# LETTERS TO THE EDITOR

## Prevalence of other birth defects among relatives of oral cleft probands

We have read with interest the paper by Stoll *et al*[1] regarding the epidemiology of oral clefts. From the genetic standpoint, one of the most interesting aspects in the article is the risk of recurrence of oral clefts, as well as the risk for the patient's first degree relatives of having other birth defects. These results prompted us to report our data from the Spanish Collaborative Study of Congenital Malformations (ECEMC). The ECEMC is a hospital based, case-control study and surveillance system that was started in April 1976. All liveborn infants in approximately 56 collaborating hospitals all over Spain are examined during the first three days of life to identify major and minor congenital defects. Each case has as a control the next non-malformed infant of the same sex born at the same hospital. A physician collects data on each child and interviews the mothers of cases and control babies to obtain prenatal, obstetric, and family histories. Descriptions of the ECEMC have been published elsewhere.[2,3]

From April 1976 to December 1990 a total of 853 360 liveborn infants was registered; 447 of them (5·24 per 10 000) had cleft lip with or without cleft palate (CL/P) and 393 (4·61 per 10 000) had cleft palate (CP). Cases were classified according to their clinical pattern. If the oral cleft was the only anomaly in the child, the case was considered to be isolated. If the child had an oral cleft as part of a pattern of multiple anomalies, the case was considered to be associated. The Pierre-Robin sequence was classified as a separate entity. Children with recognised syndromes were not included in this study.

In 392 CL/P and 336 CP cases, information on the family history was available. We used as controls those control children who were born within 45 days of each case with an oral cleft in the same hospital; thus, we had 4894 control children for CL/P and 4434 for CP.

The recurrence risk for isolated CL/P in our data was 1·4% (5/363 sibs), a figure not significantly different from the 3·9% found by Stoll *et al*[1] ($p = 0·21$). For isolated CP the recurrence risk in the ECEMC data was 1·4% (3/211).

To estimate the risk for non-clefting congenital malformations in the first degree relatives of probands with oral clefts, we divided the number of first degree relatives (mothers, fathers, and sibs) who had any type of congenital anomaly apart from CL/P or CP by the total number of first degree relatives (table 1). The results show a risk of 1·5% for CL/P and 1·2% for CP relatives. These figures are lower than the 11·1% given by Stoll *et al*, but, apparently, these authors used the number of families as the denominator. If they had used the total number of first degree relatives, the risk would have been lower, approximately 1/3 of 11·1% (assuming that each child had a previous sib), a figure closer to the one obtained from our data.

Menegotto and Salzano[4] observed that the risk for sibs is higher than the risk for all first degree relatives (including parents). We obtained the same result (table 2) and agree with the reason given by these authors, that the sibs had not yet been completely subjected to the action of natural selection as the parents had.

*Table 1 Risk for first degree relatives (FDR) of oral cleft probands of having non-clefting congenital malformations (NCM)*.*

| | FDR of CL/P or CP | | FDR of controls | | |
|---|---|---|---|---|---|
| | With NCM | Total FDR | With NCM | Total FDR | p |
| CL/P | 19 (1·5%) | 1232 | 109 (0·8%) | 14 499 | 0·003 |
| CP | 13 (1·2%) | 1056 | 106 (0·8%) | 13 269 | 0·14 |

* FDR with oral clefts additional to other birth defects are not included.

*Table 2 Risk for sibs of oral cleft probands of having non-clefting congenital malformations (NCM).*

| | Sibs of CL/P or CP | | Sibs of controls | | |
|---|---|---|---|---|---|
| | With NCM | Total sibs | With NCM | Total sibs | p |
| CL/P | 15 (3·3%) | 448 | 65 (1·4%) | 4711 | 0·0013 |
| CP | 10 (2·6%) | 384 | 70 (1·6%) | 4401 | 0·14 |

*Table 3 Risk for sibs of isolated and multiple oral cleft patients of having non-clefting congenital malformations (NCM).*

| | Isolated | | Multiple | | Pierre-Robin sequence | |
|---|---|---|---|---|---|---|
| | With NCM | Total sibs | With NCM | Total sibs | With NCM | Total sibs |
| CL/P | 10 (2·8%) | 363 | 5 (5·9%) | 85 | – | – |
| CP | 3 (1·4%) | 211 | 4 (4·4%) | 90 | 3 (3·6%) | 83 |

An important factor to consider in the estimation of recurrence risk is the clinical presentation of the oral cleft. In our data, the risk for non-clefting congenital malformations is higher for sibs of patients with oral clefts as part of a non-syndromic pattern of multiple anomalies than for isolated clefts (table 3). This suggests that in some of these families the oral clefts are part of a pattern of multiple congenital anomalies with variable degree of expression.

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1 Stoll C, Alembik Y, Dott B, Roth MP. Epidemiological and genetic study in 207 cases of oral clefts in Alsace, north-eastern France. *J Med Genet* 1991;**28**:325–9.
2 Martínez-Frías ML, Frías JL, Salvador J. Clinical/epidemiological analysis of malformations. *Am J Med Genet* 1990;**35**:121–5.
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4 Menegotto BG, Salzano FM. Clustering of malformations in the families of South American oral clefts neonates. *J Med Genet* 1991; **28**:110–3.

## Microtia, absent patellae, short stature, micrognathia syndrome

I was intrigued by the reports of Cohen *et al*[1] and Hurst *et al*[2] regarding the syndrome of microtia, absent patellae, short stature, and micrognathia. For more years than I care to remember, I have been looking for a match to a patient we reported in *Birth Defects* (1975;**11**(2):44–5) entitled 'A selected miscellany' which included a then 16 year old male who had 'microtia, absent patellae, micrognathia syndrome' (figs 1–3).[3] At that time the patient had bilateral microtia (but with essentially normal form), bilateral talipes equinovarus, somewhat reduced head circumference (53 cm), early closure of the anterior fontanelle, microsomia, micrognathia, unilateral cryptorchidism, mild scoliosis, camptodactyly of the fifth fingers, Blount osteochondritis dissecans, absent patellae, bilateral aseptic necrosis of the lateral femoral condyles, short stature (155 cm), slender bones, and delayed skeletal maturation. Parental consanguinity was denied. We further pointed out that Meier *et al*[4] described a child with remarkably similar findings. Parental consanguinity in that case suggested autosomal recessive inheritance.

I saw our patient again at 25 years of age when mandibular surgical advancement was done for micrognathia. Surgical procedures were carried out on the knees but the aseptic necrosis had progressed. He was seen again at 36 years some months ago. He still resided at home. Intelligence was estimated at the lower end of the normal range. He had held several jobs but knee pain prevented any strenuous work. Upon seeing the picture of the sisters described by Cohen *et al*,[1] the mother stated that our proband "could have been their brother".

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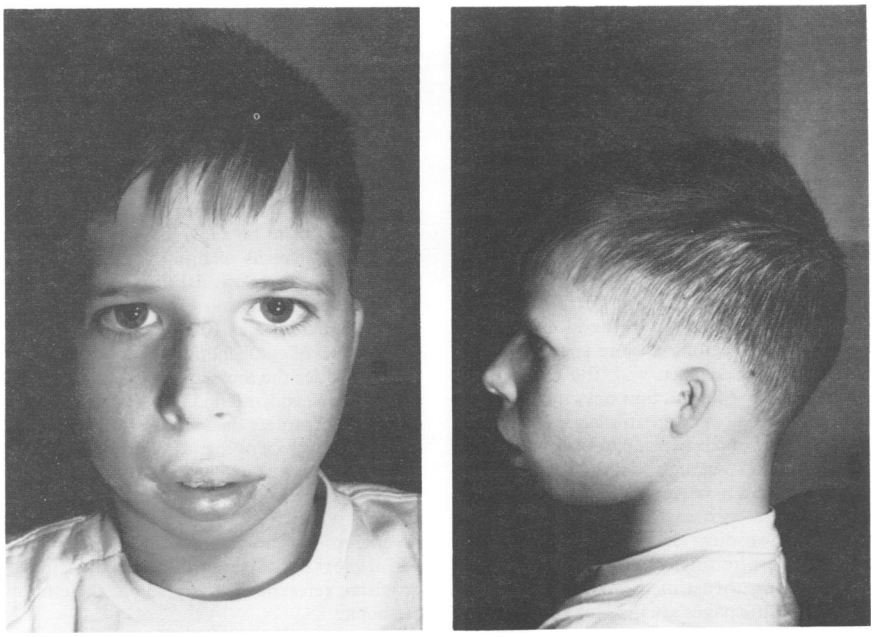

*Figure 1 Micrognathia and small, slightly dysmorphic pinna.*


1 Cohen B, Temple IK, Symons JC, *et al.* Microtia and short stature: a new syndrome. *J Med Genet* 1991;**28**:786–90.
2 Hurst JA, Winter RM, Baraitser M. Distinctive syndrome of short stature, craniosynostosis, skeletal anomalies and malformed ears. *Am J Med Genet* 1988; **29**:107–15.
3 Gorlin RJ, Cervenka J, Moller K, Horrobin M, Witkop CJ Jr. A selected miscellany. *Birth Defects* 1975;**11**(2):39–50.
4 Meier Z, Poschiavo J, Rothchild M. Ein Fall van Arthrogryposis multiplex congenita kombiniert mit Dysostosis mandibulofacialis (Franceschetti-Syndrom). *Helv Paediatr Acta* 1959;**14**:213–6.


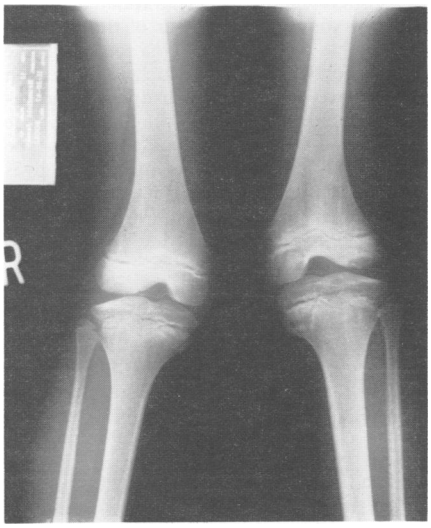


*Figure 2 Note genu valgum, agenesis of patellae, and osteochondritis dissecans.*

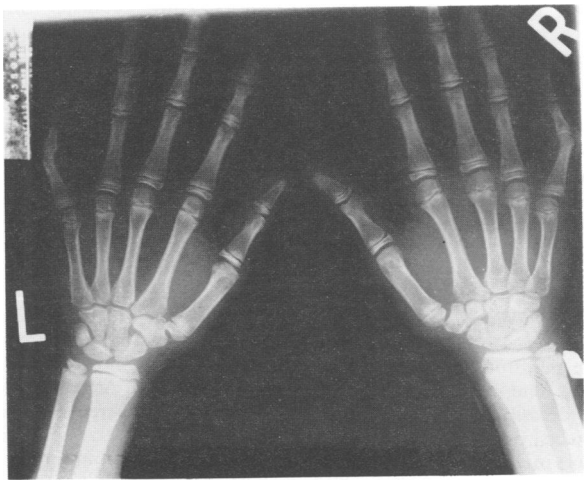


*Figure 3 Especially note camptodactyly of fifth fingers and flattening of radial epiphysis.*