and a proper segregation analysis are essential to answer the original question. A model involving more than one locus might also be necessary.

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This letter was shown to Dr Cox, who replies as follows.

SIR,

As discussed in our paper (*J Med Genet* 1987;24: 52-9) and in the comments by Dr Harris, the number of cases available for obtaining risk figures is very small and inadequate. Furthermore, there is considerable variability between the results of various studies. Statistical tests may not be appropriate until a larger sample size is available.

Although the statistical analysis does not show a clear difference in risk for families with and without a severely affected child, we feel it could be misleading to give all parents a risk of 29%. Because of the recurrence of severe liver disease in certain families, some other genetic or environmental predisposing factor may be present in these families and should not be ignored. In addition to the series we have included, there are a number of single families reported with multiple sibs affected with severe liver disease. The less favourable prognosis in Great Britain (*Arch Dis Child* 1983;58:882) may be due to differences in the referral pattern, in which children with transient or mild symptoms may never be referred to major centres. There would therefore be a selection for those families with a severely affected child, particularly when there is more than one. For parents who have had a child with severe liver disease, a risk of 29% or 40% would probably lead to consideration of prenatal diagnosis. However, a 29% risk for parents who have not had such a child is probably unduly pessimistic.

We have made approximate estimates given the data available. Careful follow up studies of patients in many centres is mandatory to obtain improved risk figures and we hope other investigators will initiate such studies.

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Possible evidence for genetic predisposition to non-disjunction in man

SIR,

Preliminary data from a community genetic survey at two district hospitals showed a high prevalence of chromosomal aneuploidy, particularly Down's syndrome, with marked temporal variation between the two districts.

In Jahra hospital serving an Arab population of 300 000, mostly (80%) Bedouins, 31 babies with autosomal trisomies were ascertained among 6874 consecutive live births (4.5/1000). Twenty-nine cases (93.5%) were Bedouins or Kuwaitis with Bedouin ancestors and two were other Arabs. The mean maternal age was 31.1 years. Parental consanguinity was observed in 29 cases with an average coefficient of inbreeding (ΣF) of 0.044, which is similar to that of parents with the traditional 'Bedouin' practice of consanguineous marriages. Among this group, two sibs, one with trisomy 21 and the other trisomy 18, had young first cousin parents. Another family had two sibs with trisomy 21.

In Farwania hospital serving a mixed Arab and non-Arab population of 400 000 with only 15% Bedouin, 14 babies with autosomal trisomies were ascertained among 8045 consecutive births (1.7/1000). Of these, six cases (42.9%) were Bedouins or Kuwaiti-Bedouins, six cases were other Arabs, and two cases were Asian. The mean maternal age was 32.7 years. Parental consanguinity was observed in eight cases with an average coefficient of inbreeding (ΣF) of 0.0225.

The overall prevalence of Down's syndrome in the two districts was 2.5/1000 which was more than double that of 1.1/1000 reported from Kuwait maternity hospital¹ (table). The usual prevalence of Down's syndrome is 1 to 2/1000 live births but higher prevalence rates have been reported from West Jerusalem² and among Negev Bedouins³ (2.4

TABLE Autosomal aneuploidies in Jahra and Farwania hospitals in 1986.

	Jahra	Farwania	Total
Number of live births	6874	8045	14 919
Down's syndrome			
Number	25(21*)	12(10+)	37(31)
Prevalence rate	3.6	1.5	2.5
Edwards' syndrome			
Number	4(4)	1(0)	5(4)
Prevalence rate	0.6	0.1	0.3
Patau's syndrome			
Number	2(1)	1(1)	3(2)
Prevalence rate	0.3	0.1	0.2

Prevalence rate per 1000 live births; figures in brackets are the number of cases examined cytogenetically.

*One case a de novo 14.21 translocation.

†Two cases de novo translocations (14.21, 21.21).

and 2.9/1000 respectively). In our survey the higher prevalence rate was observed in the district where the population was mostly Bedouin and where ΣF was 0.044. Trisomy 13 and trisomy 18 were also more frequent in the Jahra district. The familial clusters of chromosome aneuploidy were also noted in Bedouin families.

In Kuwait, a previous study showed that Down's syndrome was four times more frequent among children of consanguineous parents than among those with unrelated parents.⁴ Our survey confirms this observation and provides further evidence to support Penrose's suggestion⁵ of a genetic predisposition to non-disjunction. However, further studies are required before assuming that an autosomal recessive gene present in a relatively 'high

frequency' in the Bedouins predisposes them to non-disjunction.

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