The syndrome of chloride losing diarrhoea and metabolic alkalosis has been recently reviewed by Davidson *et al.*, (1972). The following pattern is thought to characterize this condition: severe watery diarrhoea with a stool chloride content of 70–150 mEq/l faecal fluid, minimal, or no urinary chloride excretion, severe hypochloraemia, hyponatraemia, and hypokalaemia of variable degree, hypovolaemia and metabolic alkalosis. Paradoxical aciduria occurs in the presence of severe potassium depletion. Correction is brought about by fluid and electrolyte therapy and potassium chloride supplements. Potassium with an anion other than chloride appears to be ineffective.

Large losses of chloride have also been reported in infants with ileostomy or colostomy after bowel surgery (Aaronson, 1971). Severe watery diarrhoea was associated with faecal chloride concentrations often exceeding 100 mEq/l of stool water, similar or slightly lower faecal sodium, and minimal faecal potassium concentrations. The infants required fluid and electrolyte therapy. No acid-base abnormalities were mentioned under these circumstances.

Our data may now be discussed in this context. The patient developed hypochloraemic alkalosis during a period of excessive watery ileostomy drainage. Although balance studies were not available, the amount and electrolyte content of the ileostomy fluid suggested that it was a major source of fluid, chloride, and some degree of sodium depletion. The low urinary chloride content was suggestive of an extrarenal loss of chloride. With intermittent dehydration and continuous weight loss, parenteral fluid and electrolyte therapy was evidently insufficient as long as the cycle of copious enteral feedings and diarrhoea was maintained. Cessation or reduction of enteral feedings minimized the ileostomy drainage and corrected the electrolyte imbalance in a reversible manner. Metabolic alkalosis did not recur after the closure of ileostomy, resumption of oral feeds, and discontinuation of parenteral nutrition. It appears that in the presence of hypochloraemia and of a sodium avid state, the criteria for the development of metabolic alkalosis have been met. There was no evidence of potassium depletion.

Metabolic alkalosis has been reported in cystic fibrosis with heat prostration, severe dehydration, and salt depletion (Kessler and Andersen, 1951; Rendle-Short, 1956; Di Sant' Agnese, 1960; Gottlieb, 1971; Arvantitakis and Lobeck, 1973). It is tempting to speculate that excessive sweat losses of chloride, sodium, and potassium, especially if superimposed upon pre-existing fluid and

electrolyte depletion, could easily create the above-mentioned optimal conditions for the genesis of metabolic alkalosis. Gastric loss of hydrochloric acid, however, might have played a predominant role in some of these reports (Kessler and Andersen, 1951; Di Sant' Agnese, 1960; Arvantitakis and Lobeck, 1973) and intestinal loss of chloride appears to be a plausible explanation in our case. Careful clinical evaluation and balance studies would be required to show a more than coincidental correlation between cystic fibrosis and metabolic alkalosis.

Summary

A case of hypochloraemic metabolic alkalosis in an infant with chloride losing ileostomy drainage and cystic fibrosis is described. It is speculated that intestinal loss of chloride played a major role in the development of metabolic alkalosis.

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Immunoglobulin E in erythema nodosum

Serum immunoglobulin E is characteristically increased in various atopic conditions (Johansson, 1967; Havnen *et al.*, 1973), sometimes as much as

tenfold. It usually correlates with the severity of clinical symptomatology, the number of systems involved, and the severity and variety of skin reactivity to allergens. Some asthmatic children however have normal or only moderately raised levels of IgE; nevertheless they have increased reagin activity as detected by the Prausnitz-Küstner reaction. It seems that not all circulating IgE is specific antiallergen (Havnen *et al.*, 1973). Parasitic infestation is another cause of huge IgE increase (Johansson, Mellbin, and Vahlquist, 1968; Ball, Voller, and Taffs, 1971). Moreover, raised IgE levels have been reported in various nonatopic conditions of which some are presumably of immunological nature, such as pulmonary haemosisiderosis (Heiner and Rose, 1970) and rheumatoid arthritis (Hunder and Gleich, 1971). The role of IgE in these disorders is not known. This report calls attention to raised IgE levels in poststreptococcal erythema nodosum (EN), another probable immunological disorder.

Materials and methods

Twenty-two children aged from 3 years 6 months to 12 years admitted during an 18-month period to the First Paediatric Clinic at Aghia Sophia Children's Hospital with a diagnosis of EN were studied. The children were divided into three groups according to aetiology of EN, i.e. streptococcal, tuberculous, and aetiology undetermined. Diagnosis of EN secondary to streptococcal infection was based on one or more of the following criteria. (i) Antistreptolysin O titre higher than 333 Todd units. (ii) Antistreptococcal hyaluronidase titre higher than 256 units. (iii) Increase or decrease of above-mentioned titres within a period of 2 to 33 weeks. (iv) Isolation of β -haemolytic streptococcus from nasopharyngeal smears. All children of the above group had Mantoux intradermal skin test negative.

Tuberculosis was considered whenever the Mantoux test was positive. 0.1 ml of 1:100 000 old tuberculin was initially injected; if the result was negative higher concentrations were serially tried up to 1:100. The diagnosis of active tuberculosis was based on a positive Mantoux test together with characteristic

chest x-ray findings. 'Non active' (tuberculin positive) tuberculosis (Lorber, 1958; Laurance *et al.*, 1961) was considered as the cause of EN in only one 4-year-old child whose Mantoux test had converted recently (9 months) to positive; nevertheless, his chest x-ray remained normal. This child had no findings fulfilling the criteria of streptococcal aetiology of EN.

No investigation was made of other possible causes of EN.

In all children with EN and in 14 age-matched controls serum IgE was quantitatively determined by the radioimmunosorbent technique (Bennich and Johansson, 1971; Wide, 1971). The kit was provided by the Pharmacia Company, Uppsala. Serum immunoglobulin G, M, and A, and salivary IgA were also determined by the radial immunodiffusion technique.

Results

Of the total of 22 children, 6 had EN secondary to streptococcal throat infection (27%); of these, 4 were female and all except one were above 7 years of age. 8 children had EN of tuberculous origin; only 2 were male and mostly were younger than 6 years. The age range of the remaining 8 children whose aetiology could not be determined was 3 years 6 months to 12 years. Clinical features such as recurrence a few months later, extension of the rash to the upper limbs, and/or joint involvement in the form of pain, periarticular swelling, and limitation of active movements were frequently encountered in the streptococcal EN group. They were rarely seen in the group of EN of undetermined aetiology. No EN case was in any way atopic.

Serum IgG, M, and A, as well as salivary IgA, were all within the normal range for the Greek population (Morphis *et al.*, 1974). Serum IgE levels were higher in streptococcal EN children than in the other two groups. The mean value was 991 units/ml (IU=2 ng) with a range from 170 to 2400 units/ml. Nevertheless, this increase did not correlate directly with the clinical severity of the case. On the other hand, IgE levels of children with EN due to tuberculosis coincided with the range of those of healthy age-matched controls, whereas those

TABLE

Mean values and ranges of IgE levels in children with erythema nodosum (EN) and in healthy controls

	No. of children	Age (years)		Mean value (units/ml)	Range (units/ml)
		Mean (yr)	Range (m)		
Streptococcal EN	6	8	7	991	170-2400
Tuberculous EN	8	6	3	68	12-160
EN of undetermined aetiology	8	8	3	97	70-150
Healthy	14	6	6	60	12-200

of children with EN of undetermined aetiology were in the upper part of the normal range for healthy children and their mean value was also slightly higher (Table). Statistical analysis was not attempted because of the small number of cases.

Discussion

Clinical symptomatology, aetiological diagnosis, age, and sex incidence in our series of cases do not differ in any respect from other reports (Lorber, 1958; MacPherson, 1970).

Specific allergic antibodies long known as reagins belong to the IgE fraction. As already stated, it has been shown that not all IgE are reagins (Havnen *et al.*, 1973), though it is not clear what other role IgE plays in the immune response. In the present study children with poststreptococcal EN had very high levels of serum IgE reaching over 10 times that of controls. We are studying whether IgE increases in other sequelae of streptococcal infections such as rheumatic fever, acute glomerulonephritis, or even during the actual course of streptococcal infection.

Joint involvement, extension of the rash, and recurrence, which are characteristic of streptococcal EN, could well represent an extension of an immune response. So could IgE production, but the two should not have a cause and effect relationship, as higher levels of IgE do not directly correlate with the severity of clinical manifestations.

Summary

Twenty-two children aged from 3 years 6 months to 12 years with erythema nodosum (EN) were grouped according to aetiology into streptococcal, tuberculous, and those whose aetiology was undetermined. Serum IgE levels were determined in all by the radioimmunosorbent technique. Levels were higher (mean value 991 units/ml) in streptococcal EN than in those of the other two groups (mean value 68 units/ml and 97 units/ml, respectively) and healthy age-matched controls (mean value 60 units/ml). Increase of IgE levels in individual cases of streptococcal EN did not correlate with severity of the clinical manifestations characteristic of that group.

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Vitamin E deficiency and thrombocytosis in Caffey's disease

Infantile cortical hyperostosis, described first by Caffey and Silverman in 1945, affects both sexes equally and onset is always before the age of 5 months. It is characterized by soft tissue swellings overlying cortical thickening which has been observed in all tubular bones except phalanges and vertebral bodies. It also affects flat bones. Infants usually exhibit irritability, pallor, and fever. There may be unpredictable remissions and relapses. Cases have presented with periorbital swellings and proptosis (Minton and Elliott, 1967). Associated thrombocytosis has been observed (Pickering and Cuddigan, 1969), but to our knowledge vitamin E deficiency in Caffey's disease has not previously been described.

Case report

A female, the fourth child of healthy parents, was born by normal delivery at term after a normal pregnancy. She was small-for-dates with a birthweight of 2640 g (<10th centile). After initial feeding difficulty she progressed well until 2 months when she presented with irritability, nasal obstruction, slow feeding, and intermittent swelling around the right eye with dropping of the eyelid on that side.