1949

Prevention of bronchial asthma in children

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PREVENTION OF BRONCHIAL ASTHMA IN CHILDREN

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Senior Thesis

Presented to the College of Medicine

University of Nebraska

Omaha 1949

C O N T E N T S

INTRODUCTION

The History of Asthma

Bronchial asthma may be defined as "a syndrome characterized by dyspnea, either recurrent or continuous, with wheezing rales, a sense of suffocation and usually cough".(32) The word asthma is derived from a Greek word which means "panting", and originally referred to dyspnea in general. This led to confusion in medical literature as well as in practice. Not until the development of the concept of allergy early in the present century was real progress made in the treatment of asthmatics.

The story of asthma can best be divided into three periods:

I. Ancient and Medieval Period to 1500 A.D.

Bergson traced the earliest reference of asthma to the term "anguish" in the book of Leviticus IX:6. He also found reference to asthma in two passages of Homer and in the writings of Herodotus. Hippocrates mentioned asthma in four of his aphorisms. He considered cold and moisture its principal causes, especially in children. Galen believed in the humoral doctrine of disease. He apparently produced asthma artificially by severing the medulla spinalis. He mentions two causes of asthma, each distinguished by a material "producing irritation, thick and pituitous, and a

crude tubercle in the lung". Stolkin quotes Aurelianus Caelius, a Roman physician of the 4th century, as describing asthma as being acute in nature, with a "feeling of suffocation, heaviness, burning heat in the chest, and a feeling of spasm in the bowels. It begins with violent suffering, with wheezing and hissing in the chest, and the voice is weak, the neck and face stretched and red and the expression anxious - there are tears and the pulse is weak. Asthma is distinct from other diseases where there is difficult breathing, as well as from pneumonia, orthopnea, etc." Galen's opinion, however, went unchallenged, even throughout the 17th century.

II. Pre-Industrial Period, 1500 to 1800 A.D.

During this period modern science began to emerge. Thomas Willis in the 17th century was the first to suggest that asthma has a nervous origin. He differentiated two forms of asthma and gave a clear physiological description. The first was due to mucous plugging and swelling of the walls; the second a convulsive type and due to cramps of muscle fibers of the bronchi and also of the vessels of the lungs, diaphragm and muscles of the breast. Withers in 1786 stated that dust and metallic fumes can cause asthma. He proved beyond doubt that asthma in one patient was due to new feathers in strange beds.

III. Modern Period - Since 1800

This period began with the introduction of auscultation by Laennec, and percussion by Auenbrugger. These proved of great value in diagnosis of asthma. Laennec believed in the spasm theory of asthma and thought the will has some control over this contraction. Animal experimentation showed the effects of section of the vagus and contraction of bronchi upon vagal stimulation. In 1849 Todd theorized that asthma is primarily humoral and is caused by poison or morbid matter acting on the nerves of respiration, either centrally or peripherally. This theory presages the modern "H" substance theory. (I am indebted to Unger (74) for much of the above information.)

Salter (67) wrote a comprehensive treatise on bronchial asthma in which he describes very accurately the signs and symptoms, as well as the forms of treatment which were employed in his time. Being himself an asthmatic, he carefully describes the paroxysms which were produced by proximity to a cat. Unintentionally he thus developed the scratch test technique by noting the effect of scratches of the cat on his skin. Elliotson discovered that pollen causes hay fever and that guinea pig and rabbit hair can cause asthma. Charcot-Leyden crystals were discovered in the 1870's. The discovery of adrenaline by Takamine in 1901 was a real help to asthmatics. (Unger, 74)

The 20th century saw the development of the theory of anaphylaxis and allergy, which resulted in real progress in the treatment of bronchial asthma. Therapy now is based on three principles:

1. Discovery of the offending allergen(s)
2. Avoidance or elimination thereof
3. Hyposensitization where elimination is not possible

However, in the field of preventive medicine bronchial asthma has received scant attantion. With united effort and new discoveries will the future asthmatic enjoy the freedom from symptoms now enjoyed by the tuberculous patient?

BRONCHIAL ASTHMA

Before considering the prevention of bronchial asthma in children it may be profitable to discuss the disease itself. We shall consider its a). etiology, b) pathology, c) symptoms, and d) diagnosis.

A. ETIOLOGY

It is evident from the foregoing that much progress has been made in the care and treatment of asthmatics. As to its etiology, however, there are still some questions. What makes one individual allergic and another not allergic? This is still a matter of dispute. Considering numerous factors involved may shed light on this subject. We shall consider the following factors:

1) predisposing, 2) constitutional, 3) contributory, 4) exciting

1. Predisposing Factors

The presence of asthma has been reported from all parts of the globe. Although the incidence varies in different regions, no Race is exempt. Unger (74) quotes Walzer to the effect that hay fever and asthma are rare among full-blooded American Indians and Eskimoes. In Africa the negroes are less affected than the whites, but the American negro is by no means exempt. Absence of house dust may be a factor with the native African. Yogi (Unger, ibid) observed that the incidence of asthma was greater in Formosa than in Japan, and greater among Japanese immigrants in Formosa during their time of acclimatization. In Denmark the incidence of asthma is nearly 2% of the population.

As to Sex, most statistics show a slight preponderance of males, but the incidence varies with the age group. Tuft (73) states that up to puberty males predominate, nearly 3:1, from puberty to menopause, females (5:4); after age 50, males (5:4)

Age is a very important factor, figures for which from various sources are in fairly close agreement. Tuft (73) found that one third of the cases developed before the age of 10. In Ratner's series (54) the average age

of onset of symptoms was 3.6 years. Peshkin (43) noted the majority had symptoms before the sixth year. Unger (74) found that 63% developed symptoms before the 15th year. All are agreed that the younger the patient at onset and treatment the better the prognosis.

Social Status seems to play no favorites in predisposing to bronchial asthma. But in those already predisposed the parents with means are better able to provide medical treatment and adjust the patient's environment and thus lessen the exposure to antigens. Unger (74) cites a report from Stockholm, in which a group of youngsters ages 8-14 with asthma in which nearly all had positive skin tests to house dust. House visits revealed much crowding. Twenty two patients were taken to an improvised building to be cared for. Improvement in symptoms and school attendance were remarkable, so that soon the city of Stockholm took over the enterprise. The National Home for Jewish Children in Denver (33) reports similar success in treating asthmatic children. Other cities may soon be following this lead. Efron (13) found that tests with purified product of dust extract by Endo Products Co. were 90% accurate and that in patients with asthma and / or allergic rhinitis 75% gave positive tests.

Mental Ability: Superior intelligence appears not to exempt anyone from having asthma, in fact, some of the early investigators claimed that a majority of asthmatics

possessed above average intelligence. Balyeat in 1928 (Unger, 74) reported that of 323 allergic children 68% were mentally superior as contrasted with 25% among non-allergics. Pinness et al in 1937, however, could detect no mental difference between the two groups. In school work allergics were slightly retarded, perhaps due to frequent absence from school. With this Chobot and his workers, in 1939, agreed. Shannon found that allergic children were much better mentally and physically when they were able to avoid their allergens. (Unger, 74) Hurst (31) describes what he calls the "asthma personality", which is the result of over-protection by too-anxious parents. It is characterized by: 1) intelligence above average; 2) over-anxiety; 3) lack of self-confidence. Rubin and Moses (64) studied 54 asthmatic males with EEG and personality data. EEG showed 3 times as many dominant alpha records were found as in normal persons. This, they state, indicates a passive receptive type of personality. Whether these personality traits are a result of the disease and parental influence has not been explained in the literature to my knowledge. In my opinion it might well be.

Environment: Such variables as climate, altitude and general surroundings are largely secondary causes. Climate is important in so far as it influences the production of allergens. A warm dry climate often has a low pollen and mold count. In discussing the question of patients moving

to another climate to relieve symptoms, Dr. Hull (30) states: "Climate doesn't cause it, climate won't cure it". Most asthmatics feel better in high altitudes. Partial relief may be due to freedom from allergens; increased ventilation of the lungs may aid breathing.

Seasonal variations are important in their production of allergens, such as molds and tree, grass and weed pollens. Cold weather leads to living indoors with closed windows, accumulation of house dust, closer proximity to household pets, and increase in upper respiratory infection. Sudden changes in temperature are poorly tolerated by many asthmatics, also sudden drops in barometric pressure.

Occupational exposures are highly important. Such industries include millers, pharmacists, laboratory workers, furriers, poultry farmers and those who groom or work with horses. The trauma received in such trades acts as a predisposing factor in an already sensitized individual. Pollinating plants or a stable near the home may cause increased exposure.

Relation of Asthma to Other Diseases:

Do other diseases predispose the individual to attacks of asthma? Is the asthmatic more prone to develop some other disease? These questions have been variously answered and often based on general impressions. Vaughan and Derbes (79) made a careful survey of 500 persons,

one half of which were allergics, the other half non-allergics. Their findings were tabulated and revealed the following: 1) The number of childhood diseases were nearly equal in both groups. 2) Frequency distribution of other acute infectious diseases was essentially the same. Their conclusion: There is no fundamental difference between allergic and non-allergic individuals in the matter of infectious diseases. They also report that Rackemann found no difference in development of typhoid and other agglutinins in allergic and non-allergic persons.

Tocker and Davidson(72) made a survey of 308 active tuberculous patients to determine the incidence of asthma and found that it compares favorably with that found in the general population. They add that the effect of asthma on the tuberculous process is not a favorable one. When asthma antedated the onset of tuberculosis the asthmatic symptoms improved with the onset of tuberculosis, and as tuberculosis improved the asthma returned. In tuberculosis the allergens were similar to those in non-tuberculous, but skin tests in tuberculous ~~was~~ were not so accurate.

Sequence of Allergic Manifestations:

In most instances asthma is not the first indication of allergy in the patient. The allergic response of the individual depends to some extent upon the portal of entry of the allergen. Thus, ingestion of foods often leads to

gastro-intestinal symptoms, such as pylorospasm, belching, flatulence, whereas inhalants would tend to affect first the upper respiratory tissue. The skin often reacts to allergens invading any portal, and in infants is often the first to respond in the form of eczema.

In a large series of cases Ratner (54) found the average age of onset of various manifestations to be as following: eczema at 0.7 years, asthma at 3.6 years, urticaria at 4.4 years, and hay fever at 7.3 years. He noted that every allergic child had some form of food allergy, but many were also sensitive to inhalants. He also states that "progress of allergy can be interrupted by early diagnosis of interrelated syndromes and reduction of contact with inciting substances".

Clein(8) learned that 78% of allergics had their first manifestations in the first 4 months. By the end of the first year 91% had symptoms. In 82% the first manifestation was a rash. In 24% (ages 6months to 1 year) vomiting and pylorospasm were present. In $\frac{1}{4}$ of the babies with rash there was evidence of pylorospasm.

Glaser (21) found the following sequence: Colic at about 3 weeks, atopic dermatitis at 5-6 weeks, recurrent upper respiratory infections at 2-3 years. This was followed by hay fever, allergic rhinitis, and finally asthma.

Ratner (60) states that "in many instances eczema is a forerunner of asthma". He found that asthma often begins

in the 3-8 year group and is usually preceded by multiple attacks of respiratory difficulty, repeated episodes of sneezing coughing, coryza and so-called bronchitis.

In a report of 100 cases of allergic bronchitis Thomas and Taylor (71) found that 99% had previous diagnosis of perennial allergic rhinitis, suggesting that the allergens may have descended to the bronchi. 70% had post nasal discharge, 46% had their first symptoms after upper respiratory infection. 24% developed asthma following this bronchitis, usually a gradual process. They found complications more common in the older patient or in older case. They state: "It is not uncommon to follow a case history through allergic rhinitis to allergic bronchitis, to bronchial asthma, to definite bronchiectasis". . . "Bronchial asthma is always a potent complication of any case of allergic rhinitis, regardless of treatment, but is less frequent if patient has proper management."

2. Constitutional Factors

Hereditary and Familial Incidence:

With similar predisposing factors one individual will manifest an allergic condition, while others will not. It has long been noted that there is a tendency for allergy to appear in certain families.

One of the earliest surveys made to determine the hereditary contribution was that by Cooke and Vander Veer

in 1916 (10). They found that of 504 allergic adults 48.4% gave a history of other allergy in antecedents. In 1924 Spain and Cooke (70) reported a new series and came to approximately the same conclusion, and believe that hypersensitivity is a dominant hereditary trait. In 1925 Cooke (11) reported that with bilateral history 75% had onset of symptoms before the age of 10. With unilateral history 31% had onset before the 10th year, and with no family history 20% had symptoms before the 10th year. This implied that the more dominant the hereditary factor the earlier was the onset of symptoms. Vaughan (78) found that when inheritance is unilateral about 30% of offspring develop allergy in first 10 years, if bilateral 90% show symptoms by that time. This includes all forms of allergy, as eczema, hay fever and asthma. Clein (6) found that 71% of parents of allergics had allergic tendency.

Wiener, Zieve and Fries (84) present a new theory which involves incomplete dominance. They postulate that allergic tendency is transmitted by a single pair of allelomorphic genes, H and h. H represents non allergy and h represents allergy. Hence 3 genotypes are possible: HH pure normal, hh allergic individual whose symptoms begin before puberty, and Hh are normal transmitters or those who develop allergic disease after puberty. They failed to link allergic heredity to specific blood groups or eye color.

Ratner (58), the exponent of the placental transmission theory (51), challenges the validity of the conclusion that the stronger the inheritance factor the earlier the symptoms appear. He states his agreement with Rackemann that "the clinical manifestations depend solely upon the immunologic process involved and the manner and age at which sensitivity to the particular allergen occurs". He believes that "what is inherited is the susceptibility to sensitization . . . If patients differ in the age of onset of allergic syndromes it is more likely that this is caused by variations in the type of allergen and allergic syndrome rather than by genetic differences." Ratner (57) further states:"I do not believe that inheritance per se has been proved to play a significant role in allergy. Allergy is acquired like any other disease resulting from an invasion into the body of an antigenic substance, e.g. serum sickness."

Clarke and Leopold (6) found that immigrants from Europe, where ragweed does not thrive, after entering the United States require an incubation period which is nearly equal to the average age of native American at which he develops ragweed hay fever.

Transmission:

Assuming the familial incidence of allergy, how is this hypersensitivity transmitted? All allergists do not agree on the answer. Ratner is the exponent of intra-uterine

sensitization. He believes (53) that anaphylaxis in animals is the same as allergy in man. Each animal has his own shock organ. The author succeeded in producing experimental asthma in guinea pigs by exposing their respiratory tract to dust of horse dander and castor bean, respectively. Extent of exposure determined the number which became sensitized. Subsequent exposure produced asthma. The author believes that any person can be sensitized if the exposure is sufficient to break down the physiologic barrier which which the individual possesses to resist invasion. This barrier varies greatly in individuals and at varying times in the same person. Individuals also vary in their capacity to produce antibodies. Ratner maintains that the acquisition of hypersensitiveness depends upon: 1) constitutional factors peculiar to the individual, as physiologic barriers and antibody response; 2) nature of the exciting substance; 3) amount of antigen to which the individual is exposed; 4) amount of antigen which actually invades the blood stream; 5) intervals at which such exposures occur.

Ratner, Jackson and Gruehl (51) in a series of experiments with guinea pigs showed that horse serum sensitiveness can be passively transmitted to guinea pigs in utero. From this they conclude that this is also possible in the human.

Walzer (83) disagrees with Ratner on intrauterine sensitization, for the following reasons:

1) that allergic reagins have never been demonstrated in cord blood; 2) that reagins are fixed in tissue of cord as well as elsewhere in the body; 3) that in newborn animals sensitization disappears progressively, while in humans it progressively increases, and the antigens are usually not the same in offspring as in the mother. He makes the comment that all of Ratner's cases cited were breast fed and could have become sensitized in this way. Shannon (68) cites numerous cases of sensitization via breast milk.

Sherman, Hampton and Cooke (69) studied the placental transmission of skin sensitizing and blocking antibodies. Tests of cord and infant blood were positive for blocking antibodies but negative to sensitizing antibodies. Experiments showed the presence of skin sensitizing antibody in the colostra in amounts ranging from 1/1000 to 1/100 of the amount found in human sera. Clein (8) found that 21% of all allergic infants developed symptoms from their mother's milk, and that the elimination of certain foods from mother's diet relieved the symptoms in all but 15% of the cases.

3. Contributory Factors

The response of an allergic individual to his allergens varies from time to time. A man may sleep on a feather pillow for months without symptoms, yet when he has a "cold" and sleeps on the same feather pillow he develops an attack

of asthma. The cold might then be considered a contributory factor. In the past these contributory factors were often considered to be THE cause of asthma and treatment was directed to a control of these factors, without regard to the allergens involved. And even today this is nearly the extent of therapy many patients, especially children, receive.

Contributory factors may be classified as mechanical, chemical, thermal, infectious, psychogenic, endocrine, and others.

Among mechanical factors may be mentioned such irritants as chalk dust, which, by irritation of respiratory mucosa may render it permeable to invasion of a true allergen, or set up a reflex leading to an asthmatic attack. It is possible that some form of nasal obstuction, in which symptoms are relieved by surgery, contribute to asthmatic attacks. Hansel (25) has found antigens in secretion which had failed to drain because of the obstruction, such as polyps or poorly draining sinuses.

Thermal factors, as sudden changes in temperature, especially cold air, often cause wheezing in an asthmatic.

Infections, especially respiratory, are a definite contributory factor. Ratner (60) reports many instances of food allergy developing in patients following gastro-intestinal upsets and diarrhea. He contributes this to the probable breakdown of barriers in gastro-intestinal mucosa, which permits entrance of protein molecules into

the blood stream. This condition may also obtain during coryza or bronchitis. In any event, the infection often precipitates an attack of asthma in an asthmatic or makes the condition worse. It is conversely true that most febrile conditions alleviate asthmatic symptoms temporarily. The latter may be classed as a form of fever therapy. Of 200 cases reported by Fisher (15) he found that almost one third developed first asthmatic symptoms following an attack of pertussis or measles. Peshkin (43) found asthma was precipitated in children;15% in pertussis, 4% with measles, 2% by scarlet fever, 14% by pneumonia. Recurrent rhinitis or bronchitis or both preceded onset of asthma in 33%.

The Psychogenic Factor, by some considered an underlying cause, is certainly a contributing factor. Some of the earliest references to asthma associate it with emotions. Abramson (2) states: "The early recognition that anger and hostility influence the asthmatic paroxysm goes back at least to the time of Hippocrates. This concept persisted through the Middle Ages without correlation with known physical causes. Emotional aspects were still emphasized in the 18th century." Following this there were instances recorded in which hay fever and asthmatic attacks were attributed to roses - rose fever; even the picture of a rose could produce symptoms. Mackenzie (Abramson, 2) described attacks as occurring frequently

in patients who were neurotic or unstable. Many present-day psychiatrists cite numerous cases which were completely relieved of symptoms by psychotherapy. - Abramson (1), Mayer (40), McDermott and Cobb (41).

The early allergist in his fervent search for antigens may have neglected the psyche. No doubt the patients seen by each may have a different constitutional background. Hurst (31) describes the "asthmatic personality", the result of overprotection by too anxious parents. Rogerson (62) finds that the asthmatic child is over-protected by mother, often before asthmatic symptoms appear. He considers the possibility that the symptoms may become a conditioned reflex or be used subconsciously by the patient to gain his end or avoid difficulty. These psychological factors may aggravate the physical condition. He believes the patient's nervous system is as sensitive as the physical, thus allowing a reaction to occur to physical stimuli which in the normal individual does not occur. Kuntz (36) tries to explain the hypersensitivity of the allergic on the basis of an autonomic inbalance due to electrolyte inbalance. It is difficult, however, to explain the Prausnitz-Kustner reaction on nervous or psychic basis.

At present allergists and psychiatrists are approaching common ground, among them Gillespie (19) and Henderson (27). The latter considers asthma as primarily an organic

disease based on disturbed respiratory physiology - the result of allergic factors in which psychic and emotional problems may be important in precipitating an attack. Asthma is rarely psychogenic in origin, and the the allergic cause can usually be found, in which the equilibrium is disturbed by psychic trauma. In some it may be a conditioned reflex in which the original given condition or circumstance is present after the allergic condition is removed. In children the attitude of the parents is very important. They must possess wisdom and restraint. Overprotection and apprehension may serve as a trigger mechanism, through suggestion. "A little healthy neglect may even be preferable to over-solicitude".

I am inclined to agree with Glaser (22) who recently said: "The best that can be hoped from the psychological approach is amelioration; rarely a cure, because no psychological approach can change the underlying allergic constitution. Every allergist has had the experience of seeing some new therapeutic advance relieve an occasional patient, and under these circumstances the associated psychosomatic problems vanish like mist in the sun. . . Once we are able to relieve at will the allergic manifestations, the psychological problems associated will, in most instances, solve themselves; although in a basically psychopathic individual the clinical manifestations of the abnormal psychological state will of course express itself in some other form."

Not much is known concerning the effect of the endocrines upon the allergic state. Ramirez (49) suggests that the endocrine inbalance may affect "the underlying fundamental mechanism of hypersensitiveness". In this manner, he reasons, heredity may be a factor and may also determine the shock tissue. It is true that at time of adolescence, when the endocrines are very active, marked changes often occur in the condition of asthmatics, many of which become symptom free at this age. This is especially true in food allergies; but self-desensitization may play a part in bringing this about.

In conclusion, it must be remembered that such conditions as fatigue, malnutrition, constipation, exhaustion, may be contributory factors in bringing about asthmatic attacks.

4. Exciting Factors

These may be briefly listed as being: 1) Allergens, 2) Exposure to allergens, 3) Time Element, 4) The Allergic Threshold.

"Early in the development of clinical allergy Cooke formulated postulates which must be fulfilled before a substance is recognized as a cause of allergic symptoms." These are: 1) the substance must give a positive local reaction or must be able to cause clinical symptoms; 2) the patient must be known to have been exposed to this substance. (Unger, 74)

The list of substances to which allergic persons are sensitive now contains many hundreds of things; these may be generally classified as: inhalants, ingestants, injectants, and contactants, depending upon the portal of entry. Although any individual may be sensitive to any of these substances, for purposes of testing it is found that most persons are sensitive to relatively few of these. This may be true for two reasons: 1) Extensive contact occurs more frequently with the more common substances; 2) many of these substances are weak sensitizers. Most allergens contain protein; but drugs, such as aspirin, are exceptions.

Sensitivity presupposes previous exposure. Sensitivity of infants to certain adult foods can often be traced through maternal milk. Unger (74) reports that Grove in Berlin tested 36 timothy sensitive hay fever patients with an extract of the pollen of ragweed, which does not grow in Germany, and found every one of them negative.

Time is necessary, following exposure, to permit formation of sensitizing antibodies and tissue sensitization. Repeated exposures to the same allergen are usually necessary, especially among the inhalants. Thus it usually requires considerable time before a baker develops symptoms of rhinitis or asthma from wheat products.

In every severe hay fever season many persons who usually escape symptoms suffer attacks. Some ragweed sensitive persons develop no symptoms with ordinary pre-

cautions. But should such person handle ragweeds in season he would quite surely be seized with an attack. A food-sensitive patient may tolerate a small amount of a given food, whereas an excess amount will produce symptoms. In other words, each individual appears to have a tolerance to given allergens. Unger (74) reports the case of a physician, formerly hay fever free, who accidentally spilled the contents of a beaker filled with ragweed pollen. He immediately developed hay fever, which lasted for two weeks. Each season thereafter he had hay fever. Unger attributes this to an overwhelming of the allergic threshold and thus lowering it. Unger likewise observes that a person sensitive to both ragweed and eggs may be symptom free until he eats eggs during ragweed season. Factors such as fatigue may also lower the threshold. It would seem that the tissues are able to handle a given amount of the allergen, but an excess upsets the equilibrium.

B. PATHOLOGY

The symptoms in bronchial asthma appear to be due to an increase in residual air and therefore a reduction in vital capacity. This reduction is proportional to the symptoms, and may be very marked. In uncomplicated paroxysmal asthma the vital capacity returns to normal at the end of the paroxysm. The symptoms are due to a partial

occlusion of the lumen of the bronchi, especially the smaller ones. This obstruction may be caused by spasm of the bronchioles, edema of the mucosa about the lumen of the bronchus and/or due to mucous plugs in bronchioles or bronchi.

Experiments show that stimulation of the vagi produces bronchiolar spasm, while the administration of sympathomimetic drugs relieves the paroxysm in most instances. Kuntz (36) explains the symptoms on the basis of an autonomic inbalance, in which the parasympathetic predominance leads to an attack. Ramirez (49) believes bronchospasm may result from reflex stimulation from nasal or sinal pathology.

Rackemann (48) showed from autopsy that in more than half of 50 cases death was "caused by development of plugs of tough sticky mucous which obstruct the bronchi and lead to suffocation. The pathologic picture is typical: it is characterized by voluminous distended lungs of bluish-gray color, and the cut section of which shows all bronchi, especially those of medium and small size, occluded by plugs."

Hilding (28) in a number of cases of death due to asthma found that nearly all epithelial cells in the bronchi were of the goblet cell type, with practically no cilia present. The bronchi were filled with sticky mucous. He concludes: "In my opinion this metamorphosis is the chief pathologic change and, in my opinion, death results directly

from loss of ciliary function." He found that in patients who died of chronic bronchitis the passages were filled with purulent fluid, and ciliated epithelium had sloughed off extensively. In some cases bronchospasm was the cause of death. Thus in the advanced stages of asthma there appear to be irreversible changes in the lung epithelium. Ratner (60) reminds us that in the early stage of asthma is a physiologic disturbance which can be overcome, for the child who has no further attacks has signal absence of pathologic stigmata of disease.

The exact mechanism involved in an allergic reaction is still a matter for research. The mechanism may be similar in any tissue of the body, symptoms varying with the location of the process and the organs involved. Adequate sensitization of an individual consists of invasion of the bloodstream by allergens, to which the body responds by the production of sensitizing antibodies. The majority of these antibodies become fixed to smooth muscle tissue. Their location varies with the species; in man the respiratory tract, intestine and skin are largely involved. What determines the site has not yet been learned. Perhaps the portal of entry is a factor. The skin is nearly always involved. This is the basis of skin tests.

Many allergists postulate that when the specific allergen becomes united with the fixed antibody, either

by way of the circulation or by direct contact, a histamine-like or "H" substance is liberated, which causes irritation of the smooth muscle and its contraction. Ratner (59) attempts to find a common denominator for anaphylaxis and allergy. He explains the mechanism in all instances as due to irritation of smooth muscle in the arterioles of the tissue affected. This constriction of the arterioles then leads to hemostasis, tissue anoxia and capillary permeability, to which he attributes wheal formation and edema. In asthma this edema of the mucosa in part contributes to the partial obstruction of the bronchioles. Ratner does not accept the theory of the "H" substance. However, the effective relief obtained from anti-histamine in some types of allergy, though minimal in asthma, would seem to favor the theory of "H" substance formation in at least some forms of allergy.

Physiologic Changes:

The inspiratory phase is normally more powerful than the expiratory. Partial obstruction to air passages in the asthmatic results in failure to expel the normal portion of air from the lungs. This leads to more forceful inspiration, which in turn results in more trapped air, a vicious cycle. In uncomplicated asthma there is a temporary emphysema which tends to become chronic as the elastic tissue in the lung becomes replaced by fibrous connective tissue. Alexander (3) among others believes

that in the earlier stages of the disease edema and bronchial constriction are the most important factors, since then the mucous glands are small and mucous is scant. "In long-standing asthma increased, thick, tenacious mucous is probably the most prominent factor in bronchial obstruction." Passage of air through constricted bronchioles causes wheezing. It is the mucous which causes musical rales or rhonchi. In chronic asthma the emphysema is permanent and the patient regularly feels short of breath on exertion. When a paroxysm supervenes expiration becomes well-nigh impossible. This accounts for the cyanosis and marked apprehension.

C. SYMPTOMATOLOGY

Bronchial asthma may occur at any age. It is caused by incomplete bronchial obstruction, usually due to hypersensitivity to one or more allergens and is characterized by attacks of dyspnea and wheezing. The disease may be classified according to: pathology, etiology, mode of acquisition, or clinical findings. I prefer to follow the classification of Unger (74) who divides it into paroxysmal and chronic. The symptomatology varies with the condition of the patient.

Prodromal Symptoms: Since minor allergies frequently precede the onset of asthma they should alert the parent or physician. Gastro intestinal symptoms or eczema are

often present in an allergic infant. Another frequent forerunner of asthma is nasal congestion, which causes sneezing, watering and stuffiness. These signs of a cold are often not associated with fever and often clear during the day. Thomas (71) reports 100 cases, of which 99 had previous diagnosis of perennial allergic rhinitis, suggesting that the allergens may have descended to bronchi. Gray (24) calls this the "preasthmatic state", in which prophylactic measures are often effective. Frequently asthma is preceded by nocturnal cough; auscultation may reveal slight rales, but the patient may not be aware of respiratory difficulty. This condition may continue for months or even years. Frequent sinusitis in a patient should also alert the physician. Many of these patients have had tonsillectomy without relief of symptoms. The nasal and pharyngeal mucosa is often pale and boggy. A careful history is most informative.

Paroxysmal Asthma:

This is the most common form in children and young adults, and is usually due to pollen, molds or food.

In the mild form there is a little dyspnea on exertion, a slight cough, some heaviness over the chest preceding wheezing, which is best heard with stethoscope, and often some expectoration of mucous. With the help of a little medication the patient is able to carry on his activities.

In the moderate form the symptoms are more pronounced. The patient experiences dyspnea and orthopnea with possible cyanosis. The attack lasts longer but can be relieved by epinephrin. In children there may be fever.

In the severe form dyspnea and cyanosis are marked. All accessory muscles function to capacity to force air out of the lungs. The expiratory phase is much prolonged and difficult. The patient is apprehensive and may assume a position in which he rests his elbows on the table. The cough at first is unproductive but when mucous is finally raised relief occurs. The wheezing can often be heard across the room. Cyanosis and perspiration are marked. In children there is often elevation of temperature. The attack may last a few hours to a few days if not relieved by medication. Between attacks physical findings are negative. Xray reveals depressed diaphragn, some mottling due to mucous plugs. During an attack there is marked reduction in vital capacity. Secretions often reveal the presence of Laennec's Pearls, Curschmann's Spirals and eosinophiles. If many neutrophils are present in secretions one should suspect infection. Peripheral blood may contain 5-10% eosinophils. In the prodromal stage a high eosinophil count in secretions is strong evidence for allergy.

Chronic Asthma:

In this stage the symptoms described for the paroxysmal type usually occur perennially, more frequently, and the patient is never symptom-free. He is unable to do

much manual labor; exertion may precipitate an attack. With proper management they may become symptom-free if the offending allergens are removed and their age is less than 40. Many of them succumb to the complications which chronicity brings.

In the mild form the patient has slight dyspnea most of the time but is able to carry on with limitations. His sleep is frequently disturbed by an attack of dyspnea and cough in the early morning. Proper treatment may bring much relief. The A P diameter of their chest is often increased, especially with onset in childhood.

In moderately severe form symptoms are more severe and never absent. Nutrition is usually poor, and dyspnea, orthopnea, wheezing and cyanosis are more marked. He has tendency toward self-medication; over-medication often results in palpitation and headache. Proper treatment may give much relief. Some terminate in a severe chronic state, others succumb to infection or develop serious complications.

Status Asthmaticus: This is the most severe of the chronic states. With onset of asthma after 40 this state may be quickly reached. This patient is truly to be pitied. He is critically ill and confined to bed most of the time. The vital capacity during attacks may be reduced to 300cc. Attacks occur more frequently and last longer. Apprehension is marked and during an attack many prefer to die. The patient is poorly nourished and medication is ineffective.

Skin tests are often negative, and infection is often superimposed upon allergy. Death is often the result of complications, of which there are many.

Laboratory findings are similar to those for the paroxysmal group, except that many neutrophils may be found in secretions. Xray shows emphysema of varying degree.

The most common complication of chronic asthma is emphysema. Its deformity varies with the age of onset; in the very young the sternum may be depressed; older children develop pigeon breast; adults barrel chest.

Serious complications may arise as a result of infection. Among these are bronchitis, bronchiectasis, sinusitis and pneumonitis. Sinusitis may be a part of the allergic syndrome and not the cause or result of asthma. Cardiac complications are rare in spite of the frequent strain placed upon the heart. Unger (74) reports EKG evidence of right heart strain. This is largely the result of emphysema. Alexander (3) concludes: "When heart failure does occur (in asthma) it is due to the mechanical factors of pulmonary emphysema".

D. DIAGNOSIS

In making the diagnosis it is important to:

1) establish or rule out bronchial asthma
2) determine the presence and extent of complications
3) arrive at a specific diagnosis as to the cause of attacks

Procedures employed in diagnosis include:

1) Careful and painstaking history

2) Thorough physical examination

3) Selected laboratory procedures

In taking the history the patient (or parent) should be permitted to tell what he knows about the condition and then should be asked pertinent questions, to include: duration of disease, frequency and duration of attacks, circumstances during first attack, condition between attacks, are attacks seasonal and when, cause if known; presence and productivity of cough, nature of sputum; how is cough related to attacks; history of weight loss, fever, chills, night sweats. History of conjunctivitis, coryza, itching nose, frequent colds and headaches, otitis media; ENT surgery; food or drug idiosyncrasy. What gives relief? Prolonged asymptomatic period. Where were you living then? Home conditions; limitation of activity; relation to menstrual cycle; previous tests and treatment; family history of allergy.

The physical examination should be complete with special attention given to respiratory tract and heart. The most important findings in asthma are wheezing, dyspnea, orthopnea, cough and cyanosis. Fineman (14) advocates the so-called pressure test as a valuable aid in clinical diagnosis of bronchial asthma when ordinary auscultation is negative. Manual pressure is applied to the chest

anteriorly or also posteriorly. This forces air out of the lungs and bronchi. If sibilant rales are heard with stethoscope the test is positive for asthma. A negative test, however, does not rule out asthma. Chest deformities, lowered vital capacity and cyanosis indicate chronic asthma in most cases. Fluoroscopy will reveal a depressed diaphragm and increased hilar shadows. In the paroxysmal type radiologic findings between attacks are normal. Xray may rule out carcinoma, tuberculosis, and detect bronchiectasis.

Laboratory work should include: 1) Complete blood count - leukocytosis may indicate infection; eosinophilia is common in allergy.

2) Kahn or Wasserman will determine serology

3)Sputum may reveal evidence of asthma or tuberculosis

4) Examination of nasal secretion may reveal eosinophilia

5) Sedimentation rate may exclude infection

In most instances a thorough history and careful physical examination are sufficient to determine the presence of asthma.

Differential Diagnosis:

Bronchial asthma must be differentiated from the following diseases, which may also cause dyspnea and wheezing (Unger, 74):

1. Nasal deformities and enlarged tonsils and adenoids, by physical examination.

2. Laryngeal stridor; the obstruction is largely inspiratory. It may occur with onset of asthma.
3. Tumors, by their continuous presence, and examination.
4. Syphilitic strictures, by serology, absence of rales.
5. Laryngeal diphtheria, by throat culture, membrane, absence of wheezing.
6. Enlarged thymus, by xray findings and therapy, sibilant rales.
7. Substernal goiter, by inspiratory stridor, no rales.
8. Bronchogenic carcinoma, by persistence of cough; bronchoscopy and xray.
9. Tuberculosis, by tuberculin test, sputum, fever, weight loss, xray.
10. Foreign body, by history, onset, xray, bronchoscopy.
11. Cardiac asthma, by evidence of congestive failure, history, age, rales moist and coarse at bases, shock, no eosinophilia. This condition more than any other resembles bronchial asthma.
12. Silicosis, by occupational history, onset, xray, absence of allergic findings.
13. Chronic bronchitis, by its association with other disease, as emphysema, bronchiectasis, pulmonary tuberculosis, cardiac decompensation, or asthma; purulent sputum, mild fever, leukocytosis. It may be a forerunner of asthma.

Tests for specific diagnosis will be discussed in connection with preventive measures.

PREVENTION OF BRONCHIAL ASTHMA

An important phase in the treatment of disease today is that called preventive medicine. One need but compare the incidence of small pox, diphtheria and tuberculosis a century ago and now to recognize the value of prevention. Even the complications of syphilis are less common today. But the incidence of bronchial asthma seems not to have been reduced. Is the concept of allergy and its implications not yet fully understood, or is asthma so mild an affliction that it does not merit serious consideration? The child will outgrow it?

Incidence and Morbidity

Complete statistics on the incidence of bronchial asthma are not available. Vaughan found that the incidence in the 21 - 31 age group, based on army figures in World War I, showed an incidence of about 0.5%, who were either rejected or later hospitalized for asthma. Other investigators, as Rackemann, Hoffman, Spain and Cooke, and Vaughan in surveys among civilians in America arrived at approximately the same figure. This implies that there are approximately 700,000 asthmatics in America. Hoffman found that each asthmatic in the army had an average of 25 disabling days per year. (Unger, 74), Rudolph (66) studied 200 cases in an army hospital and reports that 61% were discharged because their symptoms "were so severe

that it was believed these men could no longer perform satisfactorily the duties of a soldier in the army".

The loss in working days, however, is only one aspect of the disease. Although the death rate in asthma is very low, the morbidity is often distressingly high. One must not only take into account the slight inconvenience which the patient with the mild paroxysmal symptoms experiences, but one must also consider the bleak prospect which he faces, if no preventive measures are taken early, of the possibility of physical deformity and the dreaded status asthmaticus. No one who has cared for a patient with status asthmaticus can think lightly of bronchial asthma.

Ten years ago Kern (35) made a plea for prophylaxis in the treatment of asthma. He said: "When an allergist, confronted with the difficult and at times hopeless problem of the patient with advanced allergic disease, traces back the story to its beginnings - the severe and perennial asthma, that a few years ago was only an occasional attack, and before that, mild nasal symptoms, untreated because they seemed so insignificant - he cannot help but think how much easier it would have been to help this patient in those earlier stages, and why was nothing done to prevent the onset and progress of his various sensitivities? Although our knowledge of the development of the allergic state is as yet defective and fragmentary, nevertheless enough information is at hand to warrant its

practical application. And so some allergists in their writings (Cooke, Rowe, Tuft, Vaughan et al) have mentioned and most allergists in their clinical practice have advised measures which they felt might prevent the onset of allergic disease. Unfortunately the possibility of prophylaxis has not been brought with sufficient insistence to the attention of internists, pediatricians, general practitioners, and others not primarily interested in allergy. As a result, prophylaxis has been least attempted in the very persons most in need of it: those not yet afflicted with clinical hypersensitiveneness, or only in its milder forms."

A. METHODS OF PREVENTION

1. Avoidance of Intermarriage

In the prevention of asthma as in any other disease it seems but logical that treatment should be aimed at the etiologic as well as the contributory factors. We have seen that the chief etiologic factor in bronchial asthma is heredity, and that if the heredity is bilateral the family incidence of allergy is much greater, It therefore seems reasonable that the incidence and severity of asthma could be considerably reduced by encouraging an allergic individual to marry a non-allergic. Adequate education of the public in this respect might eventually prove to have considerable effect. Unger (77), Glaser and Landau (21).

2. Recognition of Allergic Families

It is of great value for a physician to know that a patient comes from an allergic family, for every child from an allergic family is potentially allergic, and may develop allergic symptoms, including asthma. It is a relatively simple procedure for the physician to inquire as to allergic manifestations in the patient's antecedents. Specific symptoms should be mentioned, for many individuals may fail to recognize that infantile eczema or chronic sinusitis may be of allergic origin. It is as important for a physician to know that there is allergy in the background as to know that a forebear had hypertension or cancer. This knowledge may aid in the early diagnosis of allergy which might otherwise be overlooked or mistreated.

3. Control of Allergic Mothers

The theory of intrauterine sensitization, strongly defended by Ratner (51, 52, 56) has not found general support. But there is ample evidence to show that infants may be sensitized via the mother's milk. (70, 86). Nursing mothers should eat a great variety of foods, with no indulgence in any one food; avoid eating unusual foods during period of lactation; eggs should be well cooked.

4. Preventing Direct Exposure to Common Antigens

Since the probability is so great that the allergic child will develop hypersensitivity to some allergen, it would be unwise to expose him needlessly to the allergens which most often produce hypersensitivity, especially during infancy, illness and convalescence. In the small child foods are especially important. Parents should, therefore, be instructed to watch the baby's diet closely. Foods should be introduced one at a time and be well cooked. Ascorbic acid should replace orange juice and Provatol, by Wyeth (Bowen, 4), may well replace cod liver oil. Only the yolk of the egg should be introduced at first, and it should be hard-boiled. Clein (9) in a study of 100 allergic children for 10 years, found that by eliminating raw egg yolk in infancy the incidence of eczema was reduced by one third. Any food which is found to produce colic or diarrhea should be eliminated from the diet for several months and then only gradually reintroduced. Food idiosyncrasies may well be honored until shown to be harmless.

Parents should be instructed to watch carefully for signs of allergic reaction, such as rash, eczema and gastro-intestinal disturbance. In this way offending allergens may often be detected and eliminated. The child's surroundings should be as dust free as possible

and pets and toys covered with animal hair should not be permitted in the home. (Brown, 5) Parents should avoid living in a weed infested neighborhood. Exposure perhaps explains the greater incidence of hay fever among boys than girls. The allergic child should not attend camp during the ragweed or hemp season. Older individuals should avoid entering an occupation where there is great exposure to allergenic dust, as bakeries, furriers, grain mills. Onset of symptoms in any condition should be a warning to discontinue exposure promptly.

5. Searching for Allergens on First Symptoms

In the allergic individual many symptoms may be forerunners of asthma. Among those already mentioned are: repeated gastro-intestinal upsets following the ingestion of a given food, eczema, protracted and frequent colds, rhinitis, sinusitis, allergic bronchitis, hay fever, urticaria. These illnesses in themselves seldom appear serious and, if parents are unaware of their importance, often fail to seek relief for the child. Physicians frequently treat them symptomatically. (Early symptoms of tuberculosis are also frequently mild.) Rudolph (65) states: "The early recognition of the allergic state in childhood, with proper diagnosis and treatment, may prove to be the principal factor in the prevention of asthma and other major disturbances of the body. It becomes,

therefore, of paramount importance for physicians to interpret and properly treat the earliest allergic manifestations."

Unger (74) deplores the results of procrastination which he often sees: "Children, however, are frequently permitted to have many attacks and may be given epinephrin first by the physician and later by the parents. When some of these youngsters finally report for skin tests they may be so emphysematous and pigeon-breasted that a measure of relief is all we can offer. Whenever I see one of these deformed children my heart sinks as I know that with prompt efficient preventive treatment this stage should never have been reached."

Various procedures may be employed in the search for offending allergens. They include: 1) careful history, 2) food diary and elimination tests, 3) skin tests. Conditions vary, such as the age of the patient, but first and foremost should be a complete history. Rackemann (46) gives some valuable suggestions. He emphasizes the value of specific dates in the history. One should account for all of the time, which may give a clue as to why the attack began and ended and why the free period ended. If the history is brief, history can be made by making changes in the patient's environment. In dermatitis the history may be as important as in asthma. Inspecting the patient's home and furniture is important. Old cotton and kapok are more allergenic than the new. "Allergenic cleanliness" is important.

In a small child, whose contacts are limited, whose diet is simple, and whose sensitivities fluctuate, a food diary and the elimination of one food at a time may be advisable. In the older individual skin tests should be employed. The scratch test is more easily administered, especially to small children and gives less false positive reactions; the intradermal test is more sensitive in the hands of a competent technician but may give more false positives. Each method has its advocates. This test should comprise as complete a list of substances as possible and should include all allergenic substances to which the individual is exposed.

If skin tests are all negative or if avoidance of substances found to give a positive test do not relieve symptoms then a food diary or food elimination test should be employed. The history should be carefully reviewed to find possible inhalants, contactants, drugs. Complicated situations may arise, as when several allergens in combination are needed to produce symptoms. The important thing in all cases is that the offending allergens be discovered and eliminated, or contact reduced, or the individual rendered less sensitive to their presence.

6. TREATMENT WHEN ALLERGENS ARE KNOWN

When a child presents symptoms of hypersensitivity in any form and the offending allergens have been discovered, prompt treatment should be instituted. This consists chiefly in:

1) elimination of the offending antigens
2) hyposensitization
3) removal of psychogenic factors
4) antihistaminic therapy
5) symptomatic treatment to relieve attacks

a. Elimination

"If there were no exposure there would be no attacks. Removal of the cause, if feasible and if complete, brings quick relief, and no symptoms will occur as long as the cause is avoided (unless the patient develops new sensitivities") (Unger, 74), in which case trial diets or testing must be repeated. Education of the parents is an important step in securing their cooperation in this matter. Printed instructions are of great help.

If the allergen is a food it should be replaced by a suitable substitute. Many diets have been developed for allergics and can be obtained in printed form by the physician. This information should be incorporated in the instructions to the parents. Minute amounts of the

offending foods, if they produce no symptoms, often lead to hyposensitization, and may account for the so-called "outgrowing" of symptoms seen in some individuals as they grow older. Some foods which produce symptoms in the raw state are tolerated when well-cooked.

If the allergen is an inhalant, it also should be avoided, but is a more difficult procedure. Animal dander and feathers may be avoided by keeping away from the animal and using impermeable covers or one filled with sponge rubber. Specific pollens may be avoided by moving to an area where they are not found, but development of new sensitivities may destroy the temporary benefits. Molds are also difficult to avoid. Keeping windows closed during the pollen season or using air filters helps to lower the pollen count in a given room or home, but this restricts the patient's environment. The wearing of a mask is a burden. Hyposensitization is the reasonable solution.

House dust is perhaps the most universal antigen in civilization (Brown, 5). It should be reduced to the minimum in the home and especially the patient's bedroom. No rugs, drapes or overstuffed furniture should be permitted there. It may be necessary to cover living room furniture. A good vacuum cleaner, preferably one which catches dust in a water trap, is essential. Face powder containing orris root should be replaced by non-allergenic powder now available.

It is advisable that the physician make a personal survey of the patient's home conditions. In this way conditions may be recognized which the parents did not notice. The allergic child should be advised against choosing a vocation in which allergenic dusts are a factor, such as furrier, baker, etc.

b. Hyposensitization

This procedure should be employed whenever the allergen cannot be completely or satisfactorily avoided. It may be done by the oral or hypodermic route and consists of the administering of minute, subminimal and progressively increasing amounts of the offending allergen. By this method the patient's threshold of tolerance for the allergen is raised, usually to the level that normal exposure no longer produces symptoms. These treatments may be given as pre-seasonal or, preferred, perennially. Kahn (35) found that the dosage required in children was equal to that in adults.

Frank and Gelfand (16) have reviewed the literature on the mechanism involved in hyposensitization. It has been found that in response to injection of a given antigen the individual responds by producing specific antibodies, which are heat stable. Cooke called these, "blocking antibodies". Normal (non-allergic) individuals and sheep are also capable of producing them. This anti-

body competes with the sensitizing antibody of the individual for combination with the antigen and usually succeeds, thus preventing the reaction which otherwise would occur. Loveless (37) found that blocking antibody titre was higher following perennial injections than after the preseasonal method. She also (38) showed that the titre of blocking antibody varies with the patient's symptoms. This latter result is questioned by some investigators.

c. Removal of Psychogenic Factors

It has been previously shown that in some patients psychogenic factors play an important part in prolongation of symptoms. These, as well as the organic allergens, should therefore be removed as much as possible. Prickmann (45) advises the prevention of emotional upsets. Since the allergic usually possesses a hypersensitive nervous system as well as other tissue, Fisher (15) believes that reduction of symptoms often seen in adulthood may be due to stabilization of the nervous system, if the home and environment aid the process by adequate rest and a calm reaction to stimuli and attacks. The family must avoid fear of the onset of attacks and apprehension of outcome. The diet should not be overemphasized to the child. Thus the prognosis may be greatly influenced by parents, home and environment. Improvement should be assumed during adolescence in the presence of proper treatment.

d. Antihistamines

The theory of histamine, or "H" substance, as being the causative agent in producing symptoms in allergy led to extensive experimentation. Histamine desensitization did not prove effective (Peshkin, 44). Likewise, injection of histaminase to destroy histamine was disappointing. The search then led to substances which would inhibit the action, ostensibly by competing with histamine for union with the smooth muscle cells. Amino acids, as histidine, cysteine and arginine were found to be too toxic. Synthetic products were then attempted, of which at present there are a large number available, many still in the experimental stage. Considerable success has been obtained with some of these products in the treatment of allergic rhinitis, dermatitis and conjunctivitis; but in the treatment of asthma the results have been unimpressive in most instances. These products are still new and reports by various authors show wide variation. Most of them have considerable toxic side reactions. Their efficacy merits further study.

7. Symptomatic Treatment During Attacks

While studies, tests and treatment of the asthmatic patient are under way, and never as a substitute for these, the patient should be treated symptomatically, to remove apprehension and prevent the onset of chronic asthma.

Epinephrine or ephedrine should be employed to reduce bronchospasm and bronchedema. A preparation such as amodrine, which contains aminophyllin, racephedrine and phenobarbital, may be given upon retiring if the patient is subject to coughing spells every night, or whenever wheezing is detected. Paroxysms may thus be prevented. Expectorant, as an iodide, should be administered prophylactically to prevent the formation of mucous plugs.

8. Protection During Critical Times

We have seen that infectious diseases and the period of convalescence predispose the individual to attacks of asthma and that a large percentage of cases appear to have their onset following such diseases as pertussis, measles and pneumonia. Allergic children should therefore early receive preventive therapy to render them immune to as many diseases as possible. To prevent severe shock no horse serum should ever be administered to an allergic; therefore diphtheria and tetanus toxoids should be given early in life. Upper respiratory infection should be treated symptomatically and at the first indication of involvement of the bronchi antibiotics should be given. Prolonged or untreated respiratory infection may herald the onset of so-called intrinsic asthma

9. General Hygienic Measures

It is important in the treatment of the asthmatic patient that his health and nutrition be kept as near normal as possible. Poor nutrition, lack of sleep, fatigue make the child an easy prey to infection, which often precipitates attacks. Good oral and mental hygiene should be promoted. Indications for tonsillectomy or adenoidectomy are the same in the allergic and non-allergic individual and should not be expected to cure the allergic condition. Hansel (25) recommends surgery for removal of nasal polyps or drainage of sinuses which may serve as depot for storage of allergenic substance, if other means fail. The well-nourished child usually has a wholesome attitude toward his surroundings and possesses a reserve should subsequent attacks come. The child's activities should be guided but he should be permitted to lead as normal a life as his physical condition will permit. He should not be pampered or made too conscious of his handicap.

B. SUCCESS OF PROPHYLACTIC MEASURES

In the preceding pages we have stressed the importance of preventing bronchial asthma in children. We have advocated measures which should prevent its development or make the attacks less frequent and severe. What evidence is there to show that such treatment is effective? Statistics to this effect are rather meager, perhaps because its

principles have not been clearly enunciated to the practicing physician. There has been no concerted effort to this effect as in the campaigns for tuberculosis and poliomyelitis. Leading men in the field of allergy, however, are hopeful.

As early as 1923 Ratner (50) reported 6 cases of infantile eczema developing into asthma due to foods. Elimination and desensitization helped to clear it up. In 1938 he (57) stated: "Early diagnosis and treatment (of hay fever) may well decrease the incidence of asthma in later childhood and adult life." In another article (54) he states: "Progress of allergy can be interrupted by early diagnosis of interrelated syndromes and reduction of contact with inciting substances." To which (ibid) Cohen of Cleveland added: "It can be recognized early, and if managed early many of the changes which occur in adult life may be avoided." Criep (12) states: "We are glad to see an allergic child, because we know we can do something for it, and the time to treat allergy is in its early stages - not after secondary complications have developed."

Clein (9) reports his observation on 100 allergic children whom he treated and followed for 10 years. He found that 98% developed a major allergy, 26% developed asthma. The present condition of these children, he states, is equivalent to any normal group, physically and mentally.

The result of treatment was: milder symptoms, better reaction to therapy, fewer recurrences, fewer sick days, fewer absentees at school, more normal child life. He concludes: "With our present knowledge we cannot prevent development of major allergic disease in infants who have an inherent allergic constitution. . . Prophylactic treatment in its present state of development will probably minimize or ameliorate the allergic symptoms, allowing the child to grow and develop normally, both physically and mentally."

Unger (76) reported on 459 patients who had been under observation and treatment for 1-20 years. Approximately one third of the 298 cases of paroxysmal asthma obtained 100% relief of symptoms, whereas only 1 in 80 of the chronic group had such relief. The percentage of Improvement was also much greater in the paroxysmal group. Death, from all causes, occurred in 23% of the chronic group, and in 3.7% of the paroxysmal. Death due mainly to asthma occurred in 21 cases. Unger reminds us that we can scarcely speak of an asthmatic patient as being "cured", although he may remain symptom-free: massive exposure may give temporary symptoms. Such persons (like diabetics) must be kept under observation to prevent carelessness and relapses. He agrees with Vander Veer, who says: "Once an asthmatic, a patient is usually an asthmatic for the rest of his life", and with Rackemann, who says: "The results in the extrinsic

group show that cure has been accomplished by the removal of the trigger which fired the attack, but obviously the gun remains loaded in most and probably in all cases."

In order to determine the extent of prophylaxis practised locally in the treatment of bronchial asthma in children, I made a personal inquiry of 10 pediatricians in Omaha. I obtained the following results: For the child of allergic parents only one stated that he routinely prescribes ascorbic acid instead of orange juice, drisdol instead of cod liver oil, heating of allergenic foods, no pets in the home. Others wait for the development of symptoms. When symptoms, such as eczema, develop several of the others try to determine the allergenic food involved, by elimination, or treat the dermatitis by medication. Two stated that they refer intractable cases to allergist if parents insist. The above procedures are fairly representative, I believe, of the amount of prophylaxis in allergy as applied by practitioners throughout the country.

An encouraging trend, however, may be noted as it appears in the discussion recorded in the July 1948 edition of PEDIATRICS, p. 119, where a Round Table discussion is reported concerning the treatment of asthma in children. Says Dr. Bost: "Is the man in pediatric practice able to take care of an asthmatic child properly? Does he know how and where to start and what to do? I think the answer is yes. The practitioner is the one who most often sees the

child in his home, and as (others) have mentioned, this is a peculiar and particular advantage. Treatment of the acute attack - so important in the minds of the parents - is so small a part of the problem of the asthmatic child. We must be thinking of a plan for study of the asthmatic child even during the acute attack." He then describes the Program for Care of the Asthmatic Child, which includes A. Prophylaxis, B. Plan for Study, C. Treatment.

He states: "Prophylaxis heads the list because the items outlined serve to warn, alert and acquaint the family with the nature of asthma: 1) Warning physician and parent alike, that colic, eczema, rhinitis, chronic sneezing, chronic nasal itching, cough on exertion, frequent colds, persistent night cough, etc., may all mean allergy: may all be predisposing the child to occasional asthma. 2) Alerting parents concerning the certain pitfalls and wise avoidances for the allergic child." He further describes a pamphlet given parents, and also outlines a "plan for study" wherein he describes the procedures to be taken by parents and physician (not allergist) to remove allergens and test child for sensitivities.

This is indeed a noble beginning. With intelligent and united effort on the part of practitioner and parents much may be done to permit potential asthmatics children to develop normally and lead normal lives, and to prevent many proxysmal asthmatics from becoming chronic invalids.

S U M M A R Y

A brief review is given of the history of bronchial asthma. A detailed description is given of bronchial asthma to provide a basis for discussion of its prevention in children.

Under the etiology of asthma the following factors are considered: 1) Factors which predispose the individual to acquire asthma. Race, sex, social status, mental ability, other disease have little dffect. Age and environment play a minor role. 2) Among constitutional factors heredity plays the major part. The tendency to hypersensitivity seems to be ingerited. The type of direct exposure seems to influence the type of allergy to be manifested. 3) Contributory factors include infection, especially respiratory, and those of psychic origin. 4) Exciting factors include the allergens, proper exposure, a time element, and the allergic threshold.

Pathology in asthma consists of partial occlusion of the bronchioles by edema, smooth muscle contraction and mucous plugs. There appears to be a predominance of parasympathetic stimuli. In the chronic condition emphysema is present and may be marked. Many complications may occur.

The symptoms of asthma are described as they occur in the paroxysmal and chronic types. In the paroxysmal the

symptoms are usually present only during an attack and consist of dyspnea, orthopnea and wheezing, and may be mild or severe. In the chronic type symptoms are always present in varying degree. Attacks are more prolonged and severe. Complications are often present, especially infection. Prognosis is much better in the paroxysmal type.

Diagnosis is usually not difficult and is based on: history, symptoms, physical and laboratory findings. Differential diagnosis includes all diseases producing symptoms of dyspnea and wheezing. Cardiac asthma may bear close resemblance.

The prevention of bronchial asthma in children is important because of its possibility at this age and because of the high morbidity associated with this disease. Among the methods to be employed in the prevention of asthma are the following:

1) Avoidance of intermarriage between allergic individuals.
2) Recognition of allergic families.
3) Control of allergic mothers during lactation.
4) Preventing direct exposure to common allergens.
5) parents and physician should be alert to detect first symptoms of allergy and should then at once search for causative allergen. History, food diary, elimination tests and skin tests are all means by which search may be made.

6) Once the allergen is discovered it should be avoided if possible, or the individual should be hyposensitized so that symptoms do not occur.

7) During critical times, such as infancy, illness and convalescence, the child should be protected from common allergens. Good physical and mental hygiene are important.

8) Medication, such as expectorant and sympathomimetic drugs, should be employed to abort attacks and thus prevent emphysema and other complications.

An attempt is made to evaluate the success of the above procedures in the prevention of asthma. Unavailability of accurate statistics may be attributed to general lack of application of the above principles. Leading allergists and some pediatricians are hopeful that general application of these principles will result in keeping the allergic child from symptoms so that he may lead a normal life, although in every allergic individual the "gun remains loaded".

C O N C L U S I O N

Bronchial asthma is an allergic disease, the etiologic factor of which concerns the inherited tendency of the individual to be hypersensitive to substances in his environment. To successfully prevent the development of bronchial asthma requires the prevention of exposure or a reduction in sensitivity so that no symptoms occur.

We have presented evidence from recent medical literature which, we believe, justifies the conclusion:

1) That with proper treatment in the early stage of allergic manifestation, and thereafter, it is possible, in nearly all cases, to maintain an a-symptomatic condition in the allergic individual, or to keep the symptoms at a minimum so as not to interfere with his normal growth and development, although the tendency to hypersensitivity remains.

2) That neglect to carry out these principles will result in much needless human suffering.

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