rare event in a BMD carrier. I also became aware of a condition of autosomal recessive origin[3] that fitted the clinical and CK findings in the proband and his affected sister. Nevertheless, because BMD was thought to be more common than ARMD, BMD remained a signficant possibility. When RFLP technology became really powerful, with the identification of flanking markers to the BMD locus, I decided to apply it to this diagnostic problem. The findings argued against BMD.

The table compares the probabilities of the RFLP findings, CK readings, and pedigree pattern on the assumption that the sisters are both carriers for BMD and on the assumption of the autosomal recessive form. ARMD is 55 000 times more likely than BMD. The most important single factor contributing to this difference is the double recombination deduced (if BMD) in the affected younger sister. There seems to be much geographical variation[4-6] in the prevalence of ARMD. In the north of England the BMD:ARMD ratio is roughly 2:1, so the relative likelihood of ARMD falls to 27 000 for this family from Hull/Grimsby.

I have not been able to confirm, or deny, the possibility that the mother's maternal uncle had a similar condition to the proband. Nor was I able to obtain information as to whether the parents of this uncle were blood relatives. I have therefore relied on the data given in the table. A paternal relative had a neuromuscular disorder designated Duchenne muscular dystrophy. The elder sister has had a third son, normal on CK assay at six months of age, and I hope to examine RFLP patterns in these three sons.

A diagnosis of BMD remains very unlikely. When RFLP findings do not correspond to a putative diagnosis then that diagnosis must be in doubt, and very much in doubt in this instance.

With respect to the points raised by Dr Cummings and Dr Hodgson I can say that the paediatric neurologist's clinical examination and the histochemical and histological findings strongly favour muscular dystrophy. I know of no form of X-linked spinal muscular atrophy with the family pattern described above.

The findings in this family will be reported in detail elsewhere.

I thank Dr Andrew Read for discussing my approach to the data and Dr Gwilym Hosking for his neurological opinion.

Centre for Human Genetics,
University of Sheffield,
117 Manchester Road,
Sheffield S10 5DN

C. E. BLANK

1. Bayes T. An assay towards solving a problem in the doctrine of chances. *Phil Trans Roy Soc* 1763; **53:** 376–418.
2. Emery AEH. Methodology in medical genetics: an introduction to statistical methods, 2 ed. Edinburgh: Churchill Livingstone, 1986: 93.
3. Gardner-Medwin D, Johnston HE. Severe muscular dystrophy in girls. *J Neurol Sci* 1984; **64:** 79–87.
4. Gardner-Medwin D, Penning RJ, Walton JN. The detection of carriers of X-linked muscular dystrophy genes: a review of some methods studied in Newcastle upon Tyne *J Neurol Sci* 1971; **13:** 459–74.
5. Hamida MB, Fordeau M, Attia N. Severe childhood muscular dystrophy affecting both sexes and frequent in Tunisia. *Muscle Nerve* 1983; **6:** 469–80.
6. Bundey S. Genetics and neurology. Edinburgh: Churchill Livingstone, 1985: 126–29.

GENE LOCATION IN TOURETTE SYNDROME

SIR,—Your editorial (Feb 7, p 308) reviewed the genetic aspects of Tourette syndrome. The hypothesis that the syndrome is caused by a highly penetrant dominant gene depends on the acceptance of chronic tics or obsessive compulsive behaviour as part of the syndrome. Comings et al[1] have suggested that the gene responsible is at 18q22·1. We have further evidence that this is the gene location.

A 23-year-old woman presented with a one-year history of mild obsessive compulsive behaviour and a two-month history of more severe behavioural problems. She repeatedly rearranged the furniture, was restless, unable to remain seated, and constantly plucked at her clothes. She had panic attacks and reported visual hallucinations. Her early development was reported as slow compared with her two normal elder brothers. Talipes of her left foot had been treated by tendon transplant in childhood. She had attended a normal primary and secondary school. Her nose was small and her mid-face mildly hypoplastic. Cytogenetic analysis of cultured lymphocytes revealed a deletion of the long arm of chromosome 18 at 18q22·2. Her mother and two brothers have normal karyotypes; examination of the father was not possible and therefore the deletion may have been de novo or the result of a paternal translocation.

This patient had the behavioural characteristics described in members of Tourette families and a chromosome deletion at a breakpoint very near one described in a family with Tourette syndrome.[1] Thus the Tourette gene may be on the long arm of chromosome 18.

Department of Medical Genetics,
St Mary's Hospital,
Manchester M13 0JH

DIAN DONNAI

1. Comings DE, Comings BG, Diez G, et al. Evidence the Tourette syndrome gene is at 18q22·1. 7th Int Congr Hum Genet, Berlin, 1986; part II: 620 (abstr).

HLA-DR2 AND RAPID-EYE-MOVEMENT SLEEP LATENCY: FAILURE TO REPLICATE

SIR,—We reported (Oct 4, p 803) that HLA-DR2 positive normal subjects had shorter rapid-eye-movement (REM) sleep latencies than HLA-DR2 negative subjects. This difference suggested stronger inhibition of REM sleep release in HLA-DR2 negative subjects. No other sleep variable differed between the groups. Because of the near perfect association between HLA-DR2 and narcolepsy,[1,2] a disorder with notoriously short REM latency, and the important theoretical implications of a link between the HLA system and REM sleep, we repeated the study with a new sample of normal subjects with the same protocol except that two nights rather than one were spent in the sleep laboratory.

20 DR2 positive and 20 DR2 negative healthy subjects (age and sex matched) entered this study. With the new sample, there were no significant differences in any sleep variable that we had measured before, including REM latency, between DR2 positive and DR2 negative subjects on either of the nights. The mean REM latency on the first night was 111·2 min (SD 45·9) for the DR2 positive group and 95·7 min (32·7) for the DR2 negative group. The values for the second night were 100·4 min (45·4) and 87·0 min (39·8).

Since many variables (eg, laboratory environment, scoring procedure, age) were similar, we conclude that the significant difference in REM sleep latency in the first study appertained only to that sample and that the finding should not be generalised.

H. SCHULZ
P. GEISLER
T. POLLMAECHER
A. ANDREAS-ZIETZ
E. KELLER
S. SCHOLZ
E. D. ALBERT

Max Planck Institute for Psychiatry,
8000 Munich 40, West Germany;
and Immunogenetics Laboratory,
University of Munich

1. Juji T, Satake M, Honda Y, Doi Y. HLA-antigens in Japanese patients with narcolepsy. *Tissue Antigens* 1984; **24:** 316–19.
2. Langdon N, Welsh KI, Van Dam M, Vaughan RW, Parkes D. Genetic markers in narcolepsy. *Lancet* 1984; ii: 1178–80.

IN-UTERO EXPOSURE TO BENZODIAZEPINES

SIR,—The letter by Dr Laegreid and colleagues (Jan 10, p 108), describing abnormalities in children exposed to benzodiazepines in utero, contains a photograph and some case details of a 1-week-old infant (case 2) who has the facial features of Zellweger syndrome.[1] The brief clinical and pathological details provided—ie, lissencephaly, distortion of neuronal migration, absence of the caudal part of the cerebellum, Dandy-Walker malformation, and polycystic kidneys—are all consistent with this diagnosis. Zellweger syndrome is an autosomal recessive syndrome caused by a deficiency of plasmalogens.[2] Was this diagnosis excluded biochemically in this infant? The abnormalities described may have had nothing to do with benzodiazepines.

Kennedy-Galton Centre
for Clinical Genetics,
Harperbury Hospital,
Radlett, Herts WD7 9HQ;
and Clinical Research Centre,
Northwick Park Hospital

R. M. WINTER

1. Wilson GN, Holmes RG, Custer J, et al. Zellweger syndrome· Diagnostic assays, syndrome delineation, and potential therapy. *Am J Med Genet* 1986; **24:** 69–82.
2. Heymans HSA, Schutgens RBH, Tan R, et al. Severe plasmalogen deficiency in tissues of infants without peroxisomes (Zellweger syndrome). *Nature* 1983; **306:** 69–70.