ALLERGY IN CHILDREN

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We wish to report our observations in a study of 203 cases of clinical allergy in children whose ages varied between 8 months and 15 years. These patients were seen in the Department of Allergy from January 1, 1934, to November, 1935. Although follow-up observations have not been obtained in a small number of these patients and another group has been under allergy control for too brief a time to evaluate the results of therapy, these cases have been included because of points of interest in the histories and clinical findings.

THE APPROACH TO THE STUDY OF THE ALLERGIC PATIENT

The allergic states have been classified with a view to presenting the outstanding clinical features of each problem. Allergic manifestations are numerous, due to the diversified phenomena occurring in many organs, and the fact that the majority of patients present multiple evidences of an allergic condition. We classified our cases in three groups—respiratory allergy, gastro-intestinal allergy and cutaneous allergy, and attempted to establish a working plan for the diagnosis of definite clinical states.

The approach to the diagnosis of an allergic state can be followed in a very definite manner.

PERSONAL HISTORY—FAMILY HISTORY—ALLIED CONDITIONS

One cannot help but feel that the clinical history is the most important of all the procedures in the diagnostic survey. Through this, one may first obtain knowledge as to whether or not the patient is an allergic individual. Such information is strengthened by a close inquiry regarding a family history of allergy, and in a large percentage of our cases, a family history has been elicited through persistent effort, interest and coöperation of the patient. The history must be very complete, not only in regard to the suspected allergic state, but any condition of the system that may alter the patient's state from that of normal. Failure to evaluate the importance of associated disorders results in poor clinical relief; this is particularly true in the presence of metabolic disorders, glandular dysfunction, focal or systemic infections. In taking the history, emphasis must be placed not only on environmental factors, dietary habits and modes of living, but inquiry must also be made regarding the ingestion of unsuspected, apparently harmless medication.

PHYSICAL EXAMINATION

In our cases, a complete physical examination is made routinely This consumes only a short time and occasionally some further light is

thrown on the problem. Special examination can be advised only after a complete history has been taken and a physical examination has been made. The laboratory procedures we employ routinely are a Wassermann test, estimation of the blood sugar, complete blood counts and urinalysis. Other tests are made which are indicated by the history and physical examination. If there is any evidence of the presence of an infection, a red blood cell sedimentation rate is indicated. This often gives further clues as to whether a low-grade infectious process is present or one that is due simply to a hypersensitive reaction. In cases of bronchial asthma, a nose and throat examination, and a roentgenogram of the chest are always indicated. Often, we find that a hay fever patient apparently is completely immunized against the suspected allergen, but has symptoms which are influenced by mechanical barriers such as a markedly deflected septum, a spur or polyp, or an old sinus infection. We do not concur with the opinion of many workers in the field of allergy that correction of these conditions should not be carried out, but we believe that mechanical defects in the nose and throat can prevent satisfactory clinical results. It is obvious that the patient must be assured of coöperation between the allergist and the otolaryngologist. When the clinical history indicates disorders of metabolism, the basal metabolic rate should be determined. In patients with migraine and gastro-intestinal disturbances or in the more rare genito-urinary problems, a more complete study is indicated. We do not feel that a diagnosis of allergy should be established in any case until the possibility of organic lesions has been excluded.

Tests for Allergy

From the foregoing discussion, it is obvious that we consider allergy tests as only part of the investigation of the patient's problem. *Each patient must be individualized.* It should not be inferred that tests are carried out in an incomplete manner, but several methods of testing may necessarily be used in the same patient. In the majority of patients, the scratch method is employed first, but if sufficient information is not obtained, or if the clinical history cannot be correlated with the results of the tests, further testing by the intracutaneous method is indicated. The intracutaneous method is that used by the majority of allergists today. The passive transfer method has not gained popular approval as a common procedure, but the indications for its use are many: in children in whom the physical and mental shock from direct testing is great, in patients with eczema where lichenification of the cutaneous surfaces is so marked as to render sites for testing unsatisfactory, in the acutely ill patient, and in cases where a hypersensitive reaction of the skin is noted to every substance applied, as demonstrated in some

cases of urticaria. We have used the passive transfer method on an average of one or two allergy problems daily, and we consider our clinical results to be more satisfactory than those secured by direct methods of testing.

Through these three methods of testing—scratch, intracutaneous and passive transfer—allergens can be identified in the majority of cases with consequent good clinical results. In conditions such as migraine, gastro-intestinal allergy, cutaneous lesions and less frequently the ocular and respiratory conditions where food allergy is suspected, and when skin tests have failed to give satisfactory results, further methods of investigation are employed. The digestive leukocyte response, the elimination or trial diet and food diary lend further aid in the diagnostic survey. Emphasis should be placed upon the necessity of patch testing with ingredients of proposed local medication, this being particularly important in cutaneous and ocular allergy. Not infrequently, patients have returned with an involvement which was more severe than that prior to admission, and this was due to a hypersensitive reaction to drugs used locally.

Routine testing with bacterial vaccines often throws light upon a patient's problem, particularly where chronic focal infection is encountered or has been removed. Included in the allergy tests are bacterial vaccines of standard type, such as the strains of streptococcus, staphylococcus, micrococcus catarrhalis, influenzal and the gonococcus filtrates. Routine tuberculin tests are also done with the Mantoux method in any patient where tuberculin sensitivity is suspected. The tests are made with strengths of 1:100,000, 1:10,000, 1:1,000 and 1:100 as is indicated in each individual case.

After taking the allergic patient's history, making the physical examination, laboratory tests, and allergy tests so that we have available information as to the causes of his symptoms, only 50 per cent of the problem has been solved. In our experience, the greatest cause for failure to obtain reasonable clinical success in patients who are definitely allergic is not due entirely to inadequate investigation, but to the failure of the physician to convey to the patient the understanding of allergic reactions, of allergenic substances and what is to be done about them. This phase of the program demands time and detail on the part of both the patient and the physician. The patient should be acquainted with the fact that his problem has been covered from every viewpoint, and we have made a policy of giving not only complete verbal instructions to the patient, attempting to educate him in regard to the meaning and procedure of allergic study and thought, but also to give complete written instructions. A satisfactory allergy regimen and control can-

not be accomplished unless this policy is strictly adhered to. The average time required for instructing patients is more than that consumed in taking the history and making the physical examination.

Allergens which Can Be Avoided or Eliminated

As a rule, common inhalants with the exception of pollens can be avoided unless the patient is extremely sensitive, and in such instances one must resort to further measures.

In regard to the diet—only simple elimination is necessary, and this is particularly true of every patient, whether he be an adult or a child. In substitutions in the diet, special attention must be given to assure a diet that is both adequate and nutritious. We employ not only the physician's knowledge of this, but also the assistance of our Dietetic Department. In these patients, added vitamins A, B, and D and calcium are of distinct value, not only because they insure against disturbance of diet where major foods are removed, but some beneficial influence to the general physical well being may be derived. The length of time that foods must be avoided in the diet is dependent upon the individual patient and his symptoms. It is reasonable to state that no food which has definitely been proven to be the specific factor should be returned to the diet in less than six months. The program to be followed in each particular case can be determined only by experience.

Allergens which Cannot Be Avoided or Eliminated

Sensitivity to pollens of trees, grasses, weeds and occasionally to pollens of flowering plants necessitate desensitization. It is recognized that pollen hay fever or asthma or infrequently encountered conditions due to pollen sensitivity can be adequately treated by the perennial method of desensitization. It is necessary to have a thorough knowledge of the patient's problem and to continue therapy over a length of time sufficient to render the patient immune to the offending substances.

House dust sensitivity in a number of cases, particularly in chronic respiratory and ocular conditions, demands special consideration. We do not advise house dust desensitization in many patients, but those who are treated obtain good clinical relief. The necessity of desensitizing the patient to house dust can be determined by eliciting a careful history of symptoms on exposure to dust and by judging the degree of skin reaction to house dust antigen.

Occasionally, we encounter allergic patients with ocular, respiratory and cutaneous conditions which require desensitization to one or more of the inhalants—orris root, feathers, animal hairs, silk, kapok and cottonseed. We have used this therapy in several instances and have obtained consistently good results. One point concerning desensitiza-

tion therapy which should be emphasized is that symptoms or signs of too great local reaction should be avoided and certainly any symptoms or signs of systemic reaction should be avoided. It is obvious that signs and symptoms of systemic reaction are evidence of shocking the tissues and not stimulating immunity. This particular principle has a counterpart in that it renders any type of desensitization treatment a long, tedious process. With desensitization therapy, it is necessary to treat the patient at least six months and preferably twelve months, eighteen months, two years or longer.

In patients with pollen hay fever, the therapy may necessarily be instituted for greater lengths of time. Encouraging results are noted in from 80 to 90 per cent of patients who have received desensitization therapy.

In the majority of patients, multiple skin reactions are present. By correlating the results of the tests and the clinical history, the examiner often has difficulty in evaluating the importance of the allergens to which the patient is sensitive. It is often true that no single outstanding allergic reactions appear. In all patients, the substances to which the patient shows a definite, positive reaction by allergy tests should be eliminated or avoided as thoroughly as possible. Elimination of all offending allergens demonstrated by skin tests will result in a strict routine. It is advisable to establish such a regimen and after clinical relief has been obtained for a definite period of time, to attempt a more liberal type of management. The patient who experiences clinical relief needs no additional stimulus to encourage him in the study of his problem.

RESPIRATORY ALLERGY

Seasonal Hay Fever

Fifty-five patients with seasonal hay fever have received complete allergy investigation, and the majority of these, 51, were tested by the direct, scratch and intracutaneous method. Passive transfer was used in four cases. The ages of these patients ranged between 2 and 15 years, with an average age of 10 years. A history of allergic disease in the family was elicited in 35 or 63 per cent of the patients, and in the majority of those giving a positive family history, both the maternal and paternal branches of the family showed evidence of considerable allergic disease.

The symptoms in these patients were those typical of seasonal hay fever—sneezing, watery nasal discharge and nasal fullness and obstruction, burning and smarting of the eyes, lacrimation, itching of the palate and pharynx.

The average duration of symptoms was three and one-half years. Although the majority of our patients have had a fall type of seasonal hay fever, the routine skin tests have included extracts of tree and grass pollens as well as extracts of the weed family or group. We have found that, although only mild symptoms may be present in the spring or early summer, reactions to the tree and grass pollen extracts will be noted in a number of subjects. Because of multiple sensitivity, results will not be satisfactory if only the weed type of pollen antigens is used in the therapy of these patients. The treatment for each individual is based upon the history and upon the results of complete pollen tests.

During the past three years, we have made daily pollen counts from early April until after a heavy frost in the fall, and we have found this to be helpful, not only in the regulation of dosage of the extract used in treatment, but also as an aid in the explanation of any unlooked for symptom during the hay fever season.

Associated allergic conditions were noted in 57 per cent of these cases, and in 32 per cent, associated conditions other than those of allergic origin were found to be present.

Physical examination in these cases revealed the typical findings of seasonal hay fever. Laboratory work in most of the 55 cases was routine, and the significant features revealed by these procedures was that 26 of the 55 patients had a blood eosinophilia which varied from one to 30 per cent. In two cases in which other associated states indicated a metabolic disturbance, the basal metabolic rates were minus 29 per cent and minus 32 per cent.

In the treatment of these patients, perennial desensitization and adherence to an allergy regimen were carried out in 43 cases. In four patients, the allergy regimen alone without pollen therapy was considered advisable and adequate for satisfactory control. Eight of the total number of patients received no treatment, either because of lack of coöperation or because the condition was not of such severity to warrant strict therapeutic measures.

Several of these patients received treatment under our personal supervision, but the majority have had equally as good results under the care of their family physician who coöperated with us.

Of the group of 55 cases, 15 patients or 54 per cent secured results that can be classified as excellent; 12 or 42 per cent had good results and one or 4 per cent had fair relief. None failed to show any improvement. We received no coöperation in seven of these 55 cases, the treatment either being refused entirely or not conscientiously applied. Twenty of our patients have been treated for too short a length

of time to evaluate the results, or follow-up observations have not been obtained, so that the results in these cases can only be classified as questionable.

In conclusion, we feel that of those patients who have received adequate treatment and have given conscientious coöperation, 96 per cent have shown excellent or good results.

Seasonal Hay Fever and Asthma

In this series of cases only those have been included in which bronchial asthma of a seasonal type was the outstanding symptom. A distinction has been drawn between those patients who experienced attacks of asthma chiefly in the pollen hay fever seasons, those who experienced mild attacks at intervals throughout the year, and those patients who had perennial asthma as the outstanding symptom, but who also had a mild seasonal aggravation due to pollen sensitivity. Eighteen cases of the latter sort are presented in the summary of 42 cases with perennial bronchial asthma.

The observations made on 12 patients with the outstanding symptoms of seasonal asthma due to pollen sensitivity are presented here. Although these patients had symptoms which appeared only in the pollen season, they were thoroughly investigated from the allergic viewpoint, and a strict regimen was enforced in all cases. The average age of these 12 patients was 9 years. Six patients or 50 per cent of the total exhibited associated clinical manifestations of allergy, while four or 33 per cent exhibited clinical states not related to allergy—one patient had a deviated nasal septum, one had a colloid goiter, one had Fröhlich's syndrome, and in one case a diagnosis of glandular tuberculosis was made.

A positive family history of allergy was elicited in nine or 75 per cent of the cases. The average duration of symptoms had been 5 years. The symptoms were those typical of hay fever and demanded medication for relief (usually ephedrine orally and often adrenalin subcutaneously).

Roentgenographic studies of the chest were made in the majority of cases and in one patient a roentgen diagnosis of questionable pulmonary tuberculosis was made. Eosinophilia was noted in six cases or 50 per cent; the average eosinophil count was 8.

Allergy tests were made routinely by the scratch method and were supplemented by the intracutaneous or passive transfer method as the individual case demanded. Complete tests by passive transfer were carried out in three subjects. The average number of proteins tested

in each patient was 150, except in the case of those tested by the passive transfer method.

Of the 12 patients in this group, one refused the advised course of therapy, and we were not able to secure follow-up observations on two others. Of the remaining nine, six or 66 per cent secured excellent relief, two or 22 per cent noted good results, one evidenced fair results and none was unimproved. Therefore, excellent or good results were noted in eight of the nine patients or 88 per cent. Every patient in this series is continuing therapy as originally instituted. It is interesting to note that one patient, a girl aged 12 years, received four or five injections of adrenalin daily over a period of from three to four weeks each ragweed season. She suffered complete exhaustion at the close of hay fever season and a loss of 15 to 20 pounds in weight as the result of her illness. Following treatment this patient found it unnecessary to use adrenalin; she had no asthmatic attacks, and the results secured can therefore be classified as good.

Perennial Allergic Rhinitis

Of 514 allergic patients seen in a six-month period in 1933, 137 or 26.9 per cent had perennial allergic rhinitis and bronchitis. These patients were of all ages. In a survey of 203 allergic children seen in 1934 and 1935, 41 or 20.2 per cent presented the major clinical manifestations of perennial allergic rhinitis and bronchitis. These figures show a striking similarity between the incidence of perennial allergic rhinitis and bronchitis in the adult and in the child. Thirty cases in which chronic nasal allergy was the dominant symptom are reviewed in the following discussion.

A carefully elicited history reveals the following symptom-complex to be fairly typical. Symptoms of nasal congestion, sneezing, nasal discharge of serous or mucoid character, postnasal dropping, and often dull frontal headache are noted. Sneezing is not as prominent a symptom as is nasal congestion or nasal obstruction. Eyelid or bronchial symptoms may be present to a lesser degree. Just as pollen allergy has a distinct seasonal variation, these patients experience a definite aggravation of their symptoms during the fall, winter and spring months. In this section of the country, climatic conditions are unfavorable to this group of patients. To all practical purposes, there is no sunshine, out-of-door exercise is curtailed, and contact with house dust due to our heating systems is more imminent; furthermore, infectious colds are more prevalent, and these patients as a rule, contract more colds than the average child. Symptoms resultant from physical agents such as changing temperature, cold wind and wet feet, are evidenced by

the sensitive mucous membranes and are noted in a large percentage of patients. The symptoms are not constant, but vary from day to day or week to week, and the patient never gains a normal state of nasal breathing. Varying mild attacks of bronchitis and asthma were noted in a small percentage of patients and a few patients exhibited mild pollen sensitivity with aggravation during the hay fever season. Cases where definite sinusitis of a purulent nature was demonstrated were not included in this series. Intranasal surgery had not been performed in these patients, but tonsillectomy and adenoidectomy had been performed in the majority of cases.

The average age of the patients in this series was 10 years. Positive family histories of allergy were obtained in 20 or 67 per cent. Associated clinical manifestations of allergy, which were noted in 19 or 63 per cent of the patients, were hay fever, eczema, urticaria, gastrointestinal allergy and bronchial asthma. Associated findings which were not a part of the allergic state in 16 or 53 per cent were malnutrition, obesity, deviated septa, otitis media, hypometabolism and hypertrophied tonsils and adenoids.

The average duration of symptoms was three and one-half years and the symptoms in the majority of patients were typical of this condition. The signs on physical examination were typical of chronic nasal allergy—swelling of the turbinates was an outstanding feature. Transillumination of the sinuses revealed dimming in a number of patients; irrigations revealed no purulent material. Other physical findings not a part of the allergic state have been noted above. Laboratory studies revealed eosinophilia in 16 or 53 per cent of patients, the average eosinophil count being 5 per cent. A basal metabolic rate of minus 18 per cent was noted in one patient. No positive x-ray studies of the chest were noted. The red blood cell sedimentation rate was normal in the cases where such study was made.

Allergy tests were carried out according to the indications in each individual problem. Seven or 23 per cent were investigated for allergy by the passive transfer method, 60 to 80 tests being made in each instance.

Allergy regimens based upon the results of the allergy studies were instituted in all patients. Results of allergy control could not be evaluated in 13 patients due either to failure to obtain complete follow-up observations, or the period of the allergy regimen was too short. Of the remaining 17, five patients or 29 per cent obtained excellent relief; eleven or 65 per cent obtained good relief, and all patients noted fair results. Of the 17 patients observed over a sufficient length of time to

evaluate results, 16 or 94 per cent obtained good or excellent relief. Results of allergy control in this group of patients have been most encouraging.

Perennial Allergic Rhinitis and Bronchitis

Recurring attacks of allergic bronchitis without asthma is recognized as a common problem in children. A diagnosis of infectious bronchitis had previously been made in many of these cases, but why these had been diagnosed as infections is not clear. Possibly the fact that the symptoms occur chiefly in the fall, winter and spring seasons influenced the choice of diagnosis. The therapeutic procedures employed range from the use of tonic measures such as cod-liver oil to the more drastic surgical measures in the hands of the otolaryngologist. The case histories support the contention that these measures are of little avail in the average patient; however, we do not see the patients that respond to such therapeutic measures.

A family history of bronchitis was noted in the majority of patients. It is interesting to note the frequent occurrence of croup and other forms of laryngitis in this group of patients as revealed by the histories. Tonsillectomy and adenoidectomy had been performed on two patients.

An analysis of symptoms in the patients with rhinitis and bronchitis presents a typical picture. A child enjoys fair health during the warm summer months, but after entering school in September, he fatigues easily, and with first weather change of any note, coryza develops as well as some pharyngitis and within 48 hours, there is an irritating, non-productive cough. Systemic symptoms other than malaise are not common; fever may appear in the first 72 hours, but it is usually present only until the fourth or fifth day and seldom longer than the first week—in a number of patients, the course is afebrile. The nasal symptoms persist, with nasal congestion, nasal obstruction, and mucoid nasal discharge. A dry, irritating cough, usually non-productive, continues. If sputum is noted, it is only mucus. The course of symptoms is protracted, the usual duration being three to four weeks. The appetite is variable, inconstant, and at its best, is only fair. The child recovers slowly, is permitted activities, is noticeably fatigued, and in a few weeks, similar series of symptoms develop, and so this sequence of events is repeated throughout the winter and spring months. Our patients had suffered an average of four attacks each winter.

The question of infection is immediately raised. In two of our patients, questionably infected tonsils were present, and one patient had signs of a sinusitis. Glandular tuberculosis must always be considered; peribronchial adenitis following the acute infectious diseases

of childhood must likewise be excluded and other possible infectious influences should be given every consideration.

An analysis of the findings in 15 patients with typical, severe, allergic rhinitis and bronchitis discloses some interesting facts. The average age of the patients was nine and one-half years. A family history of allergy was elicited in 11 or 73 per cent, and the average duration of symptoms was three and one-half years. Associated clinical manifestations of allergy, namely seasonal hay fever, eczema, urticaria, and gastro-intestinal allergy, were noted in 10 or 67 per cent. Other association conditions were exhibited by 5 or 33 per cent, two patients had questionably infected tonsils, one exhibited signs of sinusitis, one had definite malnutrition, and one had progressive high myopia. A roentgen diagnosis of glandular tuberculosis had been made in three instances.

The physical findings in all patients were those typical of nasal allergy. Roentgen studies demonstrated fibrosis at the hilium of the lungs in the majority of patients. Laboratory studies, other than x-ray, demonstrated secondary anemia in one patient. Eleven patients or 73 per cent, had blood eosinophilia, the average count being 3.6. The red blood cell sedimentation rate was increased in the one patient with sinusitis. Mantoux tuberculin tests were made in all patients, and the results were negative in all except one.

Allergy tests were performed by the scratch, intracutaneous, and passive transfer methods. Because of age, it was deemed advisable to do allergy tests by the passive transfer method in seven patients, or 47 per cent. Tests were made for bacterial antigens, either autogenous or stock as the individual case demanded.

Of the three patients in whom roentgen examination gave evidence of glandular tuberculosis, two received deep x-ray therapy, and the third was followed by an added rest regimen. All patients followed a strict allergy regimen based upon results of allergy studies, and generous quantities of vitamins A and D were administered. Calcium, iron and, occasionally, iodides were employed as the individual case demanded and this therapeutic routine has been continued up to the present time.

Of the 15 patients, we were unable to obtain a follow-up observation on four and of the remaining eleven, seven or 64 per cent obtained excellent relief with complete alleviation of symptoms; four patients, or 36 per cent, experienced good relief. There were no unimproved cases. To sum up, allergy investigation and control gave good or excellent relief in eleven patients who had suffered recurring attacks of allergic rhinitis and bronchitis for a period of three and one-half years.

Perennial Bronchial Asthma

Bronchial asthma presents one of the interesting phases of the study of allergy in children. The majority of patients who presented themselves for study were found to have had asthma over a long period of time. The symptoms had been typical, the attacks had been severe, and the usual type of medication had been used without any longer giving symptomatic relief. Often the patient had been submitted to surgery without relief and in the majority of patients the symptoms had only been intensified. Allergy investigation had been neglected or inadequate.

Our series includes 42 children with perennial bronchial asthma. The average age of these patients was nine years. Twenty-two patients, or 53 per cent, had other associated allergic manifestations. Ten of the 42 patients had other associated states; eight of these had tonsils which were questionably infected in a few and apparently normal in the others; one had a definite sinusitis; and one had contracted undulant fever 4 months previously which aggravated the asthmatic state.

A family history of allergy was positive in 35 cases or 84 per cent. The average duration of symptoms was 5 years, and the symptoms were typical. In practically 100 per cent of the cases, an allergic rhinitis was associated with the condition. The asthmatic attacks in every case were becoming increasingly frequent and severe.

Physical examination revealed questionably infected tonsils in eight patients, sinusitis in one; signs of a febrile disease which proved to be undulant fever in one; typical signs of rickets in one, and various states of malnutrition in three.

A roentgenogram of the chest was made in the majority of patients and in eight, the findings were interpreted as puerile tuberculosis. The tuberculin test using the Mantoux method, (0.01 mg. tuberculin, 1-1,000 dilution) gave a negative skin reaction in all these patients. The red blood cell sedimentation rates were normal, indicating the absence of any infectious element. Progress roentgen studies at three, six and twelve month intervals following control of allergy showed a clearing of the findings that had been interpreted as tuberculosis. The only method of therapy used was control based on the results of the allergy studies. The difficulties encountered in interpreting x-ray studies of the chest in children suffering with respiratory allergy is significant of the necessity of close correlation of clinical history, physical findings, and laboratory and allergy studies before a definite diagnosis is established.

Laboratory findings disclosed that 35 patients or 84 per cent had blood eosinophilia, the average being 6 per cent. Questionable mild

secondary anemia was present in only a few patients. One patient with undulant fever had a strongly positive agglutination test and a very marked skin reaction to 0.05 cc. brucellin vaccine administered intracutaneously.

Allergy tests were carried out by the scratch, intracutaneous and passive transfer methods. Quite often, the problem necessitated the use of all the methods. In 18 patients, where seasonal aggravation was noted and pollen sensitivity was demonstrated, the scratch method was employed routinely, and was followed by intracutaneous or passive transfer methods as the individual case demanded. The average number of protein substances for which tests were made varied between 110 and 160. The passive transfer method was used completely in 18, or 43 per cent of the patients.

The results of the allergy tests and a correlation of the findings with the clinical history indicated a multiplicity of reactions. Definite seasonal aggravation of symptoms during the tree, grass, and weed pollen seasons had been noted by 18 patients. These patients were advised to institute the perennial method of desensitization and followed this advice. Occasionally, patients with marked reactions to epidermals and miscellaneous inhalants which could not be completely avoided were given desensitization therapy. Bacterial sensitivity was rarely encountered as a major factor; hence, bacterial vaccine therapy, either with autogenous, pool, or stock vaccines, was carried out. A strict allergy regimen was instituted in all patients. Vitamins A, B and D, calcium, iron and iodides were prescribed as the individual case demanded. Routinely in the past year, we have employed generous doses of calcium and vitamin A and D in all patients with bronchial asthma. The value of this procedure has not yet been determined.

The results secured in the 42 cases are as follows: In eight patients, or 19 per cent, the allergy regimen has either been instituted for too brief a time to evaluate results, or follow-up observations have not been available. Seventeen or 50 per cent obtained excellent results; 12 or 35 per cent obtained good results; 3 or 9 per cent noted fair improvement; one patient was unimproved. This particular patient had suffered from asthma since infancy and had a great deal of bacterial infection within the bronchial tree and a degree of pulmonary emphysema which was quite marked for a child of 10 years. In one patient, no coöperation could be obtained. In spite of this, a very complete study of the patient was made, and the results appeared promising. To sum up, excellent or good results were obtained in 85 per cent of the sub-

jects and only one patient failed to show any definite, satisfactory degree of improvement.

Nasal Allergy and Sinusitis

The association of allergy and infection in the nasal sinuses has been recognized by many workers. Today we accept the dictum that success of treatment depends upon the recognition and control of both the infection and the allergy. The successful approach to this group of patients includes a thorough investigation for allergy and a regimen based upon the results of such studies before any surgery is advised. Likewise, continuance of the strict allergy routine following surgical procedures is imperative. Swollen, boggy, edematous mucous membranes due to allergic reaction prevent proper healing of tissue following operative intervention, make drainage from the sinuses impossible, and render local tissue vitality and resistance a complete failure. In the Department of Allergy and Otolaryngology, we have seen many patients who had allergy associated with sinusitis, and who had had repeated intranasal operations and radical surgical procedures, all of which resulted in failure to relieve the symptoms. The late Dr. William V. Mullin presented the case summaries of a few of these patients whom we have seen.[1] The remarkable results obtained following institution of an allergy regimen, and conservative, operative measures, if any at all were considered necessary, brings forcibly to the attention of every otolaryngologist and allergist the necessity for careful consideration of each phase of this problem and its influence upon the individual case before methods of treatment are enforced.

By what means can one determine the association and relative influence of allergy and infection? Only through careful evaluation of the history, a complete physical examination, special examination of the nose and throat, laboratory studies both of the blood and nasal secretions for eosinophilia, and interpretation of complete allergy tests can one determine the presence or absence of allergy in these problems. As in every allergic state, the careful history is the most important of the diagnostic measures. Not only a personal manifestation of an allergic state, but the eliciting of a strongly positive family history strengthens the contention that the suspected subject may have allergy. A family history of allergy has been obtained in a high percentage of these patients. The personal history usually discloses the story of frequently recurring and protracted colds since early childhood, which improve in summer and are aggravated in the winter, with poor response to routine therapeutic measures. Then follows the history of an acute infection, obstruction, purulent nasal discharge, local treatments, irrigations and finally surgery. In spite of repeated surgical measures

and local therapy, the symptoms continue without clinical relief. This history is typical for the patient who presents himself with allergy and infection and suggests to the examiner that he is not dealing with infection alone. We have found that the patient with nasal allergy has a stormy and protracted convalescence following nasal surgery, owing to the previously marked edema of nasal membranes, and consequent poor drainage.

Laboratory tests are indispensable. Roentgen studies of the sinuses are often misleading—the clouding of sinus areas, as shown on the x-ray may be due to infection or to a thickened edematous membrane which is an expression of allergic reaction. Only through evaluation of clinical history, physical examination and the results of laboratory and allergy tests can roentgen studies be interpreted. Study of nasal secretions for eosinophils is a routine procedure with many workers, but it should be remembered that such a finding may be changed in cases where an infection is superimposed upon allergic tissues. Purulent secretions may obscure local eosinophilia. Allergy is a systemic state with local expressions in many organs. We have relied upon studies of blood for eosinophilia and have found this test to give findings consistent with the clinical findings in about 50 per cent of the cases. Repeated examinations of the blood disclose a higher percentage of positive findings. Blood eosinophilia is inconstant and variable, so that the absence of such a finding does not exclude the presence of allergy, but a positive finding strengthens the evidence. The red blood cell sedimentation rate is of distinct value in patients where allergy and infection are associated. We have found this test to be of value in determining the presence or absence of infection as well as the degree of infection, and it is an indispensable index in determining prognosis. More than 200 determinations of the sedimentation rate have been made and the results have been consistent with the clinical findings and diagnosis.

The occurrence of allergy and chronic sinusitis in children is not so frequent a problem as it is in the adult, and surgical measures are likewise more conservative in the child. The majority of children in our group had received only local nasal packs, irrigations, or the intranasal surgical procedures. In classifying our cases, we have included only those patients who had definite sinusitis, as evidenced by history, physical findings, and the presence of pus within the sinus cavity. In many patients, transillumination shows clouding of the antrum or other sinuses, or roentgen studies reveal clouding of the sinus areas, but no further evidence of infection can be demonstrated. Such cases have not been included in our classification of nasal allergy and chronic sinusitis.

In our series of 203 allergic children, 12 had sinusitis and nasal allergy. The average age of these patients was 12 years and the average duration of symptoms of nasal allergy was six and one-half years. Symptoms of sinusitis had been present in only two patients for the same length of time as had the symptoms of nasal allergy. Local treatment had been employed in every case, and no patient had been subjected to any radical surgical procedure. Attacks of sinusitis tended to recur over a period of years after an acute infectious disease or a severe head cold, and there was a distinct winter and spring aggravation of symptoms. Tonic measures had been used in all patients. One patient had had polyps removed. Associated clinical allergic states were present in six or 50 per cent of the patients, and was evidenced by such conditions as seasonal hay fever, asthma, eczema, and bronchitis. Three patients had conditions not associated with allergy—two had definite hypothyroidism and one had epilepsy.

A family history of allergy was noted in 10 or 83 per cent of the cases. The family history of allergy usually indicated both paternal and maternal influences.

Physical examination revealed the edematous, swollen mucous membranes typical of allergy. The findings of sinusitis were typical. Nasal polyps were present in one patient. Roentgen studies of the chest and sinuses were made in practically all cases. In one patient, roentgen studies indicated the presence of pulmonary tuberculosis, but the tuberculin test gave a negative reaction. Following the institution of an allergy regimen, roentgen studies revealed these findings to clear rapidly. Physical examination and roentgen studies suggested the presence of bronchiectasis in one patient. Two patients had signs of hypothyroidism and their basal metabolic rates were minus 21 per cent and minus 17 per cent. Laboratory studies, other than x-ray and basal metabolic rate determinations revealed secondary anemia in four patients. Eight patients, or 66 per cent, had blood eosinophilia, the average percentage being 5. The red blood cell sedimentation rate was mildly increased in a few patients.

Allergy studies were made with the three methods. In one patient, it was necessary to make the complete studies by the passive transfer method. The results of allergy studies were consistent with those obtained in the cases of bronchial asthma and perennial allergic rhinitis. An allergy regimen and tonic measures were instituted in all patients. In two patients it was necessary to use pollen desensitization and the use of thyroid, iron and iodides was employed where they were indicated in individual cases. In no instance was surgery advised.

No coöperation was obtained in 2 of 12 patients; 2, or 20 per cent, had excellent relief from their symptoms; 3 or 30 per cent,

noted good relief from symptoms; 2, or 20 per cent had fair relief, but some symptoms still persisted; in two patients the therapeutic regimen has been employed for too short a time to permit an evaluation of results and in one patient, no follow-up observation is available. Good or excellent results were obtained in 50 per cent of patients and fair relief in 20 per cent. In 30 per cent, the outcome is yet to be determined. We feel that the results obtained with allergy control are gratifying.

Gastro-Intestinal Allergy

The person who is experienced in taking histories is able to elicit mild symptoms suggestive of gastro-intestinal allergy in the majority of children who present evidences of allergy, regardless of the major problem—respiratory, cutaneous, ocular or cerebral allergy. It has already been stated that allergic manifestations are likely to be multiple, due to the diversified phenomena seen in many organs in the presence of an allergic state. Gastro-intestinal symptoms, due to disturbances in the stomach and colon, pylorospasm, cramps, colic, gaseous distention, mucous colitis, and acute and chronic diarrhea alternating with chronic constipation, may be produced by allergic factors. One likewise recognizes the symptom-complex of acute gastro-enteritis due to food allergens to which the patient is more acutely sensitive. This not infrequently occurs in children despite the fact that the parent is well acquainted with the nature of such extreme reactions. Canker sores and the more discomforting herpetic stomatitis with lesions as large as one and one-half centimeters in diameter are often due to food allergy. Investigation and control of diet in these cases has been most encouraging.

One finding has been particularly outstanding in these investigations of clinical allergy in children: invariably there is a history of inconstant, variable appetite, of food dislikes, fondness for other foods, of apathy towards eating, and then a return of appetite which is followed again by a period characterized by capriciousness. Present also, are one or more of the mild symptoms enumerated in the preceding paragraph. The major complaint may be bronchial asthma, seasonal hay fever, ocular allergy or a cutaneous lesion, but the constancy of the changeable attitude towards food persists in the majority of patients. One may immediately ascribe this finding as being due to the child's general problem and this is probably true, but it is accepted in the light that food allergy is a factor which contributes largely to the entire symptom-complex. Investigation of suspected food allergens and correction of diet based upon the results of allergy studies has given in the majority of patients, an entirely different attitude toward food, and this is characterized by constant and improved appetite and disappearance of the mild gastro-intestinal symptoms.

In this discussion of gastro-intestinal allergy, no attempt is made to analyze and present the findings in all cases in which gastro-intestinal symptoms were present. Such an analysis would necessitate a review of the majority of the 203 cases. Interest is stimulated however in a group of 20 patients who presented a very definite symptom-complex of gastro-intestinal nature. This is referred to most commonly as severe recurrent vomiting or severe cyclic vomiting.

Severe cyclic vomiting is not a disease, it is a symptom-complex dependent upon underlying systemic factors. In contrast to the clearly defined and accepted clinical picture that the patient with cyclic vomiting presents, there are diversified opinions regarding the etiological factors. On the Continent, the majority of workers describe a background of a highly sensitive, nervous child of neurotic parents, and upon this background, they consider the acute upper respiratory infections as precipitating factors. In our series of 20 patients, no history of symptoms suggesting the influence of acute respiratory infections could be obtained. It is true that a close analysis reveals a hypersensitive individual in some instances, but no more than is commonly seen in allergy of any type. American workers have approached the problem in a more analytical manner. Excessive fat, and carbohydrate diets, absorption of faulty metabolic products and hypoglycemia have been accorded consideration in the etiology of these attacks. Few workers here considered and pursued allergy as a factor in these cases. A close survey of the work presented by investigators on the Continent prove their investigation and trial of food allergy to be inadequate.

Analysis of symptoms in a child with severe cyclic vomiting suggests more than a casual relationship between this symptom-complex in childhood and the occurrence of migraine in the adult. In our series, hemicrania was not an infrequent symptom. It was particularly true of the older children that gastro-intestinal symptoms became less severe and cerebral symptoms more marked in direct relationship to age. In a recent review of patients with migraine, a percentage were noted to give a history of recurrent attacks of vomiting in early childhood. A more carefully elicited history would probably result in a higher percentage of patients experiencing such a symptom-complex in childhood.

No effort is made to explain the mechanism by which protein substances reach the tissues. That there exists some undemonstrable biliary dysfunction permitting passage of unsplit protein substances into the blood is without doubt. It is likewise conceivable that there exists an increased permeability of the intestinal mucosa, and with any de-

gree of intestinal stasis or reverse peristalsis, an overload of non-split protein substances or faulty metabolic products is thrown into the circulation, reaching the tissues as toxins and producing a violent reaction. That cyclic vomiting is a result of severe toxemia is beyond pale of doubt. The prodromal period marked by anorexia, restlessness, irritability, languor, the early appearance of fever, the active state characterized by epigastric discomfort, gaseous distention, cramps, colic, often diarrhea, nausea and extreme emesis, lasting twenty-four to forty-eight hours, and the final stage, with severe exhaustion and profound prostration followed by a slow and gradual return to a normal state within a period of several days, strengthens the contention that such a clinical picture could only result from a severe toxemia. What part food allergy plays in influencing the precipitation of this chain of symptoms, or food allergens in rendering the intestinal mucosa permeable to the passage of toxic products to the tissues cannot be definitely determined at this time. Our studies lead us to believe that severe cyclic vomiting is largely influenced by food allergy and relief of symptoms can be obtained with allergic control. Further study and longer periods of observation will aid in evaluating the influence of food allergy.

Cyclic Vomiting

We wish to submit the observations and results of twenty cases of severe cyclic vomiting in children seen since January, 1934. That these comprise 10 per cent of the total number of children treated for allergic disease in these last two years, impresses one with the frequent occurrence of this condition.

The average age of our patients was seven and one-half years. In several of these patients, symptoms had been present since infancy and in others the complaints had appeared comparatively recently, the average duration of symptoms being three and three-fourths years. The positive family history of allergy which was found in 13 or 65 per cent of these patients is approximately the same as that in any allergic condition occurring in children. Fifteen or 75 per cent of the patients with cyclic vomiting exhibited clinical manifestations of allergy. These were allergic rhinitis, asthma, urticaria, allergic conjunctivitis, and eczema. The diagnosis in these cases can usually be established by a carefully elicited personal and family history, physical examination and allergy investigation.

Complete and thorough skin tests with 120 to 150 extracts were carried out in these cases. In ten or 50 per cent of the cases, the passive transfer method was employed. In these instances, testing was necessarily limited to from 60 to 80 foods or groups of foods. In cases

where limitation of testing is encountered, we have found that the group type of food extracts is valuable.

The physical findings in these patients, at the time of their visit to the Clinic, were negative in 14 instances. Of these 14 patients in whom physical examination revealed no abnormality, diagnoses of pyelitis had been made previously in two instances. During the time these two patients have been under our observation, no evidences either by laboratory procedures, roentgen examination or complete genito-urinary investigation have been revealed which would substantiate such diagnoses.

Six or 30 per cent of the total number of patients with cyclic vomiting gave evidence on physical examination of associated pathological conditions. Three of these patients had hypertrophied tonsils and adenoids, one was suffering from malnutrition, one had rickets, and one had a deviated nasal septum. In only seven of these patients, or 35 per cent, did we find it necessary to employ complete gastro-intestinal roentgen studies to exclude any possible organic lesion, and in each of these seven cases, the findings were normal.

The routine laboratory tests were employed. In nine of the 20 patients, or 45 per cent, the blood eosinophilia varied from 2 to 11 per cent.

The treatment instituted for these 20 patients was a strict allergic regimen based upon the result of the allergy tests. General hygienic measures were routinely employed. Adequate and nutritious diets with normal gastro-intestinal elimination were emphasized.

The results of the treatment of cyclic vomiting in children indicate that food allergy is a large factor in a high percentage of patients. Thirteen patients or 76 per cent secured excellent results, four or 24 per cent showed improvement, and in three instances the patients did not coöperate with us. Therefore, all the patients who have followed the allergy regimen have noted excellent or good results.

We feel greatly encouraged with the results in this small series of patients with recurring attacks of vomiting and wish to further our observations over a greater length of time and in a larger series of cases in order to evaluate more fully the significance of food allergy in the etiology of cyclic vomiting.

CUTANEOUS ALLERGY

Allergic Eczema

It is commonly recognized that skin lesions of supposedly allergic origin are more resistant to treatment than any other allergic state.

This feature of allergic eczema in children may be due in part to the difficulty of obtaining adequate balance in a child's diet even under normal conditions. The age of the patient, the familiar background and the environmental factors are all obstacles to the successful treatment of allergic skin diseases. It is generally conceded that a higher percentage of satisfactory clinical relief is obtained in the group where personal and familial allergic states are manifested.

In our series, we have reviewed 21 cases of allergic eczema in children. The condition was present in varying degrees of severity —in some patients the lesions were present only in the antecubital fossae; in others, the lesions were limited to the face or neck, while in others, the eczematous areas were far more extensive. The average age of our patients was 7.5 years and in many of these, the personal history of eczema could be traced back to infancy. In the majority of cases, the usual onset was early in the first years of life, but in a few, the first eczematous areas were noted after the child had been capable of encountering a wider scope of environmental factors. The average duration of symptoms was five and one-tenth years.

Usually, in the allergic child, one finds a definite family history of allergic disease, and this was true in 52 per cent of our patients (11 cases). As further evidence of the association of allergic conditions, in seven of the 21 patients, 33 per cent, associated allergic states were identified. In three of the cases or 14 per cent, other skin afflictions were present—pyodermia, psoriasis and impetigo respectively as complicating factors. Hypertrophied tonsils and adenoids were present in one case.

Routine physical examinations revealed normal findings except for the eczema in 14 of the remaining 17 cases. In one, a mild degree of furunculosis was present and in two cases, urticarious lesions gave further evidence of a hypersensitive child.

Laboratory tests were made routinely and of the 21 cases, six or 34 per cent showed a blood eosinophilia of from 1 to 8 per cent (average 4 per cent). These figures are compatible with those found in eczema in the adult patient. Basal metabolic rates on two of the patients whose general condition suggested the presence of hypometabolism were recorded as minus 19 and minus 9 per cent.

Complete allergy tests were carried out by the scratch, intracutaneous and passive transfer methods. In the infants, or in those children in whom it was indicated, the passive transfer method of testing was employed. Of the 21 cases, six or 28 per cent were tested by the passive transfer method.

The parents of three children made no effort to coöperate from the

onset. A strict allergy regimen was advised and carried out in 16 of the 21 cases. In the other two, mere changing of the formulae resulted in marked improvement, both in the skin and in the general condition. The results of a strict allergy regimen were not only encouraging, but in a few cases were striking. Two of our patients secured excellent results with no return of the lesions as long as they adhered strictly and conscientiously to the dietary instructions. Nine secured improvement following allergic management and in two cases, there was no improvement. Five patients have not been followed for a sufficient period of time to warrant classification.

When those patients are included whom we have followed for a period of several months, we find that 84 per cent have secured good or excellent results, and we feel that this percentage is sufficiently high in view of the difficulties encountered in the management of this perplexing problem.

No report of our findings in ocular allergy is given here because a complete summary of this work will be published as a separate paper.

Summary

We have presented our observations made from examination of 203 allergic patients whose ages ranged from 8 months to 15 years.

Adequate investigation has been carried out in every instance. Follow-up observations over a sufficient length of time to evaluate the therapeutic regimen has been obtained in the majority of patients. A small percentage have been under control for too brief an interval to determine results, or follow-up observations have been unavailable.

Of the 203 patients, 162 or 79.8 per cent presented major symptoms of respiratory allergy, namely seasonal hay fever, seasonal hay fever and asthma, perennial allergic rhinitis, perennial allergic bronchitis, perennial bronchial asthma, chronic nasal allergy and sinusitis.

Twenty-one of the 203 patients, or 10.3 per cent, presented cutaneous lesions as the major complaint, chronic allergic eczema being most commonly noted. Atypical cutaneous lesions are not presented in this study.

Twenty or 9.9 per cent of the patients presented the symptom-complex of mild and severe cyclic vomiting. Mild symptoms of gastrointestinal allergy were present in the majority of the 203 patients. No attempt is made to analyze and classify the mild intestinal disorders.

Allergy investigation was carried out by the scratch, intracutaneous, and passive transfer methods of testing. The use of the passive transfer method was indispensable in young children where direct testing resulted in too great mental and physical shock. We employed the passive

transfer method in 57 or 28.1 per cent of the patients, using from 60 to 80 allergens in each instance. Allergic control based on the results of the passive transfer method was as accurate and satisfactory as it was following the direct methods of testing.

The results of treatment have been reviewed under each section of discussion. We feel that encouraging results have been secured in the majority of these patients, and the findings in this study emphasize the importance of complete and thorough allergy investigation in the determination of the etiology of certain respiratory, gastro-intestinal and cutaneous diseases of childhood.

Reference

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