Utilization of Birth Certificates in Epidemiologic Studies of Cleft Lip and Palate

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The limitations of birth records as sources of information about the biological or demographic characteristics of newborn babies and their parents have been discussed by several authors (*1*, *6*, *8*, *10*). Every person familiar with vital statistics is aware of at least some of the analytical problems which result from the incompleteness, inaccuracy, illegibility, and unintelligibility with which information often is recorded on birth certificates.

Instead of trying to add to the list of indictments against birth records, we should like to take a more positive approach and describe some of the work we have done and are doing with birth certificates at the Dental Health Center. We believe that we can demonstrate that these records serve as an important source of data for epidemiologic studies, in spite of all the problems associated with their use.

Development of the National Cleft Lip and Palate Intelligence Service

Three years ago at the Dental Health Center cleft lip and palate investigations were begun with a study based on certificates of live birth recorded in four states over the five-year period, 1956 through 1960. That study (*4*), published in 1964, included 4,451 babies with cleft lip or palate and a one-half percent sample of all live births (17,859) as a group against which to compare characteristics of the babies born with clefts. The study provided a large number of cleft lip and palate cases and made it possible for appropriate data to be analyzed on the basis of cleft type, parental age, race, birth order, occupation of father, birth weight, length of gestation, and other variables. However, the number of cases was not large enough and the number of states

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represented was not adequate for a satisfactory analysis to be made of certain other variables. For example, little was learned about the relative frequency of cleft occurrences in specific racial mixtures, about parental age disparity and its possible relationship to the occurrence of clefts, or about the geographic distribution of clefts. In addition, the study was not designed to provide information about other malformations which may be associated with clefts.

Even before the four-state study was completed, plans were made to obtain birth certificates from a broader geographic area of the United States and to analyze the data derived from them on a continuing basis or until such time as the effort became unproductive. It also was decided that plans should be made for field studies of cleft lip and palate which would not rely on the birth record as a primary source of data but which might be based on hypotheses which grew out of the birth certificate study. To carry out these activities, the National Cleft Lip and Palate Intelligence Service, or NIS, was established at the Dental Health Center in 1963. The expanded birth record study, with which this report is concerned, is only one part of the NIS program and was the first element of the program to be initiated. Other elements are currently in the planning stages.

The birth record study component of the NIS was begun in January 1963. The National Center for Health Statistics (NCHS) of the Public Health Service and the health departments of 29 states and two cities on whose birth certificates are recorded descriptive data regarding congenital malformations are cooperating in the study. The participating birth registration areas are shown in Figure 1. Arrangements were made

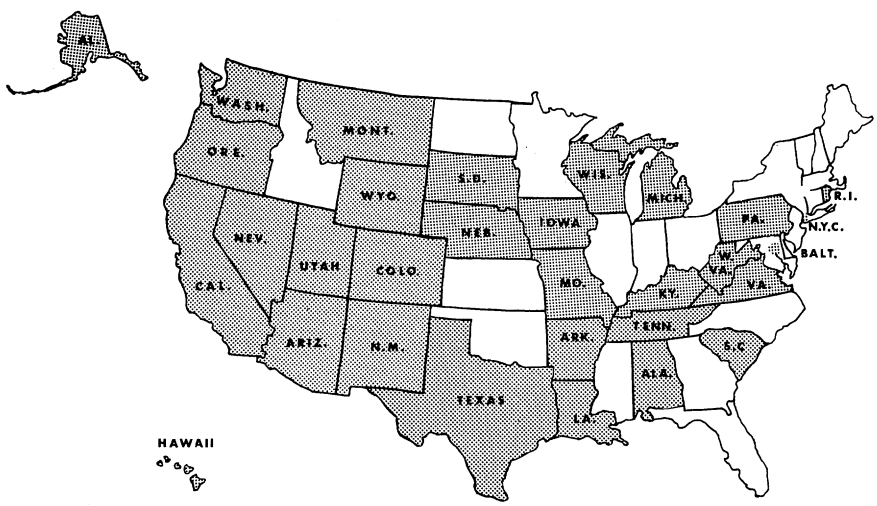

FIGURE 1. Birth registration areas participating in the national cleft lip and palate intelligence service.

with the NCHS to obtain from the 31 participating areas copies of all certificates of live birth on which a congenital malformation of any kind was recorded. Arrangements also were made to obtain a one percent systematic sample of all live birth certificates filed in these jurisdictions to serve as a comparison or control group. This control group consists of every certificate whose state file number ends in the digits 00. If a malformation is recorded on a selected control certificate, the next succeeding certificate is selected as a control. The Division of Vital Statistics of NCHS agreed to accept responsibility for screening microfilms of live birth certificates, for making photocopies of the selected certificates, and for routing the photocopies to the Dental Health Center with as little delay as possible. Certificate copies for 1963 births began arriving at the Dental Health Center in May 1963. By August 15, 1964, all of the 1963 certificate copies had been received and processed, and nearly 20% of the expected 1964 certificates had been received.

To date, special analyses of the data by economic sub-region, estimated date of conception, and by other variables have shown nothing remarkable though they have provided much interesting and perplexing information. Small numbers and lack of similar data for earlier years have contributed to the inability to produce significant results so early in the study.

This report, therefore, is not meant to be an exhaustive presentation of important research findings. Rather, it is a description and discussion of recently acquired data which exemplify types of information which can be obtained from live birth certificates, and which we at the Dental Health Center believe will markedly affect the direction of our epidemiologic research program in cleft lip and palate.

Findings and Discusion

On July 1, 1964, the cut-off date for data included in this report, birth certificates for 18,234 malformed babies and 19,654 controls, representing 1,965,400 live births in all participating areas except Nevada and Missouri, had been processed by the NIS. These records account for 83% of the total birth certificates received from the NIS reporting areas for the year 1963.

The findings presented in this paper are related primarily to clefts of the lip and palate. Findings related to other selected congenital malformations also are presented in order to make contrasts and comparisons to clefts. The other malformations selected for such comparisons are the following: anencephaly, spina bifida, hypospadias, mongolism, positional foot defects, polydactyly, and reduction deformities. Principally two criteria were used in the selection of these malformations: a) ease of detection at the time of birth, and b) high frequency of reporting on birth certificates. Naturally, not all of these malformations meet

these criteria with equal precision. For example, anencephaly is more easily detected than mongolism, but the latter is reported almost twice as frequently as the former.

In this report, the term *clefts* includes clefts of the lip, clefts of the lip and palate combined, and cleft palate without cleft lip. In most of the tables which follow, the clefts are separated into these three types. Alveolar clefts and bifid uvulae were not included, nor were ambiguously described anomalies such as possible cleft lip, defect of palate, or spontaneously healed cleft lip, even though many of these defects might indeed have been true clefts. The term *anencephaly* includes cases described as absence of cranial vault as well as those described as anencephaly or anencephalic monster. *Spina bifida* includes cases of spina bifida with or without meningocele or meningomyelocele. *Hypospadias* includes all degrees of hypospadias and the few reported cases of epispadias. *Mongolism* includes cases reported as Down's Syndrome, Trisomy 21, and mongoloid appearance. The category called *positional foot defects* is not easily described because of the difficulties of diagnosing clubfoot at birth and may include some defects which are only transient conditions resulting from the position of the fetus in utero. *Polydactyly* includes fully developed extra digits as well as extra digital tags. The final category, *reduction deformities*, includes absence of bones of the extremities which may range from a single missing distal phalanx to the complete absence of one or more limbs.

RACE. The frequencies with which selected malformations were reported for white, Negro, and other racial groups are shown in Table 1. Approximately 85% of the controls and total malformed babies were born to white mothers, but 93% of the babies reported to have clefts were born to white mothers. By contrast, only 45% of the babies reported to have polydactyly were white. In Table 2 and Figure 2, the relative incidence of each of the selected malformations for Negro and

TABLE 1. Number of controls, malformed babies, and selected congenital malformations by race of mother.

Race of Mother	*Controls*	*Malformed Babies*	*Selected Congenital Malformations*							
			Clefts	*Anencephaly*	*Spina Bifida*	*Hypospadias*	*Mongolism*	*Positional Foot Defects*	*Polydactyly*	*Reduction Deformities*
Total*	19,654	18,234	2,164	439	1,167	1,237	836	2,462	1,736	593
White	16,614	15,592	2,003	403	1,093	1,167	788	2,231	785	510
Negro	2,701	2,334	111	24	54	63	36	203	919	69
Other	327	295	48	11	20	6	11	26	30	14

* Totals include babies with race of mother unknown.

TABLE 2. Relative incidence of malformed babies and of selected congenital malformations by race of mother where incidence in white babies = 1.00.

Race of Mother	*Malformed Babies*	*Selected Congenital Malformations*							
		Clefts	*Anencephaly*	*Spina Bifida*	*Hypospadias*	*Mongolism*	*Positional Foot Defects*	*Polydactyly*	*Reduction Deformities*
White	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Negro	.92	.34	.38	.30	.33	.28	.56	7.23	.84
Other	.96	1.21	1.42	.92	.26	.72	.60	1.96	1.39

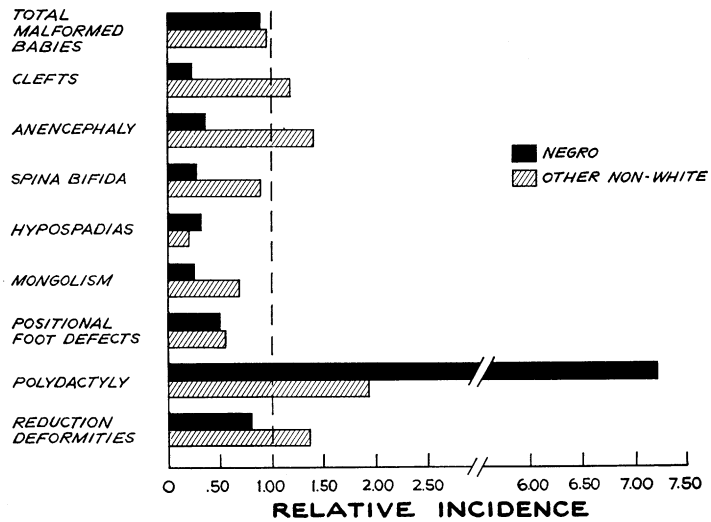

FIGURE 2. Relative incidence of selected congenital malformations among negro and other nonwhite babies where incidence among white babies = 1.00.

other nonwhite babies is presented, using the incidence of each malformation among white babies as the standard. For total malformed babies, the incidence among the Negro and other nonwhite groups is only slightly less than among whites. However, the relative incidence of the selected malformations varies considerably.

The chi-square test was used to test the significance of differences in the reported frequencies of each malformation for whites and Negroes, whites and other nonwhites, and Negroes and other nonwhites. Throughout this report, the term significance indicates statistical significance at the one percent level.

The white-Negro differences were significant for each malformation except reduction deformities. Particularly striking is the high relative incidence of polydactyly among Negroes. The white-other nonwhite

differences were significant only for positional foot defects, hypospadias, and polydactyly. The Negro-other nonwhite differences were significant for each malformation except hypospadias, positional foot defects, and reduction deformities. Only reduction deformities failed to show a significant difference in reported incidence between any of the racial groups.

These variations in the relative frequency with which selected malformations are reported as occurring in various racial groups tend to discount the notion that the difference in the frequency with which facial clefts are reported for Negroes and for Caucasians results only from differences in completeness and accuracy of reporting. It is difficult to believe, for example, that there might be a selection factor at work which would result in a greater proportion of polydactyly malformations than facial clefts being reported for Negroes than for Caucasians. Neel (*9*), reporting on his study of congenital defects in Japan, made similar observations about the variation in relative frequency with which specific malformations occurred, and he interpreted the findings as indicative that different populations have evolved significantly different genetic systems. Of course, the existence of environmental influences cannot be ruled out by such data.

SEX. The sex distribution of the selected malformations is shown in Table 3. For white babies, the sex ratio for each of the selected malformations except mongolism and reduction deformities is significantly different from the expected sex ratio (51:49) based on all live births in 1962 in states participating in the NIS. Among nonwhites, there was a

TABLE 3. Sex distribution of selected congenital malformations among white and nonwhite babies.

Selected Congenital Malformations	*White Babies*						*Non-White Babies*					
	Number			*Percent*			*Number*			*Percent*		
	Total	*Male*	*Female*	*Total*	*Male*	*Female*	*Total*	*Male*	*Female*	*Total*	*Male*	*Female*
Total Clefts	2003	1167	836	100.0	58.3	41.7	159	74	85	100.0	46.5	53.5
Cleft Lip	539	336	203	100.0	62.3	37.7	41	16	25	100.0	39.0	61.0
Cleft Lip & Palate	842	561	281	100.0	66.6	33.4	71	34	37	100.0	47.9	52.1
Cleft Palate	622	270	352	100.0	43.4	56.6	47	24	23	100.0	51.9	48.9
Anencephaly	403	155	248	100.0	38.5	61.5	35	21	14	100.0	60.0	40.0
Spina Bifida	1093	478	615	100.0	43.7	56.3	74	40	34	100.0	54.1	45.9
Mongolism	788	374	414	100.0	47.5	52.5	47	23	24	100.0	48.9	51.1
Positional Foot Defects	2231	1260	971	100.0	56.5	43.5	229	120	109	100.0	52.4	47.6
Polydactyly	785	484	301	100.0	61.7	38.3	949	533	416	100.0	56.2	43.8
Reduction Deformities	510	289	221	100.0	56.7	43.3	83	49	34	100.0	59.0	41.0

significant difference only for polydactyly. The difference between whites and nonwhites in the proportion of males in each malformation group is significant for total clefts, for cleft lip, and for cleft lip and palate combined.

The sex distribution, by type of cleft, shown for the white babies follows the pattern well established by other studies (*2*, *3*, *4*). Each of these studies has shown that more clefts of the lip occur in males, but more clefts of the palate occur in females. These studies also have shown that when clefts of all types are combined, the majority of them are in males. The different patterns shown here for nonwhites, though it may result only from the small sample, is of interest and bears watching as additional nonwhite cleft cases are reported to the NIS. Because so few nonwhite cases are included in the NIS data at this time, the remaining discussion will focus only on babies born to white mothers.

ASSOCIATED MALFORMATIONS. Of particular interest in our investigations are the frequency with which the various types of clefts were reported to have occurred with other malformations and the types of malformations which commonly occurred with clefts. For all malformed babies, 1.2 malformations per baby were reported. The proportion of babies born with cleft lip or palate who have at least one other malformation is shown in Table 4. The values are lowest for cleft lip alone (8.2%), greater for cleft lip and palate (13.9%) and greatest (27.3%) for cleft palate. These figures compare favorably with those reported in our four-state study. The five malformations reported with clefts with the greatest absolute frequency were positional foot defects, other and unspecified malformations of the extremities, polydactyly, circulatory defects, and deformed ears. Taking into account the expected frequencies of the malformations based on overall reported incidence of malformations among all live births, nearly all malformations were reported relatively more frequently among babies with clefts. The following defects were reported with the greatest relative frequency: micrognathia; defects of the eye (including microphthalmos, anophthalmos, congenital

TABLE 4. Proportion of babies (white only) born with clefts of lip and palate having other congenital malformations, by type of cleft.

Type of Cleft	*Total Babies with Clefts*	*Babies with Clefts and Other Congenital Malformations*	
		Number	*Percent*
Total Clefts	2,003	331	16.5
Cleft Lip	539	44	8.2
Cleft Lip and Palate	842	117	13.9
Cleft Palate	622	170	27.3

cataracts, other defects of the globe of the eye and extraocular and extrabulbar eye defects); malformed nose (which includes such anomalies as absence of nose and choanal atresia rather than merely misshapen nose as a result of a severe cleft lip); and encephalocele and microcephaly. All of these malformations occurred with the greatest relative frequency in cases of cleft palate except for eye defects which showed a slightly higher association with cleft lip and palate combined.

These malformations, which occurred relatively most frequently with clefts, all involve the head and were reported with frequencies greater than 50 times what was expected on the basis of the overall reported incidence. It may be that they are related etiologically or developmentally to clefts, but one must take into account the possibility of an increased index of suspicion resulting from the discovery of any single malformation and thus the increased chance of other malformations being discovered in the same child. At the same time, one must not discount the logic of expecting birth defects to occur in combination or overlook the potential significance of learning which malformations occur in combinations with any particular malformation being studied. To pursue this line of investigation, we have just developed a computer program which will show all reported combinations of congenital malformations. The data in this report have not been submitted to this analysis yet, but it is expected that when they are, certain combinations of malformations will be shown to occur with relatively high frequency. Study also will be made in greater depth of other differences between babies whose clefts occur as a component of what might be considered a syndrome and those whose clefts occur as an isolated event.

Parental Age. The role of parental age in the etiology of cleft lip and palate continues to be unclear. Some investigators have reported no relationship between parental age and the frequency of occurrence of clefts. Others have shown a relationship between advancing parental age and one or more cleft types. In our four-state study we, as Fraser and Calnan (*3*) before us, showed a relationship between both maternal and paternal age and total clefts, cleft lip and palate combined, and with cleft palate, but not with cleft lip alone. In the four-state study, a relationship was found between clefts and paternal age when age of mother was held constant. In Tables 5 and 6, clefts and the other selected malformations are shown by age of mother and by age of father respectively. These tables also include the ratio of observed to expected number of cases where the expected is based on the age distribution of the parents of the controls. In Table 5, an obvious and statistically significant relationship is shown between advancing maternal age and mongolism. The age distribution of positional foot defects also deviates significantly from the expected distribution, and the excess of observed over expected frequencies occurs for the very young mothers as well as for the older mothers. There also is a suggestion of an age effect for all other

TABLE 5. Number of controls, number of babies born with selected congenital malformations, and ratio of observed to expected number of babies born with selected congenital malformations, by age of mother. Only white babies with age of mother known are included.

Age of Mother	*Number of Controls*	*Number of Babies with Selected Congenital Malformations*										
		Total Clefts	*Cleft Lip*	*Cleft Lip & Palate*	*Cleft Palate*	*Anencephaly*	*Spina Bifida*	*Hypospadias*	*Mongolism*	*Positional Foot Defects*	*Polydactyly*	*Reduction Deformities*
All Ages	16,605	2,003	539	842	622	403	1,093	1,167	788	2,231	785	510
Under 20	2,382	253	63	108	82	44	172	165	57	385	105	81
20–24	5,992	739	211	302	226	153	399	419	132	847	310	191
25–29	4,167	492	142	208	142	108	258	303	115	490	170	116
30–34	2,419	283	74	119	90	54	144	177	99	286	117	67
35–39	1,255	179	43	72	64	34	86	80	179	146	63	42
40 and over	390	57	6	33	18	10	34	23	206	77	20	13

Age of Mother	*Ratio of Observed to Expected Number of Babies*										
	Total Clefts	*Cleft Lip*	*Cleft Lip & Palate*	*Cleft Palate*	*Anencephaly*	*Spina Bifida*	*Hypospadias*	*Mongolism*	*Positional Foot Defects*	*Polydactyly*	*Reduction Deformities*
All Ages	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Under 20	.88	.81	.89	.92	.76	1.10	.99	.50	1.20	.93	1.11
20–24	1.02	1.08	.99	1.01	1.05	1.01	.99	.46	1.05	1.09	1.04
25–29	.98	1.05	.98	.91	1.07	.94	1.03	.58	.88	.86	.91
30–34	.97	.94	.97	.99	.92	.90	1.04	.86	.88	1.02	.90
35–39	1.18	1.06	1.13	1.36	1.12	1.04	.91	3.01	.87	1.06	1.09
40 and over	1.21	.47	1.67	1.23	1.06	1.27	.84	11.13	1.47	1.08	1.09

TABLE 6. Number of controls, number of babies born with selected congenital malformations, and ratio of observed to expected number of babies born with selected congenital malformations, by age of father. Only white babies with age of father known are included.

Age of Father	Number of Controls	Number of Babies with Selected Congenital Malformations										
		Total Clefts	Cleft Lip	Cleft Lip & Palate	Cleft Palate	Anencephaly	Spina Bifida	Hypospadias	Mongolism	Positional Foot Defects	Polydactyly	Reduction Deformities
All Ages	16,137	1,955	523	820	612	390	1,054	1,144	764	2,150	752	498
Under 20	582	68	21	27	20	8	46	49	13	100	27	18
20–24	4,483	501	137	212	152	116	323	309	97	639	200	147
25–29	4,666	537	148	223	166	103	293	345	112	615	224	147
30–34	3,228	397	115	151	131	82	176	229	130	380	138	90
35–39	1,891	252	66	113	73	51	120	130	145	218	98	51
40–44	849	129	26	58	45	19	57	56	148	117	43	21
45 and over	438	71	10	36	25	11	39	26	119	81	22	24

Age of Father	Ratio of Observed to Expected Number of Babies										
	Total Clefts	Cleft Lip	Cleft Lip & Palate	Cleft Palate	Anencephaly	Spina Bifida	Hypospadias	Mongolism	Positional Foot Defects	Polydactyly	Reduction Deformities
All Ages	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Under 20	.96	1.11	.91	.91	.57	1.21	1.19	.47	1.29	1.00	1.00
20–24	.92	.94	.93	.89	1.07	1.10	.97	.46	1.07	.96	1.06
25–29	.95	.98	.94	.94	.91	.96	1.04	.51	.99	1.03	1.02
30–34	1.02	1.10	.92	1.07	1.05	.83	1.00	.85	.88	.92	.90
35–39	1.10	1.08	1.18	1.02	1.12	.97	.97	1.62	.87	1.11	.87
40–44	1.25	.94	1.34	1.40	.93	1.03	.93	3.68	1.03	1.09	.80
45 and over	1.34	.70	1.62	1.51	1.04	1.36	.84	5.74	1.39	1.08	1.78

malformations except hypospadias and cleft lip, but none are statistically significant. These same relationships are shown for paternal age in Table 6. Positional foot defects, mongolism, and both total clefts and cleft lip and palate combined show a paternal age distribution significantly different from the expected.

Because of the strong positive correlation between maternal and paternal age in the United States, observed/expected ratios were calculated for both parents taken together, assuming a basic dichotomy for mothers of under 35 and over 35, and for fathers of under 40 and over 40 (Table 7). The differences between the age distribution of cases and controls were statistically significant for total clefts, cleft lip and palate combined, cleft palate, and mongolism. The apparent age effects of the very young parents shown in Table 5 and 6 for positional foot defects were masked in these cruder age groupings. It is possible, by looking at the observed/expected ratios, to observe which age group combinations contribute most to the significant age differences between cases and controls. In mongolism, for example, it is the older mothers, regardless of the age of the fathers, who contribute to the difference in the distributions. On the other hand, it is the fathers' age, regardless of the age of the mothers, which apparently is of significance among cases of cleft lip and palate combined. For cleft palate, older mothers as well as older fathers seem to show an effect on the frequency of reported cases (Figure 3).

These findings raise many questions. For example, are there some social or environmental differences between people who rear a family early and those who rear a family relatively later in life? Do we see evidence here of what might be some biologic mechanism which develops with age such as the chromosomal abnormalities described for mongolism? Penrose's (*12*) speculations on parental age and fresh mutations and other recent observations by Legros (*7*) on the subject of teratospermia provide some support for such an hypothesis. From study of these questions, much could be learned. It is this type of follow-up activity which the NIS eventually will attempt to do when sufficient background information has been developed to make such studies productive.

Geographic Variations. If specific malformations actually occurred with equal frequency from one geographic area to the other and if accuracy and completeness of reporting were the sole reasons for variations in case rates, then one would expect that a state which reported a high incidence of one malformation also would report a high incidence of all other malformations. This is not the case, however. In Table 8, the upper quartile of NIS reporting areas are ranked according to the rate per 100,000 live births for each of the eight selected malformations. Iowa, which ranks first for reported incidence of clefts, is in the upper quartile for only two other malformations: polydactyly and reduction

TABLE 7. Ratio of observed to expected number of white babies with selected congenital malformations by ages of mother and father. Only babies with ages of both parents known are included.

Age Groups of Mother and Father		*Total Clefts*	*Cleft Lip*	*Cleft Lip & Palate*	*Cleft Palate*	*Anencephaly*	*Spina Bifida*	*Hypospadias*	*Mongolism*	*Positional Foot Defects*	*Polydactyly*	*Reduction Deformities*
Mother	*Father*											
All Ages	All Ages	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
<35	<40	.97	1.01	.96	.94	.98	.99	1.01	.55	.99	.99	.99
<35	40+	1.35	.98	1.43	1.56	1.03	.97	.96	.81	1.14	1.02	1.03
35+	<40	1.12	.97	1.08	1.31	1.35	1.00	.90	3.59	.84	1.07	.97
35+	40+	1.25	.80	1.44	1.37	.93	1.23	.87	6.25	1.16	1.12	1.23

TABLE 8. Ranking of the NIS reporting areas in the upper quartile according to reported rates per 100,000 live births for each of eight selected congenital malformations for white babies only. Shown in parentheses are rates per 100,000 live births.

Total Clefts		*Anencephaly*		*Spina Bifida*		*Hypospadias*	
Iowa	(181)	Rhode Island	(67)	South Carolina	(99)	Alaska	(191)
South Dakota	(172)	South Dakota	(60)	Virginia	(98)	Wisconsin	(110)
Alaska	(170)	Washington	(43)	West Virginia	(95)	Montana	(108)
Montana	(169)	Pennsylvania	(40)	Baltimore	(90)	Pennsylvania	(103)
Arkansas	(163)	South Carolina	(37)	Alabama	(85)	Baltimore	(101)
Wisconsin	(160)	Virginia	(33)	Wisconsin	(84)	South Dakota	(99)
Baltimore	(156)	New York City	(31)	Texas	(82)	Arkansas	(91)
All NIS Areas	(121)	All NIS Areas	(24)	All NIS Areas	(66)	All NIS Areas	(70)
Mongolism		*Positional Foot Defects*		*Polydactyly*		*Reduction Deformities*	
Wisconsin	(93)	Colorado	(200)	Wyoming	(100)	Wyoming	(57)
South Dakota	(73)	Wyoming	(200)	South Dakota	(93)	South Dakota	(53)
Washington	(72)	Wisconsin	(190)	New York City	(70)	Iowa	(46)
Arizona	(63)	Utah	(176)	Iowa	(68)	Montana	(46)
California	(57)	New York City	(173)	Arizona	(63)	Nebraska	(42)
Nebraska	(57)	Montana	(169)	Wisconsin	(61)	Oregon	(42)
Pennsylvania	(57)	Baltimore	(161)	California	(60)	Arkansas	(40)
						Wisconsin	(40)
All NIS Areas	(47)	All NIS Areas	(134)	All NIS Areas	(47)	All NIS Areas	(31)

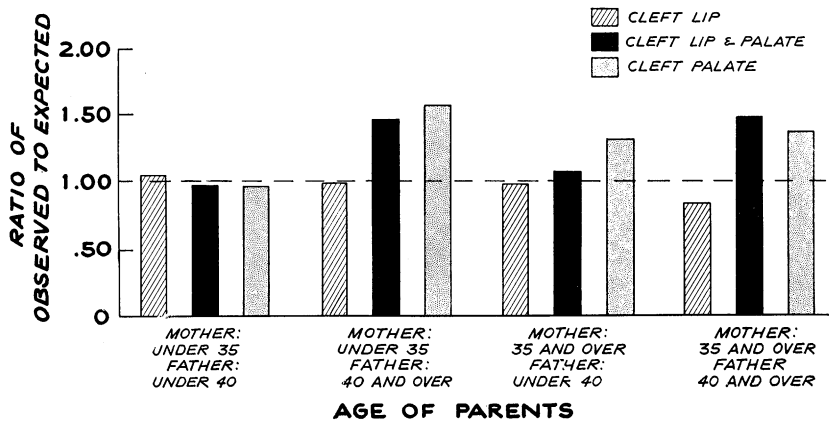

FIGURE 3. Ratio of observed to expected number of babies born with clefts of the lip and palate by age group of parents.

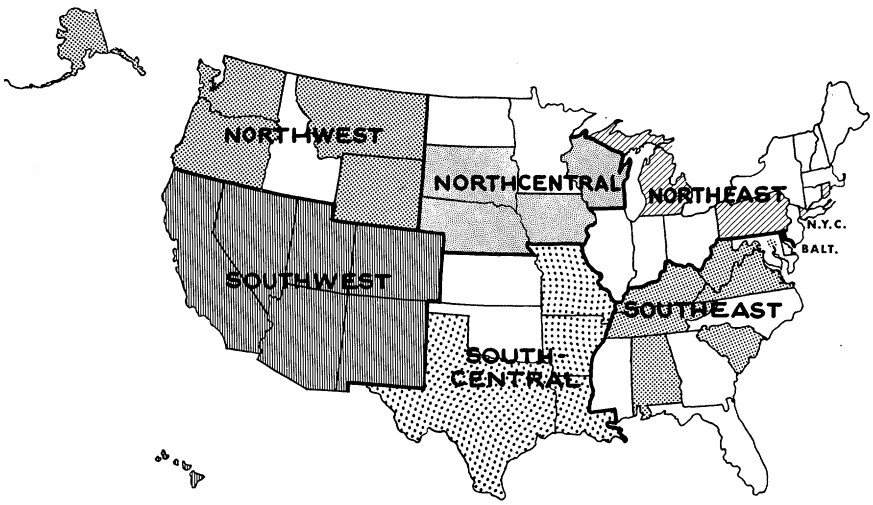

FIGURE 4. NIS birth registration areas by geographic region.

deformities. No reporting area is found in the upper quartile for all of the eight malformations, although Wisconsin appears in the top quartile for seven of them. Seven states appear in the upper quartile for only one malformation each (Alabama, Colorado, Oregon, Rhode Island, Texas, Utah, and West Virginia).

To analyze these apparent geographic variations further, the United States was divided arbitrarily into six sections at approximately 90° and 105° longitude and 40° latitude (Figure 4). If one of the dividing lines cut through a state, the state was assigned to the section into which the larger part of the state fell. Rates were calculated for each of the eight selected malformations in each of these six geographic regions. The

TABLE 9. Selected congenital malformation rates per 100,000 live births, by geographic regions of the United States for white babies only.

A. Clefts				*B. Anencephaly*			
	West	Central	East		West	Central	East
North	145	165	113	North	25	26	34
South	132	107	94	South	16	20	23
C. Spina Bifida				*D. Hypospadias*			
	West	Central	East		West	Central	East
North	52	69	67	North	79	84	86
South	47	78	81	South	76	46	48
E. Mongolism				*F. Positional Foot Defects*			
	West	Central	East		West	Central	East
North	56	73	52	North	148	164	145
South	53	27	32	South	156	95	101
G. Polydactyly				*H. Reduction Deformities*			
	West	Central	East		West	Central	East
North	43	61	55	North	36	43	32
South	57	32	29	South	34	24	20

total number of controls in each of these regions was multiplied by 100 to yield the number of live births to serve as the denominator for the rates, and the total number of each of the malformations served as the numerator.

Table 9 shows the rates for each malformation in each of the six geographic regions. The North-Central area tended to have higher rates than the other regions for each malformation except anencephaly and spina bifida. For clefts, the rate was 165 per 100,000 live births compared to the overall rate of 121. The South-East and South-Central areas tended to have low malformation rates with the notable exception of spina bifida. For spina bifida, the rates were considerably higher in those two regions than in any of the others. For anencephaly, the North-East area had the highest rate—twice as high in fact as the rate for the South-West. Marked geographic variations in the occurrence of anencephaly and in spina bifida or in deaths from these defects have been documented by other investigators but they have only been able to speculate about the reasons why these differences seem to exist (*5*, *11*). If it can

be determined that these apparent geographic differences are real differences, then field studies—both of the genetic component of the populations in the various geographic regions and of the physical environment should be undertaken.

Comments

Variables other than those discussed in this report will be analyzed in the near future. These include seasonal or temporal variations measured by approximate date of conception; birth order, controlling on maternal age; and occupation of father, using a detailed occupation code. These particular variables were examined in the four-state study but failed to reveal any significant relationships to the occurrence of clefts, with the exception of occupation of father for which there was some suggestion of higher than expected incidence of clefts among children of farm laborers. Perhaps more fruitful lines of investigation utilizing the birth records are those alluded to previously: namely, more detailed analysis of combinations of malformations, more studies of parental age, and finer analyses of geographic variations.

Although the full value of the NIS birth record study cannot be determined yet, we believe it already has provided some worthwhile information. However, interpretation of many of the findings is dependent on our achieving better understanding of the influence of completeness and accuracy of malformation reporting on birth certificates. Presently, such studies of completeness and accuracy are being planned.

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