DR. SEDLIS: A brief review of the clinical features of a group of patients with eczema will be followed by a report of special studies of the pathology of the skin. Eczema is a frequent, important skin disease in early life. It has been a puzzling problem for the physician and an exasperating one for parents and patients alike.

We began our study of eczema about 1 year ago. During this year, we have accumulated and organized the study material, and we have tried to learn about the clinical picture of eczema and to evaluate certain concepts of its etiology, pathogenesis and therapy.

Our study is far from complete, and I will therefore try to avoid drawing definite conclusions from the data presented.

Our material to date consists of a clinic population of 169 patients, 91 males and 78 females, who made a total of 646 clinic visits. Fifty-four of these patients required hospitalization in the University Hospital. Thirty of the hospitalized patients were males, 24 were females. I do not know whether the prevalence of boys in our census is significant.

The distribution of the patients by race is:

Puerto Ricans, 102;
Negro, 40;
White, 25;
Others, 2.

The distribution by age shows that the majority of patients were under 1 year of age on their first visit to the clinic:

91 patients were 1 year or less;
36 patients were between 1 and 2 years, making a total of 127 patients under 2 years;
42 patients were over 2 years, the oldest child being 6 years.

I would like now to give you some data from an analysis of the histories and physical findings in the patients.

It has been said that in the majority of cases of eczema the onset is around 6 months of age; 99 (60%) of our patients had their first manifestation within the first 3 months of life and 29 (15%) between 3 and 6 months. Thus approximately 75% had the first manifestation within the first 6 months of life.

During the first month of life, 47 patients developed eczema; during the second month, 30; during the third month, 22; and during the second half of the first year, 11 patients developed eczema. A total of 139 patients developed eczema during the first year of life; 30 patients developed eczema after the first year.

On the controversial subject of allergy as one of the contributory etiologic factors in eczema, this group reveals the following: In 20% of the patients, at least one of the parents had either asthma or hay fever; 16% gave a similar history of allergy in grandparents, cousins, uncles or aunts. Thus 36% had a positive family history of allergy. Taking into consideration the character of our clinic population, a negative family history of allergy is not always reliable.

In 14% of the patients we elicited a history of associated allergic manifestations; 4% had asthma, and 10% had numerous bouts of asthmatic bronchitis.
Forty per cent (28 of 67 patients) had eosinophilia in the peripheral blood which ranged from 8 to 41%. In contrast, Burkhart and Montgomery rarely found eosinophilia above 8% in their series of patients with eczema. In our experience, eosinophilia could be correlated with the severity of the eczematous process. We often observed that a patient showed a significant drop in the eosinophil count in the blood within a relatively short period of time, and this coincided with a remission of the clinical manifestations.

The importance of food both as an etiologic factor and an approach to treatment has been emphasized through the years. Twenty-four of the patients gave a history of having received an elimination diet at one time or another prior to their visit to our clinic. Significantly enough, only one mother claimed temporary improvement during such a dietary regimen.

Twenty-eight of the patients were breast-fed for a period ranging from less than 1 month to 1 year. Six of these patients developed eczema while they received breast milk alone. In five patients, the onset of eczema occurred between 1 and 2 months of age and coincided with changing from breast to cow's milk. Eleven patients who were breast-fed for more than 5 months developed the first manifestation of eczema after 2 years of age. In four patients, the onset of eczema in relation to the change from breast feeding was not known.

I don’t know the significance of these observations as the onset of eczema in relation to the introduction of cow’s milk into the diet is so variable. I think it would be necessary to have a large series of breast-fed patients in order to arrive at definite conclusions.

While talking about food, it is worthwhile mentioning that the majority of observers agree that infants with eczema tend to be overweight; our observations support this. Forty-four of the patients could be considered overweight, based on height-weight tables; usually many more could be called overweight in comparison with the average of our clinic population.

The clinical course of eczema is characterized by remissions and exacerbations. In 54 of the patients we were able to observe exacerbations. Many more have given histories of an exacerbation during the interval between clinic visits. “The rash comes and goes” is the favorite expression used by mothers in describing what was happening to their children.

The aggravating factors described by the mothers are rather difficult to evaluate because we do not know how much is based on observation and how much is the result of the influence of information received from friends and physicians.

The ingestion of certain foods (eggs, tomatoes, orange juice, etc.), emotional upsets, teething, febrile illnesses, immunization procedures and climatic variations were listed by the mothers as coinciding with the exacerbation of eczema. It seems worth mentioning that intense pruritus usually precedes the skin eruption.

It is too early for us to correlate remissions and exacerbations with climatic factors, namely with temperature and humidity, because of the short period of our study. As many authorities claim that high humidity and temperature, with consequent sweating, have deleterious effects on eczema, we think it worth while to include observations on this as part of our study.

In our experience, measles was the only disease consistently associated with spontaneous remission. The most severe cases of eczema cleared spontaneously, and remained clear for about 3 to 6 weeks after the onset of measles.

Skin infection was a frequent complication in our series. We have had 28 patients with impetiginous eczema. An additional five patients developed multiple abscesses; four of these had lesions requiring incision and drainage.

Among infections other than that of the skin, the single largest group was otitis
media. We have had 14 patients with otitis, and in some of them recurrences were observed.

I shall leave the detailed description of the morphology of the skin lesion for Dr. Prose, but I would like to show you two main types of eczema seen in this group of patients. Figure 1 shows the acute, erythematous, confluent, papular eruption which in more severe cases was accompanied by oozing and crusting. It was localized mainly on the face, behind the ears, and over the extensor surface of the extremities; occasionally it was generalized. This type of eczema has been called the infantile variety. It occurred more often in the patients under 1 year of age.

Figure 2 shows the chronic flexural type of lesion which is characterized by thickening, lichenification, hypo- and hyper-pigmentation of the skin. This lesion is localized mainly in the popliteal and antecubital spaces and occasionally over the wrists, ankles and gluteal folds. This type was seen more often in children over 1 year of age.

However, it must be stated that we occasionally noted the chronic flexural type of eczema in the young infant (Fig. 3) and the infantile type in the older child (Fig. 4).

We have had 84 patients with the infantile type, and we have had 44 patients with chronic type of eczema. Some of the patients could not be fitted into this simple classification. These cases were either

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**Fig. 1 (Left).** Eczema, infantile variety. Six-month-old boy with acute, exudative lesions involving the face. From Kodachrome taken on October 29, 1957.

**Fig. 2 (Right).** Eczema, chronic lichenified. One and one-half-year-old boy with thickened, infiltrated skin showing prominent skin markings.
Seborrheic eczema is not included in this oversimplified classification; there has not been much agreement amongst the dermatologists and pediatricians regarding this entity. I can only state that about 60 of this group of patients have had "cradle cap" as related to us by the mothers or as seen by other physicians or ourselves.

One of the purposes of this study is to find a therapeutic regimen which would relieve the misery of the patient and would be simple enough to be carried out at home. With this objective in mind, we have adopted the plan suggested by Dr. Holt, who has had very good results with it:

1. On admission of the child to the hospital, he receives a regular diet.

2. Some general measures include: restraints, if necessary; and on rare occasions a sedative (phenobarbital) is prescribed. We have been using soap "substitutes," Acidolate® routinely and pHisoHex® for infected eczemas.

3. As a routine, topical therapy consisted of a 5% alcoholic solution of coal tar in a vanishing cream; this solution contained several tar fractions but no known carcinogenic or photosensitizing tars.

In addition, the laboratories of Mead Johnson and Company have supplied us with ointments in which they have incorporated different combinations of tar fractions. We have used the paired-comparison method to see which fraction is the most beneficial. I don't think we have enough data yet to tell you more about it, but I would like you to see some of the results.

Usually we have noticed that the acute cases were the ones who benefited most (Figs. 5 and 6). We noticed marked improvement in nearly all of our hospitalized patients within approximately 24 to 72 hours after the onset of therapy.

As an illustration of the usefulness of the paired-comparison method for evaluating therapy, we wish to show the results of therapy in a 6-month-old infant with a severe exudative eruption on both cheeks. The 5% alcoholic solution of coal tar ointment was applied to one cheek; an ointment containing certain tar fractions was applied to the other side. The latter oint-
ment appeared to be irritating (Fig. 7) and had to be discontinued; subsequently, this cheek lagged in its response to therapy.

While we are satisfied with our preliminary results, we are fully aware that our treatment gives the patient only temporary relief. The disease is not eradicated and exacerbations occur at varying intervals. However, the exacerbations are rarely as severe as the first episode. We hope that the histochemical study which will be done by Dr. Prose will give us some ideas about eczema and help us find a better therapeutic approach.

**DR. PROSE:** We started this study of the histology and histochemistry of infantile eczema fully realizing that the histology had been studied previously by others. We wished to re-examine the subject in the light of what is known about the pathology and pathophysiology of skin at the present time.
We have received approximately 69 specimens of skin from 39 patients. Two of these specimens were large scalpels biopsies which are ideal for study; subsequently, the biopsy specimens (3 by 5 mm) were obtained by an electrically driven punch. The latter procedure is relatively painless and results in minimal scarring.

Nineteen of the specimens were from patients under 1 year of age; nine were taken from patients between 1 and 2 years of age; the remainder of the specimens were obtained from patients 2 to 6 years of age. The youngest patient from whom a biopsy was obtained was eight weeks of age.

We have examined a single biopsy from each of several patients, namely a specimen of diseased skin. We have also obtained two or three biopsies from the same patient taken at the same hospital visit, namely un-

Fig. 8. Eczema, "infantile variety." Involved skin of the thigh of an 8-month-old boy showing parakeratotic scale, partly intact keratohyalin layer, two sweat pores (V-shaped dips seen just below surface of epidermis) with subjacent elongated sweat ducts in an acanthotic epidermis. Note the absence of vesicles in the epidermis. The perivascular infiltrate is more marked in upper cutis when compared with that in the papillae. (H. & E., ×100.)
involved skin and involved skin. We have taken as many as four biopsies from the same patient at the same hospital visit: one of uninvolved and one of involved skin before and after sweating.

I would like to show you some of our main findings, and perhaps I can discuss their significance. It has been stated by some in the past that one could differentiate the infantile variety of eczema from the chronic and lichenified type by the character of the acanthosis (thickening of the stratum spinosum). However, that has not been my experience. The magnitude of the acanthosis would appear to be a function of the edema rather than a function of the site of the lesion, age of the patient, or the clinician's classification of the process.

The keratohyalin layer was usually intact beneath a parakeratotic zone. Vesiculation within the epidermis was rarely encountered. There were instances in which dissolution of basal cells and adjacent prickle cells in focal, small zones appeared to be the result of edema.

A statement has been made by MacCardle et al. that the lesions histologically appear depigmented; such has not been my observation.

Sections stained with the periodic acid-Schiff stain revealed red granules in the epidermis of involved skin; the granules were digested by diastase and thus are presumably glycogen. The glycogen in the epidermis is only present in considerable amount in involved areas. Similar observations have been made as regards glycogen in the epidermis whenever keratinization proceeds at a more rapid pace than normal.

Another characteristic of eczema is the denser infiltrate in the cutis when compared with that in the papillae (Fig. 8). The infiltrate is usually perivascular and consists mainly of lymphocytes. The num-
number of eosinophils is variable. The number of mast cells seems to be proportional to the intensity of the infiltrate. However, where the infiltrate is extremely sparse, e.g., in receding lesions, there is a disproportionate increase in mast cells because many of the cells composing the infiltrate will probably be mast cells.

The significance of this is at present unknown, but as the mast cells contain (manufacture and/or store) many substances (e.g., histamine, serotonin, hyaluronic acid), we hope to be able to do more work on this aspect. The mast cells in many of the specimens seem to be extremely numerous about hair papillae.

In the youngest patients, the capillaries in the involved skin were dilated and lined by a swollen endothelium. In the older patients, endothelial proliferation was more prominent and the surrounding collagen appeared denser than usual.

There was another finding which was of great interest to us, and that is the usual absence of active sebaceous glands in areas that are involved by eczema. One sees either little buds of basal cells, which eventually might go on to form sebaceous glands, in a position usually occupied by sebaceous glands (Fig. 9), or an absence of sebaceous glands; rarely, a poorly developed sebaceous gland was observed.

If one examines healthy skin from the same patient, active sebaceous glands are present. Whether these sebaceous glands are normal in size as compared with other individuals of the same age group is another problem to be investigated. We have all heard that people with atopic eczema have dry skins. Perhaps this is the explana-

Fig. 10. Sweat gland. Secretory portion (and part of duct) in healthy skin of 7-month-old girl showing small amount of fibrillar material between coils. (Alcian Blue-periodic acid-Schiff, \( \times 450 \).)
tion for it. When the involved skin of a patient with eczema becomes grossly normal the sebaceous glands are usually present and active.

It has been said by many investigators that much of the symptomatology of eczema, e.g., the itching and the elevation of body temperature occasionally noted in the summertime, may be associated with obstruction of sweat ducts.

In miliaria, as you know, the sweat pores become obstructed by scale, and the sweat duct may become dilated and rupture. It has been postulated that in infantile eczema the process is the same.

Of course, this was important to us, and we examined all of our serial sections to see whether or not we could observe these phenomena. In only one sweat duct, in one individual, were we able to discern rupture of the sweat duct.

Because some of these biopsy specimens were taken in warm weather, and because some were taken after profuse sweating, one would have expected that if this were a problem in eczema, we would have uncovered it. But thus far, on the basis of our observations, we are inclined to feel that obstruction of the sweat ducts is not a factor in infantile eczema.

In regard to the sweat apparatus, many of the specimens of involved skin (when compared with specimens of healthy skin removed from the contralateral site or an adjoining site of the same individual during the same hospital visit) revealed greatly increased amounts of acid mucopolysaccharides about the secretory portion of the sweat glands (Figs. 10 and 11). In addition, in the involved skin there were usually small amounts of acid mucopolysaccharides between the collagen bundles. These muco-
polysaccharides were stained blue-green by the Alcian Blue technic and they occasionally were metachromatic when stained with toluidine blue. Incubation of the sections with hyaluronidase caused the disappearance of these staining characteristics. In view of the increased water-binding capacity of the mucopolysaccharides relative to the collagen or adipose tissue that normally surrounds this portion of the sweat gland, the role played by these substances in either decreased sweat secretion or increased reabsorption of sweat should be investigated.

A marked histologic change in the skin following sweating was noted in one of the patients; the involved skin and to a much lesser extent the healthy skin of that individual revealed perinuclear edema of the prickle cells. As the cutis was edematous, it is possible that epidermal change was a secondary one. However, it is also possible that the superficial water-barrier layer in this patient was defective and may have accounted for the perinuclear edema.

The biopsies also permit us to check on the diagnosis. In one of the biopsies we noted a subepidermal bulla and monilia within the keratin layer.

In summary, there are certain preliminary observations that we have made: A histologically depigmented area is not necessarily seen in infantile eczema; the involved areas show increased amounts of glycogen in the epidermis; there appears to be a change in the sebaceous glands of the involved skin; obstruction of the sweat ducts does not seem to be a problem in these children; and there appear to be increased amounts of acid mucopolysaccharides (hyaluronidase-labile) about the sweat glands in involved skin. However, none of these changes are specific for infantile eczema.

We hope to be able to enlarge on what we have presented by studying more biopsies and by doing more work on the material we have already collected. Histochemical studies are now in progress and may give us some of the answers to the eczema problem.

REFERENCES

THE YEAR BOOK OF PEDIATRICS, 1958-1959

This is a handy and well-selected collection of abstracts from the world's literature on pediatrics during the years 1957 and 1958. The abundance of editorial comments and the comments of others solicited by the editor make this collection of abstracts a special delight to those who would like to know what other people think about some of the papers they may have read. This publication is now too well established to require extensive review of each new volume in the series.

CHARLES D. MAY, M.D.
CLINICAL CONFERENCE: Infantile Eczema with Special Reference to the Pathologic Lesion
Emilia Sedlis and Philip Prose
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