CLEFT LIP PALATE IN CAPE TOWN*

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A search of the records of the plastic surgery units of Red Cross War Memorial Children's Hospital and Groote Schuur Hospital for the decade 1958 - 1967 yielded a total of 490 cases of CL ± P.‡ Of these, 332 lived in the Cape Town area and it was possible to locate 298 for the present investigation. There were 9 individuals from 4 families, in whom CL/P was part of a special syndrome showing the autosomal-dominant pattern of inheritance (2 families with lower-lip pits, 1 with a 'new' syndrome of camptodactyly, cleft palate and club foot, and 1 family with the CL/P, microphthalmia and polydactyly syndrome). These 9 individuals have been excluded from the present study and will be reported elsewhere. The remaining 289 index cases are the subjects of this report.

Race

There were 196 index cases with CL ± P, including 89 Whites, 75 Cape Coloureds, 16 Cape Malays and 16 others (i.e. of Indian, Jewish, Bantu or mixed racial origin). Among the 93 CP index cases, there were 29 Whites, 44 Cape Coloureds, 11 Malays and 9 others. Thus, compared with the CL ± P cases, there was a relative excess of Cape Coloureds with CP.

Sex

There were 119 male and 77 female index cases with CL ± P; i.e. a sex ratio of 1·5:1. In the CP series there were 25 male and 68 female index cases; i.e. a sex ratio of 4·4:1. The CL ± P sex ratio is similar to ratios reported from other countries, but the CP sex ratio is much lower than has been found elsewhere. This unusually large preponderance of female CP index cases is due mainly to a remarkable excess of Coloured females with CP. Of the 44 Coloured index cases with CP, 37 were females; a sex ratio of 0·2:1. No explanation has yet been found for this relative excess of CP in Cape Coloured females.

Family History

In 40% of the CL ± P index cases there was at least one other relative known to have a facial cleft; in 15% there was an affected first-degree relative. Among the CP index cases the family history was positive in 20%; in about half of these there was an affected first-degree relative. Among the CL ± P cases, the proportion with affected relatives was approximately the same in all 4 racial groups, but in the CP series there were far more Cape Coloureds (27%) with a positive family history than Whites (7%). In almost all cases, the family history was corroborated by our own examination of the persons concerned, or by a report from their family doctor, or by inspection of their hospital record or death certificate. With rare exceptions, the lesion in the affected relatives was of the same general type (CL ± P or CP) as in the index case.

TABLE I. RELATIVE INCIDENCE OF CLEFT LIP ± PALATE

Degree of relationship	*Total relatives*	*Number affected*	*Affected per 1,000*
First degree	1,048	30	28·6
Second degree	2,583	18	6·9
Third degree	4,277	19	4·2
General population	—	—	1·0

In Table I it will be seen that the incidence of affected first-degree relatives of the CL ± P index cases is almost 30 times that of the general population, but that this relative incidence is progressively much less among the second- and third-degree relatives. In the CP series (Table II) the proportion of affected first-degree relatives is almost 40 times that in the general population, with an even sharper fall-off in the second- and third-degree relatives. These findings are consistent with Carter's polygenic hypothesis, namely that these anomalies result from the cumulative effect of a number of 'abnormal' genes. When the number of 'abnormal' genes which an individual inherits exceeds a certain threshold, he is liable to develop CL/P.

TABLE II. RELATIVE INCIDENCE OF CLEFT PALATE

Degree of relationship	*Total relatives*	*Number affected*	*Affected per 1,000*
First degree	578	11	19·0
Second degree	1,211	2	1·6
Third degree	2,083	2	0·9
General population	—	—	0·5

TABLE III. INCIDENCE OF CLEFT LIP/PALATE IN SIBLINGS

	All siblings			*Subsequent siblings*		
	Total	*Affected*		*Total*	*Affected*	
		No.	%		*No.*	%
CL ± P	660	20	3·0	208	8	3·9
CP	398	10	2·5	109	5	4·6

The incidences of CL/P in all the siblings and in the siblings born after the index case are shown in Table III. The proportion of affected subsequent siblings of CL ± P index cases is much the same as has been found in Europe and North America. The proportion of affected subsequent siblings of CP index cases is greater than in European and North American series. This excess is owing to the relatively high proportion of affected subsequent siblings of female CP index cases.

When there were affected relatives other than siblings in the CP series, it was much more likely to be a maternal relative. In the CL ± P series the maternal and paternal sides of the family were equally affected. Four of the CL ± P cases and 1 of the CP cases were the children of consanguineous (2nd cousin) marriages. This degree of parental consanguinity is similar to that in the general White and Cape Coloured population of Cape Town. There were only 3 sets of twins: monozygous males concordant for CL; monozygous males discordant for CL; and dizygous females discordant for CL.

Maternal Age

The ages of the mothers at the birth of the index cases were compared with those of the mothers of 1,000 Cape Coloured and 300 White children randomly selected from the paediatric outpatients. In the CL ± P series, the maternal ages (at the birth of the index cases) tended to be slightly greater than in the general population. Among the mothers of CP index cases this tendency was much more pronounced. When the proportion of CP mothers in each 5-year age-period was compared with the control mothers, the differences were highly significant; for Cape Coloureds chi^2 (5 d.f.) = 56·8, $p < ·001$; for Whites chi^2 (5 d.f.) = 42·6, $p < ·001$.

Birth Order

The birth order of the CL ± P index cases was not significantly different from that of the controls. The CP index cases, however, showed a much higher birth-order distribution, with considerably fewer first born, than the controls; for Cape Coloureds chi^2 (8 d.f.) = 30·2, $p < ·001$; for Whites chi^2 (8 d.f.) = 32·4, $p < ·001$.

Other Congenital Anomalies

All the index cases and a majority of their siblings were

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‡Abbreviations: CL = cleft lip only; CP = cleft palate only; CL+P = cleft lip and cleft palate; CL/P = cleft lip and, or cleft palate; CL±P = cleft lip with or without cleft palate.

examined systematically for other congenital anomalies. The findings are shown in Table IV, where it will be seen that,

TABLE IV. INCIDENCE (%) OF OTHER CONGENITAL ANOMALIES

Diagnostic class of index case	*CL*	*CL+P*	*CP*
Incidence in index cases	4·9	10·4	14·0
Incidence in sibs. of index cases	2·0	1·9	2·3

compared with CL index cases, other anomalies were twice as common in CL+P cases and almost 3 times as common in CP cases. Even in the CL cases, the incidence of other anomalies was more than twice that of their siblings. The siblings of the 3 classes of cases did not differ significantly among themselves in respect of other congenital anomalies, and they are probably not much different in this respect from the general population. However, adequate age-matched control data for the general population are not available.

SUMMARY

In the CL±P index cases, the findings of this survey are similar to those reported from Europe and North America and there were no striking racial differences. In the CP index cases, however, there were several unusual findings: (*i*) a considerable excess of Coloured females with CP; (*ii*) a positive family history in 27% of Coloured CP index cases; (*iii*) a recurrence rate of 4·6% in subsequent siblings; (*iv*) a high maternal age; (*v*) a high birth order; and (*vi*) other congenital anomalies in 14% of index cases.

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