Correspondence

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Familial Poland anomaly

Sir,

We were interested to read Dr David's¹ report on two first cousins once removed who both had Poland's syndrome (PS). We agree with his general conclusion that for purposes of genetic counselling the recurrence risk is very low. Despite this, it should be appreciated that there are an increasing number of reports of familial PS. Part of the problem lies in the interpretation of the limits of PS. For example, Temtamy and McKusick² define it as "unilateral aplasia of the sternocostal head of the pectoralis major and brachydactyly $\pm$ syndactyly of the ipsilateral hand". It is recognised by most workers in the field that the hand malformation is variable and not confined to that which was described by Alfred Poland. It can range from brachydactyly, usually of the middle phalanges, to a severe malformation comparable with a split hand or even monodactyly. The question as to whether those persons with isolated pectoralis major deficiency (PMD) are part of the Poland spectrum or whether they are a separate entity is unanswered, though information is emerging which suggests that some cases of isolated PMD are part of the Poland spectrum.

It seems likely that the original patient of Fuhrmann *et al*³ should be considered as having PS. Two of this man's five children had anomalies consistent with partial expression of PS, and while David¹ concedes that the man had PS, he suggests that he and his children were sufficiently atypical to suggest a different condition, in part because none of the three had syndactyly. We disagree with this view. We are in agreement with David in rejecting the report of Trosev *et al*⁴ as an example of PS, and hopefully he has corrected this misinterpretation that has crept into the literature. The report of Sujansky *et al*⁵ of familial PS is analogous to that of Fuhrmann *et al*,³ that is, there is one typical PS case plus one partial case. The two affected persons are first cousins once removed. These authors considered the aetiology to be possibly the result of delayed mutation.

Further published reports show the familial association between complete and partial cases of PS. Mustata *et al*⁶ reported a man with brachydactyly and partial syndactyly of digits 2 to 3 of the right hand, absence of the sternocostal and clavicular

parts of the right pectoralis major muscle, hypoplasia of the right nipple, and absence of hair in the right axilla. He also had scoliosis, pectus excavatum, and synostosis of the left first and second ribs. Probably all observers would accept this man as having the full PS. His three daughters (aged 25, 18, and 16 years) all showed hypoplasia of the right breast and nipple, and in addition the 18-year-old girl had brachydactyly of the right hand. Liebenham⁷ reported a pair of identical female twins who were apparently discordant for PS. The normal co-twin may, in fact, have been minimally affected because Liebenham⁷ says, "the right thorax appears to be somewhat thinner in its total formation and the right mamilla is somewhat lower than the left". She noted a difference in the shoulders and in the position, form, and size of the shoulder blades. Thus there may be concordance but extreme variable expression.

The late David W Smith⁸ mentions two sibships in the third edition of his classic textbook *Recognizable patterns of human malformation*, in which the proband had the full PS whereas a sib in one instance had only absence of the pectoral muscle, and in the other instance only syndactyly of the hand. These four reports^{3 5 6 8} illustrate the concept of variable expression and should be counted as examples of familial PS and not dismissed as a different condition as David¹ has done with the report of Fuhrmann *et al*.³ Liebenham's case⁷ is less certain but it should not be dismissed completely as an example of discordance.

In an earlier publication, Bouvet *et al*⁹ mentioned three familial examples of PS but few details were given. In two families both affected persons had the full PS.

Family G. An affected brother and sister. Both had absence of the left pectoralis major; the girl had a type III hand malformation (classification of Bouvet *et al*⁹) with an absent nipple, whereas the boy had a type I hand malformation. There was no parental consanguinity.

Family P. Affected first cousins (male and female). Both showed right-sided absence of the pectoralis major muscle, and type I hand malformation with syndactyly between digits 2–3–4. The affected female had absence of the right breast although a nipple was present. Neither had any associated malformations and there was no parental consanguinity.

The third family of Bouvet *et al*⁹ is much less certain, as it involves one case of the full PS and a second cousin once removed with syndactyly of all digits of one hand. This may be a fortuitous event and should not necessarily be construed as an example of familial PS.

The two families of Bouvet *et al*⁹ (G and P) thus bring the total number of familial instances of PS to eight. At the moment the explanation for the fact that the vast majority of PS cases are sporadic and only a very small minority are familial is unknown. The delayed mutation theory of Auerbach proposed by Sujansky *et al*⁵ may be operative, but it could equally well be a two locus model such as that demonstrated by Chai¹⁰ in the case of mouse ectrodactyly. It still does not explain the strict laterality of the syndrome which is unusual for either a gene(s) or a teratogen. As always, there are exceptions: Hecht and Scott¹¹ have described unilateral hand malformations in sibs where there was parental consanguinity, suggesting an autosomal recessive trait. The situation in PS is somewhat analogous to that of Down's syndrome before its chromosomal basis was demonstrated, that is, the vast majority of Down's syndrome cases were sporadic but there were a few familial cases. This defied genetic explanation at the time until techniques had advanced which made the whole matter quite clear. Although the aetiology remains unclear, nevertheless the pathogenesis may well be on a vascular basis as proposed by Bouvet *et al*.¹²

Castilla *et al*¹³ have published additional evidence suggesting that isolated PMD and isolated symbrachydactyly may represent partial expression of PS. They showed that the cases with full PS, those with PMD only, and those with symbrachydactyly only had a similar pattern with respect to asymmetry, sidedness, and syndactyly type as compared to isolated finger syndactyly. Castilla *et al*¹³ also showed a correlation between pectoralis muscle deficiency $\pm$ the hand anomaly and an increased frequency of sex hormone ingestion by the mother in the first trimester. They found no correlation with any other drug and did not confirm David's¹ earlier suggestion of ergot (or one of its derivatives) as a teratogen. McGillivray and Lowry¹⁴ did not find the ergot association or any other teratogen. Recently David¹⁵ has shown that Debendox is not causally implicated in PS.

Finally, a comment on the incidence. There were some errors in the calculations of incidence in the paper by McGillivray and Lowry.¹⁴ Corrected incidence figures showed there were 24 cases with the full Poland syndrome born in the years 1952 to 1975, and since there were 853 895 livebirths in that period in British Columbia, this gives a minimal

incidence for the full Poland syndrome of 1/36 000. There were an additional nine cases of pectoralis muscle deficiency only, giving a combined incidence figure of 1/26 000. These figures are comparable to those published by Castilla *et al*,¹³ which were 1/50 000 for the full PS and 1/22 000 for all PMD infants. These two studies, from British Columbia, Canada and from South America, are the only large scale population studies that the authors are aware of. The figure of 1/17 000 from Japan¹⁶ and 1/3000 from France¹⁷ are prevalence figures rather than incidence. One reference, from West Germany,¹⁸ to a frequency of 1/9300 births gives no data and the supporting reference does not mention this figure at all.

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Craniosynostosis

SIR,

In their interesting paper on families with craniosynostosis, Professor Carter and co-workers¹ suggest that our higher incidence of apparent autosomal dominant coronal synostosis may result from our inclusion of patients with Saethre-Chotzen and other syndromes among our study group.² Certainly, if the minor hand anomalies to which we referred have the same aetiology as the craniosynostosis, then some families had 'private' syndromes. We agree that family number 1 has what the authors call the 'split face syndrome', and that it is like the family reported by Slover and Sujansky.³ However, in the interest of clarity, we would like to point out that we did not make a diagnosis of Saethre-Chotzen syndrome unless at least one family

member had the typical syndactyly. Therefore, as the title implied, our families with Saethre-Chotzen syndrome were not included in the paper and we do not believe that families 4, 8, or 10 had this condition.

The degree to which the reported heterogeneity of the craniosynostosis syndromes represent true genetic heterogeneity must await biochemical or linkage markers for the genes or both. In the meantime it remains true that patients who have craniosynostosis in association with other dysmorphic features, notably of the hands, are more at risk to represent a single gene mutation than are those with isolated craniosynostosis.

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Pericentric inversion of chromosome 13

SIR,

In 1972 a paper from our laboratory described a large family with a pericentric inversion of chromosome 13, leading to a duplication deficiency

FIG 1 Pedigree of family.