Inv dup (15)

SIR,

With reference to our paper published in the June issue of the journal (1984;21:213–4), we would like to thank you for bringing the paper of Maraschio *et al*¹ to our attention.

These authors described eight new cases of inv dup (15). All were mentally retarded with few or no dysmorphic features and in six cases cytogenetic evidence for the maternal origin of the extra chromosomal material was presented.

In our analysis (using the method of Smith²) of the parental age effect in 16 other sporadic cases of inv dup (15), we found a highly significant maternal age effect. These two lines of evidence then favour an error in maternal gametogenesis as the usual cause of inv dup (15).

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References

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- ² Smith CAB. Note on the estimations of parental age effects. *Ann Hum Genet* 1972;35:337–42.

Prevention of midline defects

SIR,

The relationship between different dysrhapic malformations, such as anterior and posterior midline defects, represents a difficult genetic problem in view of the obvious heterogeneity of these disturbances. Nevertheless, an increased liability to midline defects may manifest itself within one family even with different primary causes.

This issue is of particular importance for genetic counselling and it assumes a new dimension when prevention of these developmental disturbances is considered. The use of multivitamin preparations (or folic acid alone) in early pregnancy has been advocated for pregnancies at risk for neural tube defects^{1 2} as well as for cleft lip with or without cleft palate.³ But when do we consider a pregnancy to be at risk? What kind and degree of malformation has

to have occurred in the sibship or in even more distant relatives?

Case report

The proband (II.3, figure) was born after an uneventful pregnancy to her gravida 3 mother. The preceding child of the same marriage had had a posterior encephalocele. Therefore we monitored the next pregnancy closely with ultrasound as well as amniotic fluid AFP determination at 18 weeks' gestation. All results indicated normal development of the neural tube.

The baby showed no abnormality at birth and developed normally during the first month. After 6 weeks the mother noticed a slowly growing bulge covering the large fontanelle. On palpation it presented as a cystic structure; there was no pulsation nor palpable communication with the fontanelle. Clinically no sign of raised intracranial pressure was observed and the baby appeared perfectly healthy in all other respects. A clinical diagnosis of a meningeal cyst was made which was supported by the preoperative CT scan.

At operation a dermoid cyst was found containing derivatives of embryonic elements. No sign of malignancy was present. The postoperative course has been satisfactory.

Might we have to consider this malformation to be based on the same pathogenetic events as the sib's encephalocele? Does a certain liability predispose to midline defects of different locations both topographically and developmentally? According to Opitz and Gilbert⁴ the midline represents a developmental field of rather poor stability. Therefore, associations of more than one defect there should occur more often than expected by chance both within persons and within families. Czeizel⁵ confirmed this general cleft disposition to be statistically

FIGURE Pedigree of the family reported.

true in his national epidemiological study. The reasons for dysrhapic developmental accidents may lie in the genotype, in the pre- or postconceptional environment, or in both. If so, is there a case for studying preventive vitamin supplementation in mothers after the occurrence of a minor developmental mishap like the one reported?

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- 2 Laurence KM, James N, Miller MH, Tennant GB, Campbell H. Double-blind randomised controlled trial of folate treatment before conception to prevent recurrence of neural tube defects. *Br Med J* 1981;282:1509-11.
- 3 Tolarova M. Periconceptional supplementation with vitamins and folic acid to prevent recurrence of cleft lip. *Lancet* 1982;ii:217.
- 4 Opitz JM, Gilbert EF. CNS anomalies and the midline as a 'developmental field'. *Am J Med Genet* 1982;12:443-55.
- 5 Czeizel A. Schisis association. *Am J Med Genet* 1981;10:25-35.

Translocations, social class, and Adam and Eve

SIR,

Two points in the paper of Tierney *et al* (Balanced rearrangements of the autosomes: results of a longitudinal study of a newborn survey population. *J Med Genet* 1984;21:45-51) require comment.

Firstly, the authors speak of a lower mean social class accentuating an apparent association of a higher IQ in children with familial reciprocal translocations (their table 5). Their mean social class differed 'significantly' from that of the Robertsonian group: 3.43 vs 2.43. But this is not a valid approach. Social class grouping is not a continuous metrical variable; it is a five-point categorisation. The difference between social classes I and II is not, say, twice as much as between II and IV. Perhaps it would be useful for editors to insist upon the convention of using Roman numerals: 3.43 may have passed muster, but I doubt that III.XLIII would.

Secondly, Tierney *et al* propose that the somewhat higher IQ in just seven children with familial balanced rearrangements might reflect evolutionary advance. Now, I am quite prepared to believe that Adam and Eve arose (as brother and sister) following a chromosomal change in an ancestral primate.

Vogel and Motulsky refer to this explicitly on page 449 of their text *Human genetics* (1st ed), and implicitly in putting Dürer's woodcut of Adam and Eve on the front cover. But that 'giant saltation' was, surely, a one-off event. It is difficult to conceive of mini-saltations (hops and skips?) occurring at a rate of several per generation, and which so reorder the genome that the cerebral phenotype is improved. Speculation is fine (and fun), but one must resist the temptation to go overboard.

Otherwise, I found this an interesting and useful paper, particularly in respect of the data concerning the phenotypes of children with de novo apparently balanced rearrangements.

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Tracheo-oesophageal dysraphism

SIR,

I am alarmed by Dr David's wish (*J Med Genet* 1984;21:74) to get his hands on "whoever first used the awful term tracheo-oesophageal dysraphism and wish to disclaim responsibility, though I cannot remember where I came across the phrase when I first used it (*Lancet* 1980;ii:80). I thought 'dysraphism' (defective fusion) was an acceptable way of getting around the clumsiness of 'tracheo-oesophageal fistula and/or oesophageal atresia'. What would Dr David suggest?

As for the 'probably spurious' increase in NTD in sibs of children with TED, both negative studies cited by Dr David came from low frequency areas, and Baird's study did not measure the number of sibs but only failed to find a sib with NTD reported to the BC registry. Drs Ilyina and Lurie (*J Med Genet* 1984;21:73-4) place our study in the 'low incidence' group, but in fact Montreal had a frequency of over three per 1000 during the time of the study. The figure for 'Canada' given is for British Columbia, a low incidence area. Before giving up the idea of an increase in NTD in sibs of children with TED, I would like to see negative data from a high incidence area.

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