We conclude that while MH is recognized as a latent genetic condition, susceptibility to this syndrome cannot be predicted on the basis of a distinctive or common HLA haplotype, since no such association was demonstrated in family members highly prone to this disease.

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Hyperkalemia: Benign, Hereditary, Autosomal Dominant

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The presence of hyperkalemia in a patient may present a medical emergency. The accepted normal value for serum potassium in individuals beyond the neonatal period is from 3.5 to 5.5 mEq/l. The narrow limit for this extracellular potassium is attributed to its rapid excretion by the kidney under the influence of adrenal hormone secretion. Serum levels can be lowered temporarily by administration of diuretics, or raised as a result of tissue damage. Persistent elevation of serum level is usually secondary to abnormalities such as Addison's disease, hyporeninemia, hypoaldosteronism, some forms of congenital adrenal hyperplasia, and renal failure.[1] Familial hyperkalemia with hypertension, hyporeninemia, and normal aldosterone levels was reported in four patients by Brautbar *et al.* in 1978.[2]

Pseudohyperkalemia is a condition in which serum potassium is elevated above normal values due to its release from the platelets, leukocytes, or erythrocytes during the clotting or separation process.[3–6] Clinically, pseudohyperkalemia may be distinguished from hyperkalemia by estimating both plasma and serum levels. In pseudohyperkalemia, only the serum levels of potassium are high, while plasma levels remain normal.

Inherited pseudohyperkalemia caused by an abnormal leakage of potassium from erythrocytes was reported by Stewart *et al.* in 1979.[7] The family of normokalemic subjects described had misleadingly high laboratory potassium levels. Serum potassium levels were normal when determined immediately after drawing, but rose in a linear direction to a very high level over a period of six hours of in vitro studies.

We report a family with true hyperkalemia not associated with hypertension or any detectable adrenal or renal abnormality. Neither the patient nor the members of his family appear to have clinical symptoms related to the presence of hyperkalemia.

Report of a Case

An 11-year-old boy with cerebral palsy, spastic paraplegia, and bilateral subluxation of the hips was admitted for bilateral varus osteotomy of the femur. He had been born prematurely; his mother had a significant antepartum hemorrhage. Birth weight was 1.62 kg. The patient was slow to reach developmental milestones, and the diagnosis of cerebral palsy was made at an early age. He had not walked without braces, and was usually confined to a wheelchair. Except for the usual childhood illnesses, he had no known medical problems other than those directly related to his cerebral palsy. His weight was 28.8 kg. (between the fifth and tenth percentile for his age) and his height was 133 cm (the fifth percentile for his age). His vital signs were within normal limits. Positive physical findings were limited to the motor system, which showed increased tone in all extremities. There were bilateral flexion contractures of the hips.

Routine preoperative laboratory studies revealed a normal complete blood count and urinalysis. Serum sodium was 140 mEq/l, potassium 6.3 mEq/l, total CO_2 23.1 mEq/l, and chloride 108 mEq/l. These studies were repeated several times, and the abnormal serum potassium

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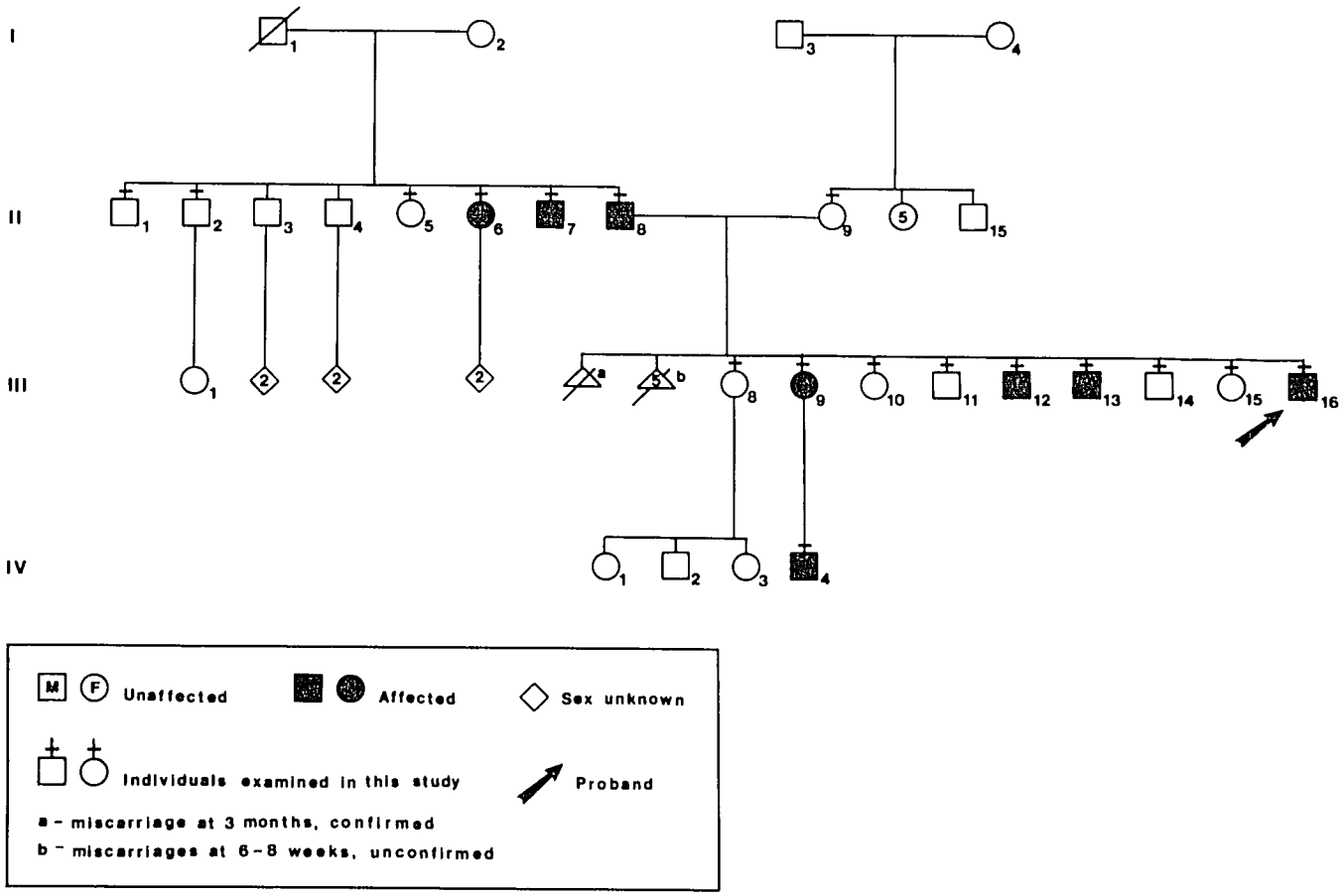

FIG. 1. Pedigree of the proband family demonstrating autosomal dominant mode of inheritance of the benign hyperkalemia.

levels persisted. Because of these findings, the patient was studied to determine the etiology of the persistent hyperkalemia.

Urine *p*H values ranged from 5.0 to 7.0, and specific gravity from 1.005 to 1.031. Several cultures were all negative, and there was no evidence of cellular abnormalities, proteinuria, glycosuria, or ketonuria. There were no unusual crystals, and an amino acid screen was negative.

Urine electrolytes were measured for a 24-hour period, with a normal diet. They were repeated on two occasions, and the volume varied from 590 ml to 640 ml. The urinary creatinine for each of these specimens was 0.72 g/24 hours. Sodium levels varied from 131 to 144 mg/specimen. The potassium varied from 51 to 62 mg/24 hours. All of these values are normal in our laboratory for a child of this age.

Blood urea nitrogen varied from 7.8 to 14 mg/100 ml, and serum creatinine varied from 0.4 to 0.6 mg/100 ml with multiple determinations. Creatinine clearance was measured at 161 ml/min, corrected for a surface area of 0.89 m^2, which is just within the upper limits for normal in our laboratory.

A urine acidification test was performed to exclude renal tubular acidosis. The results of endocrine studies performed on the patient were all within normal limits.

Multiple complete blood counts were performed on this patient during the two-year study period. His hemoglobin varied from 12 to 13 g (excluding immediate postoperative values); his red cell count varied from 4.65 to 4.93 million/μl; the white cell count from 6,550 to 9,250 cells/μl; hematocrit from 37 per cent to 42 per cent, and platelet counts from 310,000 to 500,000/μl.

In order to rule out the possibility of pseudohyperkalemia, plasma potassium levels were estimated by means of flame photometry at different intervals postdrawing. Blood samples were added to four standard lithium heparin tubes and kept at room temperature. The first was evaluated at 15 min and showed 6.0 mEq/l; the second, at two hours, measured 5.9 mEq/l; the third, at four hours, and the fourth, at six hours, both showed 5.7 mEq/l. These results indicated that while the level of potassium is initially high, there is no further increase in values with time.

Biopsy of the gluteus maximus muscle was normal by both light and electron microscopy.

Several preoperative electrocardiography tracings did not show any ST segment or T-wave abnormalities. Continuous intra-operative monitoring for several hours with the oscilloscope on standard lead 2 did not reveal any changes in either the T-wave configuration or the rhythm patterns.

Several of the patient's relatives were available for examination. Of eight siblings, hyperkalemia was present in two brothers and one sister (fig. 1, III-9, III-12, III-13, and III-16). The father was also found to have hyperkalemia. Five of the father's seven siblings were available for testing. Two were hyperkalemic (fig. 1, II-6 and II-7). The patient's nephew, at the age of six months, was also found to have elevated potassium levels (fig. 1, IV-4). This infant was retested at the age of one year to confirm the hyperkalemia. Of the eighteen family members tested, eight, or 44 per cent, showed hyperkalemia. The patient's grandparents (fig. 1, generation I) were not available for study.

All of the affected individuals are in good health with no remarkable medical history. A paternal uncle of the patient was hospitalized at the age of 32 years for a fracture of the patella. During that hospitalization, a diagnosis of idiopathic hyperkalemia was made. The uncle was anes-

TABLE 1. Potassium Levels of the Affected Individuals

	Patient Number	Age	Potassium Values
Generation II	6	50	6.0 mEq/l
	7	49	6.5 mEq/l
	8	48	6.9 mEq/l
Generation III	9	24	5.8 mEq/l
	12	20	6.4 mEq/l
	13	19	6.9 mEq/l
	16	14	7.2 mEq/l
Generation IV	4	6 mo	Serum—6.6 mEq/l Plasma—6.4 mEq/l
		1 year	Serum—6.2 mEq/l Plasma—6.0 mEq/l

thetized twice with no adverse reactions. There have been no illnesses or deaths related to the potassium levels of the affected individuals. These levels are listed in Table 1.

DISCUSSION

Hyperkalemia in the preoperative screen of a patient is of obvious concern to the anesthesiologist. Preoperative hyperkalemia can lead to lethal levels of potassium under general anesthesia, particularly when succinylcholine infusion is used or when unexpected complications occur.

Our proband has been anesthetized four times, all within a one-year period, for orthopaedic surgery. In each instance, thiopental was used for induction of anesthesia. During the first procedure, fentanyl, *d*-tubocurarine, and nitrous oxide were administered for maintenance. Halothane was used for maintenance during the second and fourth procedures, and enflurane was used for the third. All of these anesthetic techniques were tolerated well by the patient. There were no abnormal electrocardiograph findings or other complications. Intra-operative monitoring of serum potassium levels revealed only minor changes.

The serum potassium level could be altered by varying the potassium intake. When the patient was placed on a low potassium diet, the serum potassium decreased to 4.9 mEq/l. When the dietary potassium increased, so did the serum potassium, reaching a high of 7.0 mEq/l. Thus, the patient seems to have at least normal control of the range of serum potassium levels, although the base line which he maintained was higher.

The presence of hyperkalemia in three generations strongly suggests an autosomal dominant mode of inheritance. We were unable to detect an etiology for this family's hyperkalemia. Due to the benign nature of this particular condition, and the fact that it would not have been brought to anyone's attention except for the patient's need for a preoperative work-up and routine screening for serum electrolytes, we suspect that the situation may occasionally be present in the general population.

Since certain induction techniques and methods of anesthetic depression may lead to lethal or near-lethal levels of potassium in hyperkalemic patients, it is especially important for the anesthesiologist to be aware of the condition. Because the elevated potassium levels associated with benign hyperkalemia are, in effect, normal and safe levels for the affected individuals, it may be dangerous to aggressively treat these patients with the intention of reducing potassium levels; such treatment is likely to result in relative hypokalemia.

The elaborate endocrine and renal studies performed on our proband would hardly be practical, or necessary, in most cases. However, since the autosomal dominant form of benign hyperkalemia reported here had not been documented previously, the extensive laboratory work-up was necessary in order to rule out all other possible etiologic factors, due to the inherent risks of hyperkalemia during anesthesia. The relatively simple family screening performed subsequent to this extensive laboratory work proved to be the key to identifying the condition. When there is no apparent cause nor any signs and symptoms of hyperkalemia, screening of family members, where possible, would seem to be sufficient in establishing the diagnosis of benign autosomal dominant hyperkalemia.

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