

THE EFFICACY OF ORAL ADMINISTRATION OF ADRENAL HORMONES IN
TREATMENT OF BRONCHIAL ASTHMA, PARTICULARLY IN CHILDREN

Is there a constitutional state that predisposes an individual to allergic manifestations? Do the diathesis formerly so commonly spoken of have a real basis? ^{D.} ~~Are~~ the sensitivities to protein substances, seemingly both psychic and physical, to meteorologic conditions and chemical substances represent the trigger mechanisms which allow a disturbed general physiology to react? These are questions which demand an answer.

Our studies lead us to believe that the underlying physiology is the important factor and that the allergic response is the result of abnormal physiology, not merely chance sensitization. Possibly a condition that is transmitted from one generation to the next ^{is} not inherited, but by virtue of physiologic deficiency in the mother. We have by just such means produced asthma experimentally in cats. Here infantile asthma requires a second generation.

For the above reasons we have treated our patients from the standpoint of physiologic imbalance, attempting to render the patient insensitive by the restoration of balance, rather than treating the sensitizing factors either by elimination or desensitization.

The elimination and desensitization methods have taught us much in regard to the factors of sensitivity but little in regard to the fundamental physiology and though the treatment is successful temporarily, new trigger mechanisms or sensitivities may take the place of the old. On the other hand the physiologic method has in our hand shown a tendency to render one less sensitive to all agents. How permanent this mode of treatment will be, time alone can tell.

The various precipitating factors -- physical, chemical, meteorologic, psychic and *biologic* -- act upon the sensitized cells thus setting up the allergic manifestation. We must not consider that precipitating factors are always *protein* in nature. The degree of reaction, and the duration too, depends upon the ability of that disturbed physiology to respond.

Asthma, for instance when due to a single pollen is seasonal, depending upon that factor. However, other types have a tendency to show a seasonal variation, being more severe in the winter and spring. With reference to the *diurnal* variation, night attacks too, are more frequent, and after meals. These phenomena are associated with a relative increase in tissue alkalosis, a loss of sodium and an increase in potassium. Likewise exhaustion of the

sympathetico-adrenal system renders the allergic individual more susceptible to attacks. Alkalosis interferes with calcium assimilation and ^{favors} ~~promotes~~ an excess parasympathetic action. These factors depress the sympatheticotropic hormones.

Such chemical factors in theory at least, justify any measure which will stimulate the lessening of the relative tissue alkalosis and ^(Such as adrenal and thyroid) ~~store~~ ^{stimulate} endocrine glands ^{which} ~~will~~ exert a sympathetic effect on his autonomic nervous system.

Similar chemical changes are among the striking features in the adrenalectomized animal. The rapid loss of sodium chloride which is temporarily followed by an acidosis, and finally potassium poisoning, brings about the death of the adrenalectomized animal. In the adrenalectomized animal, and in Addison's disease ^{is this correct?} these effects are explained solely on a basis of sodium loss. Likewise we have an ever increasing literature suggesting the adrenals as being primarily involved in mineral metabolism, particularly sodium.

Though there are certain physical and chemical similarities between the adrenalectomized animal, Addison's disease and the allergic individual, in that ^{all} ~~both~~ show a predominating effect of potassium and an increase of parasympathetic stimulation, low total blood chlorides and other clinical and chemical similarities. None the less, when an adequate sodium chloride intake is offered, ^{to} ~~these~~ patients we do not find the allergic ^{individual} ~~response~~ with a rapid increase in blood chloride such

such as is found in the adrenalectomized animal or ^m case of Addison's disease.

Our treatment commenced with the purely empiric observation that whole adrenal raw/gland relieved the asthmatic paroxysm of a child who had been in status asthmaticus three months when usual methods had failed. This child responded promptly and unlike the result from injections of adrenalin, remained free from attacks for a period of 4 days instead of a few minutes to an hour.

What was the cause of this response? Did epinephrine do it? We had been taught epinephrin was ineffectual by mouth. Was the cortin responsible? Were the various vitamins, a,b,c,d,e and g responsible? Was some other unknown factor responsible? Were all these factors in combination ~~the~~ responsible?

We investigated epinephrine by mouth and found it to be successful in relieving both the severity and frequency of attacks. We extracted the glands for their cortin. We tried this, and found it effective, more so than epinephrin. *mb for acute attacks?* We tried a diet rich in the vitamins reported to be found in the adrenals. It too was helpful but not as noticeable as either cortin or epinephrin. And we have tried all combinations and have found a combination of all three factors best.

(In the dietary measures we use a high NaCl intake, because of its supposed effect on the adrenals). However, the raw whole gland itself is the most effective in

giving immediate relief. Though estimates are difficult, it is apparently as effective as the cortical extract from 100 times as much glandular substances, inasmuch as its effect lasts longer.

However, the effects of the therapy are more than just immediate. We have not use it for the immediate effect, but in an attempt to alter physiology. We feel that that is what we are accomplishing in those children whom we have followed from one to two years. In the latter, our sequence of events has usually been (1) relief from asthma which may or may not be precipitated by colds and other factors -- usually second attacks are lessened in intensity.

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(2) after/colds fail to precipitate more than mild wheezing, though the bronchitis may continue. Later, even the mild symptoms of wheezing disappear.

(3) Gradually the child becomes less susceptible to colds and even though all other members of the family come down, he may completely avoid the episode or respond lightly. (4) There are two factors that are more refractory, mainly the bronchitis and nasal symptoms presented by most of the group. Sometimes one or the other may be less prominent, however when there is a considerable degree of bronchiectasis the pulmonary symptoms are slower. When the narrowing of the nasal passages is the chief trouble, nasal symptoms disappear last. The symptoms begin to show definite clearing in from 9 to 18 months. The breath sounds lose their harsh

emphysematous character early as the asthmatic phase passes off. The roughness particularly over the large bronchi, continues for a longer period especially when the bronchitis was severe to begin with. These however, gradually revert into smoother breathing.

What happens to the physiology of these children during this period?

They gain weight -- not fat but flesh at a rate which is greater than the expected normals for their age and their height seems to increase a little more rapidly. These gains however, seem to be due to general tissue stimulation toward what would be normal for a robust child. The muscles increase and the bones increase in size and thickness of cortex, at a rate which seems to be greater than normal. However, these children are deficient in these factors to begin with. Their blood chlorides gradually increase from the lower limits of normal to limits nearer the midpoint of normal. Their eosinophils diminish. Their red count is frequently high, 5 to 5,500,000 or 6,000,000 with a hemoglobin of from 80 to 110%. In every instance, we have seen this drop about the 3rd month to 3,000,000 or 4,000,000 with a hemoglobin of 60 to 80%, to return to normal. Some of the children are really anemic, to begin with, but most belong to the class of angio-spastic-psuedo-anemia with their pale skins and delicate complexion. As their changes are taking place, there are great changes taking place in the child's potential

physical energy. Their energy increases greatly and it is sometimes with difficulty that the parents can keep the children from overdoing. However, as they continue with their improvement the over-exercise factor becomes less important. Exhaustion prevents sleeping and that in turn provokes more bronchial secretion; early it tends to set off the asthmatic paroxysms. Many of the children are restless and sleep poorly, having nightmares, night sweats, coughing paroxysms and other episodes that interfere with rest. These lessen very rapidly. In a like manner, the child relaxes, is less tense and irritable. Events that formerly were very upsetting lessen in effect. Children become more manageable. One of the earliest effects of the regime is an increase in appetite - this however, is followed by a lessened demand for food. It apparently is associated with better assimilation. As above suggested, as a group, these children have narrow dental arches and high vaults. Associated with the other factors of bone growth (show slide) there seems to be a widening of the arch, from the narrow transverse diameter with a high vault toward the broad arch with a low vault. As the slide shows, a decrease in the width of the arch, and an increase in the height of the vault, narrows the air passages in 2 directions,^{so} that the air flow through the nose is greatly restricted. The width of the arch at the level of the second bicupid seems to determine the width of the nasal passageway and the antra.

Many procedures have been proposed to correct the deformity and in our cases we have noted a general tendency toward widening of the dental arch and air passages without operative interference. Likewise the tonsils have been studied though they have frequently been removed before we have seen the children; in most instances where they remain, they have been large and inflamed. As Todd of Cleveland, states, the size of the tonsil is inversely proportional to the mineralization of the skeleton, so we have noted that the tonsils decrease in size as the children develop. However, like normal tonsils do, they respond to infection by increasing during that period. In one instance, tonsils so large that the child could scarcely swallow, have subsided in 18 months time, so as to be visible only by mirror.

X-ray of McWhorter (severe bronchiectasis)

X-ray of Newsome (severe nasal)

X-ray of Roper, (nose change shown)

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There is a constitutional state that predisposes an individual to allergic manifestations. Sensitivities to protein substances, to stimuli, both physhic and physical, to meteorologic conditions and to chemical sutstances, represent only the trigger mechanisms which allow a disturbed general physiology to react by allergic manifestations.

Our studies lead us to believe that the underlying physiology is the important factor and that the allergic response is the result of abnormal physiology, not merely chance sensitization. Possibly this condition is transmitted from one generation to the next, not by inheritance, but by virtue of physiologic deficiency in the mother, and continued deficiency through early childhood. Following this suggestion we have produced asthma experimentally in cats. In these animals, deficient physiology must be established in the mothers, and carried through infancy to create asthma in the kittens. In several instances the female cats had had one or more normal litters before the experimental deficiency was imposed upon them; also normal litters have been had after deficient litters.

For the above reasons, we have treated our patients from the standpoint of physiologic imbalance, attempting to render the patient insensitive by the restoration of balance rather than treating the sensitizing factor either by elimination or by specific desensitization. The elimination and desensitization methods have taught us much in regard to the factors of sensitivity but little in regard to the fundamental

physiology, and though the treatment may be successful temporarily, new trigger mechanisms or sensitivities may take the place of the old. On the other hand, the physiologic method has in our hands shown a tendency to render children less sensitive to all agents.

The various precipitating factors, physical, chemical, meteorologic, psychic, and biologic, act upon the sensitized cells, thus setting up the allergic manifestation. We must not consider that precipitating factors are always protein in nature. The degree of allergic reaction and the duration depend upon the ability of that disturbed physiology to respond.

Asthma, when due to a single pollen, is seasonal, depending upon that factor. However, other types have a tendency to show a seasonal variation, being more severe in the winter and spring. With reference to the diurnal variation, attacks at night, early morning and after meals are more frequent. These phenomena are associated with a relative tissue alkalosis, a loss of sodium and an increase of potassium. Likewise, exhaustion of the sympathetico-adrenal system renders the allergic individual more susceptible to attacks. Alkalosis interferes with calcium assimilation, and promotes an excess parasympathetic action. These factors depress the sympathetotropic hormones. Such chemical factors, in theory at least, justify any measure which will lessen the relative tissue alkalosis and stimulate those endocrine glands, such as adrenal and thyroid in particular, which exert a sympathetic effect on the autonomic nervous system.

Similar chemical changes are among the striking features in the adrenalectomized animal. The rapid loss of sodium chloride, which is temporarily followed by an acidosis, and finally potassium poisoning brings about the death of the adrenalectomized animal. In the patient suffering from Addison's disease, the symptoms shown by the patient are also explained on a basis of sodium loss. Likewise, we have an ever increasing literature suggesting the adrenals as being primarily involved in mineral metabolism, particularly sodium.

There are certain physical and chemical similarities between the adrenalectomized animal, the patient suffering from Addison's disease and the allergic individual, in that they all show predominate effects of potassium and an increase of parasympathetic stimulation, low total blood chlorides and other clinical and chemical similarities. None the less, when an adequate sodium chloride intake is offered the allergic patient, we do not find the rapid increase in blood chloride such as is found in the adrenalectomized animal, or patient with Addison's disease.

Our treatment commenced with the purely empiric observation that whole raw adrenal glands relieved the asthmatic paroxysms of a child who had been in status asthmaticus three months, when usual methods had failed. This child responded promptly and unlike the response to injections of adrenalin, the patient remained free from attacks for a period of four days, instead of a few minutes to an hour.

What was the cause of this response? Did epinephrin do it? Was the cortin responsible? Were the various vitamins, A, B, C, D, E and G responsible? Was some other unknown factor responsible? Were all these factors in combination responsible?

We investigated epinephrin by mouth and found it to be successful in relieving both the severity and frequency of attacks. We extracted the cortin from steer glands. We found the cortin more lastingly effective than epinephrin. We tried a diet rich in known vitamins; though this was helpful, the effects were not as pronounced as those obtained from cortin or epinephrin. We have tried the various combinations of the three factors and have found that therapeutic measures incorporating all three factors are best. In the dietary measures, beside giving a high vitamin intake, we use a copious sodium chloride intake because of its effect on the adrenals. The raw whole gland itself is the most effective in giving prolonged relief. Though estimates are difficult, it is apparently as effective, inasmuch as its effect lasts longer, as the cortical extract from one hundred times as much glandular substance. On account of technical difficulties of obtaining suitable glands we have largely used a crude oral extract.

The effects of the therapy seem quite general. We have not used it for its immediate effect, but in an attempt to alter physiology. We feel that that is what we are accomplishing in those children whom we have followed from one to two years. In these latter, our sequence of events has usually been:

1. Relief from asthma which may or may not be precipitated by colds and other factors; usually following attacks are lessened in intensity.

2. After a while, colds fail to precipitate, more than mild wheezing, though the bronchitis may continue. Later, even the mild symptoms of wheezing disappear.

3. Gradually the child becomes less susceptible to colds and even though all other members of the family succumb, he may completely avoid the episode or respond but lightly.

4. There are two factors that are more refractory, namely, the bronchitis and nasal symptoms. Sometimes one or the other may be less prominent. However, when there is a considerable degree of bronchiectasis the pulmonary symptoms are slower to yield. When the narrowing of the nasal passages is the important factor, with an accompanying severe hay fever, nasal symptoms disappear last. These symptoms begin to show definite clearing in from nine to eighteen months, depending upon age and severity. The breath sounds lose their harsh emphysematous character early as the asthmatic phase passes off. The roughness particularly over the large bronchi continues for a longer period especially when the bronchitis was severe to begin with. These, however, eventually revert into smooth breathing.

As a group these asthmatic children are undersized, with small, poorly calcified bones and weak muscles. The gains noted in these children seem to be due to a general tissue stimulation toward what would be normal for a robust child. The muscles and the bones increase in size. The thickness of the osseous cortex grows at a rate which seems to be greater than normal for this group. The eosinophiles diminish. The red count at the beginning of treatment is frequently high, 5,000,000 to 5,500,000 or even 6,000,000 with a hemoglobin of from 80 to 110%. In many instances we have seen the red count drop by the third month to 3,000,000 to 4,000,000 with a hemoglobin of 60 to 80%, to return to normal in six to nine months. This apparent anemia is accompanied by an

apparent increase in actual blood volume as shown by the xray of the heart. Microscopic evidence of blood regeneration is likewise frequently seen. Some of the children are really anemic to begin with but most belong to the class of angio-spastic pseudo-anemic children with their pale skins and delicate complexions. As the changes are taking place, there is a great increase in the child's potential physical energy. The heightened energy that these children experience frequently presents a difficulty inasmuch as parents can scarcely keep the children from overdoing. Overdoing is a detriment during the early months of treatment. However, as these boys and girls continue with their improvement the over exercise factor becomes less important. Exhaustion provokes more bronchial secretion; early it tends to set off the asthmatic paroxysms. Many of the children are restless and sleep poorly, having night-mares, night sweats, coughing paroxysms and other episodes that interfere with rest. These lessen very rapidly. In a like manner, the child relaxes, is less tense and irritable. Psychic events that formerly were very upsetting lessen in effect. Children become more manageable. One of the earliest effects of the regime is an increase in appetite; this however, is often followed by a lessened demand for food which is apparently associated with better assimilation. As a group these children have narrow dental arches and high vaults. Associated with the other factors of bone growth (show slide) there seems to be a widening of the arch from the narrow transverse diameter with a high vault, toward the broad arch with a low vault. As the slide shows, a decrease in the width of the

arch and increase in the height of the vault narrow the air passages in two directions so that the air flow through the nose is greatly restricted. The width of the arch at the level of the second bicuspid seems to determine the width of the nasal passageway and the antra. Many dental and surgical procedures have been proposed to correct the deformity. In our cases we have noted a general tendency toward widening of the dental arch and air passages without operative interference. Likewise, the tonsils have been studied though they have frequently been removed before we have seen the children. In most instances where they remain they have been large. As Todd states, the size of the tonsil is inversely proportional to the mineralization of the skeleton, so we have noted that the tonsils decrease in size as the children develop skeletally. In one instance, tonsils so large that the child could scarcely swallow have subsided to normal in eighteen months of treatment.

Children, because of their natural power to grow can effectively respond to a program such as we use. Their bones are not set. Their muscles are developing. Their entire organic and nervous structure is in a state of flux, and more easily stimulated to change. As a corollary, the younger the child, the more rapid the change. For instance, if a child is placed on the therapy before the permanent teeth erupt, the influence in the width of the face is much greater than in a child of, say fourteen.

Adults on the other hand, do not readily change their skeletal

shape. They do, however, change the degree of calcification of their bones varying with sickness and health such as is admirably demonstrated by the development of carious teeth. Although we may be able by prolonged treatment to induce recalcification in adults, whether or not changes in shape and size of bone can take place, we cannot tell. On the other hand, a certain degree of relief is obtained in many cases. This relief too is of a different character than that obtained from the usual measures.

One of the fundamental factors in dealing with the adult asthmatic is that we are dealing with an exhausted individual. Exhaustion plays as great a factor in the adult if not greater, than in the child. To get a good result in adults, bed rest is essential in establishing this therapy. This bed rest must be continued until definite signs of bronchitis are disappearing if we are to get best results. From then on the ^{same} gradual increase in exercise ^{as that} followed by the tuberculous patient is essential.

Such treatment is foreign to the asthmatic and it sometimes takes one to two months for the patient to begin to really get rested and cooperating, even though he already has seen a great lessening in the severity and frequency of his attacks. However, as soon as the patient begins to get real nerve stability we always feel that much has been accomplished. As in the childhood type of asthma we usually see a gradual increase in weight, many times with actual lessening of bodily dimension, especially abdominal and trochanteric diameters. They gain in energy and stability. Attacks lessen and gradually disappear. Nearly all asthmatics show some degree of nasal disturbance. A continued hay fever has a tendency to be a

threat to the adult of recurrent attacks. These attacks are usually less intense after treatment is instituted. In one instance, a woman sixty-five years old who had had three years of the severest asthma, never with relief for more than two to three hours, even from large doses of hypnotics and anti-spasmodics, after the first week of treatment has been free from asthmatic symptoms for two and one-half years.

Several cases of severe emphysema and pulmonary sclerosis without asthma have also obtained considerable relief, more especially from the oral use of epinephrin.

The diet used in all these cases can be classified as a hydrophilic colloidal diet, rich in mineral bearing foods and vitamins. Natural vitamins are used, fortified by Vitamin A, B, D and G from natural sources.

The medication consists of the alcoholic extract of whole adrenal glands devoid of epinephrin given in two and one-half to twenty grams equivalent of raw gland daily, depending on the patient's age, and epinephrin in doses of 1/64 grain in a cherry syrup three times a day. Except for smallest children, children seem to tolerate epinephrin well.

Before closing this discussion I must speak a word as to a possible cause of asthma. Adequate vitamin intake (A, D and C) will not prevent the development of infantile asthma in kittens if the meat used to feed the mother cats is cooked. On the other hand, cats fed raw meats are maintained in excellent shape and the kittens are normal.

We have long been taught the value of the vitamins and according to theory, cod liver oil and orange juice added to boiled milk and our standard formulae are sufficient to develop healthy children. Are the

hormones excreted in the milk sufficient for the proper development of the child, particularly if the mother is deficient? Some of the hormones are destroyed at the heat of pasturization. What factor is pasturization, boiling and canning of milk in this disease particularly in infants? By giving raw, certified milk undiluted to infants, omitting cod liver oil or orange juice, I have seen babies from potentially asthmatic families where the mother feared asthma in the baby, develop into husky children with normal skeletons and no asthmatic symptoms.

Our studies suggest that the heating of milk and the feeding of cows should be accorded as much attention as the reduction of bacterial count and tuberculin tests. Public health demands that all raw milk be produced under cleanest (certified) conditions. The heat of pasturization is sufficient to destroy cortin of the adrenal gland. Our studies suggest that cortin is very important in the proper calcification of the skeleton and the prevention of the development of the allergic manifestations.