Daily inspection of the infant's mouth by the mother or nurse, with mycological confirmation of suspicious patches and immediate treatment, will probably control all cases. The daily routine swabbing of infant's mouth for *C. albicans*, and treating when found, or the routine use of prophylactic nystatin has proved successful (Harris *et al.*, 1958; Larroche, 1957, quoted by Drouhet, 1958), but it is doubtful whether such measures are necessary. No great harm will ensue if the lesion is missed for a day or two. The microscope and medication should complement and not replace the clinician. (Again, we may produce a resistant strain by these techniques.)

Summary

The incidence of thrush in the offspring of mothers with untreated monilial vulvovaginitis is very high, decreasing towards zero as the treatment becomes more adequate. Prematurity, breast- or bottle-feeding, antibiotics, or pH of the baby's mouth are *not* predisposing factors. The vaginal route of infection appears to be the most common. Early clinical detection of infected mothers and infants, and treatment with gentian violet or nystatin will control the disease.

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SCLEREMA NEONATORUM TREATED WITH CORTICOSTEROIDS

BY

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Before 1948 the survival rate for sclerema neonatorum was about 25% (Hughes and Hammond, 1948). Infants who recovered were full-term with birth weights of over 5½ lb. (2,500 g.). Since then case reports have appeared of patients treated with A.C.T.H. and corticosteroids. We have been able to trace 17 infants in the English medical literature who have received these hormones for the treatment of sclerema neonatorum, and 16 of them survived—some of them being premature. The greatest number of cases in any given series was four (Kendig and Toone, 1951; Kendall and Ledis, 1952; Glynn Williams, 1953; Kurzrok, Marshall, and Becker, 1954; Eisenoff, Aaron, and Green, 1954; McDonald, 1955; Buess, 1955; Davis, 1955; Wickes, 1956). So far as we are aware no statistically valid series has been published in which the value of corticosteroids in the treatment of sclerema neonatorum has been assessed.

We are fortunately placed for assessing the value of corticosteroids in this condition, because cold injury in the newborn infant is of common occurrence in the African population served by this hospital. This is particularly so in premature infants, of whom 635 were admitted during 1959, most of them less than 4½ lb. (2,040 g.) in weight. In this paper we compare the results of treatment of sclerema neonatorum with and without corticosteroids.

Material and Methods

During a nine-month period in 1959 we were able to collect 25 neonates with sclerema neonatorum who were admitted to the lying-in wards, the premature-baby unit, or the paediatric wards of Baragwanath Hospital. The diagnosis was made by at least two of us, and we were guided by Hughes and Hammond's (1948) definition of this condition—namely, that it is "characterized by a diffuse rapidly spreading, non-oedematous, tallow-like hardening of the subcutaneous tissue of infants in the first weeks of life. The skin in involved areas cannot be picked up and the subcutaneous tissues seem bound down to subjacent muscle and bone." All children in this series had non-pitting induration of the skin and subcutaneous tissues in several of the following sites: cheeks, deltoid and scapular regions, arms, forearms, buttocks, and lower limbs. The sclerema was widespread in all but five cases—that is, three or more sites were extensively involved. Of the five infants with less extensive sclerema, two had involvement of the cheeks alone, one showed sclerema of the lower limbs, one of the cheeks and legs, and one of the forearms, legs, and scapular region.

The general therapeutic measures carried out on all the babies in this series were as follows: (1) warming by means of an electric pad, blankets, and cotton-wool

wrap; (2) administration of oxygen through a funnel at the rate of 2 litres a minute for cyanotic attacks; (3) omission of feeds where the rectal temperature was below 95°F. (35°C.), and (4) intravenous-fluid therapy via a scalp vein in the presence of dehydration.

It was our plan to treat alternate cases with and without steroids. Owing to staff changes this plan was not always adhered to, some cases being treated by our colleagues according to their own preference. As these

All were premature infants whose birth weights ranged from 2 lb. 6½ oz. to 4 lb. 15½ oz. (1,090 to 2,250 g.), six of the infants weighing 3 lb. (1,360 g.) or less. The total dose of hydrocortisone administered ranged from 50 to 275 mg., while a total dose of 60 units of A.C.T.H. was given to the single patient treated with this hormone alone.

The most frequent associated illnesses noted in this group were diarrhoea, usually with dehydration, and

TABLE I.—Group A—11 Infants Treated with Corticosteroids or A.C.T.H.

Case No.	Birth Weight		Day of Onset of Sclerema	Associated Clinical Features	Anti-biotics	Hormone Total Dose	Result	Post-mortem Findings and Remarks
	lb. oz.	g.						
1	2 6½	1,090	2	Mother had positive Wassermann test	Pen.	Hydrocortisone 75 mg.	Died	Lungs: Foci of atelectasis. Gangrene in toes of left foot. Skin and subcutaneous tissue, normal
4	2 10	1,190	11	Vomiting day 5. Cyanotic attacks day 10	Pen.	Hydrocortisone 150 mg.	"	Blood sugar: 61 mg. day 1; <10 mg. day 3
5	3 5	1,500	9	Hyperbilirubinaemia. Diarrhoea and dehydration	Pen. Chloro.	Hydrocortisone 200 mg.	"	Lungs: Foci of atelectasis and congestion of alveolar capillaries. Liver: Bile stasis. Skin and subcutaneous tissue normal
6	3 15	1,785	16	Gastroenteritis and dehydration. Cyanotic attacks	Pen. Strep. Chloro.	Hydrocortisone 100 mg.	"	Lungs: Confluent bronchopneumonia and foci of atelectasis. Liver and large bowel: moderate congestion
8	3 0	1,360	2	Hypothermic. Rectal temp. 90° F. (32.2° C.)	Nil	A.C.T.H. 60 units	"	—
9	4 15½	2,250	2	Hypothermic	Pen. Strep.	Hydrocortisone 75 mg.	"	—
12	2 8	1,135	2	Regurgitation through the nostrils. Later blocked nose	Pen. Strep.	Hydrocortisone 275 mg.	"	Sclerema resolved before sudden death on day 8
13	3 5	1,500	12	Hyperbilirubinaemia. Frequent stools. Creps both bases	Pen. Strep.	Hydrocortisone 50 mg.	"	Lungs: Bronchopneumonia, intra-alveolar haemorrhage, and atelectasis
14	2 9	1,160	1	Hypothermic. Rectal temp. 88° F. (31.1° C.)	Nil	Hydrocortisone 100 mg.	"	—
18	3 14	1,760	2	Hyperbilirubinaemia. Vomiting; blood-stained stools. Dehydration	Pen.	Hydrocortisone 175 mg.	"	Lungs: Acute inflammatory exudate in alveoli, other alveoli filled with blood. Brain: Large haemorrhage around cerebellum. Liver: Hydropic degeneration of parenchymal cells. Adrenal: Agonal haemorrhage. Skin and subcutaneous tissue normal
21	2 10½	1,205	3	Blocked nose. Thrush	Pen.	Hydrocortisone 175 mg. A.C.T.H. 30 units	Alive	Sclerema of cheeks and legs; resolved in 4 days (see text)

Pen.=Penicillin. Strep.=Streptomycin sulphate. Chloro.=Chloramphenicol.

cases occurred at random, they did not, we think, introduce a bias into the treatment groups.

There were 11 patients in the series receiving corticosteroids (group A), and 10 of them were given 50 mg. of hydrocortisone sodium succinate by intramuscular injection when the diagnosis of sclerema was made. This was followed by 25 mg. intramuscularly every 8–12 hours for up to five days. One child in this group received A.C.T.H. by intramuscular injection in doses of 10 units every six hours, while another received 10 units daily for three days after completion of a course of hydrocortisone. Penicillin was administered to 9 of the 11 infants in doses of 50,000–100,000 units every eight hours by intramuscular injection. In four of them 50 mg. of streptomycin sulphate was given every 12 hours by intramuscular injection, and in two cases chloramphenicol was given additionally in doses of 30–50 mg./lb. (66–110 mg./kg.) body weight per 24 hours.*

The 14 infants in group B did not receive corticosteroids. Five were not given antibiotics, and penicillin was administered to the remaining nine by intramuscular injection in the doses mentioned previously. Four infants received streptomycin in addition, while two others were given chloramphenicol by mouth.*

Results

Table I summarizes the body weights, clinical features, extent of sclerema, and post-mortem findings (where available) of the 11 infants in group A.

*Chloramphenicol was administered in these relatively high doses before reports appeared of its toxicity in neonates (Kent and Wideman, 1959; Sutherland, 1959; Burns, Hodgman, and Cass, 1959).

clinical "bronchopneumonia." All patients with adventitious sounds in the lungs were regarded as cases of "pneumonia." However, we were aware that pulmonary haemorrhage, a common complication of neonatal cold injury (Mann and Elliott, 1957; Bower, Jones, and Weeks, 1960) could not be excluded as a cause of the crepitations. Pathological changes in the lungs were found in all five cases on whom necropsies were performed. There was either foci of atelectasis, or congestion of alveolar capillaries, or intra-alveolar haemorrhage, or frank bronchopneumonia.

In this group one infant (Case 21) survived. This baby, whose birth weight was 2 lb. 10½ oz. (1,205 g.), was admitted to the ward with a rectal temperature of 87°F. (30.6°C.). Three days later mild sclerema was noted on the cheeks and legs, the rectal temperature then being 96°F. (35.6°C.). Treatment was started with hydrocortisone and penicillin. The sclerema was much less 48 hours later and had disappeared by the fourth day of treatment. Hydrocortisone was given for five days, and this was followed by three daily injections of A.C.T.H. each of 10 units. The baby was discharged quite well after 47 days in hospital.

There was resolution of the sclerema in one other infant (Case 12), but it died on the eighth day of life. Necropsy was not carried out.

Table II summarizes the clinical findings and the outcome of the 14 infants in group B who received no corticosteroid hormones. Their birth weights ranged from 1 lb. 15½ oz. to 8 lb. 14 oz. (895 to 4,030 g.). Of these infants, six were less than 3 lb. (1,360 g.) in weight, while three weighed more than 5½ lb. (2,500 g.).

The most common associated illness in the infants was "bronchopneumonia" and two infants had passed blood-stained stools. Necropsies were carried out on only two of the 11 babies who died. In both instances the lungs showed some degree of intra-alveolar haemorrhage with or without frank evidence of bronchopneumonia. In addition, one child developed gangrene of the toes and haematuria resulting from a thrombus in the descending aorta and left renal artery.

legs, when the rectal temperature was 97.6° F. (36.4° C.). This disappeared 24 hours later without any special treatment. The child required two exchange transfusions for hyperbilirubinaemia on the sixth and seventh days of life. He was discharged fully breast-fed on the 26th day.

One other infant (Case 24) had sclerema of the cheeks which resolved without any specific therapy. However, this baby, whose weight fell to 1 lb. 11 oz. (765 g.), died on the 10th day of life.

TABLE II.—Group B—14 Infants Treated without Corticosteroids

Case No.	Birth Weight		Day of Onset of Sclerema	Associated Clinical Features	Anti-biotics	Result	Post-mortem Findings and Remarks
	lb. oz.	g.					
2	2 6	1,075	2	Cyanotic attacks; vomited feeds	Nil	Died	Lungs: Acute inflammatory exudate in alveoli and bronchioles; areas of atelectasis and intra-alveolar haemorrhage. Liver: mild fatty change. Skin and subcutaneous tissue: normal
3	4 13	2,185	13	Creps and bronchial breathing left lung. Blood-stained stools terminally	Pen. Strep.	"	"
7	7 3½	3,275	5	Badly asphyxiated at birth. Tachypnoea. Creps both lungs	Pen. Strep.	"	"
10	2 2	965	2	Hypothermic. Rectal temp. 90.6° F. (32.6° C.). Creps left lingula	Pen.	"	"
11	2 7	1,105	1	Hypothermic. Rectal temp. 85° F. (29.5° C.). Dyspnoea and cyanosis	Nil	"	"
15	Not known	895	11	"	Pen. Strep.	"	"
16	1 15½	895	2	Blood-stained stools. Creps both lungs	Nil	"	"
17	3 12	1,700	1	Salmonella enteritis. Dehydration.	Pen. Chloro.	Alive	See text for details
19	6 0	2,720	46	Marasmus	Pen.	"	"
20	On admission 8 14	4,025	12	Badly asphyxiated at birth. Dehydration. Creps right lung. Septic umbilicus. Gangrene of toes	Pen. Chloro.	Died	Lungs: Marked congestion; some intra-alveolar haemorrhage. Thrombosis of aorta and left renal artery. Renal infarction. Liver: congestion of sinuses
22	4 4½	1,940	2	Hyperbilirubinaemia. Hypothermic. Rectal temp. 89° F. (31.7° C.)	Nil	Alive	Sclerema of buttocks, thighs, and legs resolved in 2 days (see text)
23	2 12	1,245	7	Vomiting. Dehydration. Creps right lung	Pen. Strep.	Died	"
24	2 3	995	2	Hypothermic. Temp. 90° F. (32.2° C.). Jaundice. Sudden vomit and collapse on day 10	Nil	"	Sclerema of cheeks resolved in 3 days
25	4 1	1,845	4	Hypothermic. Cyanosis. Bilateral conjunctivitis	Pen.	Alive	Sclerema resolved in 24 hours (see text)

Pen. = Penicillin. Strep. = Streptomycin sulphate. Chloro. = Chloramphenicol.

Brief case histories of the survivors in group B are given.

Case 19.—A male infant, 34 days old and weighing 6 lb. (2,720 g.), was admitted suffering from a salmonella enteritis and failure to thrive. Sclerema developed eight days after admission, first on the legs and later on the buttocks, upper limbs, and cheeks. The onset of the sclerema was associated with a recurrence of diarrhoea and dehydration. Before the starting of intravenous therapy the serum sodium level was 127 mEq/l., the plasma chloride level was 111 mEq/l., and the carbon dioxide content was 5.0 mEq/l. The blood urea level was 206 mg./100 ml. Apart from intravenous replacement of fluid loss, the child was given chloramphenicol orally in doses of 125 mg. every six hours as well as penicillin in doses of 250,000 units every eight hours by intramuscular injection. The sclerema regressed on this treatment and disappeared six days later. However, this infant failed to gain weight because he ruminated. Gain in weight occurred when the feeds were thickened with cereals. When seen again at the age of 7½ months the child weighed 14 lb. 9 oz. (6.6 kg.) and he appeared to be thriving.

Case 25.—This infant, one of twins, weighed 4 lb. 1 oz. (1,845 g.) at birth. On the second day of life the rectal temperature had fallen to 93° F. (33.9° C.). Sclerema of the legs, forearms, and back was observed on the fourth day, when the child's rectal temperature was 98.4° F. (36.9° C.). The only form of treatment was penicillin by intramuscular injection in doses of 100,000 units every eight hours. Signs of sclerema had disappeared 24 hours later, when the only abnormality noted was a bilateral conjunctivitis. The infant began to gain weight after the eighth day of life and was discharged from the ward on the 26th hospital day.

Case 22.—A male premature infant weighing 4 lb. 4½ oz. (1,940 g.) was admitted from the district. Rectal temperature on admission was 89° F. (31.7° C.). By the third day of life patchy sclerema had developed on the buttocks, thighs, and

Discussion

Table III shows that both groups were well matched with regard to the premature infants including those below 3 lb. (1,360 g.) in weight, and the extent of the sclerema and the associated illnesses. The groups differed in that all three full-term infants were in group B, which also contained more patients who received no antibiotics.

The mortality was high in both groups, and there was no significant difference between the patients treated with or without corticosteroids. Most of the 17 cases recorded in the literature that were successfully treated with cortisone or A.C.T.H. were isolated cases, and it is possible that only the successes and not the failures were published.

Before 1948 only full-term babies with sclerema appear among the reported survivors. Six premature infants are included among the cases treated successfully

TABLE III.—Comparison of 25 Infants in Groups A and B

	Group A (Hormones)	Group B (No Hormones)
Total number	11	14
Premature infants	11	11
Birth weight < 3 lb. (1,360 g.)	6	6
Full-term infants	0	3
Extensive sclerema	10	10
Survivors	0	1
Mild sclerema	1	4
Survivors	1	2
Antibiotics	9	9
No antibiotics	2	5
Associated illnesses:		
Respiratory	6	7
Gastro-intestinal	3	3
Others	4	6
Survivors	1	3

with corticosteroids (Kendig and Toone, 1951; Kendall and Ledis, 1952; Eisenoff *et al.* 1954; Glynn Williams, 1953; Kurzrok *et al.*, 1954). It might therefore be argued that premature infants with sclerema can now be saved with corticosteroids. However, in our series premature infants have survived without the use of these hormones.

The use of antibiotics might influence the course of sclerema neonatorum. Bower *et al.* (1960) had 9 survivors among 14 full-term infants with sclerema and cold injury who received antibiotics without the addition of adrenal steroids. Fairchild (1955), in commenting on a report of Buess, who treated three full-term infants successfully with cortisone and antibiotics, stated that "the incidence of increased cures comes at a time when antibiotics are used more frequently in the newborn period." Wickes (1956) in reporting the case of an infant with sclerema who survived after the use of cortisone and tetracycline, admitted that antibiotics played their part, but felt that improvement coincided with the hormone therapy. This investigation was not designed to test the efficacy of antibiotic therapy and no definite conclusions regarding its value can be drawn from our series.

The percentage of body surface affected by the sclerematous process seemed to influence the prognosis. Whereas there was only one survivor (full-term) among the 20 cases with extensive sclerema, three of the five premature infants survived when not more than three different areas of the body were involved. Of these latter babies, two received no hormonal therapy.

It might be expected that the prognosis of sclerema neonatorum would be better in full-term than in premature infants, and it is of interest that the only survivor in our series with extensive sclerema was a full-term baby.

Thus on the basis of our study and a critical review of the literature we conclude that there is as yet no certain evidence that corticosteroids are of value in the treatment of sclerema neonatorum.

Summary

The efficacy of treatment of sclerema neonatorum with or without hydrocortisone or A.C.T.H. was assessed in a series of 25 infants.

Of 11 children treated with hydrocortisone or A.C.T.H. there was remission of the sclerema in two cases. In a control group of 14 infants not receiving these hormones, there were three survivors.

The prognosis is influenced by the extent of the sclerematous process.

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CUSHING'S SYNDROME IN CHILDHOOD DUE TO ADRENAL HYPERPLASIA

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Cushing's syndrome is rare in childhood. All the cases reported in children under 10 years of age have been due to an adrenal tumour, except four which were associated with adrenocortical hyperplasia. Chute, Robinson, and Donohue (1949) first reported a case in which the syndrome was not due to a tumour, in an 8-year-old girl who died post-operatively after partial adrenalectomy. Hubble and Illingworth (1957) described two examples of adrenal hyperplasia in children. One of these was an 8-year-old boy with Cushing's syndrome who presented with arrested growth. He was treated by adrenalectomy; seven-eighths of the left and the whole of the right adrenal were removed. He afterwards required maintenance therapy by cortisone and grew rapidly. Goldblatt and Snaith (1958) described a case in an infant, and Silver and Ginsburgh (1960) described another in an 8-year-old girl. Both these cases were treated by bilateral adrenalectomy in two stages.

We now report a case of Cushing's syndrome due to adrenocortical hyperplasia, with onset at age 9, in a boy who was treated with total bilateral adrenalectomy when he was 11 years old.

Case History

The patient was referred to hospital at the age of 10 years 2 months with a history of excessive gain in weight for one year. Previously he had been rather thin, with a poor appetite. His mother had noticed that he had stopped growing. He also had a history of periodic pain and pyrexia. On examination he was found to be obese, weight 121 lb. (54.9 kg.), height 55 in. (140 cm.), B.P. 145/112. He had a slight buffalo hump but no striae. He was put on a 1,000-calorie diet, to which he strictly adhered. During the next four months he lost 14 lb. (6.4 kg.) in weight and his blood-pressure fell to 125/95. In this period he developed frontal and temporal headaches and also complained of pains in the back, of increasing severity. There was a marked increase in growth of body hair.

On October 6, 1958, when he was aged 10 years 8 months, he was admitted to hospital for investigation.