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

- ¹ Maraschio P, Zuffardi O, Bernardi F, *et al*. Preferential maternal derivation in inv dup (15): analysis of eight new cases. *Hum Genet* 1981;57:345–50.
- 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.