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## MAIN HEAD DIMENSIONS IN RELATIVES OF CHILDREN WITH CLEFT LIP AND PALATE

Because of the wide spectrum of problems associated with the occurrence and development of inborn anomalies both the therapeutic approach and basic research require a close co-operation of several scientific disciplines (Karfík, 1971). It proved the possibility to utilize all approaches which could be helpful in providing a deeper understanding or a full elucidation of the nature and causes of the development of these anomalies. Anthropologic and anthropogenetic studies belong among those which contributes to new knowledge in this branch of investigations and thus form an inherent part of complex studies (Burian and his co-workers, 1964 a).

The studies of inborn anomalies should not be limited to the examination of the individual involved, but an equal attention should be paid to the next of kin and to the other relatives of the patient. Of particular importance is the recording of aetio-pathologic and genealogic data (Burian et coll., 1964 b; Farkaš et coll., 1970). It is also necessary to determine the general state of health and the somatic state of normal relatives of the afflicted individual, since both visual inspection and measurements might provide important informations on the presence of some deviations from normal. It is assumed that significant differences of the morphologic characteristics and of the measurements occurring in the parents, sibs, or in some other relatives of the afflicted children might represent a marker of the genetic predisposition of inborn anomalies. Fraser (1970) assumes on the basis of animal experiments that in humans the shape of the face could represent an indicator of this predisposition in individuals with cleft of the primary palate (i.e. of the lip and alveolus).

There are only a few reports in the literature supporting the advanced hypothesis and they do

not provide definite conclusions (see discussion). The studies reported so far disclosed, however, that certain craniofacial deviations from normal might be seen in parents of cleft children. In spite of their minor degree these deviations are not necessarily unimportant. In the case that they are statistically significant they will play a similar role as microforms (they show in individual situations rather a hereditary background, Šmahel 1974). They provide further the possibility to confirm or to exclude the hypothesis on the genetically determined predisposition of a certain somatic or morphologic type to an inborn malformation. Further, they are helpful in the discrimination of phenocopies from hereditary determination of malformations and thus allow a more accurate prognosis in genetic counselling. They contribute also to the identification of those craniofacial structures which are of importance for an appropriate morphogenesis (and which might exert adverse effects on the latter), since they will show more frequently a shift towards the limit of normal range of variations in relatives of cleft individuals than in normal controls.

As the basis for similar determination can serve only comparative studies including a group of controls and an experimental series (i.e. families with the occurrence of clefts). This type of investigations is further necessary for the detection of microforms. This term is used, at the present time, for anomalies occurring in a significantly increased frequency in relatives of cleft patients, compared to the normal population. These comparisons were carried out e.g. by Niswander (1968), Mills et al. (1968) and by Pashayan and Fraser (1971). It seems appropriate, however, to reserve the term of microforms only to minimal forms of malformations and to designate the other cases as

associated signs. This approach was suggested by Tolarová (1969) who specified a microform eighter as a combination of two atypic features in the region of the maxilla, or a single sign in a definite carrier. It remains to be settled empirically how far the occurrence of a microform in relatives of the probands influences the recurrence risk figures. This is associated with difficulties, however, because of the small numbers of cases. Finally it should be mentioned that a higher frequency of other inborn anomalies in relatives of cleft children was ascertained in similar comparative studies e.g. by Niswander, Adams (1968). The same was reported in the so-called minor defects by Smith and Bostian (1964).

The present communication reports the results of cephalometric studies in parents and other relatives of cleft children and supplements our previous report (Figalová, Šmahel, 1974).

#### MATERIAL AND METHODS

Our report is based on the results of cephalometric studies of 93 families having a child with cleft lip and/or palate. All children were born in Bohemia in 1966 and were seen at the Clinic of Plastic Surgery at Prague. Out of the total number of recorded cases in the year mentioned above (166 probands; frequency 1 : 500, Klásková-Buriánová, 1973) our series form the representative majority (31 children had a unilateral and 9 had a bilateral cleft lip and palate, 34 had a cleft lip  $\pm$  the alveolus and 19 had an isolated cleft palate). The measurements were carried out in probands with malformations, in their sibs, parents, grandparents, as well as in sibs of their parents, i.e. in three generations. Because of the small numbers the sibs of the probands were not evaluated (a heterogeneous group according to age). This holds true equally for the families of proband with bilateral cleft lip and palate compared to the results according to the type of cleft. Thus it was possible to evaluate a series of 571 normal relatives of cleft children. They were subdivided according to sex, father's and mother's side, and coefficient of relationship (parents = 0.5; other relatives = 0.25). The subdivision was carried out separately in horizontal and vertical line. The numbers of individuals in individual groups of relatives and their mean age are presented in *table 1*. The data illustrate equally the willingness to co-operate which was less in father's than in mother's parents and generally in males than in females. During the evaluation of this series the numbers of individuals with clefts within one family were not taken into account (there were 15 cases of familial occurrence, i.e. 16.1%), since this allows to enlarge expected differences (they will be absent in true phenocopies). Clefts occurring as an inherent part of a syndrome, conceivably, were excluded from our study.

The measurements included the maximum length of the neurocranium (g-op, M 1), the maximum width of the neurocranium (eu-eu, M 3), the width

of the cranial base (t-t, M 5), the minimum width of the forehead (ft-ft, M 4), the width of the face of the forehead (zy-zy, M 6), the width of the mandibular angles (go-go, M 8), the morphologic height of the face (n-sto, M 18), the height of the upper face (n-gn, M 18), the height of the nose (n-sn, M 21), the height of the inner canthi (en-en, M 9), the distance between the outer canthi (ex-ex, M 10), distance between the nose (al-al, M 13), the width of the width of the nose (ch-ch, M 14), the subnasal arch (t-sn-t) the oral slot (ch-ch, M 14), the submandibular arch (t-gn-t). The dimensions and the submandibular arch (t-gn-t). The dimensions ascertained by measurements were used for the computation of the cephalic index  $[(100 \times \text{eu-eu}) : \text{g-op}]$ , facial index  $[(100 \times \text{n-gn}) : \text{zy-zy}]$ , nasal index  $[(100 \times \text{al-al}) : \text{n-sn}]$  and intercanthal index  $[(100 \times \text{en-en}) : \text{ex-ex}]$ , characterising the structural proportions of a given part. Since both visual inspections and measurements disclosed in cleft probands deviations of the auricle (Farkaš, Lindsay, 1973), the height (sa-sba, M 29) and the width of the pinna (pra-pa, M 30) were measured as well. The measurements were carried out according to Martin and Saller (1957).

The same examinations were carried out in a group of controls, consisting of 50 normal adult males and 50 females ranging in age from 20 to 40 years, with a predominance of the age group of 20–30 years. The range of age corresponds approximately to that of the parents and of parental sibs of the cleft children. The control group of males was compared with all groups of male relatives (i.e. father, father's brother, mother's brother, father's father and mother's father) and in a similar way all groups of females were compared with the group of control females (thus there was no agreement in the age of controls with that of grandparents). The differences of the mean values were tested with Student's t-test. *Table 1* presents the final results of the t-test in groups with ascertained significant differences. The numerical value denotes the significance level, the marks + and – denote whether the assessed value is lower or higher than that obtained in the group of controls (width of the oral slot and the dimensions of the auricle were not included because of the lack of a personal or some other adequate controls). The data were further subdivided into three groups according to the type of cleft of the proband (lip, palate, lip + palate unilateral). They were subjected to a statistic analysis and tested by the same procedure as all our cases. The results are not presented because of the small numbers of cases in individual groups but some differences are described in the text. Since there are no data on the circumference of the neurocranium in the investigated series we have used for their supplementation the values obtained by measurements in a small group of parents of cleft children seen in our genetic consultation. The results are given in *table 3*.

The statistical analysis of the recorded data disclosed in some features significant differences between the mean values in parents and their sibs compared to those ascertained in grand-parents. The differences were equally reflected in the results

TAB. 1 *Craniofacial characteristics in relatives of cleft children — results of the t-test yielding a significant difference compared to controls (all types of clefts conjunctly).*

Relationship	mother	mother's mother	mother's sister	father's mother	father's sister	father	father's father	father's brother	mother's father	mother's brother
Mean age	24,26	50,93	22,03	55,14	28,53	27,86	57,95	26,10	53,89	25,17
Number of probands	80	60	60	50	58	79	35	59	46	44
g-op	-0,05		-0,01		-0,001	-0,05		-0,001		-0,001*
eu-eu	-0,001	-0,02	-0,001		-0,02	-0,05				
t-t	-0,02		-0,05			-0,001				-0,001
ft-ft				-0,01						
zy-zy						-0,05				
go-go	-0,01									
n-gn										
n-sto	+0,05		+0,02	+0,005	+0,02	+0,05	+0,001		+0,005	
n-sn			+0,05	+0,05		+0,02	+0,01		+0,05	
ex-ex				-0,01				+0,01		
en-en	+0,02									
al-al		+0,001*		+0,01			+0,001		+0,001	
t-sn-t			-0,005							
t-gn-t										
i. cephalicus									-0,05	
i. facialis										
i. nasalis			-0,05			-0,001				
i. intercanthalis				+0,01						
t-sn-t**	-0,05			-0,02	-0,02			-0,05		

\*) only in these situations the difference attains approximately 1 standard deviation compared to the corresponding group of controls (in other cases it is 0.4—0.8 SD).

\*\*) in unilateral cleft lip and palate.

of the t-test. It is therefore apparent that also in adults some craniofacial dimensions undergo changes with age. The assessment of these characteristics is reported in the second part of the present communication. Table 2 include the mean values and the standard deviations of the basic dimensions of the head and of features showing significant deviations compared to controls or undergoing changes with age. We have therefore added the dimensions of the right auricle which were compared with the corresponding age group

of the series described by Hajniš (1969) as well as the width of the oral slot. The data at the same time provide the possibility to assess the absolute magnitude of the significant deviations recorded in table 1 and their eventual practical utilization. For simplification we use in the following text the term 1st generation for the grand-parents of the proband and the term 2nd generation for the parents of the probands and their sibs. The difference between the age of these two generations is approximately 30 years (see Tab. 1).

TAB. 2

*Craniofacial characteristics in relatives of cleft children — mean values and corresponding standard deviations, + and — indicate significant plus or minus differences compared to controls (the numbers of individuals examined are identical with those in table 1, the group of controls included 50 males and 50 females).*

metric character	control females	II. generation			I. generation		control males	II. generation			I. generation	
		mother	mother's sister	father's sister	mother's mother	father's mother		father	father's brother	mother's brother	father's father	mother's father
g—op	179,6 5,7	177,5- 6 2	176,7- 5,6	176,5- 5,0	178,9 6,3	178,8 5,8	188,1 5,2	186,5- 7,0	184,9- 6,6	184,0- 4,5	186,8 6,6	188,3 4,0
eu—eu	155,2 4,2	152,6- 4,5	152,6- 5,0	153,2- 4,9	153,1- 4,8	154,5 6,8	161,3 4,6	158,9- 7,2	159,7 6,2	159,8 5,1	158,7 7,1	159,8 6,8
t—t	133,8 5,4	131,3- 5,8	131,4- 5,5	131,6 6,8	134,1 6,4	133,2 6,2	142,2 4,6	138,9- 7,9	140,1 8,4	138,4- 5,7	141,0 9,0	142,3 8,3
zy—zy	134,8 4,9	134,4 5,1	133,8 5,3	133,9 6,6	135,1 6,0	135,3 6,2	142,8 4,9	140,8- 5,7	141,9 6,6	141,7 4,8	142,6 6,5	143,9 5,2
go—go	103,2 4,4	101,0- 4,8	102,9 5,2	101,4 5,0	104,6 5,4	103,7 5,3	109,2 5,0	108,0 6,1	107,7 7,5	107,8 4,9	109,2 6,8	110,8 6,4
n—gn	111,8 5,3	112,0 6,1	112,8 6,8	112,5 5,4	111,2 6,4	111,6 5,5	119,6 5,9	121,0 6,2	120,0 7,9	121,5 6,3	122,4 8,4	121,2 5,8
n—sto	68,1 4,1	70,0+ 5,4	70,3+ 5,3	70,2+ 4,8	69,5 5,6	70,7+ 4,8	73,5 4,7	75,2+ 4,4	74,7 5,0	75,0 3,4	77,4+ 5,8	76,6+ 5,5
n—sn	48,7 3,5	48,9 4,2	50,1+ 3,9	49,1 3,5	49,5 3,4	50,1+ 3,6	52,2 3,3	53,8+ 3,6	52,3 4,1	53,4 3,2	54,3+ 3,7	53,9+ 3,9
al—al	32,3 2,0	32,8 2,5	31,8 2,2	32,7 2,9	34,5+ 2,5	33,9+ 4,1	35,7 2,6	35,1 2,6	35,0 3,0	35,4 2,5	37,9+ 2,9	37,5+ 2,8
ch—ch*	48,2 3,2	46,6 3,7	45,6 3,2	46,0 4,2	48,1 3,6	49,1 3,4	50,9 2,7	48,8 3,0	48,4 5,0	49,7 3,5	50,6 3,7	50,7 4,8
t—sn—t	272,1 9,2	270,4 10,9	266,0- 12,9	268,5 13,8	271,0 13,0	270,8 11,6	283,3 8,7	282,5 12,1	281,5 17,1	280,7 13,5	283,1 14,6	285,0 14,7
t—gn—t	289,6 10,2	290,4 12,4	287,1 14,3	288,5 16,8	290,4 13,5	289,8 12,3	309,1 11,5	309,7 14,6	309,5 21,8	307,6 14,7	314,1 13,5	313,5 14,4
sa—sba	not own control	59,9 3,7	59,4 3,5	61,0+ 3,8	65,0 4,1	65,1 4,5	not own control	65,3 4,5	66,3 4,2	64,4 4,0	71,5 3,8	68,8 5,0
pra—pa	not own control	31,4* 2,6	31,7* 2,6	31,8* 2,7	34,3 2,7	34,5+ 2,7	not own control	35,2 3,0	35,7 2,3	35,0 2,5	37,2 3,3	36,2 2,8

\* ) not tested because of a different method used for the measurements of controls (or in the dimension pra—pa because of the significant difference between both sides in the compared series described by Hajniš).

## RESULTS

*Dimensions of the neurocranium (Tab. 1—3).*  
The length of the neurocranium of the parents of the probands and of their sibs, i.e. of the 2nd generation is significantly lower compared to the corresponding value in controls. However the difference between control values and those ascertained in grand-parents is not significant. This is probably due to the further slight apposition growth of this dimension with age when it attains in grand-parents almost the size observed in compared controls. A similar apposition growth is less clearly

evident in the width of the neurocranium. Lower values of this dimension were among all groups of relatives ascertained only in parents and in female relatives (with the exception of the father's mother). The cranial base was also significantly narrower in parents and sibs of the mother of the probands, while the minimum width of the forehead, with the exception of one case, showed no deviations from normal. When the described significant differences are expressed in terms of the standard deviation from the corresponding group of controls it amounts regularly to 0.4—0.8 SD, which is in practice negligible. These findings are illustrated

on table 2 (those cases where the deviation attains approximately 1 SD are marked on Tab. 1). The circumference of the neurocranium is also slightly smaller in parents seen in the genetic consultation, however, the difference is not statistically significant (Tab. 3).

*Facial dimensions (Tab. 1, 2).* The significant difference in the bizygomatic width in fathers of the probands and in the bigonial width in mothers are rather an exception. On the contrary it was possible to ascertain some variations of the vertical dimensions of the face. The differences of the total height of the face are not significant, but there is mostly an increase of the height of the upper portion of the face and often equally of the height of the nose. Compared to the controls the differences attain, however, equally only 0.4–0.8 SD.

Among the other investigated features some deviations of the width of the nose were observed. The mean values are significantly higher in grand-parents of the proband, while there was only a little difference in the 2nd generation. This is due to the slight growth of the width of the nose in adults resulting in a wider nose in grand-parents, as is shown in Tab. 2. A similar dependence was found in the oral slot and thus both features are not considered as significant in the investigated connections. The distance between the inner and outer canthi equally does not differ from the values in controls, with the exception of the intercanthal width in mothers. Thus it is not possible to conclude that the relatives of cleft children show a tendency towards a widening of the interocular distance (Figalová, Šmahel, 1971).

Facial arches show no changes in spite of the somewhat lower mean values of the subnasal arch in the second generation compared to control (the change is significant in a mother's sister), indicating a flattening of the maxilla. But for occasional exceptions there are no deviations of the auricular dimensions; there is however a strong dependence on age (compared with the data reported by Hájniš, 1969).

*The indexes (Tab. 1).* No changes in the proportions of the neurocranium and of the face were demonstrated in parents and in other relatives of cleft children (only the above mentioned deviations of the height and width of the nose are reflected sometimes by the values of the nasal index).

*Comparison according to the type of cleft.* The described smaller dimensions of the neurocranium are not pronounced in relatives of probands with cleft lip, while this trend is obvious in the two other groups (cleft palate, cleft lip + palate). Signs of an increase of vertical dimensions of the central portion of the face are present in families with all types of clefts, however because of the small numbers of cases there are only a few significant results. On the contrary changes of the width of the nose were found practically only in relatives of probands with cleft lip and palate, but they were limited equally to the first generation with a wider nose. In the same type of clefts, i.e. in the most severe form, all groups of relatives had a smaller sub-

TAB. 3 *The circumference of the neurocranium in parents of cleft children (a series seen at the genetic consultation; all types of clefts conjunctly).*

	n	$\bar{X}$	SD	t-test
mother	23	545,0	18,3	1,81 not significant
control	50	552,6	12,6	— (but smaller)
father	21	566,3	14,4	0,84 not significant
control	50	569,3	12,2	—

nasal arch. This reduction was significant in four cases. These data are included into Tab. 1 and are suggestive of a flattening of the maxilla.

No proportional deviations were found in relatives of children with cleft lip, while in several groups of relatives of probands with cleft palate the calculated indexes showed significant differences (more frequently in isolated cleft palate than in combined cleft lip + palate). The frequency of these findings was low, however, and thus they represent only occasional, even though not very rare exceptions. Compared to the controls the slightest changes in general were observed in families with isolated cleft lip, but this could be due to the smaller numbers of individuals within these groups (in spite of the highest frequency of families with this type of cleft, the lowest numbers of relatives responded to the invitation for examination, which was most probably due to the fact that it represents the slightest type of malformation). However, the groups of relatives of children with isolated cleft palate, which were even smaller in number, showed significant differences in a higher frequency than in all other types of clefts included in our comparison.

*Comparison according to the coefficient of relationship (Tab. 1).* Parents ( $r = 0.5$ ) showed regularly smaller dimensions of the neurocranium with the exception of the bifrontotemporal width. Compared to the other relatives of the 2nd generation ( $r = 0.25$ ) these differences however are not substantial. Of the facial dimensions the increased interocular distance in mothers is worth mentioning. The width of the nose was not increased in parents of the probands. This finding is in agreement with the above discussed little importance of this feature for the purpose of our study. The reduced bizygomatic width in fathers and bigonial width in mothers, together with the ascertained dimensions of the neurocranium may indicate that these individuals were of smaller stature. This finding is due to the composition of the examined series rather than to characteristics of the population with clefts. In various groups of relatives no gradation of facial features according to the degree of kinship was found.

*Comparison of the 1st and 2nd generation (Tab. 2).* The comparison of the two generations disclosed

that some craniofacial dimensions continue to increase with age in adults. This has the opposite effect as the simultaneous secular trend. Even though these changes are small they should be taken into account during the evaluation and testing of the results obtained. They provide equally evidence that it is necessary to use a group of controls of an adequate age. The maximum length of the neurocranium increases by apposition while both the width of the neurocranium and the minimum width of the forehead show no changes of this type. This could possibly explain the lower values of the cephalic index reported in old individuals. The values of the bitragic distance are equally distinctly higher in grand-parents than in parents. This is most probably due both to the accumulation of fat and to the growth of the cranial base.

The characteristics of facial heights show no changes, while the width of the mandibular angle, and to a lesser degree also the bizygomatic width are increasing (most probably by appositional growth). No differences of the distance between the inner and outer canthi were found in the compared generations, while, the width of the nose and of the oral slot showed a significant increase. With regard to the standard deviation, contrary to expectation, facial arches showed only minor deviations which could be due to the amount of subcutaneous fat tissue. The dimension of the pinna showed a significant increase. The discussed changes were reflected, conceivably, by the values of the pertinent indexes, in particular by the higher values of the nasal index and by the somewhat lower mean values of the cephalic and facial indexes in the older generation. The differences between generations can be found in table 2 and their degree can be estimated by the comparison with controls according t-test, or by means of the standard deviation.

## DISCUSSION

Of the deviations investigated within the scope of our study we consider as particularly important with relation to clefts the increase of vertical dimensions of the central part of the face and the reduction of the subnasal arch. The first characteristic was ascertained in the series as a whole, as well as in groups of relatives subdivided according to any type of cleft which was present in individual patients. The latter was present only in relatives of children with cleft lip and palate. A significant increase of the interocular distance in mothers does not allow any definite conclusions because of its occurrence only in the above mentioned group (after the subdivision of the group according to the type of cleft a significant difference was recorded only in mothers with cleft lip). Proportional deviations characterized by the values of indexes were present in several groups of relatives of patients with palatoschisis and only occasionally in families of children with cheilognathopalatoschisis (they were not demonstrated in probands with cheiloschisis and in the series as a whole). This finding together with the smaller subnasal arch and, eventually, with an

increased interocular width which were recorded in some groups of relatives of children with cleft of the primary palate provided the possibility to discriminate within the scope of our study between the 1st and 2nd genetic group of clefts and justified the hypothesis proposed by Fraser (on the predisposition to clefts of the 1st genetic group, i.e. to cleft lip  $\pm$  palate).

The ascertained significant differences differed mostly from controls by 0.4—0.8 standard deviations, only very rarely by 1 standard deviation (see table 1). Thus they are of no use in practice (e.g. in genetic counselling). The comparison of the dimensions obtained after the subdivision of the series according to type of cleft indicated that relatives of probands with palatoschisis have more gracile face which is often described in these patients (and which might be due to hereditary transmission to a certain degree linked with clefts). In the other significant deviations, than those discussed above, it is not possible to consider a direct relation to clefts. The width of the nose, of the oral slot and the dimensions of the pinna are in the first place dependent on age; smaller dimensions of the neurocranium are due rather to the composition of the investigated series as it was already mentioned above.

Among the reports in the literature dealing with these subjects Pashayan, Fraser (1969) and Fraser, Pashayan (1970) described the results of an examination of 25 parents of children with cleft lip  $\pm$  palate. Compared to controls these individuals had a more marked flattening of the maxilla, higher values of facial height and width and a thinner and less prominent upper lip, as well as a higher frequency of a trapezoid and rectangular shape of the face. Coccaro and his co-workers (1972) ascertained during their roentgenoccephalometric studies of 20 fathers and 20 mothers of children with cleft lip and palate compared to controls that the parents of cleft children had a less convex facial profile with a tendency toward mandibular prognathism, smaller vertical dimensions of the upper part of the face, reduced antero-posterior dimensions of the palate and a smaller length of the nose. Erickson (1974) found in sibs of children with clefts of the primary palate ( $\pm$  secondary palate), deviations of the form of the palate, of the dental arch and of the facial profile (a lesser prognathism) compared to the general population of children (he evaluated casts and profile photos of 53 probands and of 40 controls).

Because of the differing methods and items the results of individual studies are not fully comparable. A consistent finding represents the flattening of the maxilla reported by Fraser and Pashayan (1970). This is in agreement with the less convex profile of the face described by Coccaro et al. (1972), with the reduced profile angle reported by Erickson (1974) and with the smaller subnasal arch ascertained in our study. The latter quoted author mentions the results obtained by Dixon, who observed equally a relative maxillary hypoplasia in parents of cleft children.

The statements on deviations of vertical facial dimensions vary in individual studies. The increased height and width of the face in the series of Fraser and Pashayan (1970) provides evidence of symmetrical changes of these characteristics (the serie could possibly consist of individuals of more than average stature), while on the contrary disordered proportions could be considered of importance in the relation to the inborn defects, and could be utilized in practice (the relations between individual characteristics are inherited to a greater extent than their absolute size).

On the basis of the above mentioned findings it is recommended to devote in the future more studies to the investigation of the profile and of the vertical dimensions of the face which might show significant deviations. Moreover special attention should be paid to the central part of the face and to the interocular distance. The increase of the latter is associated in affected children always with cleft of the primary palate — Dahl (1970) and Figalová et al. (1974). A technique for an individual assessment of the interocular distance is proposed in another report by Šmahel and Figalová (1975). For the verification of the proposed hypothesis it would be necessary to study separately families with a familial occurrence of clefts, as well as to use some additional methods (especially studies of facial physiognomy and topography). At the same time it is obvious, however, that the results obtained should be interpreted with caution since it might always be possible to disclose occasionally significant differences in any individual characteristic. The literature contains, so far, no reports on the examination of other relatives than of the next to kin (parents and sibs), or on the demonstration of gradation of deviations from normal situation according to the degree of relationship. Thus the presented results might be regarded as assumption, with the exception of the flattened maxilla which was mentioned consistently in all reported studies. Further it would be necessary to state accurately the age distribution of the compared series, since some dimensions show signs of a continuing slight growth even in adult and old age. The use of sufficiently large series would provide equally the possibility to avoid errors due to random selection.

The comparison of mean values ascertained in generation of parents with those found in grandparents served for the evaluation of characteristics undergoing changes with age in adults. There is a significant growth of the dimensions of the pinna, as well as of the width of the nose and of the oral slot. By appositional growth are increasing: the length of the neurocranium, the width of the mandibular angles and to a slighter extent equally the width of the face. Changes of other dimensions are believed to be due to the accumulation of fat (facial arches and in combination with growth equally the bitragic distance). Vertical dimensions of face were constant (the devastation of teeth and the atrophy of the jaws might lead to their reduction in old age).

In agreement with our findings Hajniš (1969) demonstrated that the pinna continues to grow until very old age, and Suchý (1967) mentioned a relatively narrow neurocranium and a wider nose in old individuals. We have observed in our series that of the other characteristics the oral slot (in agreement with Vondráček, 1927) and the bigonial distance continue to increase. The difference of the first dimension between the 1st and 2nd generation ranged from 1 to 3.5 mm. The tests showed regularly that this increase was statistically significant (with the exception of the mean value recorded in mother's brother — tab. 2). The results of the t-test disclosed that the difference of the second characteristic between the groups of relatives of the 1st generation and of the 2nd generation often attains the significance level (seven out of 12 tested combinations were significant). The degree of all differences is evident from tab. 2.

#### SUMMARY

The hypothesis that the shape of the face could serve as the marker of a genetic predisposition to cleft of lip was tested in a series of 571 normal relatives of children with cleft lip and/or palate, by cephalometric studies. The comparison with controls revealed increased vertical dimensions of the central part of the face and a flattened maxilla. The differences of the other investigated characteristics were not considered as significant within the scope of our study. An increased interocular distance was found only in mothers of the probands and therefore do not justify any definite conclusions. The indexes provided no evidence of any craniofacial shape deviations from normal in the series of relatives of cleft children as a whole. All significant differences were regularly within the range of 0.4—0.8 standard deviation compared to controls and thus are of no use in practice (genetic counselling). No gradation according to the degree of relationship was observed in any of the demonstrated deviations. The differences related to clefts of the 1st and 2nd genetic group were limited to the subnasal arch and to the indexes and did not concern vertical dimensions of the face. The demonstration of a flattened maxilla is in full agreement with previously reported findings.

The comparison of mean values of individual craniofacial characteristics in the generation of parents with those obtained in the generation of grandparents provided the possibility to identify those characteristics which undergo in adults changes with age. The dimensions of the pinna, the width of the nose and of the oral slot showed signs of significant growth. An increase by apposition occurred in the length of the neurocranium, the width of the mandibular angles and to a slight degree in the width of the face. An accumulation of fat may result in changes of some other dimensions, as the facial arches and in association with the growth of the cranial base also the bitragic distance. The reported results demonstrate the necessity to use for the comparison and testing groups adequately matched for age.

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