Congenital Chloride Diarrhea

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1 Introduction

Specific disturbances of intestinal electrolyte transport are very rare. More often, absorption of water and electrolytes is impaired along with the absorption of amino acids, fatty acids, sugars, and vitamins in states of generalized malabsorption, as in familial enteropathy with hypoplastic villous atrophy (Davidson et al. 1978). Chronic inflammation of the gut, e.g., colitis ulcerosa, may also be accompanied by malabsorption of electrolytes and water (Dutchie et al. 1964; Edmonds and Pilcher 1973; Harris and Shield 1970; Rask-Madsen 1973). In addition, reversible electrolyte malabsorption, "secondary chloride-losing diarrhea" may result from intestinal surgery even in normal children (Aaronson 1971). Other factors causing secondary impairment may be increased levels of gastrointestinal hormones, VIP, GIP, gastrin, secretin (Walsh 1981), and calcitonin (Gray et al. 1973) produced by tumors, diseases with increased intestinal bile acid concentrations (Binder 1980), and infections with intestinal toxin production such as cholera and E. coli gastroenteritis (Fishman 1980; Sack 1975). The only ions known to be involved in specific malabsorption states are Zn⁺ (Rahanzadeh and Danzig 1974), Cu²⁺ (Danks et al. 1972) and Cl⁻. Malabsorption of Cl⁻ is known as congenital chloride diarrhea (CCD). This disease was at first named "congenital alkalosis with diarrhea" (Darrow 1945; Gamble et al. 1945). Later, it was called "congenital chloridorrhea" and "familial chloride diarrhea." Today the name "congenital chloride diarrhea" appears to be generally accepted.

The early patients presented with intractable diarrhea, extremely low serum Cl⁻ concentrations and severe metabolic alkalosis. Patients who survived were retarded in growth and in psychomotor development. In some patients renal function deteriorated and arterial hypertension developed. Renal biopsies revealed hyalinized glomeruli, hyperplasia of the juxtaglomerular apparatus, calcium deposits and thickening of the arteriolar walls.

The last two decades have brought new insight into epithelial (including gastrointestinal) electrolyte transport. Intestinal perfusion studies have been performed in several patients with CCD and have extended our knowledge of the primary defect in this disease. Its pathophysiology is now largely understood. All other manifestations are secondary to the hypovolemia caused by the diarrhea. The crucial realization has been that the salts and water lost through diarrhea have to be fully replaced both quantitatively and qualitatively in order to avoid even slight hypovolemia, hyperreninism, and hyperaldosteronism. The diarrhea is inevitable. If the diagnosis is made in early neonatal life and adequate therapy is instituted immediately, these patients' kidneys and their growth and psychomotor development will remain unaffected.

So far, CCD has been mainly a pediatric problem. Now, however, these patients should all reach adulthood and the internists need to be aware of this rare disease, which has been reported from most parts of the world.