INFANTILE ECZEMA TREATED WITH ORAL CORTISONE

A CLINICAL REPORT

BY

BETHEL SOLOMONS, jun., M.D., F.R.C.P.I.*Dermatologist to Dr. Steevens' and the Royal City of
Dublin Hospitals*

The dramatic but unfortunately temporary improvement which occurs in infantile eczema when cortisone is administered has already been reported by Glaser *et al.* (1951). The purpose of the present trial was to observe the clinical transformation which they found.

Some cases urgently call for temporary improvement because of the severity of the skin lesions and the distressingly poor general condition of the infant. For these, short courses of cortisone may be considered, but, bearing in mind the potential dangers of the drug and the relative harmlessness of infantile eczema, it should be administered only to carefully chosen cases.

All the 15 cases in this series were severe and, except for the two with hay-fever, had had a good deal of treatment. The routine management of the condition, which was carried out before it was thought necessary to administer cortisone, consisted in a carefully taken history, general examination, skin-testing, local and general forms of treatment, as well as a period in hospital. Each patient was also regularly weighed, and regular eosinophil counts and routine blood pressure estimations were made. There were 10 males and 5 females. Five were between 6 and 12 months old; two were between 1 and 2 years, and seven were between 2 and 3 years.

The most difficult point to arrive at in these cases was to determine upon a dose unlikely to produce toxic effects, and it was thought wisest not to exceed 75 mg. a day. This was adhered to except in three cases, in which 87.5 mg. daily was given for a short time. No other treatment was given, except when weeping lesions were present and local applications were essential.

In the following three groups of cases only observations referable to the clinical response of the eczema have been noted. The first group describes a number of infants whose response to cortisone was slow, unconvincing, and not maintained. In none of these was an exacerbation seen after treatment. The third case produced toxic symptoms.

Group 1

Case 1.—A 7-months-old boy had had weeping lesions on the face and flexures of the elbows for four months. His mother and sister had asthma. On June 3, 1952, 50 mg. of cortisone daily was started. As there was little change two weeks later, 75 mg. was given daily. A slight improvement resulted, and after six weeks, although the lesions were drier, cortisone was gradually discontinued. When she was seen two months later exudative lesions were again present.

Case 2.—A boy aged 8 months had had eczema of the face, flexures, and trunk for the previous three months. From April 2, 1952, he was given 75 mg. of cortisone a day. There was no improvement after fourteen days, and the dose was increased to 87.5 mg. daily. After another fortnight the condition was much the same, and the drug was gradually discontinued.

Case 3.—A 2-year-old boy had suffered from eczema of the face, neck, and flexures of arms and legs for twenty

months. There was a lot of crusting and scaling. He had a moderate degree of ichthyosis. From March 12, 1952, he was given 75 mg. of cortisone daily. A month later the skin was much improved, but, alarmingly enough, there was a rounding of the face, with increase of the scalp and eyebrow hair. He gained 2½ lb. (1.1 kg.) in seven days. The cortisone was discontinued within a week. The eczema relapsed within ten days. At the end of a month his weight was the same. By the beginning of August his face was normal, and the excess hair had markedly diminished.

Case 4.—A boy aged 2 had had severe atopic dermatitis of the face, flexures of elbows, and forearms for eighteen months. His father had eczema and asthma. On January 6, 1953, 75 mg. of cortisone daily was started. At the end of a week he was much better, and the dose was reduced to 50 mg. daily. Three days later exuding lesions were again present. The dose was raised to 75 mg. daily, but as this did not control the rash, at the end of a week it was increased to 87.5 mg. daily. After 16 days with no improvement the drug was gradually discontinued.

Case 5.—A 3-year-old girl had had severe generalized atopic dermatitis since the age of 18 months; her arms and legs were very excoriated, and itching had been extreme. Her mother has severe asthma. From November 7, 1952, the patient was given 75 mg. of cortisone daily. A fortnight later the itching had diminished, but the rash had not quite cleared from the legs. The dose was dropped to 62.5 mg. daily, but within five days the skin condition was worse. Again 75 mg. daily was administered, but, as it produced scarcely any improvement after a fortnight, 87.5 mg. daily was given for 14 days. Little improvement occurred, and the drug was gradually discontinued.

Case 6.—A 3-year-old girl had had severe chronic atopic dermatitis of the arms and legs, and slightly on the cheeks, for one year, with a flare-up causing oozing lesions. She was allergic to all types of fish, and had had severe attacks of angioneurotic oedema involving the face, mainly lips and tongue. She was given 75 mg. of cortisone daily from August 24, 1952. A week later there was little change, and the dose was increased to 87.5 mg. daily. Three weeks later the condition was much the same, so cortisone was gradually withdrawn. Her skin condition is now much the same as when first seen.

Group 2

These cases illustrate a moderately good response to cortisone. Exudation was abolished for considerable periods, and itching was always remarkably reduced.

Case 7.—A 10-months-old girl had had a severe dermatitis of the face, flexures of arms, and backs of knees for three months. From April 8, 1952, 50 mg. of cortisone was given daily. Within a week all the lesions were dry, and five days later the dose was cut to 37.5 mg. daily. On May 10 there was a sudden flare-up of the facial lesions, but a return to 50 mg. daily rapidly improved it. This dose was maintained for eight weeks. It was gradually reduced to 25 mg. daily and stopped on August 2. During the past 10 months she has had two mild recurrences, relieved by local treatment.

Case 8.—A girl aged 15 months had had moderately severe atopic dermatitis involving the cheeks, backs of forearms, legs, and thighs for four months. From May 28, 1952, she was given 75 mg. of cortisone daily. Ten days later there was a great improvement and the dose was cut to 50 mg. a day. Two weeks later she got worse and moist lesions appeared. The skin responded well again to 75 mg. daily, and 14 days later it was reduced to 62.5 mg. During the next three months the dose varied between this and 37.5 mg. daily. It was discontinued at the end of October. When seen in April, 1953, there was some redness and scaling, but there had been no exudation, and itching was negligible.

Case 9.—A boy aged 2½ had had diffuse papular lesions on the trunk, limbs, and face for ten months. His sister had had eczema as an infant. On September 4, 1952, 75 mg. of cortisone daily was started. Ten days later,

owing to marked response, it was reduced to 62.5 mg. and a week later it was possible to cut it to 50 mg. daily. At the middle of October the dose was further reduced to 37.5 mg. daily and, as no new lesions appeared, a month later cortisone was gradually discontinued. When last seen in May, 1953, there had been no fresh acute attacks. There was a little redness of the flexures of the arms, and occasional papules appeared on the trunk.

Case 10.—An 11-months-old girl had had itchy papular lesions of the face, neck, and interscapular regions for five months. Her scalp was covered with a good deal of greasy scales. On November 6, 1952, 50 mg. daily of cortisone was started. In ten days there was considerable improvement of the facial and interscapular lesions. The scalp also improved, but never to the degree of the other areas. At the beginning of January, 1953, there were no lesions below the scalp, and the cortisone, which had been maintained at the original dose, was gradually discontinued. When last seen in April, 1953, nothing abnormal was noticed except slight scaling on the scalp.

Case 11.—A 15-months-old boy had a sudden exacerbation of eczema, from which he had suffered since the age of 10 months. Weeping lesions developed on the cheeks, arms, and forearms. The attack may have been due to wool, to which he was extremely allergic. From October 6, 1952, cortisone was given in doses of 50 mg. daily. By the end of a week the lesions were dry, and ten days later the dose was cut to 37.5 mg. daily. A month later only redness and a few papular lesions were present in the original areas, and cortisone was discontinued. Up to May, 1953, there had been no further acute attacks, although the rash was more pronounced and itchy.

Case 12.—A 2-year-old boy had had a diffuse papular rash involving the face, arms, trunk, and backs of knees for seven months. From March 22, 1952, 75 mg. of cortisone was given daily. Ten days later, as he was much improved, the dose was reduced to 50 mg. The rash began to recur within a week. He was again given 75 mg. daily, and this was maintained for six weeks. It was very gradually reduced to 25 mg. daily over a period of seven weeks, and successfully discontinued in July. In March, 1953, he developed weeping lesions for the first time, and 75 mg. daily for a month was necessary to dry them up. Gradual withdrawal over a period of six weeks resulted in no relapse, and when seen in May there was a slight papular rash involving the cheeks and the backs of the knees.

Group 3

This group showed a very satisfying response, reacting rapidly to cortisone, without return of symptoms.

Case 13.—A boy aged 9 months had had dry papular lesions on the face, scalp, shoulders, and flexures of elbows, and slightly on the wrists, for two months. On June 11, 1952, cortisone, 50 mg. daily, was started. A week later the rash had cleared except for very slight scaling and redness of the face. Up to September it was kept in good control by 37.5 mg. or 25 mg. daily. It was slowly discontinued in October, and there had been no exacerbation up to March, 1953.

Case 14.—An orphan boy aged 2½ had a papular and scaly dermatitis of the face, arms, legs, feet, and interscapular and lumbosacral areas, associated with hay-fever. It was his second attack, the first one having occurred a year before. On May 7, 1952, cortisone, 50 mg. daily, was started. Ten days later he was practically well. By the middle of June, as pollination was over and the signs of eczema were limited to slightly scaly areas on the back of the left leg, cortisone was gradually discontinued. There was no recurrence up to January, 1953, soon after which he went to America.

Case 15.—A girl aged 3 had a severe diffuse papular dermatitis associated with severe hay-fever. It was her first attack of eczema. On May 10, 1953, cortisone, 75 mg. daily, was started. There was an immediate improvement in the hay-fever and skin lesions. Five days later the dose

was reduced to 50 mg. daily. A week later the rash had disappeared except for residual erythema. She was maintained on 37.5 mg. daily until the middle of June, when the drug was discontinued. A month later there had been no recurrence of the rash.

Comment

Owing to the dangers already mentioned, there seems to be little justification at present for administering cortisone to infants with eczema, unless the lesions are severe, the infant's general health is definitely deteriorating, and scratching has become a ceaseless habit. Then cortisone is often of great value for temporary improvement. Sometimes there is a temptation to give it in moderate cases when there is pressure from anxious parents, but it is better to explain to them that the benefits of cortisone in infantile eczema are only temporary, and indicate that exacerbations may occur after withdrawal of the drug.

One of Lever's (1951) contentions regarding the disadvantages of cortisone in atopic dermatitis is that the rebound of the disease after discontinuation of the drug is worse than in most of the other diseases. My patients, however, did not have this experience following treatment, although lesions assumed their former character in many. Unfortunately, toxic effects give no warning of their appearance. The 2-year-old boy (Case 3) developed excessive growth of hair four weeks after a relatively low dosage of cortisone. Other patients who had larger doses had no toxic symptoms. One of the infants in Glaser's (1952) series developed transient hypertension.

Generally speaking, when the patient responds to cortisone it should not be continued for a protracted period. But in very exceptional cases Baer and Leider (1951) consider it warranted so long as a maintenance dose of 25 mg. is used. Glaser (1952) has also done this when asthma was a feature of the case, and W. R. F. Collis (1953, personal communication) reports a case of infantile eczema, complicated by asthma, which has been treated with A.C.T.H. and cortisone for one year without ill effects and with much benefit. Glaser (1952) suggests that in long-term therapy alternation between courses of A.C.T.H., which causes hypertrophy of the adrenal glands, and cortisone, which causes atrophy, should be used to maintain a reasonable balance.

The euphoria which is usually so pronounced in adults taking this drug is also obviously present in infants. Also, their appetite increases and sleep is prolonged, and all these features are usually evident within two or three days of taking cortisone. When the eczema responds to cortisone the effect is so dramatic and satisfying that the underlying complex, and perhaps allergic, nature of the condition is frequently forgotten. It often requires a little reflection on the part of the administrator to realize that, unfortunately, the treatment is symptomatic only.

As will be seen from the description of these cases, there were few results which could be classified as good. Two cases which responded well were associated with severe hay-fever, and Reicher *et al.* (1952) have already shown that the latter condition frequently benefits from the judicious use of cortisone. In most of the other cases, all of which had severe skin lesions, the temporary benefits these unfortunate infants obtained appeared to justify the administration of short courses of cortisone.

The question yet to be answered is: What will be the effects produced by this early administration of cortisone as the infants grow? On account of immediate and unknown late risks, therefore, it is felt at the moment that until every other form of treatment has been tried, and except for the severe distressing generalized cases, cortisone should be withheld in infantile eczema.

Summary

Fifteen cases of infantile eczema were treated with oral cortisone. Temporary benefit usually resulted.

One case showed toxic effects by growing an excess of hair on the face.

Infections which are easily masked by cortisone should be carefully watched for.

REFERENCES

- Baer, R. L., and Leider, M. (1951). *Ann. Allergy*, 9, 399.
 Glaser, J. (1952). *J. Allergy*, 23, 222.
 — Siegel, S. C., Goldstein, J. D., and Meltzer, R. S. (1951). *Ann. Allergy*, 9, 292.
 Lever, W. F. (1951). *New Engl. J. Med.*, 245, 359.
 Reicher, J., Schwartz, E., Levin, L., Leibowitz, H., Kelly, J. F., Wallman, M., and Feinblatt, T. M. (1952). *J. Allergy*, 23, 32.

Medical Memorandum

Use of Methyl *N*-Propyl Ether as an Anaesthetic for Children

The use of methyl *n*-propyl ether in anaesthesia dates from its inclusion in a series of ethers investigated by Krantz *et al.* (1946). The physical and chemical properties are not dissimilar to those of diethyl ether, of which it is an isomer, and similar precautions against explosion risk must be observed. Its safety margin is close to that of diethyl ether, the arbitrary standard (Krantz *et al.*, 1947), and it is excreted from the body without having undergone metabolism. The chemical formulae of the two substances are:

In the present series of 378 cases in which methyl *n*-propyl ether was used as a maintenance agent all the patients were subjected to plastic surgical procedures, and the group selected for study includes ages from birth to the fifth birthday, distributed as follows: 1st year, 108; 2nd year, 87; 3rd year, 71; 4th year, 50; 5th year, 62.

By the age of 3 most of the surgery for hare-lip and cleft-palate has been completed, and the liability to burns and trauma causes the increase in surgery in the fifth year and subsequently. The duration of administration of anaesthesia varied from 10 minutes to 180 minutes, the average being 76 minutes. With the exception of eight cases, administration was carried out by means of an intratracheal tube, using the method described by Picken (1950), the vaporizing agent being oxygen or a 2:2/3 oxygen and nitrous oxide mixture at a flow rate of 4 to 5 litres a minute.

In this series 209 patients were operated upon for repair of hare-lip and/or cleft-palate, among them an Abbé repair of primary hare-lip at 5 months, in which the administration lasted 145 minutes; 80 underwent excision and/or grafting of burns; and the remaining 89 were submitted to a large variety of procedures, including a repair of spina bifida lasting 105 minutes, eleven hours after birth, and a colostomy at 26 hours.

Premedication.—Atropine alone, 1/200 to 1/100 gr. (0.3 to 0.6 mg.), was used in the smallest children. Pentobarbitone sodium ("nembutal") at the rate of 0.7 gr. per stone (7 mg per kg.) body weight, with atropine, was given orally to some; morphine sulphate, 1/40 gr. per stone (0.25 mg. per kg.), with atropine was given to others; while a few of the older children received papaveretum and scopolamine. All these drugs, with the exception of pentobarbitone, were given by the intramuscular route.

Induction.—Cyclopropane and oxygen 50:50 was used as the inducing agent in 200 cases, and ethyl chloride followed by methyl *n*-propyl ether on the open mask in most of the other 178. In a very few cases induction and maintenance were carried out with methyl *n*-propyl ether alone. Cyclopropane is preferred by one of us (H. G. M.) because it gives a very rapid induction, free from coughing or excitement. Its vapour density (21) is greater than that of air (14.3), and most of the children were anaesthetized without

the use of a mask by "pouring" the gas from a tube concealed within the hand. Intubation was carried out, using either the Magill or the Macintosh laryngoscope, as soon as the jaw was relaxed. Induction with ethyl chloride and methyl *n*-propyl ether appeared to be more rapid than induction under similar circumstances with ethyl chloride and diethyl ether. The relatively non-irritating vapour of methyl *n*-propyl ether causes less coughing and breath-holding and allows induction to proceed more smoothly.

Course.—After intubation anaesthesia was maintained with either pure oxygen or a mixture of nitrous oxide and oxygen as a vaporizing agent for the methyl *n*-propyl ether. The vapour is carried by pressure tubing to a Cardiff connector attached to the end of the intratracheal tube so that there is no resistance to breathing in the circuit. Because this ether is relatively non-irritating we have found that anaesthesia may be deepened very rapidly when required, and therefore a very light plane may be maintained when relaxation is not needed. The respiratory rate is not apparently increased to the same extent by methyl *n*-propyl ether as by diethyl ether, nor is there any apparent increase in capillary oozing in the presence of an unimpaired airway. We have observed no cardiac irregularities in the series. The response of the pupil to methyl *n*-propyl ether shows a time lag when compared with the sequence for diethyl ether (Guedel, 1937), and consciousness may be reached during withdrawal of anaesthesia from depth before the pupil contracts (Shane, 1947). Recovery from anaesthesia is rapid, and the cough reflex is quickly restored. Excitement and struggling are very uncommon. It has been found possible to begin feeds in all cases very soon after withdrawal of anaesthesia, thus minimizing nutritional loss. In the concentrations used there have been no complaints of headaches or disagreeable feelings in the surgical teams (Fisher and Whitacre, 1947).

Sequelae.—We have found no significant alteration in the incidence of post-operative nausea and vomiting when compared with diethyl ether. No vomiting persisted beyond the first post-operative 24 hours. The type of surgery undertaken in this series has necessitated the acceptance for operation of a higher than normal proportion of patients with chest infections. It is our impression that complications are few, since coughing is restored rapidly and co-operation in physiotherapy soon follows. There were no deaths immediately or remotely attributable to the anaesthesia.

We are indebted to Mr. Emlyn Lewis, consultant plastic surgeon to the United Cardiff Hospitals and the Welsh Regional Hospital Board, under whose care these patients were admitted, for his co-operation.

H. G. MIDDLETON, M.R.C.S., D.A., F.F.A. R.C.S.,

Consultant Anaesthetist, Welsh Regional Hospital Board,
St. Lawrence Hospital, Chepstow.

D. K. W. PICKEN, M.B., D.A., F.F.A. R.C.S.,

Consultant Anaesthetist, United Cardiff Hospitals and
Welsh Regional Hospital Board; Recognized
Clinical Teacher in Anaesthetics, Welsh
National School of Medicine.

REFERENCES

- Fisher, A. J., and Whitacre, R. J. (1947). *Anesthesiology*, 8, 156.
 Guedel, A. E. (1937). *Inhalation Anesthesia*. Macmillan, New York.
 Krantz, J. C., Evans, W. E., Carr, C. J., and Kibler, D. V. (1946). *J. Pharmacol.*, 86, 138.
 — *et al.* (1947). *Anesthesiology*, 8, 496.
 Picken, D. K. W. (1950). *British Medical Journal*, 1, 954.
 Shane, S. M. (1947). *Curr. Res. Anesth.*, 26, 260.

The United States Food and Drug Administration has directed that drug products containing more than 5% of oil of wintergreen must bear on their labels a warning that they should be kept out of reach of children, and that use contrary to directions may be dangerous. The methyl salicylate in the oil of wintergreen attracts young children by its smell, and a considerable number of deaths have occurred in the U.S.A., as in Britain, from young children drinking such preparations as liniments containing oil of wintergreen. Parents are not often aware of how dangerous these preparations are to children.