner (47) is convinced that the natural progress of allergy is eczema during the first year, asthma in the third and fourth years, hay fever in the second decade and urticaria may appear at any time. Rowe (49) agrees with this in stating that food asthma in children is frequently preceded by eczema or hives. He considers migraine and gastro-intestinal disorders as common manifestations in the teens and angioneurotic edema as an adult condition. Hopkins (33) accepts eczema and gastro-intestinal upsets as common infancy and childhood manifestations, and believes that hay fever and asthma are more likely to occur in grown-ups. Ratner (47), in 200 cases of food allergy, reports

that manifestations occurred in 78% before the age of four months. 85 of these cases were eczema. He found cyclic vomiting in 24, and colic in 16 cases.

Most writers agree that the symptomatology is very irregular and inconsistent. There seems to be nothing definite about the onset, character, intensity, duration or frequency.

The onset, after ingestion of the allergen, may be very sudden in highly sensitive people (1). In chronic and recurrent cases it is generally accepted that the onset may be delayed. It may also vary with the same food from time to time. It may be in a few seconds or several days.

Tuft (62) writes that the manifestations may be acute or chronic. If the allergen is common to the diet, the symptoms are more likely to be chronic, and either continuous or recurrent. As previously mentioned they are often multiple. Cyclic recurrences also have been reported, and are explained by some (54) as a desensitization following an attack. The intensity also is variable.

The duration of allergic disorders may vary from a few hours to several days. The chronic forms may con- for months and years. In some cases, the more acute the

reaction the shorter the duration. Liveing thinks the duration depends upon the amount of the offending food ingested (11).

The marked inconsistency of the symptomatology may partially be explained by the numerous contributing factors in the etiology of food allergy. This will be discussed later.

Several men have made rather extensive surveys of the incidence of allergy. Service (56), in the study of 1000 families, comprising over 3000 individuals, found 44.9% of these families manifested some form of allergic disease. 16.98% of the individuals showed evidence of some form of allergy. This would roughly indicate that only about one out of three individuals of an allergic family has allergic manifestations. It is doubtful if most allergists would agree with this computation.

In the distribution of manifestations, he reports that 32.7% of families and 10.2% of individuals complained of hay fever; 9.5% of families and 3% of individuals had asthma; 8.5% of families and 2.6% of individuals exhibited eczema; 8.7% of families and 2.7% of individuals complained of migraine; 8.5% of families and 2.6% of individuals manifested urticaria; 7.3% of families and 2.1% of individuals showed evidence of gastro-intestinal allergy.

Rowe strongly believes that food allergy is much more common than is generally recognized, and estimates that about 30% of the general populace are sensitive to foods (16). In the study of 400 student nurses he found 31% were sensitive to food (2). Ratner (48) concludes that only about 10% are affected. Duke is of the conviction that about 15% suffer from sensitization. Vander Veer and Cook found 14.5% of normal people showed positive skin sensitiveness (32). This would indicate that there is both agreement and disagreement as to the general incidence, and also that it is far from a rare problem.

GASTRO-INTESTINAL MANIFESTATIONS

Since foods are most frequently contacted by way of the gastro-intestinal tract, it would seem that alimentary signs and symptoms would be the most common manifestations of food. Few calculations as to the ratio of gastro-intestinal symptoms to other manifestations can be found. The high percentage of gastro-intestinal complaints in other forms of manifestations has been touched upon in the discussion of multiple manifestations. Piness and Miller (46) emphasize this by concluding that gastro-intestinal symptoms of food allergy are rarely present without other manifestations. Rowe (49) confirms this somewhat by finding, in 50 cases of gastro-intestinal allergy, 70% had other manifestations. Gay finds that associated allergies often give the clue to gastro-intestinal allergy. Ratner (47) in 85 cases of eczema in children found almost half of them had gastro-intestinal complaints. Moore (43) in the study of 350 cases of food allergy discovered 44.8% gave definite gastric complaints, secondary to their main complaints. Tuft (62) states that although there is little doubt that allergy to foods may produce many gastro-intestinal symptoms in a patient who has other manifestations of allergy , the possibility that symp-

toms of this type are due to food allergy when they occur in a patient whose complaints are only gastro-intestinal and shows no other evidence of allergy is controversial. This would immediately lead to the conclusion that gastro-intestinal manifestations are not the most common of food allergy. Moore (43) finds the manifestations of gastro-intestinal allergy are most irregular. No two cases are alike. The patient usually gives a history of a disease of a chronic nature with rather frequent attacks of short duration. The symptoms produced by food allergy are believed to be brought about by edema and the smooth muscle spasm. If the sensitizing agent is present in food as it is eaten, it is likely to cause upper abdominal symptoms, such as vomiting, which would come on soon after ingestion. More frequently the offending substance is a split product of digestion, and in this type of case the symptoms would be delayed in coming on and would be lower abdominal, such as diarrhea or colic (43). Various gastro-intestinal manifestations have probably been suspected for some time as being on an allergic basis. Gee, in 1882 published a paper on fitful and recurrent cyclic vomiting in children (31). In 1884, Hutchinson dis-

cussed vomiting, distress and a sinking sensation due to eggs (11). Liveing, in 1873, mentioned gastralgia along with other allergic manifestations (69). The surgeons have also long suspected the existence of gastro-intestinal allergy. Harrington, in 1903, found an urticarial swelling of the bowel wall during an attack of colic (43).

Some of the various gastro-intestinal symptoms discussed by Rowe (64) are: canker sores, coated tongue, heavy breath, distention, belching, sour stomach, epigastric heaviness, burning, nausea, vomiting, intestinal cramping, mucous colitis, diarrhea, constipation, proctitis, pruritis ani, and pain in various localities of the abdomen. Associated general symptoms are: weakness, fatigue, irritability, nervousness, mental dullness and confusion, general aching and fever. Few other contributors to gastro-intestinal allergy list such a large number of manifestations. In a later article (63), he names canker sores, gastric, diarrhea, constipation, mucous colitis, pruritis ani, abdominal pain and tenderness, ulcer type of pain and toxemia as the more common symptoms. He also mentions that vesicles, papules and canker sores may be found in the mough and pharynx, and that these

may also occur in the stomach and duodenum. He believes the mucosal capillaries may have an increased permiability which may lead to bleeding and allergic purpura. He is convinced that the gall bladder, biliary tracts and even the parenchyma of the liver are not exempt from allergic reactions. In this group of cases he mentions the frequency with which associated respiratory, dermatologic and neurologic manifestations are encounted.

What are the more common gastro-intestinal manifestations? Alvarez (2) in a series of 700 patients found post meal distress approximately four times as common as vomiting, diarrhea or severe pain. His statistics would indicate that gas and belching are six times as frequent as vomiting with diarrhea, and approximately nine times as common as diarrhea or heartburn. Regurgitation and headaches were complained of approximately one-half times as often as diarrha. Gay is of the opinion that gastro-intestinal symptomology is immensely varied, and lists pain, constipation, gas and bloating as the most common. Rowe (53) in a 270 case series, reports gastric complaints in 79%, abdominal pain and tenderness in 60%, constipation in 43%, toxemia in 2[illegible]%, canker sores in 17%, mucous colitis in

and prostration of one to three days' duration. Most cases were two to four years of age. Typical course of symptoms were anorexia, lassitude, irritability, followed in twelve to eighteen hours by extreme nausea and vomiting, and increased temperature, prostration, abdominal discomfort, constipation and diarrhea, dehydration and hypotonus. The vomitus usually consisted of mucous, which was occasionally stained with bile. Between attacks these patients enjoyed normal health. They were often diagnosed as bowel obstruction.

The pain of food allergy is explained in various ways. Crispin thinks it may be caused by distention of visceral nerve, by pseudo-obstruction of the intestine, by marked peristaltic action, or it may be a result of distention. Learmonth believes it may be due to infiltration of the stomach or bowel by serous or hemorrhagic fluid to such an extent as to stretch the parietal mesenteric attachment (43). The pain seems to be of all degrees and locations. Unna and Kimmon (27) found it most frequently in the region of the umbilicus. Moore (43) is of the opinion that it is usually mild, occasionally severe, simulating a gastric crisis.

Hollander (30) discusses several cases of mucous

DERMATOLOGIC MANIFESTATIONS

Belgrade (9), in discussing the value of skin testing states that the role the skin plays in destroying bacteria and toxic products during the process of elimination is a commonly known and accepted fact. It is also highly probably, owing to its' important function of elimination that the skin may become sensitized or allergic by the nature of the intimate part it plays during the course of disease. This seems to be a fairly good explanation for the cause of skin manifestations.

That foods are the cause of some forms of skin manifestations has undoubtedly been known by both the public and medical men for a number of centuries. This is probably substantiated by the frequency withwhich lay people know exactly which foods will cause them to have hives. Bateman, as early as 1817, recorded internal causes of eczema.

The most common cutaneous manifestations are eczema, urticaria, angioneurotic edema and pruritus (65), (52), (14), (3). Other conditions which have been ascribed to food allergy are acne, purpura, psoriasis (12), erythema multiforme, dermatitis herpetiformis and several other forms of dermatitis. Goodman and Sulzberger (30) are of the opinion that, as a general rule, lesions of skin

allergy do not seem to be limited to any particular distribution. Several of the writers disagree to some extent with this conclusion. Most allergists are convinced that eczema in infancy, up to about two years is almost entirely due to food allergy (68), (50), (33). Ratner (47), is one of the few who disagrees withthis statement. Osborne and Walker found food important in only 15-20% of cases in a large series of infant eczema (30). From infancy on, the role of food, in causing eczema, decreases in importance. Williamson (68), states that eczema of the adult is rarely due to food allergens. It must still be considered seriously as a cause of eczema during childhood and adolescence according to Hopkins (33). Eczema of infancy may disappear spontaneously later in childhood. Ratner (47), believes it is usually the first manifestation of allergy and often is found in the history of individuals who later have other manifestations.

Rowe (52), describes the lesion as being erythematous, indurated and scaling, and does not display the visible vesicles of a contact eczema. Hopkins (33), pictures the most common form of lesion as dry, lichenfied and papular, but adds, that it also may be weeping and vesicular. Williamson (68), believes that it has

predilection for the face and neck, bends of the elbow and back of the knees. Also, that it causes itching.

Urticaria, commonly named hives, especially by the laity, involves the superficial layers of the skin, and occurs as papular, itching lesions in any part of the skin of the body. The size of the lesions may vary from pinpoint to large welts the size of a hand or even larger. Vesicles may form. They may appear in conjunction with angioneurotic edema. Von Pirquet, first discussed urticaria from the standpoint of allergy in 1911. Ratner (47), writes that it may occur anytime during life and does not have a predilection for any age group. Williamson (68) remarks that urticaria is fairly common in food allergy. The attacks are usually of short duration but are noted for their frequent recurrence. Occasionally they may last as long as one month. Ratner (47), is of the opinion that the attacks are often so sudden that the patients usually make their own diagnosis as to the etiology. Rowe (49), in 30 cases found urticaria to be the sole manifestation in 75% of the cases. He also is of the conviction that in chronic cases, food is rarely the etiological agent.

Angioneurotic edema is a swelling, similar to urticaria, of the subcutaneous tissues. It is transient,

non-itching, may occur in any part of the body, but more commonly affects the face and extremities. In 1776, Milton had called it giant urticaria. Quincke, described this edema in 1882, though it had been recognized by physicians for years. In 1905, Strubing named it angioneurotic edema (54). Rowe (59), believes this type of reaction could affect any tissue, such as the alimentary tract, central nervous system or urogenital system, and thus produce most any type of symptoms.

Its' behavior is very much like urticaria in being short in duration and frequent in recurrence. He found, in a series of 20 cases, the average age to be 39 years. This lead him to conclude that it is an adult manifestation.

Purpura due to food allergy is a rather recent contribution to allergy, although Galen, in 1904, mentioned bleeding into the bowels due to angioneurotic edema, and Quincke in 1915, also reported its' occurrence (54). In 1934, Leary, reported thrombocytopenic purpura due to sedormid. Other drug purpuras have been reported since (59). This lead to the belief that foods also may cause purpura. Squier and Madison (59), discuss several cases of thrombocytopenic purpura in which dietary manifestation yielded striking clinical improvement

RESPIRATORY MANIFESTATIONS

Asthma, perennial hay fever or vasomotor rhinitis and certain types of bronchitis are described as the more common respiratory manifestations of food allergy. Hansel is of the opinion that in his otorhinolaryngology practice, he has found approximately 40% of nasal complaints are due to allergy. He also feels that 80% of chronic sinusitis is due to allergy (56). It seems that inhalants would be the predominant cause in the etiology of allergic respiratory symptoms. This supposition is largely borne out by most allergists and they relegate foods to a secondary but still important place as an etiological agent in causing respiratory manifestations, (52), (47), (66). This is especially true with advancing age. However, Chaney (16) found foods as a predominant factor in causing nose and throat symptoms in a series of 175 cases. Waters (66), advises that patients with long and protracted colds and bronchitis should be investigated from an allergic standpoint.

Salter, in 1868, though he had no conception of food allergy, connected food with asthma and wrote of stopping attacks by 36 to 48 hours of starvation. In 1908, Schofield described an acute case due to eggs (54). Since then the importance of food in causing asthma, es-

pecially in infants has been generally recognized. Rowe (52), is of the opinion that asthma occurring during first two years is almost always due to food. Ratner (47), on the other hand, stresses the importance of inhalants and contactants, even in this young group. They both agree as to the frequency with which eczema precedes the onset of asthma. With increase in age, foods play a less important role and the inhalants should be given dominant consideration. However, food may still be the sole cause in an adult asthma (52), (28). Gay (28), is sure that chronic asthma, no matter what age, is usually due to food. Deamer (20) states that the asthma of food allergy is catarrhal in type. This agrees with Eyermann (26), who finds that inhalants are more likely to cause a spastic type of asthma. Rowe (51), describes food asthma as cyclic and non-seasonal in recurrence. Recurrence becoming more frequent and finally chronic. Gastric and cutaneous manifestations are often also noted (66), (54). Rowe (52), in 1418 cases of asthma of all ages determined food was the cause in 57% of the cases. This is probably higher than most allergists would acknowledge.

Food as a cause of vasomotor rhinitis was first recognized by Walker, in 1920, when he found that ingestion as well as inhalation at times caused hay fever. Rich,

in 1922, published the first article which considered the causes of perennial hay fever with the possibility of all types of allergy in mind. Tufts (62), writes that in adults, foods are more likely to cause coryza than asthmatic symptoms. By skin testing, Rowe (52), found in 68 cases food to be the cause in 30%. Pollen was the cause in 58% of cases. Cohen (16), believes food is often a contributing factor in seasonal hay fever. The symptoms usually are sneezing, itching, nasal congestion, throbbing or blocking, or nasal discharge. It is more likely to be exaggerated following meals. Bronchitis and asthma are frequently also found in these patients (62). Ratner (47), is convined it occurs very commonly during the second decade in children who have had eczema and asthma in infancy and childhood.

NEUROLOGICAL MANIFESTATIONS

On analyzing the pathology produced by an allergic reaction, it can be understood why many and bizarre neurological manifestations can occur. These include migraine, epilepsy, meniere's syndrome, vertigo neuralgias, transitory aphasia, hemiplegia, functional paralysis, amblyopia, amaurosis, hypersomnia, insomnia, lethargy and even changes of personality. Of these, migraine is the most common and prominent (54), (24), (49), (11).

Liveing, in 1873, associated migraine with other allergies (69). French authors, as early as 1850, grouped migraine with asthma and eczema (63). Vaughan was the first to report control of migraine by diets in 1922. Rowe, Miller, Eyermann, Rinkel, and Balyeat, have also attributed headaches of migranous types to food allergy (63). Because there are few associated skin reactions, is probably the reason physicians were slow in accepting migraine on an allergic basis. Vaughan (63) finds that approximately 7% of the public suffer from chronic or recurrent paroxysmal headaches. He believes one out of five chronically recurrent headache has an allergic etiological factor, and that at least one out of three frankly allergic individuals at one time or another may experience headaches due to food allergy. Sippe (58), concluded

that migraine is a rather frequent manifestation of food allergy. Rowe (52), in analyzing 247 cases found skin positive tests to foods in 68% of cases. Inhalants gave positive tests in 45%, and miscellaneous in 24%. Vaughan (63) states headaches due to food allergy, as a class, present the true characteristics of migraine. Sippe (58), alleges that periodicity is the feature of the attacks. Sheldon and Randolph (37), studied 127 cases and analyzed them rather carefully. In all cases the headaches were frontal. 61% were unilateral. The frequency varied from daily to every three months. The average period between attacks was 18 days. The duration would vary from an hour to seven days. The average duration until all after affects left, was 46 hours. Visual disturbances were common. Nausea and vomiting were also frequently encountered at some time. 34% of the patients had other manifestations. The most common of these were hay fever (22 cases), and urticaria (17 cases). 74.8% of the cases were females, 24.2% were males. The onset of the recurrent headaches occurred before 16 years of age in 58% of the cases. Eyermann and Liveing, found the duration of symptoms depended upon the amount of offending food taken (11).

Other manifestations such as epilepsy and meniere's syndrome and many others are reported in limited numbers (24), (49).

MISCELLANEOUS MANIFESTATIONS

In this group are included those illnesses attributed to food allergy which cannot well be classified with the previously discussed manifestations. These conditions are not common to food allergy, but food should be suspected as the etiological agent if other allergic disorders are present.

The etiology of arthritis is still a mystery, though allergy to bacteria has been strongly suspected for sometime. Talbot, in 1917, and Cooke, in 1918, first suggested arthritis may be due to food allergy. Turnbull (61), in 1924, reported checking the progress and even restoring movement in arthritics by diet. Wooton (72), describes arthritis as a dual process of allergy and hyperparathyroidism. He notes that a serous swelling in or around a joint would be a favorite site for decalcification and again for increased calcium deposits. The decalcification is caused by hyperparathyroidism, while increased calcium deposit depends on a decreased permeability of the kidney. This would lead to atrophic or hypertrophic arthritis as the case may be.

Urinary system symptoms described as due to food allergy include pain of bladder and renal type and enuresis. Duke (23), in 1923, described 5 cases with

bladder symptoms. All had other allergic manifestations. The complaints were frequent and painful urinations and constant pain over the bladder. There is little evidence of enthusiasm for food allergy as cause of urinary system symptoms in the recent literature.

Duke, also reported disturbances in menstruation due to food allergy. Schwarz and Smith (55) discussed 35 cases of dysmenorrhea due to food allergy. These patients, as a rule, complained of three symptoms; pain, mucous discharge and irregularity. Twenty-six of the 35 cases gave a history of other allergies. After other causes of dysmenorrhea were ruled out, most of the patients were definitely relieved by the proper foods.

Various abnormal conditions of the heart have also been attributed to food allergy. Wirley (69), states that angina pectoris on the basis of food allergy has only been suspected since about 1933. He reports 135 cases studied on the basis of food allergy. 93% of these gave a history of other allergies. Gay (28), discusses 20 cases of essential hypertension, in which the blood pressure was improved in all but one case by the proper diet. At the outset, the average blood pressure was 180/90. The highest was 220/115, the lowest was 150/80. After removal of sensitizing foods the pressures ranged from 120/65 to 140/80.

Rowe, (52), also describes a condition of toxemia of food allergy. These patients feel drowsy, dull and have difficulty in thinking. They also have a lack of pep and strength, and headaches of allergic type.

Gastro-intestinal symptoms are frequently present.

Can it be concluded that certain manifestations are always due to food allergy? It is doubtful that such a conclusion is justifiable. It seems that the manifestations discussed should be considered as probably or possibly disorders of food sensitiveness.

ETIOLOGY

The mechanism of allergy has already been discussed. There are still a number of unanswered questions concerning the origin and absorption of the antigen and its relationship with the antibody. In other words, why do allergic reactions to food occur?

Goodman and Sulzberger (30) write that there is some individual factor which determines the degree of susceptibility to sensitization and this factor varies from person to person. This is similar to Williamson's statement that some people inherit the capacity to develop allergic reactions more easily than others (68). Hopkins (33) believes a person whos is sensitive to one food has a tendency to become sensitized to others.

Oelgoetz, Oelgoetz and Wittekind (44) have arrived at the conclusion that manifestions of food allergy are caused by the absorption of too large amounts of protein to be hydrolyzed to non-toxic split products by the available pancreatic enzymes. They have found by experimentation, as a normal process, pancreatic enzymes are absorbed into the blood stream and then break down the absorbed unsplit protein before it reaches the tissue cells. This lead to the conviction that serum enzymes prevent all of us from being allergic to foods at all times. Thus they base all food allergies on pancreatic hypo-

function. The hypofunction may be primary or it may be secondary to some disease or other factor.

Brown (12) (14) explains the causes of reaction in a somewhat similar manner. He conceives the disorders as due to inadequacy of an enzyme to destroy the toxic portion of the absorbed protein molecule after it has been been broken down into toxic and non-toxic portions by another enzyme. He also maintains the serum enzymes are unable to act on certain types of protein. The protein molecule, whole or at the end of the first stage of gastro-intestinal digestion reaches the blood, lymph and tissues. If the enzyme to destroy the toxic portion is lacking, accumulation occurs in the tissues and causes a reaction. His opinion that certain proteins are not acted upon by enzymes would explain why occasionally a very small amount of an offending food will cause a marked reaction. The oversupply of whole or split protein may result from too free a supply by way of the alimentary tract. Too large a supply of food, or digestive inadequacy, or both may contribute to this (11). He also believes the exciting substance need not necessarily be a foreign protein. Hopkins (33) refers to the non-protein substances as incomplete allergens and thinks they become sensitizing only after combining with a body protein.

Lippard and Schmidt (37) (20) explain it somewhat

differently. They believe in the presence of hypersensitivity, protection from disorders is closely related to the presence of antibodies in adequate amounts to neutralize the absorbed antigen before it reaches the tissues. They arrived at this concept after studying the antibody titer in the sera of treated and untreated hay fever patients. The subjects who showed improvement to treatment displayed a rise in the antibody titer, while those with no rise had no improvement in symptoms. They also detected an ascent in the antibody titer in children following the absorption of sufficient antigen to produce clinical sumptoms.

Alvarez (5) believes that many cases which are thought to be food allergy, are really due to a combination of food sensitiveness and various types of organic diseases. He also is convinced that allergic manifestations may be due to a number or a combination of factors, including actual sensitivity, emotion, strain etc.. The contributing and predisposing factors in the etiology of food allergy will be discussed in more detail later.

In the allergic infant, another question arises. Lippard found a number of infants to be sensitive to eggs, though they had never ingested eggs(20). The answer as to how the sensitivity occurred seems to be a choice

between placental and breast milk transmission of the antigen. It is now believed that both happen. Both Ratner (47) and Lippard are convinced that transmission of the antigen can occur in utero. Thus heredity may play a role not only in the tendency of susceptibility but also the actual sensitization. Donnally has shown food allergy of the infant may also arise from the transmission of allergens in the breast milk (62).

Of all the predisposing causes of food allergy, heredity is without question the most outstanding one. Its importance has already been mentioned in the discussion of manifestations and etiology. Heredity not only transmits susceptibility, but also manner of manifestation and specific sensitivity to certain foods. Most prominent is the hereditary predisposition to asthma, eczema and migraine (62). Ortan, as early as 1886, reported egg sensitiveness in three generations of a family (11). Waters' (66) 110 cases of respiratory allergy, all gave a positive family history of allergy. Many allergists feel that in infant allergy, a positive family history can always be obtained if carefully sought for. This seems logical since the infant would have little chance to develop an acquired form of allergy. In general, most of the authors found a positive family history in well over half of their cases. Typical is Sheldon and Randolphs (57) finding of hereditary history in 81% of migraine

cases.

Age seems to be a factor in determing the type of manifestation to be expected. This has been discussed in the course of allergic disorders. The incidence of food allergy seems to be equal at almost all ages.

Rowe (50) is convinced that season is also an influencing factor in bringing on manifestations of food allergy. He relates that in many patients, symptoms are definitely lessened during the summer months and increased from September to April. A very surprising statement is found by Deamer (20), which conveys the impression that in some instances attacks are produced regularly at the time of certain meteorlogic changes.

Moore alleges that allergic diseases are very common in America, prevalent in England, rare in eastern Europe and less rare in wester Europe. Brown (11) accepts that people who cannot eat certain foods in one section of the country often can partake of the same food without trouble in another. This may be related to a conviction of Rowe (50), that food allergy seems to be benefited by inland and dry climates.

Both sexes seem to be about equally affected.

The fact that some patients are sensitive to certain foods one day and not the next week, and the finding of people who have eaten certain foods with impunity all of

their life and then suddenly become sensitibe to it, has been rather puzzling to the allergist (13) (7). This is probably due to the various and numerous contributing causes of food allergy. Brown (14) believes that an oversupply of split protein may be due to inadequate digestion, overloading of the normal digestion, or too rapid absorption from the alimentary canal. The cause of slow destruction after absorption can only be due to lack of certain enzymes or antibodies.

A great many conditions may cause inadequate digestion. Poor selection or preparation of foods, or foods which are partially autolyzed, incompletely fermented and bacterially decomposed, may contribute to the production of allergic reactions (13). Foods with a high cellulose content and commonly eaten in the raw state also seem to be frequent offenders (12). Hurried eating and poor mastication may lead to poor digestion. Foods which have been treated with dyes and drugs may cause reactions (8). Absent or low gastric acidity, diminished pepsin, inadequate pancreatic digestion and liver insufficiency must also be considered (44) (11). Fatigue, emotion, strain, annoyance, worry and nervousness may be factors in faulty digestion (4) (12) (32) (44).

Sheldon and Randolph (57), in the study of 127 cases

of migraine found: In 30 cases, the headaches usually accompanied menses; 20 followed emotional upset; 13 occurred with excitement; 10 frequently attended fatigue; 7 were connected with exertion; 6 were contributed to nervousness; 3 for each, associated warm weather, cold weather, high humidity, worry, constipation and eye strain with their headaches.

Overloading of the normal digestibe system usually occurs in the individuals with an uncontrolled appetite (13). It may be a result of overeating in general, or of over-eating in one food at one time, or eating a food too frequently (14) (5). Thus food of which the patient is most fond of is often the offender. Drueck (22) observed general overeating and overdrinking in his group of pruritis patients.

Chronic and focal infections also seem to play a role in the pathogenesis of food allergy at certain times (14). As previously mentioned, Alvarez (5), believes many cases which are thought to be allergy are really due to a combination of food sensitization and various types of organic diseases. Oelgoetz etc. (44) feels hypofunction of the pancreas may be secondary to some disease such as syphilis. Hollander (32) finds that sensitivity may return with some disease. Belgrade (9) is convinced that bacteria, fungi and animal parasites may produce allergens

which act similar to food allergens. Alvarez (4) thinks a coming cold or influenza may contribute to the causation of sensitivity. He also reports 3 cases following cholecystectomy.

Another important element to be considered is hypoendocrinism, especially hypothyroidism. Gay (28) believes hypothyroidism is particularly important in children. One author, in a series of 21 food allergics found all of them to be hypothyroids (11).

Anemia is also to be regarded as a factor (11).

It must be concluded that any condition veering from the normal must be looked upon as a possible contributing cause.

How frequent are food allergens significant in producing allergic reactions in comparison to other allergens? Hinnant and Halpin (31) write that among the proteins capable of playing the role of allergens are pollens, foods, serums, animal emanations, products of bacteria and animal parasites. Of these, they believe pollens and foods are most important, and correspondingly food plays a greater part than pollen in the procuction of allergic symptoms. Piness and Miller (46) consider people who are sensitive to food alone are extremely rare. Chaney (16), in 175 cases, reports food to be dominant in the cause of allergic nose and throat symptoms. Rowe (49), in one series of 175 allergic conditions, discovered foods to be the cause in

72%. In another series (52), in 1418 cases of asthma he found by skin test, 57% were positive to food, 49% to pollen, 24% to animal emanation, 23% to house dust and 10% to other inhalants and bacterial products. In 68 cases of perennial hay fever, 30% were positive to foods, 54%to pollens, 26% to dust, 21% to animal emanations and 7% to miscellaneous. In 61 cases of urticaria, 44% were positive to food, 48% to animal emanations, 15% to dust, 15% to pollen and 15% miscellaneous. Urbach, in 500 cases of urticaria determined food as the cause in only 110 cases (30). In 247 cases of headaches and migraine, Rowe reveals 68% were skin positive to food, 45% to inhalants, and 26% to miscellaneous. Eyermann (26), in 181 cases of perennial hay fever detected, by skin testing, 74% were positive to food and inhalants other than food, 20% were positive to food and pollens and other inhalants, and 2% were positive to pollens alone. Osborne, on the other hand emphasizes the importance of contactants and environmental allergens in producing skin manifestations. He found food important in only 15-20% of a large series of cases (30). Ratner (47) also is in accord with the significance of contactants and environmental allergens. He believes the trend at the present is definitely away from the prominence of foods as causing allergic disorders, especially of the dermal type.

Which foods are the most common causes of allergy? Tuft (62) writes that practically any food is capable of procucing a reaction, but the more common offender are: Wheat, eggs, milk, chocalote, tomato, the legumes, patato, fish and meats. Most students of allergy agree that as a rule, the more commonly eaten foods are also the most frequent offenders.

Chaney (16) has a list of common offenders similar to Tufts'. He includes: Wheat, eggs, milk, chocolate, cabbage, tomatoes, oranges, walnuts, strawberries, bananas, white potato, cauliflower, oats, pork, carrots, rice, oysters, salmon, celery and lettuce.

Hughes (34), in the study of 1000 cases of gastro-intestinal allergy, found the most frequent source of disorders to be: Onions, radishes, cooked cabbage, beans, cuccumbers, cooked onions tomatoes, greasy foods, eggs and chocalate. Onions were reported to cause symptoms in as high as 24.5% of these patients, while chocolate caused symptoms in only 3.6-4.9%. He also analyzed these foods in reference to age, discovering but slight variation in their occurrence in the different age groups. Alvarez (2), presents somewhat different results in a series of 700 gastro-intestinal idiosyncrasies. According to his findings, onions again are the most frequent offender, followed by milk, apples, cooked cabbage, chocolate,

radishes, tomatoes, cucumbers, eggs, fats, cantaloupe, beef, strawberries, coffee, lettuce and a great many others which caused symptoms rather infrequently. He estimated that the onion affected about 27% of these patients. Hinnant and Halpin (31), in 30 children with mild and severe cyclic vomiting, established milk, grains, egg, white potato, chocolate, beans, peas, tomatoes, spinach, bananas, apples and oranges to be the usual sources of allergic reactions. In no instance was one food alone responsible. Fries and Zizmor (27), in 20 cases of children with gastro-intestinal manifestations, detected wheat, eggs, milk, chocolate, fish, beef, pork, and nuts to be the common sensitizing agents.

In 500 cases of cutaneous manifestations, Rowe determined wheat, spinach, eggs, milk, celery, squash, string beans, corn, cabbage, tomatoes, cauliflower, white potato, onions, rice, oranges, asparagus, turnip, grapefruit and lettuce to be the usual origin of the sensitizing allergen. Goodman and Sulzberger (30) consider wheat and eggs the cause of the majority of infant food eczemas. Hopkins (33) agrees with this but adds milk, oranges, tomatoes, chocolate, spinach, oats, potatoes and cod to the list. Williamson (68) also lists eggs, wheat and milk as the most important causes of food eczemas. Alvarez (2)

believes urticaria is mainly due to strawberries, tomatoes, eggs, fish and milk. Williamsom accepts eggs and milk are the usual causes of urticaria during childhood, and eggs, pork, fish, shellfish, nuts, tomatoes as the common offenders in adults. Hopkins (33) finds that urticaria of infancy is frequently due to eggs, milk, codfish and tomatoes, and that fish, shellfish, strawberries and nuts often produce it during adolescence. Williamson (68) reports that food causes of angioneurotic edema correspond closely to those involved in urticaria. White (67) discovered the common offenders in acne were chocolate, milk, wheat, oranges tomatoes, and nuts. Williamson lists chocolate, fish, nuts, white bread and salts of bromine and iodine as important in acne. He is of the opinion that white bread is a common source of bromides because of a bakers preparation which changes to bromides during the baking process. The ordinary source of iodides is the iodized salts so commonly used on the table. Williamson found purpura most frequently due to eggs, milk, wheat, chocolate, beef, pork, fish, onions, tomatoes and strawberries. Squier and and Madison (59), in 5 cases, discovered grains, milk and potatoes to be the offenders. Dutton (25), in another case, determined citrus fruits were producing the reaction. Drueck (22) reports shellfish,

salmon, venison, strawberries, coffee, chocolate, salt and spices to be frequent etiological agents of pruritis ani.

Eyermann (26), in 181 cases of vasomotor rhinitis, discovered wheat, eggs, tomatoes, pork and nuts to be the usual source of allergen. Waters (66) is convinced the most common foods producing respiratory disturbances are milk, wheat and eggs; other causes are potatoes, oatmeal chocolate.

Sheldon and Randolph (57), in the study of migraine, by skin testing, established the majority of reactions were due to grains, coffee, peas, celery, berries, onion, peanut, radish, cabbage, cocoa, milk and cream, tomatoes, dates, spinach and corrots. Sippe (58) reports a high percent of reactions to banana, egg white, tea, oatmeal, peas, milk, pineapple, potato and pork. Alvarez (2) finds that the most common cause of migraine is chocolate. Onions, milk, peanuts, cabbage, eggs, pork, apples, cucumbers, meat, oranges and wheat are also frequent offenders.

Sensitivity to more than one food is well known to the allergists. Eyermann (26) believes this to be the rule rather than the exception. Several students believe this may be related to food families and have carried out extensive studies in food families to determine if there is

a common allergen. This might greatly simplify the methods of diagnosis.

Withers (70) (71) studied thirteen food families with a relatively small number of 43 patients. The families are listed in order of frequency of positive skin reactions: 1. The potato-tomato group, which included the egg plant and green pepper proved to have mostly single sensitizations. 2. The cerial family with wheat, rye, corn, oats and rice had very few multiple reaction. 3. The bean group consisted of string beans, navy beans, lima beans, peas and peanuts, and showed multiple sensitivity especially in cases that were sensitive to the string bean. 4. The watermelon group tested with the watermelon, cantaloupe and cucumber. 5. The apricot-peach family, comprised of apricots, plums, cherries, and almonds, indicated sensitivity to the cherry seemed denote multiple sensitivity. 6. The apple-pear family had few multiple reactions but seemed to have a definite relationship to peaches. 7. The orange-lemon family disclosed that sensitivity to lemon seems to indicate multiple sensitivity. 8. The onion family exhibited single reactions as a rule. 9. The walnut-pecan group showed the English and black walnut to be closely related. Other families were the banana, raisin, berry and cab-

bage-turnip group. Withers concluded that if a patient is sensitive to one food of a family, he has an equal chance of being sensitive to other members of the same family, although it does depend somewhat upon which member it is. He also concluded that multiple sensitivity was most likely to occur in the bean-pea, peach-apricot, walnut-pecan and orange-lemon families. Pineas, Miller etc. (45) also have studied food family groups. Piness is convinced that each food has an individual allergen. Tuft (62) considers group reactions as being fairly common.

The factor of selection, preparation etc. of foods has been mentioned in contributing causes of food allergy. A good many of the authors are of the opinion that raw and uncooked foods cause allergic manifestations more commonly than will cooked foods. Malkins and markow (39) compared 632 pairs of tests of extracts from raw and uncooked foods. By skin test, 91% of the tests were equal, 3.9% of the raw extracts reacted positive while the cooked was negative, and 4.3% of the cooked food extract gave positive reactions while the raw extracts were negative. They concluded that heat apparently does not affect the allergenicity of foods.

From the foregoing material, could it be ascertained that certain foods produce specific manifestations?

It seems not. It seems that a good conclusion would be that common article of diet are likely to to be the etiological agents in food allergy.

DIAGNOSIS

Brown (13) feels the big problem of allergy is to get the physicians to recognize the possibility of allergy as a cause or its association with a great number of manifestations. Alvarez (5) alleges that it may well be, that hundreds of persons would be cured and perhaps spared of needless operations if the existence of allergic sensitiveness were recognized and the foods at fault identified.

Vaughan (64) expresses that the methods of diagnosis of food allergy are divided into three epochs. The first consisted of empirical diet lists which were based on experience with food idiosyncrasies. The second was ushered in by the development of the sensitization tests. This at first appeared to be a splendid sterotyped method for determining the appropriate diet in the individual case, but as time went on the enthusiast in skin testing was forced to the conclusion that some foods which definitely disagree would not infrequently fail to give positive cutaneous reactions, and some that gave positive reactions would not be productive of symptoms. So in the third epoch which we now find ourselves, we observe a combination of the methods of the first two. This brings up the question of what are the methods of diagnosis and of what value are they?

In general, the allergists choose a combination of history, skin tests, diets, and leukopenic index, in the diagnosis of food allergy. Different authors emphasize the value of certain methods, depending upon the one they are most enthusiastic about.

Most authors are of the definite opinion that good histories are indispensable in the diagnosis of food allergy. Rowe (52) believes that every history should be taken with the possibility of all types in mind. The history of any of the symptoms which are frequently due to food allergy should suggest food sensitization. In addition, history of inhalant, contact or drug allergy should suggest concomitant food allergy. History of food dislikes are often helpful because these are often due to idiosyncrosies (49). Moore (42) feels that dislikes to foods are important but must be carefully evaluated because many factors may bring on dislikes. If the dislike is constant no matter how prepared then it must be seriously considered. He found patients with urticaria presented the largest number of food dislikes, also that food experiences increase with age. Vaughan and Pipes (65) studied the likes and dislikes of foods in a large series of cases and discovered that 80% of persons, allergic or non-allergic, have one or several

food dislikes. Among the allergic individuals, 12.7% of foods mentioned as disliked gave positive or borderline skin reactions. They thus concluded that dislikes to foods cannot be relied upon as an indication of allergic sensitization. In gastro-intestinal symptoms they found a closer relationship to dislikes and idiosyncrasies. Rowe (52) states that the tendency to inherit the propensity to develop allergy of any type and even specific manifestations such as asthma, eczema or migraine, and occasionally to become allergic to specific foods or other allergens must be remembered. Karlstrom, Cutts and Stoesser (35) present a history form which they suggest to be used in the diagnosis of allergy in the child. This seems to be a satisfactory form to follow in all allergies. They use the following form:

1. Present Illness

   Time of year: Seasonal pollens and foods

   Symptoms:

2. Past History

   Infancy: Eczema, food disagreements

   Childhood: Cyclic vomitting, eczema, caryza, hay fever, asthma, urticaria, gastro-intestinal allergy purpura etc.

3. History of Systems

Head: headaches

Scalp: itching

Eyes: itching and burning

Ears: itching

Nose: blocking, itching, discharge

Mouth and throat: canker sores, dryness, irritation

Chest: dyspnea, chronic cough, expectoration

Heart: tachycardia

Gastro-intestinal: constipation, diarrhea, abdominal distress, nausea and vomitting

Genito-urinary: bladder distress

Catamenia: irregularity, pain

Bones and Joints: pain

Nervous: irritability, depression

Skin: location of lesion, characteristic lesion, pruritis

Weight:

Operations: especially nose and throat

the diagnostic program (52). He, and many others, feel that foods giving positive reactions must be tested by diet trial to determine the true role. Alvarez (2) feels that skin sensitivity tests are often useless in finding offending foods in gastro-intestinal allergy and headaches, but is of more value in finding the cause of asthma, hay fever and eczema (1). Waters (66) is of a similar impression by accepting that skin tests are often of value in people with inhalant sensitivity, but cannot be relied upon in determining foods that cause clinical sensitivity. Clein (17) stipulates that experience has taught us that more than half of allergic children between three to ten years of age do not have clinical symptoms due to foods, despite positive skin reactions. Brown (13) believes skin tests are often essential to discover offending agents. However, especially with food allergy, they cannot be absolutely depended upon. In some cases they may give a basis useful for diet trials. He advises that skin tests should not be relied upon unless they can be carried out in an exhaustive manner. Chaney (16) feels that the reason skin tests usually are not reliable is because not enough are applied. Piness, Miller etc. (45) feel that the skin test is very reliable if properly carried

out. They conclude that regardless of age, heredity, age of onset and duration of symptoms, 80% of allergic patients should give positive reactions. 70% should be positive to foods and results lower than this may be traced to promiscuous testing of non-allergies, unreliable proteins, lack of persistence and completeness, insufficiency of testing, reading and correlation.

The two methods of skin testing that are commonly employed are the intracutaneous and the scratch method. Cooke, in 1911, was the first to employ the intradermal method (9). Again, there is general disagreement as to the actual value of these techniques. Belgrade (9) feels that the intracutaneous method is much more sensitive and somewhat more reliable than the scratch technique. In the study of 50 cases, comparing intracutaneous and scratch methods, 16% of the cases had no reactions to the intracutaneous injection, while 58% had no reaction to the same allergens by the scratch method. Rowe (50) believes that more reactions are obtained by the intradermal injections than with the scratch test, but the reactions are often false and unreliable. Belgrade (9) reports that non-specific reactions often occur with the intracutaneous method. Hinnant and Halpin (30) feel this to be the most satisfactory method. Sippe (58) is of a similar opinion. This test should never be used before the

scratch method is used because of severe shock that may be produced. It is also more difficult to perform and more painful to the patient (9).

Another method, termed the passive transfer test, is performed by the injection of sera of the sensitive patient into a non-sensitive patient, followed by the application of skin tests (71). This method would be used in cases where skin test is impossible or difficult by direct method (62). The basis of this type of reaction is the transfer of the specific antibody from one person to another (37). Withers (71) in the study of a series of passive transfer tests concluded that sera does not necessarily contain a reagin to skin or clinical sensitiveness. He also found that the passive transfer of pollen reagins was easier to obtain than food reagins. This seems to correspond to the direct skin sensitivity tests.

In reading skin reactions, Belgrade (9) defines a positive reaction as being a distinct wheal surrounded by an area of erythema, in the presence of a negative control test. The wheal should be irregular in outline, an and the edges should never be sharply defined. This irregularity is produced by edema spreading along the lymph spaces. Immediate reactions occur within a few minutes with the intradermal test (not later than 20

minutes), and within 10 to 30 minutes with the scratch method. As a rule, positive reactions persist from one to 24 hours. The traumatic and non-specific protein reactions disappear within that time, thereby permitting a more accurate reading. A doubtful reaction consists of an area of erythema .5 centimeters in diameter. A delayed reaction consists of a zone of erythema at the site of innoculations resembling a beginning infection. A negative reaction with either method of skin testing does not differ in anyway from the control test.

Occasionally difficulties arise in reading reactions. In patients with dermatographia, the reading is particularly difficult, for controls may as well give positive wheals. In these, it is best to delay the reading about one hour. During that time the element of trauma disappears. Iodides and bromides also seem to affect the reactions. The site of testing also produces variable results. The skin of the back seems uniformly sensitive, while on the arm, the skin near the elbow is more sensitive than that at the wrist (9).

Generally speaking, there are two main methods of diet used in the diagnosis of food allergy. These are the elimination diets and the diet diary methods. Brown in 1922 was the first to report a diet trial, Rowe later dilated on this method and called it the elimination diet (4).

The elimination diet depends upon reducing the possibilities of the cause by placing the patient on a limited number of foods which seldom cause trouble even in highly sensitive people (1). Alvarez (11) (4) recommends a diet of lamb, rice, butter, sugar and canned pears to start on. Other foods which are known to be safe may also be added to this list. This diet should give relief from symptoms by four days. If it does not foods may be cut out all together for about two days. If no relief is then obtained, then foods may be ruled out as the cause of the allergy. After symptoms have definitely disappeared then one new food may be added each day or two. Alvarez (4) finds foods which can be added to his above starting group without much danger are: beef, potato, gelatin, carrots, turnips, asparagus, string beans, arrowroot cookies, rye krisp, toast and oatmeal. Later the more common offending foods may be added. He often finds which cause symptoms, if eaten in moderation, often do not cause discomfort.

Rowe (52) (49) has four lists of diets which he feels contain foods that ordinarily do not cause sensitiveness. He feels these diet trials are next to histories in importance in diagnosis. The diets are:

I	II
rice tapioca	corn rye
rice biscuit rice bread	corn pone
lettuce spinach carrot artichoke	corn rye muffins rye bread rye krisp tomato
lamb	squash asparagus string beans
lemon grapefruit	chicken
pears	pineapple peaches apricot prunes
cane sugar gelatin	cane sugar Masola oil Wesson oil
wesson oil olive oil pear butter	salt
salt syrup made of maple or cane sugar flavored with mapliend or maple sugar	Karo gelatin

III	IV
tapioca	milk
white and sweet potato	
lima bean potato bread soy bean, lima bean bread	
beets carrots	
lima beans	
tomatoes	
beef bacon	
lemon grapefruit peaches apricots	
cane sugar	
olive oil Wesson oil	
gelatin	
salt	
olives	
maple sugar or syrup made with cane sugar flavored with maple	

2. List of foods rarely causing allergies:

1. lamb	11. string beans
2. chicken	12. pears
3. butter	13. pineapple juice
4. cane sugar	14. beets
5. tea	15. asparagus
6. corn	16. sweet potato
7. barley	17. egg plant
8. arrowroot	18. turnips
9. tapioca	19. parsnip
10. lima beans	20. pumpkins

3. List of foods frequently causing allergy:

1. wheat	11. white potato
2. eggs	12. cauliflower
3. milk	13. oats
4. chocolate	14. pork
5. cabbage	15. carrots
6. tomatoes	16. rice
7. oranges	17. oysters
8. walnuts	18. salmon
9. strawberries	19. celery
10. bananas	20. lettuce

4. List of foods the patient thinks cause him trouble.

5. List of foods to which patient is positive by skin test.

The ultimate aim is to get patient on diet of list number one. He starts out with a diet consisting of list one minus lists four and five. This diet is used for ten to fourteen days. If the symptoms are reduced, then foods from list number two, and later from list one which are not in list four and five are added. He advises the addition of one new food in large amounts, every three days. Another plan is to use list number one minus list four. If relief is obtained, add foods in list one minus those in list four. His third plan is the diary method.

The other system of diet, used in diagnosis, is the food diary method. In this system the patient marks down the unusual foods eaten in the twenty-four hours before the upset. Most suspicion should fall on foods of the previous meal, since most reactions occur within a few hours after ingestion (4). This technique is usable only in cases where attacks come on at intervals of weeks or months. It would be of no value where the symptoms are continuous and if the offending agent is eaten daily (64). The diary method may prove to be very strenuous. It needs very good cooperation from the patient (16).

The leukopenic-index, a hematologic response, used by some as a method of diagnosis was first discovered by Vaughan in 1934 (21). He developed the original technique

of taking two leucocyte counts at ten minute intervals before ingestion of the allergen. Counts were taken at 15 minute intervals for one hour and the final count taken at 90 minutes. A fall of 1000 or more is considered positive. Rinkel modified this technique in 1935 and his mithod is now used by most allergists who are enthusiastic about this test. Rinkel recommended rest, prohibited smoking and unnecessary conversation and the avoidance of unnatural disturbance previous to the test. Loveless, Darfman and Dawning (38) used a technique of no food for twelve hours, no alcoholic beverages, adrenalin or exertion before the test. Thirty minutes of relaxed sitting before the test was required. Three fasting counts were taken at twenty minute intervals and three post-pandrial counts at twenty, forty and seventy minute intervals. They found variations only in those patients who developed explosive symptoms during the seventy minutes that post-pandrial tests were taken. They concluded no blood count was needed for diagnosis in these cases. Brown and Wadsworth (10), in the study of a series of over 2000 leucocyte counts, found no justification for the use of the leucopenic index. Theyfound no adequate proof for the existence of an anaphylactic post-pandrial leucopenia. Squier and Madison (60), in the study of 200 cases, found a hematologic response in 102 cases, questionable in four

and negative in 94 cases. They believe that the hematologic response is a definite aid in allergic diagnosis but feel it should be used only to supplement the usual methods of skin tests. They also studied eosinophilia in relation to the leukopenic index and discovered that an increase in eosinophils in the circulating blood occurs as constantly as does the reduction of total leucocytes after the ingestion of allergenic foods. They are convinced that simultaneous counting of both eosinophilis and leucocytes materially increases the diagnostic accuracy of the leucopenic index. Denny (21) believes it has a definite place in the study of food allergy. He feels it must be made under proper conditions and an accurate proceedure must be emphasized. Alvarez (1) considers it too expensive and time consuming and also too difficult to perform. Chaney (16) and Sippe (58) believe it to be of very little practical value. Gay (28) believes it is very valuable.

In gastro-intestinal manifestations, several men have in isolated cases, found x-ray to be of some value. Eyermann, in 1927, described a disharmonic colon with areas of hypo and hypertonicity (29) (43). Rowe, in 1933, demonstrated gastric retention arising from pylorospasm due to food allergy. Gay (29) reports a case of

incomplete canalization, with spasticity of the colon, and intolerance in the splenic flexure to barium, with a distinct visualization of this portion of the colon due to thickening from edema. A film taken four weeks later revealed a very normal colon. The use of x-ray is very much limited and probably mostly of accidental value.

Generally speaking, there are about four important points to consider in the diagnosis of food allergy:

1. Rule out organic diseases
2. Establish the allergic state
3. Sum up the individual as a whole, evaluate the predisposing and contributing causes
4. Employment of methods of diagnosis best suited to physician or to patient.

TREATMENT

Treatment and diagnosis are closely interrelated and many of the problems of treatment have been discussed in the diagnosis. Rowe (51) states that the problem of the physician in the treatment of food allergy is to place the patient on a satisfying and appetizing diet from foods which are not productive of evident sensitization. The menu should be comparable to meals ordinarily taken so the treatment will not become too monotonous. Undersirable weight loss, protein, vitamin and mineral deficiencies must be avoided. In some cases, to prevent this, it may be better to suffer from the effects of actual or possible allergenic foods than to develop increasing invalidism through nutritional deficiencies. The treatment, in general, of course consists of removing the specific food allergen, eliminating the contributing causes and the treatment of the symptoms.

The removal of the offending food allergen is accomplished by avoiding the food entirely and perhaps bringing about desensitization, or by employing desensitizing proceedures. Brown (13) states that unnecessary and unusual foods are easily avoided, but foods common and necessary to the diet furnishes an difficult problem. Rowe (52) is convinced that the offending allergenic foods must be

excluded entirely and the tolerance to it must not be tested oftener than every four to six months. He finds that tolerance to an offending food may return in a few weeks or it may never return. Sippe (58) believes that sensitizing foods if taken in small amounts, often do not cause harmful results. If the elimination diet is quite limited, Alvarez (2) adds uncommon offenders as rapidly as possible. A number of uncommon offenders and their method of addition were discussed in diets of diagnosis. All of the authors are in accord that chemical therapy should replace the deficiency of a limited elimination diet. If other types of sensitizations are participating in the production of allergic disturbances, then the problem becomes very complex. If the offender is a common article of diet, then desensitization should be attempted.

Rowe (53) sums up the methods by which desensitization may be accomplished in the following manner:

1. The elimination of foods from the diet. the various foods to be ommitted may be determined by the different methods of diagnosis already discussed. He is of the opinion that desensitization by this method may not occur and when it does is rarely complete.

2. Oral desensitization. Schloss first reported success by this method in 1912. In 1920, he reported 12 patients who had been desensitized from three to seven years to specific foods in this manner. Rowe feels that this method has been disappointing to most allergists. Keaton, Waters and Hopkins (36) reports a study of 50 cases, mostly children with eczema. They started with an initial dose of about one milligram of protein. Eggs required less. The protein content was increased every four of five days so at the end of a few months the patient was eating, without ill effects, a normal daily portion. If a recurrence of symptoms occurred during treatment, then the dilution was dropped. back to that used twelve to sixteen days previously. All proteins were diluted with water. The most difficulty was encountered in desensitizing to eggs. They concluded that this was an effective, inexpensive method which can be carried out in the home.

3. Hypodermic desensitization. This method is the same as with pollen extracts. The initial dose is .1 cubic centimeter of a dilution which just fails to produce a skin reaction. Results from such desensitizations have been negligible. Cooke and Racheman are of a few who have reported some success by this method.

4. Peptone therapy. This method was first reported by Lambert, Aucel and others. They found the ingestion of a small amount of a food drug or peptone one hour before mealtime prevented a subsequent allergic reaction. Richet and Urbach suggested the use of specific peptones (propeptans), prepared from the causative foods and given in one half to one drachm doses, in tablet form, one hour before the meal at which these foods are taken (62). Markins (40) reports some success with propetan therapy. The acceptance of this therapy awaits clinical verification.

5. Denaturization of foods. Some authors feel that heating of foods modifies the protein molecules so that its allergic response is prevented. This factor was discussed predisposing and contributing causes of food allergy. Rowe and others (39) find this method to be lacking.

6. General measures. The use of calcium, quartz light, vitamin therapy, non-specific protein therapy and autohemotherapy for the reduction of allergic reactions are of no definite value.

McGee (41) in discussing the management of the allergic child makes a statement to the affect that the treatment really begins with conception. This is

because of the intra-uterine sensitivity which may develop (47). He is of the opinion , since milk and eggs are the foremost causes of food allergy in infancy, it seems reasonable to suggest to the mother to boil the milk consumed in the later months of pregnency and to avoid an excess of eggs. During the first three days of life when the gastro-intestinal tract is most permiable, cows milk should be avoided. New foods should be introduced only one at a time. Foods which are regurgitated often, should be discontinued. He believes too early introduction of fruits and vegetables is apt to encourage allergic disorders. It seems the mother should also avoid excesses during the nursing period.

Contributing causes have been discussed in etiology, and most certainly they must treated as they are found. The most important ones to be combatted probably are hypoendocrinism, especially hypothyroidism, anemia, digestive inadequacy, foci of infection, and organic diseases. Nervousness, strain etc. must also be considered.

Brown (13) sums up the situation of treatment rather adequately by listing twenty principles of diet, applicable in the treatment of food allergy:

1. One must not eat too much of a food or all foods at anymeal, or of any one food in successive meals.

2. Food must be eaten slowly and must be thoroughly masticated.

3. The various foods of any one classification of food should be alternately used.

4. Do not eat when extremely tired or nervous.

5. Where a person can have but a limited number of foods, it is well to experiment with cooking for three or four hours.

6. One with inadequate digestive juices should take hydrochloric acid and pepsin. Pancreatic extracts have been found to supplement other digestants and may need be added in all or certain cases. Oelgoetz etc. (44) emphasizes the importance of pancreatic enzymes. It seems that liver inadequacy should also be considered here. The mention of liver insufficiency is mentioned but few times although Hinnant and Halpin (31) and Laroche, Richet, and Saint Gerons, quoted by Tuft(62) believe that liver inadequacy is instrumental in the mechanism of producing food allergy.

7. Foods taken from plants, trees or other original sources and kept so they undergo chemical change are more apt to produce difficulties.

8. Eat three or more meals at regular hours.

9. When on has an attack he should attempt to place the blame for it upon certain foods. This may establish a diagnosis.

10. If the diet is limited, vitamins should be added. It seems that minerals should also be included, especially calcium in the elimination of milk, and iron to combat anemia.

11. Constipation should be treated with large amounts of fluid in the morning upon arising.

12. Food addition methods should have a careful trial.

13. Food tests should be made by competent allergists if no reasonable prompt response is obtained by food trial.

14. Allergenic foods must absolutely be eliminated from the diet.

15. Strict adherence to the elimination of the reacting foods aver a sufficient period may permit them to be eaten without penalty.

16. Anemia should be thoroughly treated.

17. Bacterial foci should be eliminated.

18. Bacterial vaccines, preferrably autogenous, but made from the organism to which patient gives a positive skin test, offer hope of benefit.

19. Pollens, contactants and other substances to patient reacts to should be added to the vaccine.

20. Treatment should be followed persistently no matter how aggravated the case continues.

Since the clinical manifestations of food allergy are so varied, the type of symptomatic treatment will depend on the type of manifestation present. This would include ordinary hygienic measures to promote the general well being of the patients. Drugs would be used as indicated(62).

The prognosis of food allergy probably depends upon the number of elements involved in producing it. Cooke (15) believes that the allergic group, as a whole, represent an ingrained constitutional defect. These individuals are likely to have recurrences as well as different clinical varieties, which may reappear at any time of life. The evidence of allergy may be controlled by avoidance of the exciting agent, the sensitization is not actually cured and it may reappear in some other form and may be due to some other allergen. This represents the ultimate prognosis of the allergic. The immediate prognosis of treatment is no doubt influenced largely by the complexity of the problem. Rowe (49) feels that when other types of sensitization are participating in the production of allergic disturbances, the problem may become one of the most complicated in medical practice. If the number of

sensitizing foods are few the problem will be relatively simple. The difficulties increase with the number of food sensitivities and the number of contributing and predisposing causes. Most authors report rather favorable immediate results in a large percentage of their cases. Sippe (58), in 105 cases of migraine, secured complete relief in 61% and had complete failure in 15.2%. He found that the nervous type of patient did not do well. Sheldon and Randolph (57), in 127 cases of migraine, established definite relief in 66%. A higher percent of relief was secured in women than men. In both of these studies, elimination diets were used. Chaney (16), in treating 100 cases of food allergy, was successful in all but 2 cases. He attributed failures to lack of cooperation, lack of income and to conditions where it was impossible to remove the excitant. He also discovered that pollen therapy alone produced poor results, but along with elimination of foods, the results were good. Hinnant and Halpin (31), in 21 cases of cyclic vomiting, obtained complete relief of symptoms in 76%. 24% showed improvement although 18% failed to cooperate fully. Gay (28), in 20 cases of essential hypertension, secured complete relief in all but one case. Schwarz and smith, in 35 cases of

dysmenorrhea, established complete relie in 20 cases and partial relief in 9. 2 of these cases received partial relief on thyroid extract alone. All of the above men used the elimination diet. Brown (14) finds that as a rule, early cases of food allergy often clear up with astonishing promptness, those of long standing clear up slowly and must have their treatment followed up for a long time.

It seems that the best results in treatment are obtained by complete elimination of allergenic food from the diet. The ultimate prognosis is not good.

BIBLIOGRAPHY

1. Alvarez, W. A.: What is new in the field of food sensitiveness. Minn. Med. 22: 92, Feb.,1939.

2. Alvarez, W. A., and Hinshaw, .: Foods that commonly disagree with people. J. A. M. A., 104: 2053, June, 1935.

3. Alvarez, W. A., and Hinshaw, .: Foods that some people cannot eat. Hosp. Management, 39: 44, April, 1935.

4. Alvarez, W. A.: Ways of discovering foods that are causing distress. Proc. of Staff Meet. Mayo Clinic, 12: 88, Feb., 1937.

5. Alvarez, W. A.: Food sensitiveness and conditions which may be confused with it. Med. Clin. of N. Am., 12: 1589, May, 1929.

6. Alvarez, W. A.: Ways of discovering foods that are causing indigestion. Review of Gastroenterology, 1: 13, March, 1934.

7. Alvarez, W. A.: Which are indigestible foods? Journal-Lancet, 52: 573, Oct.,1932.

8. Baer, H.: Dermatitis due to analine dye in food products. J. A. M. A., 103: 10, July, 1934.

9. Belgrade, J. F.: Intradermal and cutaneous methods of testing in food allergy. Arch. of Derm. and Syph., 27: 206, Feb., 1933.

10. Brown, E. A., and Wadsworth, G. P.: The leukopenic index. J. of Allergy, 9: 345, May, 1938.

11. Brown, O. H.: Resume of the literature. Southwestern med., 18: 109, April, 1934.

12. Brown, O. H.: Theory, etiology, symptoms and treatment of food sensitization. Southwestern Med. J., 12: 388, Sept., 1928.

13. Brown, O. H.: What every physician should know about allergy. Southwestern Med. J., 21: 14, Jan.,1937.

14. Brown, O.H.: Sucessful treatment of eczema, angio-neurotic edema, urticaria, pruritus etc. by dietary regulation and digestants. Southwestern Med. J. 15: 261, June, 1931.

15. Cecil, R. L.: 1939, Textbook of Medicine, W. B. Saunders Co., Philadelphia and London, pp. 500-506.

16. Chaney, W. C.: How is the general practitioner to diagnose food idiosyncrasies. Miss. Doctor, 15: 68, Feb., 1938.

17. Clein, N. W.: Allergy in infants. Significance of first allergic manifestations. Northwest Med. 138: 9, 1939.

18. Cohen, A. I.: Allergy and relation to sinusitis and allied nasal conditions. Arch. of O. R. L., 21: 265, Mar., 1935.

19. Cohen, M. B., and Friednar, S.: Scorings in the long bones as a guide in management of food allergy in children. J. of Allergy, 9: 54, Nov., 1937.

20. Deamer, W. C.: Allergic diseases in childhood. J. of Allergy, 10: 605, Sept., 1939.

21. Denner, E. R.: The value of the leukopenic index in allergic diseases. J. Okla. M. A., 30: 202, June, 1937.

22. Drueck, C. J.: Pruritus ani and perinei. Urol. and Cutan. Review, 39: 490, July, 1935.

23. Duke, W. W.: Food allergy as a cause of irritable bladder. Southern M. J. 16: 776, Oct., 1923.

24. Duke, W. W.: Menier's Syndrome caused by allergy. J. A. M. A., 81: 2179, Dec., 1923.

25. Dutton, L. O.: Thrombocytopenic purpura. J. A. M. A., 111: 1920, Nov., 1938.

26. Eyermann, C. H.: Food allergy as a cause of vasomotor rhinitis. Southern M. J., 31: 210, Feb., 1938.

27. Fries, J. H., and Zizmor, J.: Gastro-intestinal allergy in children. Clinical reactions resulting from ingested foods. J. of Ped., 16: 69, Jan., 1940.

28. Gay, L. P.: Food allergy in internal medicine with special reference to paroxysmal tachycardia and essential hypertension. J. of Missouri M. A., 34: 332, Sept., 1937.

29. Gay, L. P.: Radiological demonstration of an allergic reaction in mucosa and musculature of the colon. Am. J. of Dig. Dis. and Nut., 3: 131, May, 1936.

30. Goodman, J. and Sulzberger, M. B.: Allergy in dermatology. J. of Allergy, 10: 481, July, 1939.

31. Hinnant, I. M. and Halpin, L. J.: Food allergy in mild and severe cyclic vomiting. M. Clinic N. Am., 19: 1931, May, 1936.

32. Hollander, E.: Mucous colitis due to food allergy. Am. J. of Med. Sc., 174: 495, Oct., 1937.

33. Hopkins, J. G.: The role of food allergy in diseases of the skin. New York State M. J., 38: 23, Jan., 1938.

34. Hughes, O.: Foods that disagree with healthy people. J. Am. Dietet. A., 12: 314, Nov., 1936.

35. Karlstrom, A. E., Cutts, R. E., and Stoesser, A. V.: An outline for diagnosis and treatment of allergic diseases. Arch. of Ped., 55: 233, April, 1938.

36. Keaton, B. M., Waters, I., and Hopkins, J. G.: Oral desensitization to common foods. J. of Allergy, 6: 431, July, 1935.

37. Lippard, V. W., and Schmidt, W. M.: Human passive transfer antibody. IV. Studies in children hypersensitive to foods. Am. J. of Dis. of Children, 56: 797, 1938.

38. Loveless, M., Dorgman, R., and Downing, L.: A statistical evaluation of the leukopenic index in allergy. J. of Allergy, 9: 321, May, 1938.

39. Malkins, G. I., and Markow, H.: An analysis of the comparative results of skin testing with cooked and uncooked foods. J. of Allergy, 10: 337, May, 1939.

40. Markin, J. M.: The propeptan therapy of Luithlen-Urbach in the treatment of allergic skin diseases caused by food. New York State J. of M., 32: 390, April, 1932.

41. McGee, W. A.: Allergy in childhood, prophylaxis, early recognition and treatment. J. A. M. A., 111: 1551, 1933.

42. Moore, M. W.: Food history and skin sensitivity. Northwest M., 37: 12, Jan., 1938.

43. Moore, M. W.: Gastro-intestinal allergy, points to consider in diagnosis. Northwest M., 34: 200, June, 1935.

44. Oelgoetz, A. W., Oelgoetz, P. A., and Wittekind, J.: Etiology and treatment of food allergy. Southwestern M., 20: 463, Dec., 1936.

45. Piness, G., Miller, H., Carnahan, H., Altose, A., and Hawes, R.: Relationships between foods as shown by skin testing in 1000 children. J. of Allergy, 11: 251, Mar., 1940.

46. Piness, G., and Miller,H.: Skin tests in 4589 cases of allergic diseases, with a criticism concerning elimination diets. J. of Allergy, 4: 18, Nov., 1932.

47. Ratner, B.: Allergy in children, its onset and natural progress. J. A. M. A., 111: 2346. 1938.

48. Ratner, B.: Does heredity play a role in pathogenisis of allergy? J. of Allergy, 8: 273, Mar., 1937.

49. Rowe, A. H.: Food allergy, its manifestations, diagnosis and treatment. J. A. M. A., 91: 1623, Nov.,1928.

50. Rowe, A. H.: The elimination diet in the diagnosis and treatment of food allergy. J. Am. Diet. Ass., 16: 193, Mar., 1940.

51. Rowe, A. H.: The dietary problem of the food sensitive patient. Am J. of Dig. Dis. and Nut., 4: 737, Feb., 1938.

52. Rowe, A. H.: Food allergy: A common problem in practice. Southern M. J., 28: 261, Mar., 1935.

66. Waters, W. C.: Respiratory disturbances due to food allergies. J. M. A. of Georgia, 24: 86, Mar., 1935.

67. White, C.: Acneform eruptions of the face. The etiologic importance of specific foods. J. A. M. A., 103: 1277, Oct., 1934.

68. Williamson, G. S.: The role of dietetics in dermatology, including a discussion of cutaneous manifestations in food allergy. Canad. M. J., 40: 470, May, 1939.

69. Wirley, G.: Allergy and other factors in angina pectoris. Southern M. J., 28: 1156, Dec., 1935.

70. Withers, O. R.: Food allergens: Statistical analysis of 43 cases relative to genetic classification of foods. Southern M. J., 30: 918, Sept., 1937.

71. Withers, O. R.: Food allergens, atopic reagins and botanical classification of foods. J. of Allergy, 10: 105, Jan., 1939.

72. Wooton, W. T.: The role of allergy in arthritis. J. Ark. M. Soc., 32: 119, Jan., 1939.