over, their work suggests that factors other than emulsification of the substrate alone may also be involved(20). We, too, have found that emulsification of purified olive oil did not assure hydrolysis by postheparin plasma. Thus, no lipolytic activity in postheparin plasma was detected in a turbidimetric system designed for pancreatic lipase(12). In addition, much less activity was observed with the standard titrimetric lipase method of Tietz *et al*(21) than with our present system. All 3 systems employed purified olive oil as substrate but differed in the composition of the substrate mixture and in the method of preparation. This indicates that a certain "mode of presentation" of the substrate to the enzyme as suggested by Desnuelle and Savary(14) is required for maximal activity.

Summary. A rapid, simple, reproducible and readily available substrate preparation for estimating postheparin plasma lipase is described. Ca^{++} is obligatory but can be replaced by other cations such as NH_4^+, Na^+ or Mg^{++}. No preference was shown by postheparin plasma lipase for triglycerides with a particular fatty acid chain length or degree of saturation or unsaturation.

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X-Linked Recessive Inheritance of a Syndrome of Mental Retardation With Hyperuricemia. (31204)

SAMUEL L. SHAPIRO, GEORGE L. SHEPPARD, JR., F. E. DREIFUSS, AND DAVID S. NEWCOMBE (Introduced by Alfred Jay Bollet)

Division of Neurology and Departments of Preventive Medicine and Medicine, University of Virginia School of Medicine, Charlottesville

In 1959 two separate case reports described a syndrome of choreoathetosis, cerebral palsy, mental retardation, and self-mutilation in young children with elevated serum uric acid levels(1,2). Lesch and Nyhan recently demonstrated a metabolic abnormality in purine biosynthesis in this syndrome and reported the third affected family(3). Subsequently,

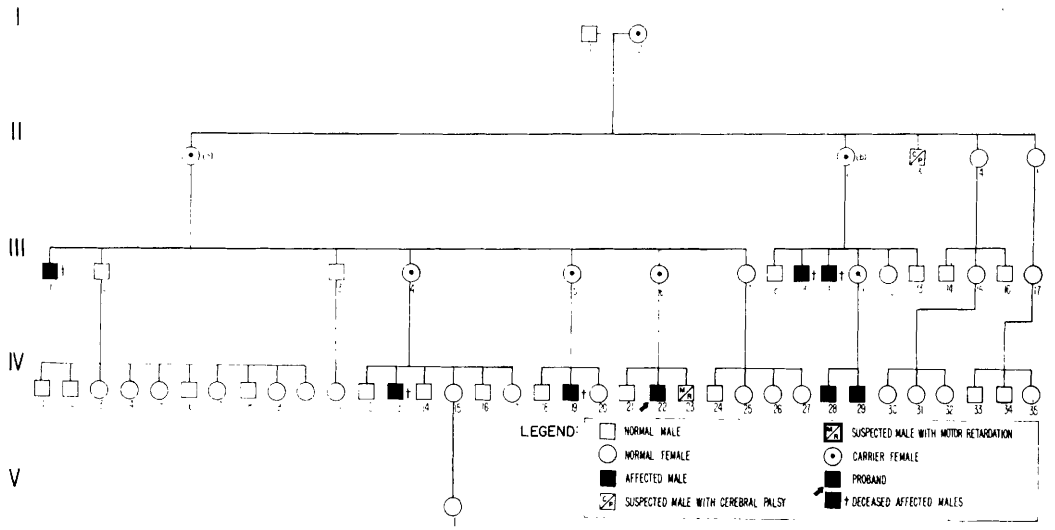

FIG. 1. The pedigree of a kindred with mental retardation, athetosis, spastic diplegia, self-mutilation, and hyperuricemia. Affected males IV 28 and 29 were confirmed by information received from Dr. Bessman at University of Maryland.

Hoefnagel *et al* published data on the fourth and fifth pedigrees, and from the combined pedigrees in the literature suggested an x-linked mode of inheritance(4). The present report describes a new pedigree, the largest known with this syndrome, and clearly demonstrates an x-linked recessive pattern of inheritance as the most likely mode of transmission for the disorder.

Methods. The pedigree (Fig. 1) is constructed from data obtained from the family of the proband, death certificates, and records from institutions for the mentally retarded. Uric acid determinations were measured by the enzymatic spectrophotometric method(5). In an x-linked recessive trait, one-fourth of the sons of all daughters of carrier females are expected to be affected, and the expected data calculated in Table I were determined on this basis.

Results and discussion. The proband of the pedigree, a 4½-year-old white male, is being investigated presently at the University of Virginia Hospital. From birth, delayed motor and mental development were noted in this child, and at present he is unable to walk, speak intelligibly, or maintain an upright position by himself. The characteristic neurological signs of the syndrome, athetosis with spontaneous leg scissoring, spastic diplegia, mental retardation, and self-mutilation, were present. The latter sign was manifested by finger chewing and teeth grinding although there was no indication of pain insensitivity; in fact, the child appeared more docile with protective hand wrappings to prevent the biting. Examination of the urinary sediment demonstrated red blood cells and numerous amorphous urate crystals, and 24-hour urine collections contained visible crystals. Alkali treatment of the urine resulted in dissolution of the crystals and higher urinary uric acid recoveries than in non-alkalinized specimens. On a low purine diet the serum and 24-hour urinary uric acids are in the range of 8.9 to 9.8 mg per cent and 426-658 mg (37 to 58 mg/kg body wt), respectively. The proband's mother had a serum uric acid of 5.7 mg per cent and a 24-hour urinary uric acid of 952 mg. One of the carrier mothers reported by Hoefnagel *et al* (4) also had an elevated urinary uric acid

TABLE I. Grandsons of Carriers Through Their Daughters.

	Grandsons through daughters		
Carriers	Total	Affected	Unaffected
I	9	3	6
IIa	10	3	7
IIb	2	2	0
Observed	21	8	13
Expected		5.25	15.75

TABLE II. Identification of Affected Kindred.

Affected numbers	Spasticity and athetosis	Mental retardation	Self-mutilation	Crystalluria	Hyperuricemia
III- 1	present	present	present	present	unknown
III- 9	"	"	"	"	"
III-10	"	"	"	unknown	"
IV-13	"	"	unknown	present	"
IV-19	spasticity only	"	not present*	"	"
IV-22	present	"	present	"	present
IV-28	"	"	unknown	"	"
IV-29	"	"	"	"	"

* Case IV-19 died at the age of 3 mo, and self-mutilation appears in the reported cases only after the age of 4 yr.

output in the face of a normal serum uric acid. The carrier and non-carrier females in the present pedigree are being studied by these determinations to determine definitely whether carrier states can be detected chemically.

The pedigree demonstrates that only males are or have been affected. Deceased affected members are identified easily from institutional records by the characteristic descriptions of athetosis with opisthotonus, self-mutilation, or gravel in the urine (Table II). Self-mutilation was of importance for the identification of the fully developed syndrome since no other disorder is known to demonstrate this feature, and the records examined described either protective devices against hand chewing or complete dental extractions to prevent mutilation. In addition, the mothers of affected children have noted a granular consistency to the urine on diapers.

A chi-square test applied to data in Table I indicated that there was no significant difference between the observed and expected figures ($= 1.92$). Thus, from a clinical test of the transmission of this trait to grandsons through carrier mothers, the pedigree fitted the pattern of an x-linked recessive trait.

Simple male-limited autosomal dominant inheritance was not eliminated by the present pedigree. However, the clinical demonstration of affected male to male transmission was unlikely, since most affected males were either institutionalized at an early age for their neurological disease or succumbed as infants from the renal consequences of urate overproduction. The critical proof for the x-linked recessive inheritance of the syndrome must come from the demonstration of linkage with a trait independently proved to be x-linked. The authors are pursuing this and other metabolic studies on members of the pedigree.

Summary. A pedigree of a heritable metabolic disorder of uric acid overproduction indicated an x-linked recessive mode of inheritance. Affected members had mental and motor retardation, a gravel-like consistency to the urine on diapers, athetoid movements with opisthotonus, and self-mutilation. Female carriers appeared to be hyperexcretors of uric acid.

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