

## EVOLUTION OF ATOPIC DERMATITIS

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In an infant, dermatitis due to hypersensitivity to "protein" substances is called eczema by most dermatologists, pediatricians and allergists, be they European or American. If the condition becomes chronic, in later childhood or adult life it may take many names, commonly, neurodermatitis, or it may still be called eczema by some physicians. If one limits the term eczema to an acute vesicular dermatitis, as some dermatologists do, the chronic condition that is seen in children and adults is certainly not eczema; but if one considers the etiology and evolution rather than the clinical appearance it is in some cases eczema.

Confusion has arisen on account of these variations of nomenclature. While the clinical picture of eczema in infants is different from that of neurodermatitis in later childhood and in adult life, it seems to us, and we wish particularly to stress it, that the fundamental basis of atopic dermatitis is the same at all ages, and in not a few cases the various changes which take place at different age periods may be followed in the same person from year to year. The infant is not merely a small man: he is a different sort of small man. He reacts differently to many diseases than does the adult. Many of his metabolic processes are different. The anatomy, physiology and chemical constitution of his skin are different from those of the skin of the adult.

It is not strange, then, that atopic dermatitis is not similar in clinical appearance at different age periods. It would be strange if it were similar.

It makes comparatively little difference what the nomenclature is, provided that one realizes that atopic dermatitis is the same disease in the infant as in the older person, modified by long duration, long continued external trauma, the differences between the skin of the infant and that of the adult and the variations in reaction that these two different skins may show to irritation by the same stimuli. In past years, when practically nothing was known concerning the etiology and much of dermatology consisted in the minute description of various morpho-

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logic pictures and classification by this method, it was not strange that so-called disseminated neurodermatitis should not have been linked so closely as now to infantile eczema.

At the present time, when what knowledge of hypersensitivity that exists has helped much in gaining at least a little understanding of some of these dermatoses, it becomes plain that in many cases there is a definite evolution from the acute, often vesicular infantile type of eczema, to the thickened, chronic, lichenified neurodermatitis. Chronic atopic dermatitis or chronic atopic eczema seem reasonable terms to use for this condition, if one does not wish to call it neurodermatitis.<sup>1</sup> These are now in use by some American dermatologists, but in Europe, where until very recently little attention was paid to scratch or intracutaneous skin tests, with a few notable exceptions, such as the work of Rost, the nosologic identity and natural history of the two conditions are not generally appreciated.

By the state of atopy is meant a certain form of hypersensitivity to substances usually protein or closely linked to protein. The tendency to sensitizations of this type is often, some think always, hereditary, and becomes manifest in the predisposed family in the occurrence of atopic dermatitis, hay fever, asthma and sometimes other conditions, such as migraine and gastro-intestinal disturbances. In atopy, reagins can usually be demonstrated in the blood. There are other states of hypersensitivity or allergy, such as allergy to various metals or drugs, allergy of infection and serum sickness. These are, however, so far as is known, not of familial occurrence and have, as a rule, no reaginic mechanism. With the increase in the knowledge of allergy in the last few years the particular type of allergy first called by Coca "atopy" has gradually assumed a fairly distinct shape, and this nomenclature is being used more and more by American allergists. Some such nomenclature to distinguish the atopic dermatitis-hay fever-asthma group is highly desirable, for this group differs in certain ways from other forms of allergy, and atopy may be looked on as a definite and familial pathologic entity. The predisposition to this type of sensitization seems in many instances to be as clearly hereditary as, for instance, the predisposition to diabetes or psoriasis.

It is our purpose in this article to trace the evolution of atopic dermatitis from its beginning, through infancy, childhood and adult life.

#### FIRST STAGE

*Infantile Eczema of Atopic Type.*—A 3 month old infant usually (in this country) fed from the bottle and receiving nothing but cow's milk with added carbohydrate, cod liver oil and orange juice, who has

1. In this paper we are not considering circumscribed neurodermatitis, which is a different and apparently unrelated disease.

possibly ever since birth had a tendency to cradle cap, begins to have a papulovesicular rash on the cheeks. Soon the rash extends to other parts of the body, notably the outer aspects of the lower part of the legs, the forearms, wrists and forehead. But by no means is it always vesicular—there may be little or no oozing on the cheeks, and there may be flattened, scaly lesions on the body. Sometimes there may be irregular areas of erythema and occasionally a tendency to wheal formation. There is a polymorphism of lesions, the most characteristic and constant of which is, however, an exudative papule. There may be intense oozing, particularly of the cheeks, which has always been greatly stressed in most textbook articles on infantile eczema, but as a matter of fact cases with very profuse oozing are not particularly common. Scratching and rubbing may give rise to a punctate appearance, which some European dermatologists regard as pathognomonic.

Atopic infantile eczema may become generalized and take on the appearance of an erythroderma, somewhat resembling the picture described by Leiner as erythrodermia desquamativa. We have the impression that the likelihood of a tendency to generalization and the production of erythroderma is particularly strong in those cases in which an atopic dermatitis is superimposed on a skin with a marked seborrheic tendency. These cases with erythroderma present the most severe and the most intractable form of the eczematous process.

*Development of Sensitivity.*—As the hypersensitive patient proceeds along his atopic career he is constantly showing new sensitivities and is losing some of those that he had in the beginning. This capacity for sensitivities we believe begins with the embryo and in many persons runs through infancy and childhood and persists well into adult life, tending to diminish, however, at middle age. It is of interest to survey the ebb and flow of sensitivity in patients of different age groups with atopy, and for this purpose we shall consider the most important food atopens—egg, wheat and milk—and silk and cat hair of the environmental group.

Skin tests are not often done on patients under the age of 3 or 4 months because, as a rule, atopic symptoms have not developed to any great extent before this time.

We tested 29 infants under 3 months of age, and found positive reactions in 19. There were sixteen reactions to egg, seven to milk and four to silk. The youngest infant whom we tested was 4 weeks old. He gave positive reactions to egg white and to lactalbumin. Of 46 infants 6 months of age or under who gave positive reactions to something, 42 reacted to egg white, 7 to wheat, 11 to milk, 4 to silk and one to cat hair.

In a similar series of 46 infants between 6 months and 1 year of age, 39 reacted to egg, 13 to wheat, 13 to milk and 1 to cat hair.

The chief facts of interest brought out by these figures are that about 85 per cent of all infants under 1 year of age who react to anything react to egg; that the incidence of sensitivity to wheat nearly doubles between the sixth and twelfth months; that there are not many reactions to the environmental exogenous atopens (inhalants) during the first year, but that of these atopens silk is apparently the most important. Taking wheat, milk and egg white as a group and cat hair and silk (which in our series are the most common environmental substances to give reactions in early life), we found that in infants 1 year old and under the ratio between the two groups is 20:1. This of course does not indicate the actual ratio accurately, as only five atopens were considered, but is intended simply to serve as a basis for comparison with the figures for the next age group. The development of sensitivity in a person is dependent as a general rule on frequent and adequate exposure to the atopen. In this connection it is interesting to note the abrupt rise in the incidence of sensitivity to wheat after the sixth month, at about which time most infants begin to eat cereal.

The frequency of reactions to egg in young infants is striking and at first glance somewhat difficult to explain, because none of the group under 6 months of age was eating or had ever eaten egg. Furthermore, in this group, of the 42 who were sensitive to egg 24 (52 per cent) were sensitive to egg alone and to nothing else. In the group of children between 6 and 12 months of age only 12 (26 per cent) were sensitive to egg alone. It is certain that in most of these infants a positive cutaneous reaction to egg white means that there is real atopic hypersensitivity to it, for Woringer of Straßbourg and Moro of Heidelberg, working independently, were almost always able to demonstrate the presence of reagins in the blood, Woringer in a series of about 40 cases and Moro in a series of 100. We also have been able to demonstrate reagins in the blood in the few cases that we have studied by this method.

While the origin and significance of sensitivity to egg white in these young infants who have never eaten egg is not entirely clear, there are enough indubitable facts on which to base a reasonably satisfactory theory of possible sensitization of the fetus in utero. Walzer has shown conclusively that in most normal persons certain substances, notably the atopen of egg white, but also others, are absorbed from the digestive tract into the blood in an unchanged condition, and it has further been shown by Ratner that the placenta is permeable to such foreign substances. As egg is eaten by almost every one and therefore by almost all women during pregnancy, it follows that most fetuses are in contact with egg white. But by no means all fetuses become sensitized, for sensitization probably depends largely on the individual peculiarity of the fetus, that is, on the hereditary predisposition to sensitization—*atopy*. The reason, therefore, why sensitivity to egg white is so common

in atopic infants is that this is probably almost always the principal foreign protein with which they come in contact in sensitization-producing quantity. Furthermore, if such a person is not sensitized to egg in utero, he is very likely to become sensitized to it in early postnatal life if he eats it, for it is well known that of all proteins egg albumin has the lowest coefficient of digestibility and is the one most easily absorbed into the blood in its native state. It is, however, usually not possible to produce atopic sensitization in a normal nonatopic person, no matter how much egg white he may have been given by injection. Precipitins are produced, but rarely reagins, and never atopic eczema, asthma or hay fever.

Notwithstanding the possible correctness of this theory, it is certain that in babies who are sensitive to egg alone and who do not eat egg, this food is not producing the eczema. There is, then, the paradox of an atopic baby with eczema who does not come in contact with the only atopen to which he can in the present state of knowledge be proved sensitive. This question will be discussed more fully in a later article, and we can only state now that from unfinished work in progress we are somewhat suspicious that an egg-sensitive atopic baby may have eczema without coming in contact with any atopen to which he is specifically sensitive. He is prepared for eczema by his atopy and his sensitivity to egg, but the actual eczema may be brought about by other causes of which nothing very definitely is known; possibly it may have some relation to the metabolism of cow's milk, possibly to non-specific external irritation. This at present is one of the most pressing and obscure problems of eczema in young milk-fed infants and needs a great deal further study before it can be thoroughly understood.

#### SECOND STAGE

*Atopic Dermatitis of Childhood (2 to 12 Years; Neurodermatitis).—* A great many infants with atopic dermatitis recover entirely toward the end of the second year or sometimes before, are able to take with impunity foods which caused them trouble as young infants, and are bothered no more with atopic symptoms of any sort the rest of their lives. They have outgrown their sensitive phase. It is probable, however, that they can pass on the atopic taint to their children.

It is not uncommon for atopic dermatitis to begin after the second year, but many cases that one sees in childhood have existed since early infancy. In 1934<sup>2</sup> one of us (L. W. H.) reported such a series. Of 210 patients between the ages of 2 and 12 years, 127 had had the condition since early infancy. Most of these were atopic. In childhood, as contrasted

2. Hill, L. W.: Chronic Atopic Eczema (Neurodermatitis) in Children, J. A. M. A. **103**:1430 (Nov. 10) 1934.

to infancy, the cutaneous condition is characterized by papulation rather than exudation. The common sites are the antecubital and popliteal spaces, the wrist and the region about the neck, but the distribution by no means always follows this rule. The eruption may occur on any part of the body and may consist of slightly scaly, infiltrated and lichenified plaques, sometimes with rather sharply defined margins, or in some cases there may be many small papules with excoriated tops, scattered all over the body, particularly on the exposed surfaces: the hands, arms, face, neck and sometimes legs. The skin in these cases is very thick and dry and usually erythematous or hyperpigmented. In short, the most varied morphologic pictures may be seen, but there is no primary vesiculation. The microscopic change is one of epidermal thickening and of infiltration; there is no primary spongiosis. The characteristics of the eruption depend to a large extent on how long it has lasted and how much secondary change from trauma and possibly secondary staphylococcic and fungus infection has taken place. The itching is intense and often continuous, and a large part of the picture is caused by secondary traumatic change from long-continued scratching and rubbing. The disease is one in which the patient is continually working against his own interests, no matter how much he wishes to be cured. This aspect of the situation is particularly difficult in young children, who are too old to be restrained and not old enough to restrain themselves, and sometimes prohibits satisfactory results no matter what local treatment is used or what offending atopens are withdrawn.

In a series of 46 patients with this type of atopy between the ages of 2 and 12 years with positive immediate wheal reactions to something, 28 reacted to egg, 6 to wheat and 6 to milk—about two-thirds as many reacting to egg as in the case of the infants previously considered, and only half as many to wheat and milk. It is, however, in the frequency of sensitization to the noningested atopens that the greatest change occurs; there were eleven reactions to cat hair and five to silk. This gives a food-nonfood ratio of 2.5:1—a marked difference from the ratio of 20:1 in the group under 1 year of age. After the second year sensitivity to milk, particularly, tends to die out. In a series of 217 patients (some atopic, some nonatopic) under 2 years of age 14 per cent gave positive reactions to milk; in a series of 76 between 2 and 12 years only 7.7 per cent reacted to milk. The same holds true for sensitivity to egg.

#### THIRD STAGE

*Atopic Dermatitis in the Adult.*—In a certain, apparently large, percentage of cases of infantile eczema the dermatosis disappears during infancy and does not recur. In some cases, on the other hand, the condition continues, often with exacerbations and remissions,

through childhood and persists, frequently with sporadic free periods, beyond the age of puberty into adult life.

The even approximate percentage of infants with atopic dermatitis who later have neurodermatitis as adults is unknown at present; unfortunately, no accurate statistics are available. However, it seems to us that infantile eczemas can be divided into four principal groups roughly equivalent to the four large groups of eczemas in adults. We name these in their order of probable frequency in adults: (1) true eczema of the contact type, (2) eczematous mycotic and bacterial dermatoses (including dermatophytids and "microbids"), (3) seborrheic dermatitis (seborrheic eczematids) and (4) atopic dermatitis. In spite of the absence of accurate statistical evidence, it is our impression that the relative frequency of these dermatoses in adults is approximately the reverse of that found in infants, in whom the atopic dermatitis takes first place. The impression, however, still awaits statistical confirmation.

For some time, it has become more and more apparent to dermatologists that the term eczema, as generally and loosely employed, is necessarily confusing, for it has included a number of heterogeneous and widely divergent disorders of the skin. From this heterogeneous assembly at least the four more or less distinct entities mentioned have begun to take shape with a definition which modern allergic studies are continuing to make sharper year by year.

The necessary statistical and other studies have been impeded by the fact that, especially in infancy but also in childhood and in adult life, the differential diagnosis of these four forms of eczematous and eczematoid dermatoses is often beset with difficulties. In many cases the superficial resemblances which have led to the common name eczema, the combination of two or more forms and the possible existence of transitional forms, all obscure the fundamental differences. These differences are, however, clearly to be seen in typical instances, and careful study has been able to bring them to light in the majority of atypical cases in adults.

We shall not enter into detail regarding the characteristics of and differentiation between the eczemas and eczematoid dermatoses of adults, classed in groups 1, 2 and 3, but shall confine ourselves to group 4, atopic dermatitis, which is the one which comes strictly within the scope of this study.

The attempt at separation of this group from the other eczemas is not a new one. Especially since the time of E. Vidal, Brocq and Besnier, dermatologists have split off from the mass of eczemas in adults a certain fairly distinct group or entity which has been variously called, in Europe, disseminate neurodermatitis (Brocq), lichen simplex disseminatus (Vidal) and prurigo diathésique (Besnier). In

America, this group of eczematoid dermatoses has been variously called hay fever eczema, pruritus with lichenification, flexural eczema and, even more confusingly, chronic eczema or just eczema, as well as many other names. In spite of this confused and confusing terminology, it was necessarily obvious to critical dermatologic observers that here was a form of eczema which was different from the others. It was not a mycotic disease, such as the older *eczema marginatum* of Hebra, or as many of the eczematous eruptions of the hand and foot have since been shown to be; nor was it the seborrheic eczema of Unna, nor the true or contact form of eczema which had been so precisely defined and studied by the schools of J. Jadassohn and of Bruno Bloch nor simply a chronic and lichenified stage of the last-named condition.

The earlier observers, such as E. Vidal, Besnier and Brocq, indicated the relationship of this particular and separate form of eczematoid dermatosis to asthma and other sensitizations. It is the more recent work of Rost, in Europe (who called the early infantile form "early exudative eczematoid" and the adult form "late exudative eczematoid"), and of Sulzberger, Spain, Sammis and Shahon, Peck, Balyeat, Piness, Rackemann and others, in America, which has emphasized the clear relationship of the adult form of disseminate neurodermatitis to certain forms of infantile eczema and the relationship of both these conditions to atopy in general. It is due, in a great measure, to these more recent studies that this dermatosis has been understood with greater clarity and has been shown to be a part of atopy, in other words, a dermatologic manifestation of this form of familial predisposition to a certain type of sensitization.

In order to maintain this dermatologic manifestation as an entity, separate and distinct from other, nonatopic eczemas and eczematoid dermatoses, and also to emphasize its atopic nature, we believe that it is today best named atopic dermatitis of the infant, of the child and of the adult.

In delineating the characteristics of atopic dermatitis in the adult, it would appear simplest to describe the composite findings based on actual studies of 32 typical cases.

Atopic dermatitis of the type here designated as the adult form appears, as a rule, during adolescence, either as a direct and uninterrupted transition from the dermatitis of childhood or as a fresh attack of dermatitis after a period of several years' freedom.

It is important to note that over 50 per cent of the patients with the classic form have a familial history of other atopic manifestations, such as asthma and hay fever, and about 50 per cent have a personal history of atopic disease and of infantile eczema. Since this characteristically high percentage of preceding infantile eczemas occurs in no other form of the adult type of eczematous or eczematoid dermatitis,



the conclusion is permitted that atopic dermatitis in infants is, in some cases, a forerunner of atopic dermatitis in the adult. This does not necessarily mean that all or even a high percentage of babies with atopic eczema of the infantile type will later have atopic dermatitis of the adult type, but it indicates that a certain as yet unknown and perhaps small percentage of babies with the infantile form will later be affected by the adult form. Thus, the prognosis in each individual case of infantile atopic dermatitis must envisage the possibility of later manifestations. This is apparently in contradistinction to the status of the purely contact and seborrheic infantile forms free from atopy; these forms, so far as it is possible to ascertain today, are not the forerunners of atopic dermatitis in the adult.

The average age of the patient at the first consultation in our 32 cases of atopic dermatitis of the adult type was 19 years; the age of onset, however, ranged between 10 and 28 years. In the majority of the cases the dermatitis begins either shortly before, or from two to three years after, puberty.

Clinically and histologically the adult form of atopic dermatitis bears a much closer relationship to the childhood type than to that seen in infants.

The sites of predilection of the dermatosis are the flexural areas, and in typical cases all the antecubital and popliteal fossae are often affected. The face, particularly the forehead, the region around the eyes and the anterior portions and sides of the neck, are also favored sites. In severe cases the dermatosis may become generalized, but even in such instances it is frequently most severe in the areas just referred to.

As is the case in atopic dermatitis in childhood, and in sharp contrast to atopic dermatitis in infancy, as well as in contrast to contact dermatitis in the adult, the cutaneous manifestation is not primarily vesicular or weeping. The histologic picture is approximately that found in the childhood form. In uncomplicated cases there is no spongiosis in the epidermis. The cardinal clinical lesions consist of slightly elevated papules and diffuse, dry and slightly scaly, hard and thickened, usually not very sharply demarcated lichenified plaques, with accentuation of the cross-markings of the skin. The papules are scattered, often irregularly distributed about the plaques, vary in size from that of a lentil to that of a pea, are sometimes roughly polygonal and vary in color from that of the skin through pink, red and tan to brown and grayish brown. Some of these papules are, as a rule, excoriated, and often nothing is to be seen but the secondary crusting which has followed the scratching and the infection. The larger and diffusely infiltrated areas often become oozing, weeping and crusty, owing

probably to the traumatization of scratching or rubbing, to secondary impetiginization or to irritation from topical applications.

The color of the larger diffuse lesions also varies from a bright pinkish red in the acute or early stages through a tannish brown to a dirty grayish brown in cases of long standing. In chronic or recurrent cases the entire skin of the facies and body of the patient may assume a dark grayish-brown color, which is often very pronounced on the face, neck and cubital areas and frequently of such a peculiar and characteristic hue that the presumptive diagnosis may be made at a glance.

Occasionally the atopic dermatosis is seen combined with contact eczema from topical remedies. More frequently, perhaps, there are to be found a superimposed impetiginization or mycotic (yeast) infection, probably due to infection from scratching, and, not rarely in severe cases, what appears to be a seborrheic condition, with scaling of the scalp and weeping of the areas around the ears and on the neck, which may be superimposed (monilia infection?).

The skin of these patients is frequently dry in general and rather thick, even on areas apparently unaffected by the dermatosis. Among those affected about 50 per cent of the children and adolescents have keratosis follicularis of the trunk and extremities. The oily skin or the moist, thin, hyperhidrotic skin so frequently seen in contact dermatitis or the oily skin accompanying seborrheic dermatitis is usually absent in atopic dermatitis.

In the foreground of the picture of atopic dermatitis stands the continued itching, which often precedes the objective manifestations and/or persists after these have disappeared. The pruritus may be continuous or in crises and can reach maddening proportions. It is often worse at night or after exertion. (Perspiration? Cold? Lack of vitamins?)

While the course of the disease is chronic, most (but not all) patients have intervals of many months or even years of more or less complete freedom. The exacerbations of the disease are not infrequently seasonal, and in our material in the majority of cases exacerbations have occurred in the late fall (ragweed? cold? lack of vitamins?) and early winter, but there are some cases with peaks in the spring and summer and some with irregular flare-ups. It is a puzzling characteristic of the disease that change of environment may produce an almost miraculously beneficial result, so that hospitalization or moving to a different climate or even to a different residence sometimes effects speedy relief. (Elimination of environmental allergens?)

It appears that the disease eventually runs itself out; that is, the patient outgrows the condition. We base this statement on the fact that during the period of more than ten years in which we have been

particularly interested in atopic dermatitis we recall having seen but one case in a patient over 35 years old. It seems to be a disease most often of the teens, but also of the twenties.

As we have stated before, these patients, although healthy in all but the aforementioned respects, generally have the characteristics of atopy. Not only do their family and personal histories often manifest other atopic disease, but skin tests and demonstrations of reagins give results indicating atopy, even in those cases in which the dermatosis has been and remains the only personal clinical manifestation. Scratch and intracutaneous skin tests in cases of atopic dermatitis show that, compared with patients who have other atopic diseases, these patients are, as a group, among those whose skins are most strongly hypersensitive, have the most polyvalent hypersensitivities and the strongest and largest number of reagins. We have seen patients with as many as fifty-six different definitely positive reactions to skin tests, and we have demonstrated as many as twenty-eight different reagins in the same serum.

In sharp contrast to the marked and polyvalent hypersensitivity to intracutaneous or scratch tests with common foods and inhalants, patients with atopic dermatitis almost always give negative reactions to patch or contact tests with large numbers of common contact substances. There is, apparently, one exception to this rule: The heavy metal salts, particularly nickel sulphate or potassium dichromate, when applied in patch tests, elicit a positive response in a fairly high percentage of cases. There is at present no explanation for this finding. We do not believe, however, that this positive reaction can as yet be considered identical with that produced by patch tests in contact dermatitis, for the reaction in atopic dermatitis does not seem to be truly eczematous but rather more papulopustular.

It is instructive to study the further course and changes of the hypersensitivity of the skin, as shown by the compilation of the substances eliciting the most frequent responses to skin tests in the adult group, as compared with those causing the most frequent reactions in the childhood and in the infantile group.

In 21 adults on whom complete skin tests could be done by the scratch or intracutaneous method and who reacted to one or more atopens the results were as follows:

Thirteen patients reacted to one or more foods, but of these only 4 reacted to egg white; only 1 reacted to egg white alone and 1 to wheat alone. None reacted to milk alone. Eleven reacted to other foods, either alone or in combination with egg, wheat and milk. All the reactions to egg white, milk and wheat were weak, never above  $\pm$  to  $+$ , while some of the reactions to other foods, such as fish, shellfish, pork, coffee and fruits occasionally gave reactions up to  $+++$ .

Fifteen patients reacted to one or more noningested environmental or inhalant atopens. The four members of this group most commonly eliciting positive reactions were: feathers (in 6 cases) and silk, horse dander and ragweed (each in 5 cases).

Silk caused the strongest reactions (a reaction of + + + + in 3 cases), and the serums of the patients contained the highest reagin titer to silk. The next strongest reactions were those elicited by horse dander and ragweed, while the reactions to feathers were by far the weakest.

Comparison with the reactions in the groups of infants and of children shows that there has again been a change in the direction of the hypersensitivities. In infants the food-nonfood ratio was 20:1; in children, 2.5:1, and in our group of adults it was 13:15, or approximately 0.87:1. The conclusion seems justified that foods are becoming less important and the noningested, environmental substances more important. Furthermore, the ratio of importance within the group of foods itself has changed. Reactions to egg have been markedly reduced, and the same applies to reactions to milk and to wheat, while other foods (fish, pork, coffee, fruits) have caused increased reactions.

Among the environmental atopens, the inhalants have assumed first place with silk, horse dander, certain pollens and perhaps feathers and certain other animal emanations causing reactions which deserved serious consideration. (We regret that house dust was not included in our tests on adults.)

In conclusion it is necessary to remark that, just as was the case in infants and as we mentioned in discussing sensitivity to egg white, it is noteworthy that even strongly positive reactions to skin tests and the demonstration of specific reagins do not necessarily prove that the substance used in testing is of causal significance. It may be stated with certainty that some of our patients improved when certain of the substances causing strong skin reactions could be eliminated, and some patients showed exacerbation on renewed contact with certain atopens which had elicited cutaneous responses. However, it is equally true that some patients have not been benefited by the removal of foods causing positive reactions and some have not been harmed by the ingestion of such foods. So the significance of the skin test and the reagin findings requires further study.

It is, in our opinion, a great defect in our own and all other previous studies that only elimination diets have received adequate attention, while the elimination of inhalants has, to a great extent, been neglected. The allergists, as a group, have hitherto gaged the importance of the inhalants more correctly than have the dermatologists or pediatricians. It would seem that no definite conclusion as to the significance of the skin tests and reagin findings can be reached until atopic dermatitis has

been studied not only with dietary eliminations but also and simultaneously by complete environmental control in the most perfect allergen-free rooms today available.

## SUMMARY

It is evident that the state of susceptibility to sensitization which has been called atopy is the base on which develops a certain type of dermatitis, from earliest infancy to middle age. By careful observations atopic dermatitis can usually be distinguished from other dermatoses. The clinical appearance and the immediate exciting agents vary at different age periods, but the fundamental predisposition which makes the development of the dermatitis possible is the same at all ages. While in many cases removal of the specific atopen or atopens to which the patient is sensitive cures or improves the dermatitis, in some cases this is not so, and there are undoubtedly other factors at work of which at present practically nothing is known. In about half the cases there is strong evidence to support the thesis that this predisposition to the development of sensitivity is hereditary; in the rest it is not known why some persons become so easily sensitized to foreign "protein."

Until there is better understanding of the fundamental variation from the normal which makes atopic sensitization possible and until this variation can be directly controlled, the best method of attack in the treatment of atopic dermatitis is symptomatic but rational local and systemic therapy plus the determination of specific sensitivities and withdrawal of the corresponding atopenis from the diet or environment—or an attempt at hyposensitization in a few selected cases. The results of these procedures, while sometimes encouraging, are by no means ideal.

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