Birth Variables and the Incidence of Cleft Palate: Part I

RICHARD F. DONAHUE, Ph.D.
Denver, Colorado

It was the purpose of this research to study in a very large human population some of the variables which may be related to incidence of cleft lip and/or palate.

Method

The investigation (*3*) was based on 5,838,855 birth records obtained from 17 state departments of vital records and statistics. Information for these records was obtained, in most cases, from the attendant at the birth who was responsible for the accuracy of the data on the birth certificate. From the 5,838,855 records, 6,070 infants with cleft lip and/or palate were identified. A control group was arbitrarily selected by taking the record fifth in order after the cleft birth record appeared. If the fifth record also noted a cleft, the sixth was used for control. The data were stored and analyzed by electronic computer systems. States were selected for the investigation on the basis, generally, of whether or not they noted cleft palate specifically on the birth record and, in the same way, the number of years surveyed in each state was determined by how long such information had been reported in that state.

Variables for Study

Factors were selected for study on the basis of two criteria: apparent significance of the variable to the etiology of cleft palate, and the number of birth records on which this significant variable was included. A total of 18 were selected; they were arbitrarily divided into three groups, generally depending upon the apparent temporal influences important in their determination: a) variables determined at conception (sex, color, plurality, maternal age, paternal age, birth order, and maternal nativity), b) variables related to gestation (length of pregnancy, associated anomalies, classification of cleft, complications of pregnancy, and prenatal care), and c) variables related to birth (geographical location, urban-rural location, legitimacy, month, weight, and attendant). This report concerns data for the *first* group of factors.

Dr. Donahue is associated with the University Park Psychological Center, Denver.

Results and Discussion

Although it is generally agreed that factors which operate initially at the time of birth have no influence on the occurrence of oral clefts, the variables considered in this report (with the exception of attendant) may exert some influences during gestation. They have been listed in this group to emphasize that the information obtained relates only to the immediate status at birth. In other words, the information obtained has to do with location, time, weight, and legitimacy at the moment of birth and, therefore, is not entirely reliable when applied to variables present at the time of oral cleft determination. The attendant factor is important only as a validity measure in the recognition and reporting of the malformation.

Geographical Distribution. A total of 17 states was included in this investigation, representing various geographical divisions of the United States. Although the study was not designed to randomly sample the births of normal and cleft children in the entire United States, it was anticipated that an adequate sample would be obtained from each of the several areas included. Presented in Table 1 are rates of incidence for each of the 17 states used for the study. The highest incidence is in Montana (1:624) and in North Dakota (1:657); the lowest incidence is in South Carolina (1:1681) and in Tennessee (1:1558). The low incidence

TABLE 1. Incidence of clefts according to state.

State	*Years of Data Available*	*Total Births*	*Cleft Births*	*Incidence*
Colorado	2	81,466	105	1:929
Indiana	5	570,501	723	1:789
Iowa	4	248,664	329	1:756
Michigan	2	400,481	480	1:834
Missouri	9	793,178	899	1:704
Montana	6	104,227	167	1:624
Nebraska	10	340,220	353	1:992
New Mexico	11	270,143	218	1:1239
North Dakota	3	49,313	75	1:657
Oregon	4	147,843	133	1:1112
Pennsylvania	1	249,600	292	1:854
South Carolina	10	681,003	405	1:1681
South Dakota	10	180,022	182	1:989
Tennessee	9	704,328	452	1:1558
Vermont	10	82,608	101	1:817
Washington	10	636,768	827	1:770
Wisconsin	3	288,430	329	1:876
Total		5,838,855	6,070	
Mean	6.41			1:929

TABLE 2. Sex distribution for the control and cleft groups.

Sex	*Control*		*Cleft*	
	N	%	*N*	%
Male	3,051	50.3	3,643	60.2
Female	3,019	49.7	2,427	39.8

of cleft palate in Tennessee and South Carolina probably relates to the proportionately higher incidence of colored births (see Table 4). In addition, there may be a relationship between the variable of attendant at birth and the incidence of cleft palate. Tennessee and South Carolina have the highest percentage of births attended by nonmedical persons, and there may be a problem of recognition not only for cleft palate but for other congenital malformations as well.

SEX. Table 2 presents data for sex distribution for control and cleft samples. There were 3,643 males born with cleft lip and/or palate in the experimental group and 2,427 females, a difference of 20.4%. The control group consisted of 3,051 males and 3,019 females, a difference of 0.6%.

Presented in Table 3 are data for the comparison of sex distribution between the results of this and other studies. It can be seen that the percentages of male and female cleft palate cases are fairly constant among the various investigations, varying between 66.9% males in the Kessler study (*8*) and 59% males in the Schwartz research (*24*).

Apparently there are two explanations for the predominance of cleft palate in males: a) the concept of the malformation as a sex linked hereditary characteristic with male dominance as proposed by Beder and associates (*1*), Mazaheri (*13*), Oldfield (*19*), and Fogh-Anderson (*5*), and b) the selective action of environmental insults to the male in utero as suggested by Palmer (*20*), Vaughan (*28*), Schwartz (*24*), and Lutz and Moor (*11*).

COLOR. The amount of information pertaining to racial background

TABLE 3. Comparison of sex distribution of clefts from eight investigations.

Investigator	*Year*	*Male*	*Female*
		(*in per cent*)	
Haug (*6*)	1904	64.3	35.7
Fogh-Anderson (*5*)	1939	62.0	38.0
Sanders (*23*)	1943	61.5	38.5
Hixon (*7*)	1951	63.0	37.0
Kessler (*6*)	1951	66.9	33.1
De Voss (*2*)	1952	62.0	38.0
Schwartz (*22*)	1954	59.0	41.0
Present study	1961	60.2	39.8

TABLE 4. Data regarding distribution by state and color for control and cleft groups, in per cent of total births.

State	*Control*		*Cleft*		*Difference between control white and cleft white*
	White	*Nonwhite*	*White*	*Nonwhite*	
Colorado	90.4	9.6	96.1	3.9	1.3
Indiana	91.9	8.1	97.4	2.6	5.5
Iowa	98.6	1.4	99.1	0.9	.5
Michigan	88.6	11.4	96.9	3.1	8.3
Missouri	86.3	13.7	96.9	3.1	10.6
Montana	93.8	6.2	90.1	9.9	3.7
Nebraska	96.0	4.0	98.3	1.7	2.3
New Mexico	88.0	12.0	89.0	11.0	1.0
North Dakota	96.7	3.3	97.3	2.7	.6
Oregon	97.3	2.7	98.5	1.5	1.2
Pennsylvania	89.8	10.2	96.2	3.8	6.4
South Carolina	55.5	44.5	82.3	17.7	26.8
South Dakota	92.7	7.3	94.0	6.0	1.3
Tennessee	78.5	21.5	93.4	6.6	14.9
Vermont	99.7	0.3	100.0	0.0	.3
Washington	94.7	5.3	96.9	3.1	2.2
Wisconsin	96.3	3.7	98.1	1.9	1.8
Total Sample	90.4	9.6	96.1	3.9	5.7

varied among states, with the most prevalent categories being 'white' and 'nonwhite'. The category 'white' includes, in addition to persons reported as Caucasian, those reported as Mexican or Puerto Rican. The category 'nonwhite' consists of persons reported as Negro, American Indian, Chinese, Japanese, and other numerically small groups.

There were 5,833 white children born with cleft palate in the present experimental group and 237 nonwhite. The control group consisted of 5,487 white children and 583 nonwhite. In terms of percentages, 96.1% of the experimental group was composed of white cleft palate babies. Whites accounted for 90.4% of the control. That difference was significant. Data are presented for color reported for the infant in Table 4, which indicate that about four out of every 100 cleft palate births are nonwhite, while the ratio is 10 in 100 for nonwhite births in the control group.

Many investigators, notably Lutz (*10*), Schwartz (*24*), Lutz and Moor (*11*), Krantz (*9*), Vaughan (*28*), and Shapiro and associates (*25*) have studied the factor of race in the occurrence of congenital anomalies. Generally, Caucasian births were found to be significantly related to the occurrence of cleft palate in the studies dealing with this anomaly (*10, 11, 24*).

Although there is no statistically significant difference between color categories in Montana, there is an interesting deviation from the pattern found in other states in that sample. That deviation has been referred to

previously by Tretsven (*27*). In Montana, the nonwhite category increased from 6.2% in the control group to 9.9% in the cleft palate group. In every other state, however, the percentage of nonwhite decreased from the control to the experimental groups. Since 5.6% of Montana's total births are Indian, only 0.6% makes up the difference in the nonwhite category. It might be hypothesized that, because there are more nonwhite records in the experimental group, the Montana Indian is responsible for the increase in relative cleft palate incidence.

The determination of race is a complex problem, as difficulties result from varying registration and enumeration methods used in collecting this information. The procedures used in completing vital statistics records result, in general, in an entry of race on the certificate that is acceptable to the family. Race reported in the census of population is recorded on the basis of observations by the enumerator. Serious differences arise in the racial classification of Indians, as well as of the others in the nonwhite group. Where Indians live among the general population, census figures are lower than those estimates made by the Bureau of Indian Affairs.

Observed differences in vital statistics for various racial groups should not be interpreted as necessarily due to inherent racial causes. Race is not independent of other variables and the economic, social, and medical circumstances of one racial group may be quite different from those of another. For example, an observed difference in mortality by race may in actuality be no more than a difference of mortality for different economic classes. For incidence of cleft palate, however, where the apparent optimal socioeconomic factors relate to a higher incidence of the abnormality, the observed difference in incidence is felt to be more dependent upon racial factors than economic variables.

Several other factors also relate to the color. For example, there is a strong geographical influence on color ratios, with most colored births occurring in the southeastern part of the country and in large cities in the remainder of the United States. Maternal age and birth order relate to the color variable since colored mothers are, on the average, one year younger than white mothers when their first child is born (*17*).

Plurality of Birth. During the past 10 years, the number of plural births in the United States has increased from 36,819 in 1949 to 43,793 in 1960. In 1958, for example, a total of 4,161,513 confinements resulted in 4,117,202 single live births and 86,610 live births from plural sets (*17*). In 1958 the total number of plural cases in which at least one member was born alive and for which all matching records for births or fetal deaths were found was 43,741. Of this group, twin sets accounted for 43,360; triplets, 375; and quadruplets, 6. In 1949 there were 10.4 plural cases per 1,000 total confinements resulting in at least one live birth. This national rate varied during the period of this research between 10.4 in 1949 and 10.9 in 1955. The rate was lowest among the youngest age group of mothers and rose with each successively older age group to

TABLE 5. Plurality of birth for control and cleft groups.

Type of birth	*Control*	*Cleft*
Plural	59	115
Single	5,187	5,131
Percentage	1.1	2.2

a peak of 15.3 among those 35 to 39 years old. The proportion of plural births was higher among confinements of the nonwhite than the white in nearly every age group in both the national averages and in the control group used in this study (*17*).

Data for plurality of birth are reported in Table 5. There were 115 cases of plurality in the cleft palate group and 5,131 single births, an incidence of 2.2% plural births in the experimental group. The control group consisted of 59 plural cases and 5,187 singletons, an incidence of 1.1% plurality. The difference between the two groups was significant, indicating that significantly more plural births are associated with cleft palate births than single births.

Steigler and associates (*26*), Murphy (*16*), Palmer (*20*), and Phair (*22*) have reported a relationship between oral clefts and multiple births. Douglas (*4*), taking issue with Metrakos, Metrakos, and Baxter (*15*), emphasized the role of environmental factors in the determination of cleft palate. In both of the studies (*4, 15*) data were obtained from comparing monozygotic and dizygotic twin sets. It is felt that a relationship may exist between plurality and associated anomalies, birth weight, and complications of pregnancy. It is beyond the scope of this study to explore those possible relationships. Generally, the results obtained in this research support the previous investigations.

MATERNAL AGE. Data regarding maternal age are reported in Table 6. Among all women, cleft and control groups combined, the most fertile ages in the period covered by this investigation were 20 to 24 years. More than one out of four women in this age category bore a child during this period. The next most fertile age category was 25 to 29. Ranking third and fourth, according to this measure of fertility, were women 30 to 34 years and 15 to 19 years, respectively. Of the 5,775 controls 34.8% of the

TABLE 6. Data regarding maternal age for control and cleft groups.

Group	*Total*	*Age of mother categories, in years*							
		10–14	*15–19*	*20–24*	*25–29*	*30–34*	*35–39*	*40–44*	*45–49*
Control	5,775	6	699	2,013	1,585	868	482	116	6
%	100	0.1	12.3	34.8	27.1	15.7	8.0	1.9	0.1
Cleft	5,777	8	728	1,872	1,458	992	549	155	15
%	100	0.1	12.6	32.4	25.2	17.1	9.5	2.8	0.3

births occurred in the maternal age category 20 to 24, while in the 5,777 clefts the percentage of births was 32.4% in the same maternal age category. The difference in per cents was significant; there is a significantly greater number of older mothers in the experimental group than in the control group.

There is a great deal of disagreement in the literature on the subject of maternal age influence on the incidence of cleft palate. Malpas (*12*), Vaughan (*28*), Murphy (*16*), Phair (*22*), and Mazaheri (*13*) report a positive relationship between the occurrence of oral clefts and advanced maternal age.

Several other investigators (*2, 5, 14, 18, 20, 21, 25*) have suggested that the slight differences which exist in maternal ages between cleft palate and noncleft palate samples are not significant or are even nonexistent.

PATERNAL AGE. Data regarding paternal age are reported in Table 7. Among all men the most fertile age category during the period covered by this investigation (as in recent years throughout the United States in the general population) is from 25 to 29 years. More than one out of four men in this category fathered a child during this period. Ranking second and third, according to this measure of fertility, were men 20 to 24 years and 30 to 34 years, respectively.

Distribution of paternal age for control and cleft groups is quite similar. The greatest difference is in the older categories (40 and older). Whether this relative increase in occurrence of cleft palate births is a function of the father's age or is merely a reflection of the probability that the older mothers had older husbands is difficult to say.

Advanced paternal age and differences in parental ages are occasionally mentioned in the literature. McEvitt (*14*), Fogh-Anderson (*5*), Mazaheri (*13*), and Peer and associates (*21*) felt that the age of the father is of little consequence in the etiology of cleft palate. Murphy (*16*), however, suggested that a relationship exists between the incidence of all congenital malformations and the age of the father.

Differences in parental ages have been examined by Murphy (*16*), who suggested that parental age difference is not an etiological factor in cleft palate.

TABLE 7. Data regarding paternal age for control and cleft groups.

Group	*Total*	*Age of father categories, in years*									
		15–19	*20–24*	*25–29*	*30–34*	*35–39*	*40–44*	*45–49*	*50–54*	*55–59*	*60–*
Control..	4,306	123	986	1,256	874	649	294	85	25	10	4
%.....	100	2.8	22.7	29.1	20.7	15.1	6.9	1.9	0.4	0.2	0.1
Cleft....	4,306	119	956	1,192	945	607	302	121	40	12	12
%.....	100	2.7	22.2	27.7	21.9	14.0	7.1	2.8	0.9	0.3	0.3

TABLE 8. Birth order for control and cleft groups.

	Total	Birth order						
		1st	2nd	3rd	4th	5th	6th, 7th	8th, higher
Control.....	4,308	1,180	1,111	838	504	279	250	146
%.....	100	27.4	25.8	19.2	11.8	6.5	5.8	3.5
Cleft.....	4,647	1,129	1,039	987	647	376	306	163
%.....	100	24.3	22.4	21.2	13.9	8.1	6.6	3.5

BIRTH ORDER. In recent years a trend for larger families has been observed. In 1960, 50% of all births were first and second children compared with 62% in 1950. Fourth and higher order births now represent 28% of the total compared with only 21% eight years ago.

Presented in Table 8 are data for birth order of cleft and control subject groups. There were significantly more cleft palate births in the upper birth orders (third or greater). This may be a function of maternal age or paternal age, or it may be a real difference in birth order itself.

There is a disagreement in the literature on this variable; Oldfield (*19*) found 2% more clefts in the first born, while Mazaheri (*13*) discovered significantly more (.05 level of confidence) cleft palate births in later pregnancies. According to Mazaheri, there is a 'strong relationship' between birth order and maternal age.

Murphy (*16*) and Phair (*22*) mentioned the increased incidence of malformations in later birth orders, while Palmer (*20*) found the difference to be significant between birth orders.

Summary

A total of 5,838,855 birth records were obtained from 17 state departments of vital records and statistics. From the group, 6,070 infants with cleft lip and/or palate were identified. A control group was selected by taking the record fifth in order after the record for the cleft birth appeared. Comparisons between the two groups were made for sex, color, plurality of birth, maternal and paternal age, and birth order.

University Park Psychological Center
2343 East Evans Avenue
Denver, Colorado

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