Reprint from California and Western Medicine October, 1938. Volume 49, Number 4 450 Sutter Street, San Francisco

ADRENAL CORTEX IN TREATING CHILDHOOD ASTHMA: CLINICAL EVALUATION OF ITS USE*

By F. M. Pottenger, Jr., M.D. and

> F. M. POTTENGER, M.D. Monrovia

HEN one faces a therapeutic problem he is inclined to try to find a single approach to its solution. Inasmuch as vital processes are complex, a single measure rarely accomplishes the end in view. Insulin simplifies the control of the diabetic, but it is far from commanding the full confidence of the physician in treating diabetes. Epinephrin has long been used in the treatment of asthmatic paroxysms, but we now find that crude extract of the adrenal cortex is an important adjunct in restoring the physiologic balance of the allergic patient. The acquiring of a comprehensive understanding of asthma has probably been delayed because we have had our minds too narrowly directed to its allergic nature. Because asthma is accepted as an allergic disease, it is natural to assume that its cause is some allergen. This thought has dominated the minds of medical men almost to the exclusion of all other ideas. The fact that the patient's general physiology might be an important part in the etiology of asth-matic symptomatology has not been sufficiently emphasized.

RECENT TREATMENT OF ASTHMA

For two decades the principal treatment of asthma has consisted of treating paroxysms with epinephrin, and attempting to desensitize the patient to specific allergens; of withdrawing the offending allergens; or of removing the patient from the environment in which the allergens are found.

A great deal of progress has been made by following this line of therapy. Many patients have been freed from their distressing paroxysms, and not a small percentage have procured a more or less permanent relief.

ASTHMATIC SYNDROME

The asthmatic syndrome is one of vegetative dysfunction. All allergies in their final analysis are due to cells whose physiologic balance is disturbed, which means that their permeability is altered. This in turn means that their function is more readily stimulated than normal.

Sensitization of cells in case of allergies may be caused by protein gaining access to the tissue, and requiring cellular digestion. Body cells are normally endowed with a power to digest proteins and accomplish it by producing antibodies, which are fixed to the cells and react with more or less violence when the same foreign protein again finds its way into the tissues. When once this function has become established it may remain for a long period of time, and may be very active when the allergens to which the cells form antibodies contact

* Read before the General Medicine Section of the California Medical Association, at the sixty-seventh annual session, Pasadena, May 9-12, 1938. them, or when stimulated by other forces. It is probable that cells digest much protein without developing a pathologic degree of sensitization. We infer this from the fact that protein is known to enter the tissues without causing symptoms. Parenteral digestions as a normal function of cells may be more active in protecting the body than is realized. This suggests that the relief of pathologic allergies might be brought about physiologically by substances which will reduce the permeability of the affected cells.

Allergies are relieved by increasing the antagonistic effects of the sympathetic nervous system in such conditions as asthma and hay fever, either by central stimulation or by using the sympatheticotropic hormone from the adrenal gland; by lowering parasympathetic action by the use of atropin; by lowering the potassium intake and increasing the calcium; by the administration of acids or ammonium chlorid; by starvation or the use of foods, which tend to decrease the alkaline balance. Such measures lessen the activity of the hypersensitive cells.

AUTHORS' ANALYSIS

Our discussion today will be limited to an analysis of a group of fifty allergic cripples complaining of asthma who have been under treatment for one year or longer. Though many have obtained relief in a shorter period of time, we have purposely chosen this group of severe refractory cases in whom we have carried out a program of prolonged treatment which has gradually evolved during the past six years. Each new feature of the treatment has been added after careful consideration, and we now attempt to explain the measures used, and to assign to them their due importance.

INITIAL METHOD

As previously reported,1 we started our treatment of asthma with the whole adrenal gland and found it to be more effective than epinephrin alone, and most effective when given with a high salt intake. Our second step was the addition of a hydrophilic colloid diet² with an acid ash residue, high in mineral and high in vitamins. The third step was the addition of a series of exercises. In evaluating the various measures used, the adrenal hormones have exerted the most favorable influence on results; next, the diet; and then, finally, the exercises. The adrenal hormones form the basis of the regimen. Fineman³ reported treating a series of four cases using a purified adrenal cortex preparation. His results were not encouraging. Wilmer and Miller* reported a series of seventy-two cases using the adrenal cortex. More recently Prickman and Koelschi³ have made a similar report. Barbour⁶ reported the use of dried adrenal material and thyroid, with favorable results in children. Todd 7 has made extensive anatomical studies of the allergic cripple, showing the marked variation in the anatomical structures of allergic children from those who are considered normal.

RATIONALE OF THE TREATMENT

The rationale of the treatment as we use it was previously described by us.¹ Though we referred but briefly to the dietary regimen in our previous discussion, we now utilize a semiketogenic diet which, on the basis of an adult diet, consists of

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approximately 2,300 calories, roughly 145 grams fat, 145 grams protein, and 100 grams carbohydrate. It is rich in known vitamins and minerals. The two main meals are built around a large, raw salad and a portion of meat consisting of not less than four ounces when cooked. Sugar and all foods high in carbohydrates except whole grain, fresh ground cereals are largely eliminated. Gelatin is used, one-half ounce or more at each meal, because of its hydrophilic colloidal properties which aid in digestion and mineral assimilation. The vitamins, other than those contained in the large green salad, are administered in the form of a high grade raw green pasture milk, and malt and cod liver oil. The use of the vitamin B complex is particularly stressed in those children showing large colons. Minerals are obtained from the milk and vegetables. Mineral concentrates are only occasionally used in the most severe cases of deficiency.

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POSTURE

Nearly all of these children have poor posture, which is either a result of developmental failure or the secondary reaction to their disinclination to exercise. We attempt to correct this by the use of appropriate exercises. We specifically attempt to secure diaphragmatic breathing. Our exercises are graded from a method of simply controlling breathing to as strenuous physical exertion as the child can bear when he becomes stronger. One must always remember that overexertion is a definite menace to these asthmatic children. Athletic coaches often attempt to push them too fast, and they may undo much that the clinician, through patience and perseverance, has accomplished over a prolonged period of time.

INDIVIDUALIZATION IN TREATMENT

The complete therapy used in any individual case depends upon the physical findings in those patients. Though all the children and adults discussed in this paper have come to us primarily for the purpose of obtaining relief from their asthmatic paroxysms, we have, by studying each patient, tried to find in what manner he differs from normal physiologic standards. This we felt was a much better approach than a simple attack upon their allergic symptomatology. Although the allergy may be the most distressing symptom, we feel that as one understands the deviations from the normal, both in physical development and physiological response, he can more properly evaluate the therapy which is to be used.

As one watches and studies the changes which take place in growth and development, he usually finds that the fundamental physiological processes are also altered. These processes and the allergic symptoms seem to respond coincidently.

It is not the purpose of this paper to evaluate the deviations from normal that the allergic individuals show, but we do desire to mention some of the more obvious changes and to discuss the effect that the therapeutic regimen which we have instituted has had on certain prominent physical characteristics.

DATES OF ONSETS OF ASTHMA

The onset of asthma in the fifty patients reported here occurred in nine during the first year of life, nine during the second year, sixteen during the third, six during the fourth year, four during the fifth year, one during the sixth year, one during the eighth year, one during the ninth year and one at the age of 61; two were unknown.

If, however, from the standpoint of the patient's history, the first indication of allergy, such as difficulty with digestion, eczema or hay fever is considered, these figures change to twenty-three during the first year, seven during the second year, twelve during the third year, three during the fourth year, one during the fifth year, one during the sixth year, one during the sixty-first year and three were unknown.

When the matter of breast feeding is considered, one patient was breast-fed for nine months, four for six months, fifteen for three months, fourteen for less than three months, and eleven not at all; five were unknown.

The intensity of the asthmatic symptoms seemed to be greater in the children who showed feeding difficulties. A comparatively accurate history of disturbance of thyroid (may this be partly vitamin B complex deficiency?) was obtained in the mothers of twenty-eight of this group, and nine reported disturbances of the generative system, without evidence of primary thyroid dysfunction. The history of seven mothers was unknown. Of this group thirty-seven mothers, or 74 per cent, gave a definite history of these disturbances.

OTHER FACTORS

Of the asthmatic group, ten showed some degree of bronchiectasis, and eighteen out of fortyfive patients tested were positive to tuberculin. Three of these have become negative under treatment.

Six of the thirty-five boys in this group showed delayed descent of the testes, while the tendency of the remaining under the age of puberty was to present external genitalia smaller than normal.

The blood chlorids varied from 370 to 492 in twenty-eight cases. On first examination twentyeight patients showed an average of 458.3, while at the end of treatment they showed an average of 458.6.

The hemoglobins of the group averaged 88.1 at the beginning of treatment, and 90.1 at the last examination. The red blood counts averaged 4,578,000 at the beginning of treatment and 4,619,047 at the last examination. The white blood count averaged 10,390 at the beginning of treatment and 9,478 at the end of treatment. The eosinophilic count averaged 9.5 at the beginning of treatment and 9.02 per cent at the last examination.

As a group at the beginning of treatment, muscular development of thirty-eight patients was poor, five was fair, and seven was good.

On the basis of the weight¹² for the height of forty-three of this group, twenty-one were above normal and twenty-two below normal. Of these patients forty were taller than standard, one not obtained, six shorter than standard and three normal. Full cognizance has been taken of the fact that children in California are, as a group, taller than children of other parts of the country.

MUSCULAR DEVELOPMENT

When muscular development, physical endurance and weight changes are considered in refer-

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ence to normal development, twenty-four patients showed marked improvement, twenty-one showed moderate improvement, and five showed no improvement. When one considers the patients' condition during treatment, fourteen had no allergic paroxysms, thirty had paroxysms of less intensity and incidence, and eight had only temporary relief.

The patients constituting this group were under active treatment with adrenal cortex therapy for a period of one year or more, using daily doses of 1¹/₂ to 10 grams of raw gland equivalent three times a day with meals, depending upon the age and condition of the patient.

TREATMENT PROCEDURES

Inasmuch as such prolonged treatment cannot be carried out hypodermically, particularly in children in whom a psychical condition is a serious complicating factor, we have used the oral method. The adrenal extract we use is known to contain active cortin which has been shown to be effective by mouth by Grollman,8 Hartman,9 Britton,10 and associates. Likewise there are probably other fractions of equal importance in this crude extract, made according to the method first described by Swingle and Pfiffner and modified by us, and described in a previous report.11

The fifty patients under discussion today have all been refractory to other methods of treatment, and this consequently means that the coöperation of the patient is difficult to obtain in some instances. Of the five patients in whom we feel that the results were unsatisfactory, our records indicate that coöperation was difficult to obtain. This is based on historical evidence of continuous overdoing, and inasmuch as we supply all the medication, we have the records of its consumption which gives us a further index of coöperation.

The factor of greatest importance in the results obtained seemed to be the coöperation. The severity of the disease seemed to relate particularly to the time of breast feeding or the type of formula used in early infancy. The response of the children of this group to therapy and subsequent attacks during the year mentioned was apparently related somewhat to the degree of bronchitis. Whether or not they had a positive tuberculin did not seem to exert any appreciable influence on the improvement of the asthma in the children.

On the other hand, recurrent attacks during treatment seemed to have a definite relationship to the degree of bronchiectasis. Alteration of the normal sexual development of the girls was inferred from their physical development, but could not be measured as in the boys. Our experience would indicate that not only in the younger boys, but the older ones as well, there is a definite evidence of sexual imbalance. This is partly brought out by the fact that these children on the whole were taller than normal standards for their age, while their weight for their height was approximately normal.

LABORATORY FINDINGS

From the standpoint of the clinical laboratory, little evidence of change is noted in the figures as presented. The general average of blood chlo-rides is almost identical. The hemoglobins are very close and likewise the total red counts. The eosinophilic count remains constant. There is a tendency for the white blood count to diminish. On the other hand, at the end of a three months' period we usually find that there is a very marked reduction in the hemoglobin and red count in many of these patients, which climbs back to original levels at the end of a year.

When one considers the physical development of these individuals, based upon their ability to perform muscular exercises, their endurance and tissue tone, improvement was shown in all but five cases.

COMMENT

When one considers the allergic cripple from the standpoint of his physiology and development, one is confronted with a symptom complex differing with each child. A thorough understanding of this symptom complex offers an intelligent basis for the application of therapy. In all of our work we have used a crude extract of the adrenal cortex because experimental and clinical evidence shows it to be a physiologic stimulant which is an important adjunct in the treatment of the symptom complex.

This method of approach, we feel, offers a hope that the allergic cripple may be gradually rehabilitated.

SUMMARY

1. A crude extract of the adrenal cortex, in conjunction with epinephrin given orally, is an important adjunct in the treatment of asthma.

2. A summary of fifty cases of refractory asthma treated over a period of one year or more showed improvement in their allergic symptomatology in 84 per cent. Physical improvement in the same group was noted in 90 per cent.

3. The routine hematology and study of the blood chlorids apparently give little information as to the progress of the patient.

4. Six of the thirty-five boys in this group presented nondescent of one or both testes, all six of which showed descent under treatment.

5. Evidence of thyroid or genital disturbance was obtained in 74 per cent of the mothers of the patients.

6. Some forty of the fifty patients were taller than normal standards.

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