mined by reassessment of symptoms after a course of therapy for *H. pylori* infection.

REFERENCES

1. Boyle JT. Nutritional management of the developmentally disabled child. Pediatric Surgery International 1991;6:76-81.
2. Halpern ML, Jolley SG, Johnson DG. Gastroesophageal reflux: a significant association with central nervous system disease in children. J Pediatr Surg 1991;26:171-3.
3. Albanese CT, Towbin RB, Ulman I, Lewis J, Smith SD. Percutaneous gastrojejunostomy versus Nissen fundoplication for enteral feeding of the neurologically impaired child with gastroesophageal reflux. J PEDIATR 1993;123:371-5.
4. Flake AW, Shopene C, Ziegler MM. Anti-reflux gastrointestinal surgery in the neurologically handicapped child. Pediatr Surg Int 1991;6:92-4.
5. Mitchell HM, Lee A, Bohane TD. Evidence for person-to-person spread of *Campylobacter pylori*. In: Rathbone BJ, Heatley RV eds. *Campylobacter pylori* and gastroduodenal disease. Oxford, England: Blackwell Scientific Publications, 1989:197-202.
6. Mitchell HM, Bohane TD, Tobias V, et al. *Helicobacter pylori* infection in children: potential clues to pathogenesis. J Pediatr Gastroenterol Nutr 1993;16:120-5.
7. Harris AW, Douds A, Meurisse EV, et al. High seroprevalence of *Helicobacter pylori* in residents of a hospital for people with severe learning difficulties [Abstract]. Gastroenterology 1994; 106:A91.
8. Vincent P, Gottrand F, Pernes P, et al. *Helicobacter pylori* infection in cohabiting children. Lancet 1991;337:848.
9. Mitchell HM, Lee A, Carrick JTI. Increased incidence of *Campylobacter pylori* infection in gastroenterologists: further evidence to support person-to-person transmission of *C. pylori*. Scand J Gastroenterol 1989;24:396-400.

Pseudohypoaldosteronism with increased sweat and saliva electrolyte values and frequent lower respiratory tract infections mimicking cystic fibrosis

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Four patients with severe pseudohypoaldosteronism caused by multiple end-organ resistance to aldosterone had frequently recurring lower respiratory tract infections and persistently elevated sweat and saliva electrolyte values. The increased saliva electrolyte values in these patients probably affect normal mucociliary function in the respiratory tract and facilitate the occurrence of frequent lower respiratory tract involvement. Patients with pseudohypoaldosteronism may require treatment similar to that for cystic fibrosis to prevent long-term respiratory complications. (J PEDIATR 1994;125:752-5)

Type I pseudohypoaldosteronism is a hereditary salt-wasting disease that includes two distinct entities with different modes of inheritance.[1] The classic form stems from an isolated target organ defect with diminished renal tubular responsiveness to aldosterone and is inherited as an autosomal dominant trait; sweat and saliva electrolyte values are normal.[1] In contrast, the more severe form of PHA is characterized by multiple target organ resistance to aldosterone and is inherited as an autosomal recessive trait; these patients have signs and symptoms of severe salt loss that may even lead to death as a result of excessive loss of electrolytes from sweat, salivary glands, colon mucosa, and the distal renal tubule.[1]

Long-term observations of four of our patients with the severe form of PHA showed that they have frequent lower respiratory tract infections. The analyses presented in this article reveal a condition that mimicks cystic fibrosis in these patients. Although CF and PHA differ in pathophysiology and outcome, the similarities in the courses of these two genetic entities suggest a linkage between increased

Supported in part by a grant from the Israel Ministry of Health.
Submitted for publication Feb. 7, 1994; accepted June 17, 1994.
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0022-3476/94/$3.00 + 0 **9/22/58438**

salivary sodium chloride concentrations and susceptibility to frequent lower respiratory tract involvement and infections.

METHODS

The diagnosis of PHA with multiple target organ resistance to aldosterone was established in all our patients according to the following criteria: (1) severe salt-wasting episodes (vomiting, dehydration, shock) starting in early infancy, which were associated with hyponatremia, hyperkalemia, acidosis, markedly increased plasma aldosterone concentrations, and hyperreninemia; (2) increased urinary sodium concentration and sodium/potassium ratio, with increased salivary and sweat electrolyte concentrations; (3) normal renal and adrenal function test results after correction of dehydration, including normal findings on renal ultrasonography and intravenous pyelography and normal serum 17 α-hydroxy-progesterone levels; and (4) parental consanguinity and normal plasma aldosterone and renin activity in the parents.

Sweat was collected by pilocarpine iontophoresis from the forearm, and saliva was collected from the sublingual region. In infants, sweat and saliva chloride concentrations were measured with a CF analyzer (Advanced Instruments, Needham Heights, Mass.), which requires small amounts of sweat and saliva. Beyond infancy, sweat and saliva electrolytes were analyzed by means of a Monarch 2000 automatic analyzer (Corometrics Medical Systems, Inc., Wallingford, Conn.) with ion-selective electrodes for sodium, potassium, and chloride.

CF	Cystic fibrosis
FVC	Forced vital capacity
FEV_1	Forced expiratory volume, in 1 second
PHA	Pseudohypoaldosteronism

CASE REPORTS

Patient 1. A 9-day-old girl was seen because of failure to thrive. The pregnancy, labor, and delivery were uneventful; her birth weight was 3 kg. The genetic and endocrine evaluation of this patient was reported previously.[1] There was no family history of chronic lung disease.

On admission the patient was severely dehydrated and weighed 2.6 kg. The laboratory evaluation revealed marked hyponatremia and hyperkalemia (Table I). Because of resistance to aldosterone, the patient's condition was stabilized only by intravenous administration of high amounts of sodium chloride (5 gm/day). She remained dependent on high amounts of sodium chloride throughout hospitalization, which lasted 4 months. During hospitalization she had two episodes of pulmonary disease. At the age of 1 month she had severe dyspnea, cyanosis, high fever, tachypnea (90/min), and severe intercostal retractions. Crackles over both lungs were heard. An x-ray study of the chest showed nonhomogeneous left lower lobe infiltrate. The patient was treated with oxygen and antibiotics. Her condition improved slowly. The second episode occurred at 3 months of age and was characterized by persistent cough and expiratory wheezing, which lasted about 1 week.

Since the age of 4 months, in addition to recurrent salt-wasting episodes requiring frequent hospitalizations (about six a year), especially during hot summer weather, the patient had frequent pulmonary infections characterized by cough associated with tachypnea, high fever, and crackles or wheezing on auscultation. These symptoms usually were not severe, and they usually did not require hospitalization. Sometimes the crackles persisted off and on for several months, with only minimal cough and low-grade fever or no other symptoms. Today, at 8 years of age, the patient still has frequent episodes of cough associated with wheezes or crackles and high fever, even though a high-salt diet (14 gm/day) has prevented severe salt-losing crises for the last 6 years.

The sweat and saliva electrolyte determinations (more than 10 determinations in an 8-year period) repeatedly showed markedly increased values (Table II). During the respiratory events and infections, throat and blood cultures did not grow any pathogenic bacteria. Pulmonary function tests at the age of 8 years, when the patient was free of symptoms, revealed normal flows and volumes (FEV_1 = 91% of the predicted value, FEV_1/FVC = 99%, maximal expiratory flow at 50% of vital capacity = 124% of the predicted value, FVC = 91% of the predicted value).

Patient 2. The patient, a girl, was the product of a consanguineous marriage. Pregnancy and delivery were uncomplicated, and she was born at term; birth weight was 3.5 kg. The parents and six siblings were all healthy. The patient was first admitted at the age of 10 days because of severe salt wasting (Table I) and remained hospitalized for almost a year. Subsequently she was hospitalized nearly 100 times for either salt-losing crises or respiratory events and infections. She was last admitted at the age of 8 years 3 months because of severe respiratory distress associated with severe hyponatremia (128 mmol/L) and acidosis (bicarbonate, 12 mmol/L). An x-ray study of the chest showed a left lower lobe infiltrate. The patient's condition improved after therapy with oxygen, antibiotics, and saline solution. A month later a roentgenogram of the chest was normal, although crackles over both lungs were heard off and on during 6 months of follow-up. Occasionally crackles disappeared immediately after vigorous chest physical therapy and postural drainage without antimicrobial therapy.

Sweat and saliva electrolyte determinations (seven and four occasions, respectively) during a 6-month period revealed markedly elevated sodium and chloride values (Table II). During the respiratory events no bacterial pathogens were isolated from blood or from the oropharynx. The results of pulmonary function tests performed when the patient was free of symptoms were also within normal limits.

Patients 3 and 4. The patients were twin boys in whom PHA was diagnosed at the age of 5 days (Table I). The parents and two healthy siblings had no history of respiratory tract infections or allergy. The infants had their first pulmonary infections at 4 months of age. Twin 1 (patient 3) had clinical and roentgenographic evidence of bilateral bronchopneumonia necessitating the administration of O_2 and antibiotics. In twin 2 (patient 4) the first episode was characterized by wheezy bronchitis. Since then, the patients have had repeated episodes of lower respiratory tract infections, associated with high fever, and respiratory distress that required hospitalization and oxygen therapy. The sweat and saliva electrolyte values have been persistently high (Table II).

DISCUSSION

These four patients with a severe form of PHA have several characteristics that mimic CF, including increased

Table I. Biochemical data of four patients with PHA at first admission

Patient No.	Sex	Serum Na^+ (mmol/L)	Serum K^+ (mmol/L)	Aldosterone (pmol/L)	PRA (ng/(L·sec))
1	F	125	10.0	39,600	41.7
2	F	116	12.3	53,100	5.8
3 (twin 1)	M	116	9.2	128,000	308.0
4 (twin 2)	M	118	8.8	69,700	47.0
Normal*	—	136-146	3.5-4.8	<3,050	<2.8

Urinary Na^+ concentrations >50 mmol/L and urinary Na/K ratio >10 in all patients.
PRA, Plasma renin activity.
*Normal values for aldosterone and PRA in infants 1 week to 3 months of age.

Table II. Sweat and saliva electrolyte concentrations in four patients with PHA with multiple end-organ resistance to aldosterone

Patient No.	Age (yr)	Saliva Na^+ (mmol/L)	Saliva Cl^- (mmol/L)	Sweat Na^+ (mmol/L)	Sweat Cl^- (mmol/L)
1	8	145-175	124-162	137-202	117-182
2	8.5	140-167	128-139	70-206	70-143
3	4	138	80-135	150	70-150
4	4	146	>100-140	112-125	120
Normal values		<40	<40	<60	<60

Serum immunoglobulin concentrations were normal in all patients.

sweat electrolyte values and recurrent lower respiratory tract infections starting in early infancy. Sometimes the pulmonary involvement was severe and necessitated hospitalization and vigorous therapy. The severe pulmonary infections were usually associated with episodes of salt loss, including severe dehydration and hyponatremia, especially until the age of 2 to 4 years. In the ensuing years the patients frequently had only persistent cough associated with crackles or wheezes, even in the absence of salt-losing episodes, and pulmonary involvement was usually mild to moderate.

The pathophysiologic abnormalities in CF include altered ionic composition of the mucus secreted by various organs;[2, 3] increased concentrations of chloride in the airway,[4] nasal mucosa,[5] and saliva[2, 6-8]; and failure to clear mucous secretions.[2, 3] Changes in the ionic composition of the salivary[3] and respiratory tract[9] secretions may compromise normal mucociliary function in the respiratory tract. Similarly, the increased saliva electrolyte concentrations in patients with severe PHA may have an effect on normal mucociliary function, leading to frequent lower respiratory tract infections.

The underlying abnormality of respiratory epithelial cells in CF is well delineated.[10, 11] The increased sweat and saliva electrolyte concentrations in PHA may also reflect an underlying epithelial disorder. However, the severe form of PHA probably does not stem from a defective response of respiratory cells to aldosterone. In vitro experiments have demonstrated that aldosterone does not affect baseline bioelectric properties of distal lung epithelium in fetal rats[12] or tracheal sodium transport in rabbits.[13] Aldosterone also does not affect potential difference of nasal respiratory epithelium in normal subjects.[14] Aldosterone does have a small effect on tracheal epithelial sodium transport in dogs, but only at high doses.[15]

Episodes of dehydration in these patients may be an additional factor affecting mucus and mucociliary function in the respiratory tract.[3] However, the lower respiratory tract involvement was observed even in the absence of severe dehydration (especially in patients past the age of 2 to 4 years), so dehydration could not be the sole factor responsible for the respiratory tract disease. These findings suggest that recurrent respiratory infections in our patients are secondary to both significantly altered composition of saliva and recurrent bouts of dehydration. However, the existence of a primary defect in the respiratory tract cannot be ruled out.

Frequent acute respiratory tract infections, including recurrent pneumonias, have been noted in three additional patients with multiple end-organ resistance to aldosterone,[16, 17] although no explanation was given for such an occurrence. On the basis of our findings in four patients with severe PHA, we suggest that lower respiratory tract involvement should be considered a significant characteristic of this disease. These patients may require appropriate treatment, similar to that for CF, to prevent long-term respiratory complications.

REFERENCES

1. Hanukoglu A. Type I pseudohypoaldosteronism includes two clinically and genetically distinct entities with either renal or multiple target organ defects. J Clin Endocrinol Metab 1991;73:936-44.
2. Boat TF. Cystic fibrosis. In: Behrman RE, Kliegman RM, Nelson WE, Waughan VC, eds. Nelson textbook of pediatrics. 14th ed. Philadelphia: WB Saunders, 1992:1106-16.
3. Sturgess JM. Mucous secretions in the respiratory tract. Pediatr Clin North Am 1979;26:481-501.
4. Gilljam A, Ellin A, Strandvik B. Increased bronchial chloride concentration in cystic fibrosis. Scand J Clin Lab Invest 1989;49:121-4.
5. Knowles MR, Gatzy JT, Boucher RC. Increased bioelectric potential differences across respiratory epithelia in cystic fibrosis. N Engl J Med 1981;305:1489-95.
6. Bardon A, Ceder O, Kollberg H. Cystic fibrosis-like changes in saliva of healthy persons subjected to anaerobic exercise. Clin Chim Acta 1983;62:815-7.
7. Davis PB. Pathophysiology of cystic fibrosis with emphasis on salivary gland involvement. J Dent Res 1987;66(special issue):667-71.
8. Davies H, Bagg J, Goodchild MC, McPherson MA. Defective regulation of electrolyte and protein secretion in submandibular saliva of cystic fibrosis patients. Acta Paediatr Scand 1991;80:1094-5.
9. Chace KV, Naziruddin B, Desai VC, Flux M, Sachdev GP. Physical properties of purified human respiratory mucus glycoproteins: effects of sodium chloride concentration on the aggregation properties and shape. Exp Lung Res 1989;15:720-37.
10. Quinton PM. Cystic fibrosis: a disease in electrolyte transport. FASEB J 1990;4:2709-17.
11. Welsh MJ. Abnormal regulation of ion channel in cystic fibrosis epithelia. FASEB J 1990;4:2718-25.
12. O'Brodovich H, Rafii B, Perlon P. Arginine vasopressin and atrial natriuretic peptide do not alter ion transport by cultured fetal distal lung epithelium. Pediatr Res 1992;31:318-22.
13. Boucher RC, Gatzy JT. Characteristics of sodium transport by excised rabbit trachea. J Appl Physiol 1983;55:1877-83.
14. Knowles MR, Gatzy JT, Boucher RC. Aldosterone metabolism and transepithelial potential difference in normal and cystic fibrosis subjects. Pediatr Res 1985;19:676-9.
15. Cullen JJ, Welsh MJ. Regulation of sodium absorption by canine tracheal epithelium. J Clin Invest 1987;79:73-9.
16. Popow C, Pollack A, Herkner K, Scheibenreiter S, Swoboda W. Familial pseudohypoaldosteronism. Acta Paediatr Scand 1988;77:136-41.
17. Hogg RJ, Marks JF, Marver D, Frolich JC. Long-term observations in a patient with pseudohypoaldosteronism. Pediatr Nephrol 1991;5:205-10.

Presymptomatic late-infantile metachromatic leukodystrophy treated with bone marrow transplantation

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At 8 months of age, before clinical neurologic deterioration, the younger of two sisters with metachromatic leukodystrophy received a transplant of bone marrow from her haploidentical, heterozygote mother. Compared with the course in the older, affected, untreated sibling, the onset of neurologic regression was delayed 1 year and progressed at a slower rate. (J PEDIATR 1994;125:755-8)

Submitted for publication April 8, 1994; accepted June 28, 1994.

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0022-3476/94/$3.00 + 0 **9/22/58758**

Metachromatic leukodystrophy is an autosomal recessive inherited metabolic storage disorder of sphingolipid metabolism. Its estimated frequency, 1 in 40,000,[1] makes it one of the more common lysosomal storage diseases. In its most common (late-infantile) form, regression manifested by incoordination and by gait disturbances first appears between