or supernumerary element, when examined with the silver NO and DA-DAPI techniques, the supernumerary is shown to consist of 15p plus centromere joined to another 15p. Such chromosomes have been observed in individuals with normal, as well as abnormal, phenotypes.

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- 2 members of a twin pair can be unequally exposed to an environmental teratogen. The explanation, I suggest, lies in the placentation: twin members do not always share the same placenta and, even when they do, their facilities are often unequal.
- If one accepts that the teratogen is dietary or hormonal in nature (and most of the points to be presented seem good evidence for such a view), then the only logical alternative to this placenta hypothesis seems to be that the teratogen is very powerful, but exists in such tiny quantities (a few molecules) in the maternal circulation that only one twin is usually affected. I can think of no good ground for this alternative, whereas the following points seem to implicate the placenta.
- (1) Anencephaly is closely associated with defective placentation. Berge (1965) examined the placentae of 10 anencephalic fetuses and found that all of them contained areas of degeneration and scar tissue. Benirschke and Driscoll (1967) offer evidence that placental infarcts are of maternal, rather than fetal, origin, and hence are not to be interpreted as an effect of the malformed fetus, but possibly as a cause.
 - (2) Placenta praevia has been reported to be common in anencephalic maternities (Smilkstein, 1962; Smithells *et al.*, 1964). Record and McKeown (1949) estimated that the incidence of placenta praevia in anencephalic maternities is 10 times that in control maternities. Again, it seems reasonable to suppose that this condition predates (and therefore may somehow cause) the malformation.
 - (3) It has also been reported that anencephaly is associated with a single umbilical artery (Cipparone, 1966). This is another condition in which the fetus is suspected of being deprived of nutrient (Benirschke and Driscoll, 1967).
 - (4) There is the observation (Talbot, 1924) that in a pair of twins discordant for anencephaly, the affected twin had a placenta that was infarcted, whereas the other placenta was normal.
 - (5) It has been noted (Mall, 1908) that ASB is disproportionately common in extrauterine pregnancy, a condition in which the placenta is usually defective.
 - (6) This placenta hypothesis would explain the apparently higher concordance rates in same-sexed than in opposite-sexed affected pairs. This phenomenon would be partially (but not wholly) explained by the hypothesised higher incidence rates in monozygotic twins (James, 1976). The additional explanation now being offered is that monozygotic pairs sometimes share the same defective placenta.

There is plenty of evidence (Coffey and Jessop,

Placentation, anencephaly, and spina bifida

SIR,

I want to suggest that the immediate cause of anencephaly and spina bifida (ASB) is typically a dietary or hormonal deficiency in the embryo brought about by defective placentation. (It should be noted that the word 'placenta' here denotes the system of nutrition immediately after implantation. Logically, the hypothesis does not require the existence of an organ of that name.)

Concordance rates for anencephaly in twins are modest. In a review of affected pairs ascertained in series, 13 of 309 same-sexed pairs, and 3 of 118 opposite-sexed pairs, were reportedly concordant (James, 1978). These concordance rates were estimated to be slightly higher than would be expected on the basis of (i) the raised recurrence rates in the sibs of affected cases; and (ii) the hypothesised higher rates in monozygotic twins (James, 1976). Nevertheless, the cause would seem to be shared only to a small extent by both members of a twin pair. At first sight this seems a very odd fact as it apparently rules out genetic causes. Moreover, it is not easy to see how the

1957; Anderson *et al.*, 1958; Richards, 1969; Smithells *et al.*, 1976) that women who have ASB infants have a poor diet. The relevance of this observation to the present hypothesis needs careful consideration. One is tempted to suggest that poor maternal nutrition leads directly to poor embryonic nutrition and from there to ASB. The difficulty with this explanation is its apparent failure to deal with the relatively low concordance rates in twins. If maternal malnourishment (an excess of some toxin or a deficiency of some nutrient) directly caused ASB, why are both twins not usually affected? Logically, it seems that one is forced back to invoke the intervention of the placenta.

These considerations unfortunately give no clue to the identity of the agent causing ASB. However, they may suggest a slightly different direction for experimental teratology. Many agents seem to produce ASB in experimental litters, but experiments have been unsatisfactory in that usually only relatively small proportions of fetuses have been afflicted with the malformation. If the placenta is intervening between the agent and the malformation in the manner suggested here, the question to be first answered may be not 'What will produce ASB?' but 'What will cause early placental damage?'.

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Reproduction in a woman with mosaicism

SIR,

Reproduction in a woman with mosaicism, in which the major cell line was 46,XX, and a few cells were 45,XX,t(21q21q), was recently published in the *Journal of Medical Genetics* (Mark *et al.*, 1977). This woman gave birth to a son with Down's syndrome whose karyotype was 46,XY,-21,+t(21q21q). Karyotypes of lymphocytes from the woman and her husband were normal. Only after multiple tissues from the woman were analysed (skin, right ovary) were cells containing the 21q21q translocation detected. The percentage of cells containing the translocation was consistently less than 10%. A subsequent fetus was also found to have 46,XY,-21,+t(21q21q) and the pregnancy terminated.

Some years ago, we reported (Wilroy *et al.*, 1969) a family in which two sibs with Down's syndrome were thought to have *de novo* 21q21q translocations. After using banding techniques, the karyotype of one of the sibs was found to be 46,XX,-21,+t(21q21q). The second sib died before the advent of banding techniques. The karyotypes of lymphocytes of both parents were normal. A skin biopsy was obtained from the mother, but the father refused to be biopsied. Only after 436 cells were analysed from the skin biopsy of the mother did we find one cell with the karyotype 45,XX,t(21q21q).

We agree with Mark *et al.* that chromosome analyses of tissues, in addition to lymphocytes, should be performed on parents of more than one child with apparently *de novo* translocation (D-21 or G-21). Down's syndrome, in an effort to detect mosaicism in the parent in which the abnormal cell line makes up only a small proportion of the total cell population. An even more prudent approach might be to monitor all future pregnancies of such parents by amniocentesis even though the low percentage mosaicism is not detected. One might consider analysing the chromosomes of other tissues, in addition to the lymphocytes of parents after the birth of only one child with a