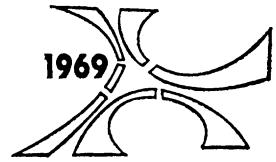
Some Genetic and Surgical Aspects of the Cleft Lip/Cleft Palate Problem in Egypt



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For a better understanding of the etiology of cleft lip and palate, genetic studies of this malformation in various populations have been recommended (*24*). It is the purpose here to present the results of such a genetic study, the first of its kind in the Egyptian population, which is characterized by a very high consanguinity rate. One of the main objectives of the study was to disclose any significant role played by recessive genes in the etiology of this malformation.

Optimum conditions for satisfactory surgical results under our present circumstances of preoperative, operative and postoperative care will also be discussed.

Material

It was possible to obtain accurate family and pregnancy histories and to examine the sibs and parents of 100 cleft lip and/or palate patients who attended the pediatric surgery outpatient clinic for surgical correction of their deformity. The clinic provides services for children from different areas of the United Arab Republic including both upper and lower Egypt, but mainly from Cairo and its vicinity. Each proband was clinically examined and special investigations were made when indicated. A case record was filled out for each patient including personal and social data, family history, pregnancy history, and an accurate description of the orofacial malformation and of any associated malformation. Also obtained were other data of genetic importance, such as mother's age and father's age at time of birth of the proband, birth order, number of sibs, parental consanguinity, and its type. Presence of family members affected with cleft lip and/or palate or other

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malformations on either the father's or mother's side was confirmed by examining affected members whenever possible. A pedigree was drawn for each proband. Cooperation of the family members was excellent.

Data from the case record of each proband were transferred to a punched card. Statistical analysis was performed when the number of cases reached 100. The study is still in process.

Only some of the patients included in the genetic study were surgically managed.

The control group comprised 200 cases of the same age group as the probands, including 100 cases attending the pediatric surgery outpatient clinic for disorders that are not congenital or genetically determined and 100 cases attending the baby welfare clinic of the same hospital.

Results and Discussion of the Genetic Study

NATURE OF THE MALFORMATION. The classification devised by Calnan (*1*), which includes complete and incomplete types of cleft lip and/or palate, has been followed. Probands were classified as having isolated cleft lip (CL), isolated cleft palate (CP), or combined cleft lip and cleft palate (CLCP). The probands' ages ranged from birth to 5 years. As shown in Table 1, there were 100 probands, 59 males and 41 females, with a marked excess of males in the group of CLCP, but not in the classes of CL or CP. A sex difference in the distribution of the type of malformation has been noted in different races. In American whites (*24*), isolated cleft lip as well as combined cleft lip/cleft palate is more common in males, while isolated cleft palate is more common in females. In the Japanese (*6*), the same tendency for an increase of females in the class of isolated cleft palate has been noted, also for an increase of males in the class of combined cleft lip/cleft palate. However, in the Japanese, as in this study, there was no excess of males in the class of isolated cleft lip. An excess of females in the class of isolated cleft palate was not evident in the present study, probably because of the very small number observed. These findings strongly suggest a race difference in the sex ratio of cleft lip and/or palate, the Japanese being similar to Egyptians in the absence of sex difference in incidence of cleft lip. How-

TABLE 1. Classification of probands according to type of cleft.

type of cleft	*males*	*females*	*total*
cleft lip (CL)	25	21	46
combined cleft lip/palate (CLCP)	26	14	40
isolated cleft palate (CP)	8	6	14
total	59	41	100

TABLE 2. Details of malformation in cleft lip (CL).

side, type	*males*	*females*	*total*
right	6	8	14
left	15	10	25
bilateral, complete	1	1	2
bilateral, incomplete	3	2	5
total	25	21	46

TABLE 3. Details of malformation in cleft palate (CP).

type	*males*	*females*	*total*
complete	3	2	5
incomplete	5	4	9
total	8	6	14

ever, in order to be conclusive, large numbers have to be studied and the incidence should be that at birth.

Table 2 shows classification of cases of cleft lip according to the sex of the probands. The side and type of the lesion show absence of sex differences in the side affected, but indicate a preponderance of left-sided lesions and a relative rarity of bilateral cleft lip. Table 3 shows the type of isolated cleft palate in the 14 probands. In all cases, the cleft was central with an excess of incomplete lesions. Table 4 shows that in combined cleft lip/palate, complete lesions are much more common than incomplete lesions and that bilateral complete lesions are more frequent in males. The preponderance of left-sided lesions has been noted by previous investigators (*6, 8*) and therefore must have an embryological significance. The observation that males more commonly have bilateral and/or complete lesions has also been noted by Fujino (*6*), indicating that males are more severely affected than females.

Associated Malformations. From other studies (*3, 8, 9, 11, 12, 14–16, 18, 20, 22*), it has been estimated that about 10 to 25% of patients with cleft lip and/or cleft palate have associated malformations: about 10% have mental retardation, 10% have congenital heart disease, and 3% have anomalies of the fingers and toes. Table 5 shows associated malformations in the probands classified according to their sex and the type of malformation. The most common associated orofacial malformation is hypertelorism, which was noted in 19% of the cases and was more frequent in males with combined cleft lip and palate. Minor ear malformations were in the form of low set ears, preauricular fistulae and

TABLE 4. Details of malformation in CLCP.

type	*males*	*females*	*total*
bilateral complete CLCP	10	1	11
unilateral complete CLCP	11	8	19
unilateral incomplete CLCP	1	1	2
bilateral incomplete CL complete CP	1	1	2
unilateral incomplete CL complete CP	3	3	6
total	26	14	40

TABLE 5. Associated malformations in probands.

type	*isolated CL*		*isolated CP*		*combined CLCP*		*total*
	males	*females*	*males*	*females*	*males*	*females*	
hypertelorism	3	4	1	1	7	3	19
hypoplastic mandible	0	1	3	1	1	2	8
tongue malformation	2	0	1	1	0	1	5
ear malformation	2	3	2	0	2	1	10
lower lip pits	0	0	0	1	0	0	1
congenital heart disease	0	0	1	0	0	1	2
skeletal malformation	1	3	3	0	2	2	11
mental retardation	0	1	2	1	0	0	4
external genital malformation	0	1	1	0	0	0	2

abnormal shape of ears, noted in 10% of the cases. Congenital heart disease was present in only two cases; in both, the lesion was acyanotic, most probably ventricular septal defect (V.S.D.). Skeletal malformations in areas other then the orofacial region were rather common and noted in 11% of the cases. In two cases, congenital ring constrictions associated with syndactyly and absence deformities of limbs and talipes equinovarus of feet were noted. It is possible that cleft lip and/or palate in these cases has the same etiology as the congenital ring constrictions, whose mechanism of production is as yet largely unknown (*17*). One case had unilateral hypoplasia of the femur associated with hypertrophy of the clitoris. Defects in skull bones were present in one case. Severe pectus excavatum was noted in one case. One case had bilateral postaxial pedunculated postminimi of the hands but no other features of D_1 trisomy syndrome. Two cases were dwarfed. One case had Roberts' tetraphocomelia syndrome (Figure 1). His parents were first cousins, thus confirming an autosomal recessive mode of transmission previously suggested by the senior author (*17*). One patient had associated pits of the lower lip (Figure 2), an indication that she was affected with an autosomal domi-

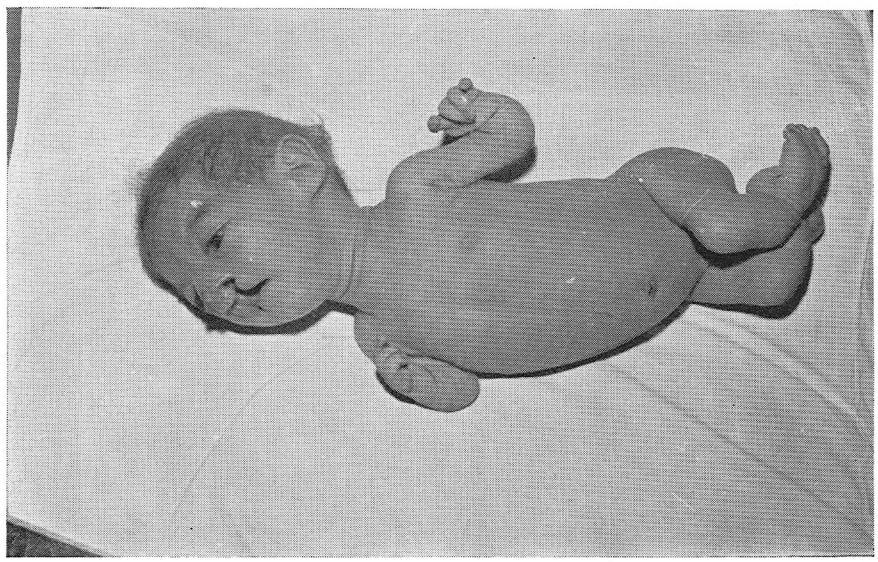

FIGURE 1. Full body view of proband with Roberts' tetraphocomelia syndrome. Note bilateral complete cleft lip/palate deformity associated with severe symmetrical absence deformities of the four extremities.

nant disorder, the Van der Woode syndrome (*19*). Her father had lower lip pits and dental anomalies without clefts (Figure 3) and her brother had posterior cleft of palate and asymmetry of the nose (Figure 4) without associated pits.

Associated tongue malformations, observed in five of the probands, were in the form of hypoplastic tongue and tongue tie due to short or short and thick frenum. In two cases, the tongue was bifid in the midline at its tip. In one of these cases, the father had the same tongue malformation as the proband (Figures 5 and 6) and, in the other case, the mother had the same malformation as the proband (Figure 7). Other members in the families of both cases had the tongue malformation without associated clefts of lip or palate. In both cases, parents were first cousins. It is therefore possible that homozygosity for a nondominant gene causing bifid tongue produces the association of bifid tongue with cleft lip and/or palate. Another possibility is that bifid tip of tongue with or without cleft lip or palate represents an autosomal dominant trait with variable expressivity.

Tongue malformations are known to be associated with cleft lip and/or palate; for example, in the aglossia adactylia syndrome and in the ankyloglossum superius syndrome (*8*), whose genetic etiology is rather complex (*17*).

Previous investigators have noted that in isolated cleft palate associated malformations occur with a frequency thirty times that in the

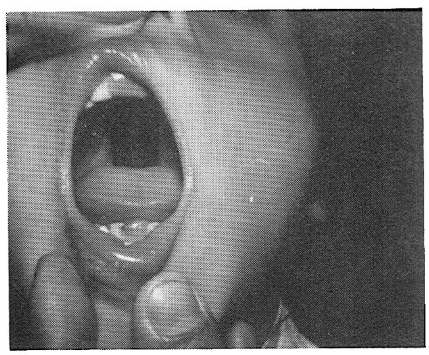

FIGURE 2. Mouth and oral cavity of proband with Van der Woode syndrome. Note cleft palate and lower lip pits, more evident on the right in the middle of a cyst.

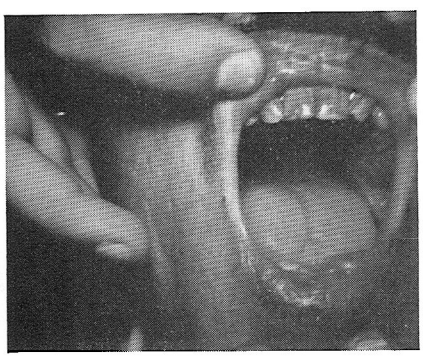

FIGURE 3. Mouth and teeth of father of proband with Van der Woode syndrome. Note lower lip pits more evident on the right of the midline and a cystic swelling on the left. Also note malposed left upper lateral incisor.

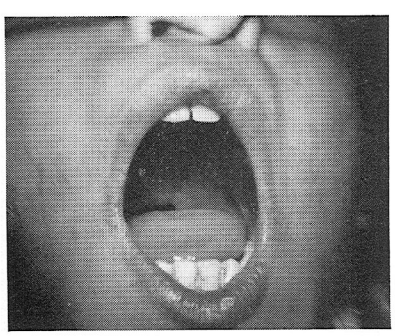

FIGURE 4. Brother of proband with Van der Woode syndrome. Note short soft palate and bifid uvula, asymmetrical nose but absent lower lip pits.

general population (*8*). In the present study, among the 14 cases studied with isolated cleft palate, other than the proband with Van der Woode syndrome and the proband with associated bifid tongue, 6 cases had a galaxy of associated malformations which do not exactly fit in known

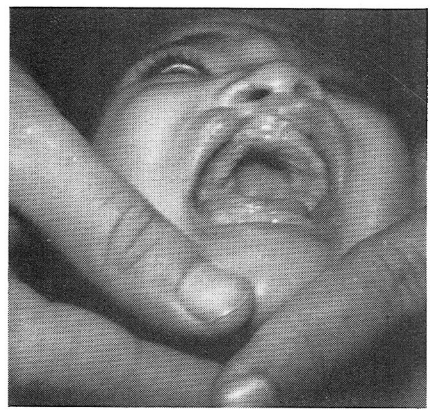

FIGURE 5. Proband with cleft lip and bifid tip of tongue with short and thick lingular frenum. His father (Figure 6) had bifid tongue only.

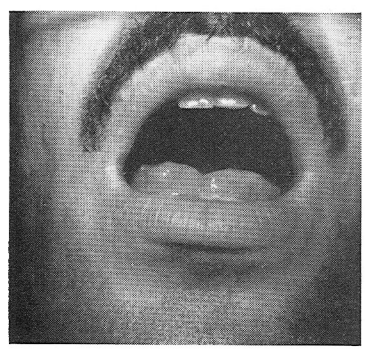

FIGURE 6. Father of proband in Figure 5. Note bifid tip of tongue in the middle line.

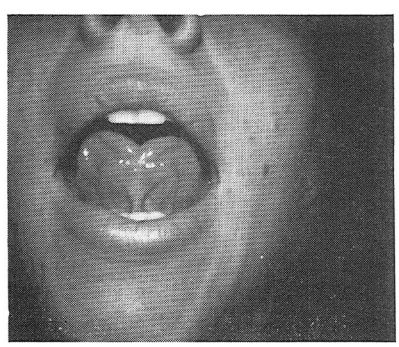

FIGURE 7. Bifid tip of tongue in the middle line, the mother of a proband with cleft palate and bifid tip of tongue in the middle line.

syndromes. These cases are: ℵ1, a female with flat facies, mental retardation, and no speech development at the age of 3 years. Her parents were first cousins. ℵ2, a male with dwarfism, narrow forehead, low neck hairline and hypospadias. His parents were not related. ℵ3, a

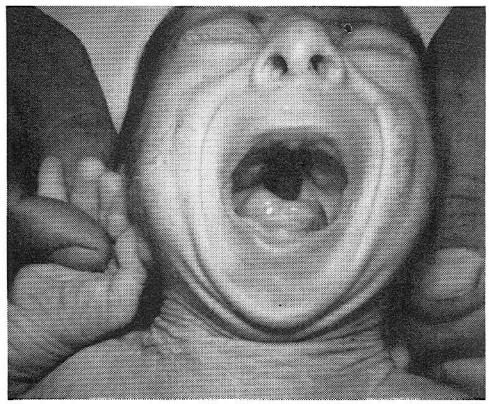

FIGURE 8. Face of case ⅋5 with posterior cleft palate and adherent tongue in its whole length. Note that left side of tongue is smaller than the right and that the upper lip is adherent to gingival margin. Also note redundant skin over neck and hypertrichosis.

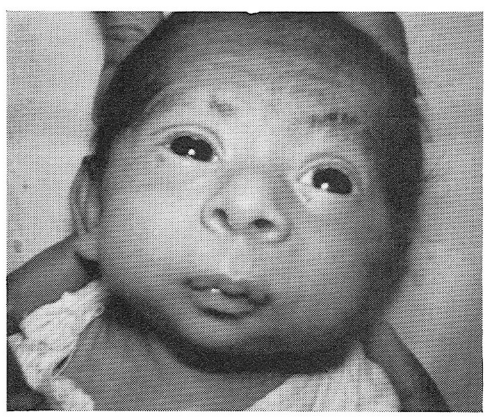

FIGURE 9. Face of case ⅋6 with cleft palate and associated anomalies suggestive of E trisomy syndrome. Note small palpebral fissures, hypoplastic mandible and low set ears.

male with antimongoloid slanting of the eyes, hypoplastic mandible, low set ears, mental retardation, dwarfism and clinodactyly of the fifth finger. Clinodactyly was also noted in his mother and some of his sibs. His parents were first cousins. ⅋4, a male with associated oxycephaly, nephrogenic diabetes insipidus, mental retardation and primary optic atrophy. His parents were first cousins. A paternal first cousin had combined cleft lip and palate without the associated malformations noted in the proband. ⅋5, a male with hypoplastic mandible and an adherent tongue in its whole length. The upper lip was adherent to the gingival margin. The left half of the tongue was smaller than the right. He also had hypertrichosis, low hairline and redundant skin (Figure 8). His parents were first cousins. ⅋6, a male with features suggestive of the E trisomy syndrome without the characteristic dermatoglyphic pat-

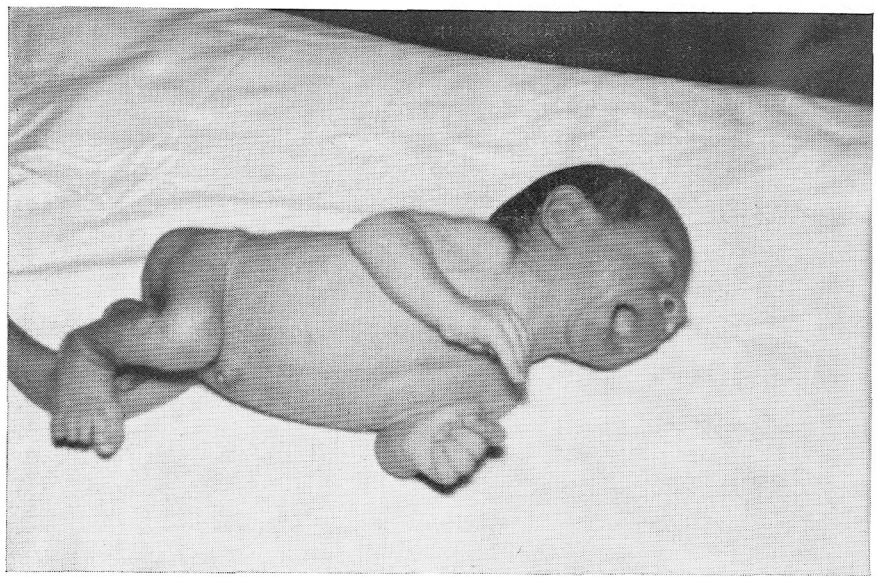

FIGURE 10. Full body view of case #6 with cleft palate and associated anomalies showing features similar to those found in E trisomy syndrome. Note clenched hands, hypoplastic mandible and low set ears.

tern. He died of pneumonia shortly after admission, before a successful chromosome culture could be done. He had small palpebral fissures, hypoplastic mandible (Figure 9), low set ears, failure to thrive, clenched hands (Figure 10), and congenital heart disease, probably V.S.D. Parents were also first cousins.

It is possible that some of these patients have minor structural chromosomal aberrations, not discovered by means of examining chromosomes. However, it is also possible that some of these cases whose parents are first cousins represent as yet unrecognized autosomal recessive disorders. More studies of details of associated malformations in cases with cleft lip and/or palate are needed to reveal the nature of these syndromal associations.

Numerous syndromes are characterized by the association of cleft lip and/or palate. In some of them, cleft lip and/or palate occur in all or in the majority of cases. A partial list of these syndromes with delineation of their genetic etiology is shown in Table 6. Cleft lip and/or palate is an occasional finding in other syndromes reviewed by Gorlin and Pindborg (*8*). These are: Apert's syndrome of acrocephalosyndactyly, an autosomal dominant disorder; diastrophic dwarfism, an autosomal recessive disorder; chondrodystrophia calcificans congenita, an autosomal recessive trait; E or 18 trisomy syndrome; Down's syndrome or 21 trisomy; aglossia adactylia syndrome; and ankyloglossum superius syndrome. In Smith-Lemli-Opitz syndrome, an autosomal recessive disorder

TABLE 6. Syndromes characterized by CL, CP, or CLCP

syndrome and reference	*main associated malformations*	*etiology*
Van der Woode syndrome (*19*)	lower lip pits	autosomal dominant inheritance
cleft lip-palate split hand-foot (*20*)	split hand-foot, lacrimal duct anomalies	autosomal dominant inheritance
popliteal pterygium syndrome (*9*)	popliteal web, digital and genital anomalies	autosomal dominant inheritance
Nager's acrofacial dysostosis (*12*)	radial defects, ear deformity	unknown, sporadic
orofaciodigital syndrome (OFDI) (*8*)	digital anomalies, hypoplasia of alae nasi, hypertrophied oral frenuli	x-linked dominant, male lethal
Mohr syndrome (OFD2) (*14*)	polysyndactyly of toes, cleft tongue, conductive deafness	autosomal recessive inheritance
Roberts' syndrome (*15*)	tetraphocomelia (severe absence deformities of upper and lower limb long bones)	autosomal recessive inheritance
Pierre-Robin syndrome (*8*)	micrognathia and glossoptosis	unknown? autosomal recessive
Taybi's otopalatodigital syndrome (*3*)	broad nasal root, broad distal phalanges, conductive deafness	unknown, sporadic
Larsen's syndrome (*11*)	flat facies, short finger nails, multiple joint dislocations	unknown, sporadic
Weyers' oligodactyly syndrome (*22*)	ulnar defects, kidney & spleen malformations	unknown
median cleft of upper lip and polydactyly (*18*)	postaxial polydactyly	autosomal recessive
chromosome 4 short arm deletion syndrome (*10*)	hypertelorism, prominent glabella, low set ears	chromosomal aberration
13 or D_1 trisomy syndrome (*16*)	micro or anophthalmia, postaxial polydactyly, holoprosencephaly (type mid-face and forebrain defect)	chromosomal aberration

characterized by mental retardation, urogenital, and skeletal anomalies, cleft palate is sometimes found (*2*). For the purpose of genetic counseling, it is important to recognize cleft lip and/or palate as a part of syndromes which have a definite genetic etiology. In the present study, these were represented by a patient with Van der Woode syndrome and a patient with Roberts' syndrome.

Familial Incidence. Positive family history of clefts in relatives of probands has been estimated to be 15 to 20% (*8*). In the present study, familial aggregation was noted in 16% of the cases. Data in Table 7 show the familial cases, indicating the relative affected in the different classes of cleft lip and/or palate and whether parents were consanguineous. In case ℵ1, isolated cleft palate in a female, the proband had Van der Woode syndrome. In case ℵ5, female with isolated cleft lip without associated lower lip pits, the pedigree pattern of affected father, paternal grandfather, and a paternal first cousin suggests autosomal dominant inheritance with incomplete penetrance. Pedigrees suggestive of autosomal dominant inheritance, where clefts are not associated with lower lip pits, have been noted by other investigators (*13*). In case ℵ5, combined cleft lip and palate in a male, the finding that the father and a maternal first cousin have clefts, in spite of the absence of parental consanguinity, suggests inheritance from both sides of the family or the

TABLE 7. Familial cases.

malformation	*sex*	*case*	*affected relative*							*parental consanguinity*	*comments*
			sib	*father*	*mother*	*1st cousin*	*uncle*	*aunt*	*others*		
CP	females	1	+	+			+			−ve	Van der Woode syndrome
CP	males	1				+				+ve	
CL	females	1							+	−ve	
		2	+				+			+ve	
		3	+							+ve	
		4					+			+ve	
		5		+			+		+	−ve	? aut. dominant
CL	males	1							+	+ve	
		2	+							+ve	
		3				+				+ve	
CLCP	males	1							+	+ve	Roberts' syndrome
		2				+				−ve	
		3	+							+ve	
		4	+							+ve	
		5		+		+				−ve	inheritance from both sides
CLCP	females	1	+				+		+	+ve	
Total		16	8	3	0	5	4	0	5	11	

effect of autosomal recessive genes. The paternal grandmother of the proband with Roberts' syndrome, whose parents were first cousins, had isolated cleft lip without skeletal malformations. It is therefore possible that homozygosity for the irregular dominant gene causing cleft lip can produce the severe skeletal disorder associated with cleft lip and/or palate. In the remaining 12 familial cases, parental consanguinity was present in 9 cases.

Incidence in Relatives of Probands. In the present study, excluding pedigrees of autosomal dominant inheritance, the proportion of affected sibs was 3.5%. Woolf and associates (*24*) found a 4.61% incidence in probands' sibs. The figures in sibs obtained by Fujino and associates (*6*) ranged between 0.84% and 2.36%, excluding cases in which one parent was affected.

The proportion of affected parents was 1% in the present study, 2.03% in the study by Woolf and associates (*24*), and 2.02% in the study by Fujino and associates (*6*). In the present study, among the 7 affected sibs, 5 were brothers and 2 were sisters. All other affected relatives of the probands in the present study were males. These findings are similar to those of Fujino and associates (*6*) in which male relatives were much more frequently affected than female relatives, suggesting a sex difference in penetrance of the malformation.

Orofacial Malformations in Probands' Parents. Minor orofacial malformations noted in the probands' parents are shown in Table 8. A total of 45, or 22.5%, of the probands' parents had minor

TABLE 8. Minor orofacial malformations in probands' parents, by sex of proband.

parent	*type of malformation*	*isolated CL*			*isolated CP*			*combined CLCP*			*total*
		M	*F*	*total*	*M*	*F*	*total*	*M*	*F*	*total*	
mother	hypertelorism	3	3	6	0	1	1	2	1	3	10
	dental malformation	7	7	14	0	0	0	7	1	8	22
	tongue malformation	0	0	0	0	1	1	0	0	0	1
father	hypertelorism	0	0	0	0	0	0	3	0	3	3
	dental malformation	2	1	3	1	1	2	3	0	3	8
	tongue malformation	1	0	1	0	0	0	0	0	0	1
total		13	11	24	2	3	4	15	2	17	45

TABLE 9. Consanguinity in probands' parents.

cleft type	*sex of proband*	*number affected*	*number of consanguineous parents*	*per cent consanguineous parents*	*per cent first cousins*	*per cent distant cousins*
CL	males	25	18	72	66	34
CL	females	21	12	57	75	25
CLCP	males	26	11	62	63	37
CLCP	females	14	8	57	75	25
CP	females	5	4	80	100	—
CP	males	8	5	62	60	40
total		100	58	58	71	29

orofacial anomalies. The dental anomalies noted were unilateral or bilateral absence or hypoplasia of lateral incisors. Other dental anomalies were supernumerary, malposed, or overcrowded teeth. These anomalies affected mainly the maxillary and/or the mandibular incisors. While these malformations were noted in 33% of the mothers, only 12% of the fathers had these changes. In the control series, only 4% of the parents had mild hypertelorism and 3% had similar dental anomalies. One father in the control group had absent upper central incisor, a malformation not noted in any of the parents of the probands. None of the parents of the controls had tongue malformations.

The observation of this high percentage of orofacial abnormalities in parents of probands is in agreement with the observations of Fukuhara and Saito in Japan (*7*), who considered these findings as microforms of cleft lip and palate. Temtamy (*17*) in family studies of 7 probands with orofacial anomalies (mainly cleft lip and/or palate), associated

TABLE 10. Comparison of parental consanguinity in probands and controls, in per cent.

	parents of probands	*parents of controls*
total per cent of consanguinity	58	32
per cent of first cousin marriages	71	71
per cent of more distant cousin marriages	29	29

TABLE 11. Birth order distribution of probands according to sex and type of cleft.

birth order	*CL*		*CLCP*		*CP*		*total*
	M	*F*	*M*	*F*	*M*	*F*	
1st	4	6	5	2	1	1	19
2nd	3	3	5	2	1	1	15
3rd	5	2	4	3	2	1	17
4th	6	6	3	1	2	1	19
5th	2	1	5	1	1	—	10
6th	1	1	2	1	1	2	8
7th	1	2	1	—	—	—	4
8th	1	—	—	2	—	—	3
9th	2	—	—	1	—	—	3
10th	—	—	1	1	—	—	2

with hand anomalies noted that both cleft lip and/or palate and dental malformations occurred in families of these cases. It is therefore possible that these microforms are stigmata for the genetic susceptibility to cleft lip and/or cleft palate, or the mildest expression of the malformation. The finding that females more frequently show these microforms while males more frequently have clefts may be another evidence of a sex-influenced or sex-modified penetrance of this malformation.

In the probands' relatives, the incidence of malformations other than in the orofacial region was not significantly higher than that in the general population. Congenital heart disease was found in the sib of one case. Hand malformations in the form of clinodactyly, camptodactyly and polydactyly were noted in some of the probands' relatives.

Parental Consanguinity. The total consanguinity rate among parents of probands was 58%, while that in the control population was 32%. This difference is highly significant. Table 9 shows the distribution of consanguinity among parents of probands, according to sex of the probands and type of cleft. The highest consanguinity rate is that among parents of females with isolated cleft palate. However, the numbers of each group are too small to allow for definite conclusions.

TABLE 12. Comparison of birth order distribution of probands and controls, in per cent.

birth order	*probands*	*controls*
1st	19	15
2nd	15	18
3rd	17	18
4th	19	20
5th	10	9
6th	8	7
7th	4	5
8th	3	3
9th	3	2
10th	2	3

TABLE 13. Mean maternal and paternal ages (in years) for parents of probands and controls.

type of cleft	*mean maternal age*	*mean paternal age*
CL	24.8	33.1
CP	26.9	32
CLCP	26.5	35.9
Controls	28.2	30.5

Table 10, a comparison of the type of consanguinity among probands and controls, shows a similar distribution of first degree and more distant cousins among parents of probands and of control subjects, indicating that the degree of consanguinity is not important in the etiology of cleft lip and/or palate.

The results of the present investigation strongly suggest a role played by recessive genes in the etiology of cleft lip and cleft palate. Such a conclusion was also reached by Fujino and associates (*6*), who noted that the rates of total consanguineous marriages among parents of probands in which both parents have no clefts was slightly greater than the frequency in the general population. In their series, this was due largely to parents of cases with isolated cleft palate. In families where both parents were normal and where two or more sibs were affected, the consanguinity rate in the same study was as high as 20% or more, irrespective of types of clefts. Consanguinity rate in the Japanese ranges from 9.94% to 12.97% (*6*).

Birth Order. The birth order distribution of the probands according to sex and type of cleft is shown in Table 11. A comparison of birth order distribution of the probands and the controls is shown in Table 12. The data indicate no evident birth order effect.

Parental Age. Table 13 shows the mean maternal and paternal ages of the probands for the three different types of clefts and their comparison with maternal and paternal age of the controls. From this table, while no maternal age effect is apparent, a paternal age effect is suggested, particularly in the group of combined cleft lip/cleft palate. A paternal age effect was previously noted by Woolf (*23*).

Pregnancy History. In three cases, a period of sterility preceded the pregnancy which terminated in the birth of an affected case. In two cases, sterility was secondary for a period of 5 years. In one case, sterility was primary for 17 years. In two of the cases preceded by a period of sterility, congenital ring constrictions were associated. Oral contraceptives (anovular)[1] were erroneously taken by two mothers during the first three months of pregnancy (pregnancy occurred during a period of lactation amenorrhea). Two mothers had attempted abortion by drugs and by mechanical means. Two mothers had received broad spectrum antibiotics for a period of one week to ten days during the first trimester of pregnancy. Two cases received sedatives during the first three months of pregnancy. One mother had antiallergics throughout the pregnancy. One mother had influenza during the first trimester. Three cases received hormonal treatment for threatened abortion that had occurred during the second or third months of pregnancy, for periods ranging from one to three months.

From such a retrospective study, it is difficult to incriminate certain environmental factors as being teratogenic, particularly with the small number studied. No single environmental factor is as yet known to produce cleft lip and/or cleft palate in humans. In experimental animals, clefts have been produced following treatment of the pregnant mother with a variety of agents. Examples are vitamin deficient diets (*21*), cortisone injection (*4*), and many other agents (*5*). Further studies are needed to determine a causal relationship between certain environmental factors and clefts in humans.

Surgical Aspects

Simple cleft lip or cleft palate is a relatively minor deformity. However, the more common combined cleft lip and palate, especially the severe degrees, is a serious disfiguring deformity that requires skillful correction. The parents, in the case of the minor deformities, are indifferent about them while in the latter they are deeply concerned, not only about the disfigurement but also about feeding problems.

Parents in the rural provinces often believe their child to be the product of venereal disease and sometimes seem to hope that the child will not survive. They become careless about the child, who in turn is

[1] Anovular (Schering, Berlin, manufacturer) is norethisterone acetate 4 mgm and ethinyloestradiole 0.05 mgm.

exposed to infection, loses weight from underfeeding, and becomes a poor surgical risk patient. This is further aggravated by the fact that specialized centers for correcting these serious deformities are not always accessible to the parents, who may live far away and who hesitate to bring their child for surgery until his health is impaired.

On the other hand, the warm climate, particularly in the summer, predisposes the children to develop postoperative hyperpyrexia. Gastroenteritis is common and easily leads to dehydration, dryness of the mouth, and susceptibility to thrush with greater risk for the wounds to disrupt. Moreover, the relatively frequent occurrence of infectious diseases among the childhood population, particularly of measles, may affect the patients postoperatively with the possibility of interference with proper healing of the wound. The nursing of the patients in open wards increases the likelihood of cross-infection. Despite all these detrimental factors, the wounds of the patients usually heal satisfactorily. However, the patients are always under antibiotic cover postoperatively. Of 64 operations for cleft lip and palate performed, there has been only one complete breakdown of the palate and one of the lip; four have had partial breakdowns. Three of these healed spontaneously while the fourth required a second operation.

The optimal age for surgery for cleft lip is between 3 and 5 months of age, while for cleft palate it is from 18 to 24 months.

Different surgical procedures were performed. Years ago, the surgeon had to rely on his own skill and worked alone. Subsequently, orthodontic problems arose that would have been better managed from the start. At the present time, we are working in collaboration with the orthodontist to plan the treatment. Better understanding by the parents of the etiology of this malformation and of the risk of its recurrence is provided by the geneticist. The help of the social worker in studying the environment and in following up our patients is indispensible. To obtain better results, our team needs completion by the speech therapist.

Summary

A genetic study of 100 children with cleft lip and/or cleft palate was undertaken for the first time in the Egyptian population. The results of the present study are remarkably similar to studies in other parts of the world, suggesting similar etiological factors and a major role played by genes. The significant increase in consanguinity rates among parents of probands when compared to the controls strongly suggests a role played by recessive genes. A sex difference in expressivity of this malformation was also evident, males being more severely affected than females. The present study confirmed a paternal age effect and an increase of minor orofacial malformations in parents of probands. Treatment of cleft lip and palate in Egypt is also described.

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