Cleft Lip and Palate Mortality Study

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Background and Purpose

Information obtained from matched birth and death certificates for a large population of infants born with cleft lip or palate has special value for an investigator. The composite data provide an opportunity (a) to describe the infants who died in terms of their characteristics at birth, their ages at death, and causes of death, (b) to compare deaths in the study population with those of the general population from which they were drawn, and (c) to compare the birth characteristics of the deceased children with those children who presumably did not die. Previous studies of this type are listed in Appendix 1 shown on page—.

Methodology

Through the National Cleft Lip and Palate Intelligence Service, a large collection of birth certificates was available for analysis. Birth certificates that reported the presence of congenital malformations were drawn from twenty-eight states and two cities for varying periods between 1956–1965 (Appendix 2 shown on page —). Among these certificates was a total of 12,553 on which clefts were recorded.

Vital statistics registrars in each area in which the birth certificates were registered searched their records through 1966 for deaths occurring to the infants whose birth certificates reported cleft lip or palate. Death certificates were found and copied for 1,838 children. Thus, the population of children born with clefts in the present study is larger than any that has previously been followed.

The births and deaths were classified by the following types of clefts: isolated cleft lip, combined cleft lip and palate, isolated cleft palate, and Pierre Robin syndrome. Included in these categories were a few cases assumed to be bona fide clefts but reported in vague terms such as deformity, dysplasia, or defect of the lip or palate, healed harelip, pseudoharelip, or fusion line on upper lip. Although Pierre Robin syndrome was diagnosed specifically for a number of children, combinations of cleft palate with micrognathia and glossoptosis were removed from the isolated cleft palate group and were reclassified as Pierre Robin syndrome.

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Trained nosologists in a state department of public health coded all the death certificates for underlying cause of death according to the *Seventh Revision of the International Classification of Diseases* (19). All congenital malformations were coded according to *A Classification of Congenital Malformations* (8).

Selected data from the birth certificates and similar data from the death certificates, including any mention of congenital malformations, were keypunched. Summary cards, representing each child's malformations and the certificates on which they were reported, were prepared and used to produce the tabulations for this study.

Mortality rates for all deaths under one year of age in the United States were used as a baseline for evaluating the mortality patterns during the first year of life of children born with cleft lip or palate. The appropriateness of using the entire United States as a standard was substantiated by the close agreement of infant death rates for the thirty registration areas incorporated in the study with those for the total United States for the years 1962–1965. However, it should be noted that three States—California, Hawaii, and Wisconsin, comprising the birth areas for the period 1956–1961, had somewhat lower infant mortality rates than those which the whole country experienced.

Several limitations are inherent in the design of this study. Only those cases of clefts reported on birth certificates were searched in the death records, whereas, it has been estimated that about 20 percent of clefts are not reported on birth certificates (7). The number of deaths in this study are also probably underreported inasmuch as only those deaths occurring in the same registration area as birth could be traced. Thus, the data might be biased in favor of deaths to younger children and deaths in the least mobile families. Children for whom no death certificates were located in the area of birth were presumed to be alive.

Ten different cohorts were traced through 1966. The group born in 1956 was reviewed for eleven years. Succeeding cohorts of infants born with clefts were traced for shorter periods of time, ending with babies born in 1965 who were traced only from one to two years, depending upon date of birth.

There are also limitations to the use of death certificates as sources of information about congenital malformations. There is no place for recording congenital malformations on death certificates unless a malformation is the underlying cause of death, or if a physician considers the malformation to be a contributing cause. In the event there are multiple malformations contributing to the death, lack of space often discourages the recording of individual malformations. Furthermore, malformations may not be recorded for deaths from traumatic causes because circumstances leading to the trauma take precedence over prevailing health conditions. Also, nothing is learned concerning malformations when death is attributed to an unqualified "immaturity."

TABLE 1. Births, deaths, and death rates by type of cleft and sex of children born with clefts, 1956–1965.

type of cleft	*total*			*male*			*female*		
	births	*deaths*	*death rate**	*births*	*deaths*	*death rate**	*births*	*deaths*	*death rate**
all clefts	12,553	1,838†	146.4	7,438	1,003	134.8	5,115	829	162.1
isolated cleft lip	3,378	239	70.7	2,073	128	61.7	1,305	111	85.0
cleft lip and palate	5,328	800	149.4	3,509	473	134.7	1,819	323	177.5
isolated cleft palate	3,646	740	202.4	1,761	372	211.2	1,885	366	194.1
Pierre Robin syndrome	201	59	293.5	95	30	315.8	106	29	273.6

* Rates are per 1,000 births with clefts.
† Total includes 6 of unknown sex.

Results and Discussion

During the period of review there were 1,838 deaths among the study population, resulting in a death rate of 146.4 per 1,000 babies born with a cleft lip or palate. Table 1 shows that children with isolated cleft lip had the lowest death rate; those with Pierre Robin syndrome had the highest.

SEX. At birth the sex distribution followed the classic pattern of male predominance in clefts involving the lip and female predominance in isolated cleft palate. In contrast, female death rates exceeded those for males in cases of isolated cleft lip and combined cleft lip and palate, whereas the male death rate slightly exceeded the female death rate in cases of isolated cleft palate. The rate of deaths for males with Pierre Robin syndrome was higher than that for females. Among other investigators only Ivy (9) and Shorting (15) mentioned finding no sex differences in deaths of children born with clefts.

RACE. Table 2 shows the racial distribution of births and deaths among the children with clefts. Whereas only eight percent of the children who were born with clefts were non-white, they comprised 11 percent of the deaths. Non-white children with clefts had a death rate 1.4 times higher than that of white children.

TABLE 2. Births, deaths, and death rates by race of children born with clefts, 1956–1965.

race	*births*	*deaths*	*death rate**
all races	12,553	1,838	146.4
white	11,564	1,641	141.9
other races	989	197	199.2

* Rates per 1,000 births with clefts.

TABLE 3. Age at death of deceased children born with clefts, 1956–1965.

deaths	*number*	*percentage*
all deaths	1,838	100
under 1 year	1,743	95
under 28 days	1,314	71
under 1 day	623	34
1–11 months	429	23
1 year and older	95	5

AGE AT DEATH. Most of the deaths among children born with a cleft lip or palate occurred early in life. Table 3 shows that 95 percent of the children died before their first birthdays. About one-third of the children failed to survive the first day of life.

The 1,743 infant deaths were compared with infant mortality in the United States. Table 4 shows that during the ten years, 1956–1965, the infant mortality rate for the United States averaged 25.7 per 1,000 births; during the same period the mortality rate for infants with cleft lip and palate was 138.9 per 1,000 births. In other words, a child born with a cleft had more than five times the risk of dying during his first year of life than his counterpart in the general population.

Survival did not improve appreciably during the ten year period. Between 1956 and 1965 the proportion of children with clefts who survived for one year increased by only three percent.

CAUSE OF DEATH. Table 5 shows that a greater number of deaths was attributed to congenital malformations than to any other cause of death among the children born with a cleft lip or palate. With the exception of accidents, other causes of death among infants with clefts produced rates that were about two or three times the prevailing death rate for all infants

TABLE 4. Infant mortality rates by age at death, United States and infants with clefts, 1956–1965.

age	*United States**	*infants with clefts†*
under 1 year	25.7	138.9
under 28 days	18.6	104.7
under 1 day	10.2	49.6
1–6 days	6.3	37.4
7–13 days	1.0	7.8
14–20 days	0.6	5.4
21–27 days	0.4	4.4
1–11 months	7.1	34.2

* Rates are per 1,000 births.

† Rates are per 1,000 births with clefts.

TABLE 5. Infant mortality rates for selected causes of death, United States and infants with clefts, 1956–1965.

ICD code number, seventh revision	*cause of death*	*rate**
	all causes	
	United States total	25.7
	infants with clefts	138.9
750–759	congenital malformations	
	United States total	3.6
	infants with clefts	87.5
760–773 (X763)	certain diseases of early infancy	
	United States total	9.9
	infants with clefts	22.7
763	pneumonia of the newborn	
	United States total	0.8
	infants with clefts	3.5
774–776	prematurity	
	United States total	4.8
	infants with clefts	9.1
810–985	accidents	
	United States total	0.9
	infants with clefts	1.2
	all other causes	
	United States total	5.7
	infants with clefts	14.8

* United States rates per 1,000 births; rates for infants with clefts per 1,000 births with clefts.

in the United States. Deaths from malformations, however, were nearly 25 times greater than in the total infant population.

The preponderence of deaths from congenital malformations in infants with clefts led to an examination of the coded classifications included within that broad category. Table 6 presents the six best defined malformations within the ICD 750–759 group (Seventh Revision). All deceased children born with clefts, not just infants, are shown distributed by type of cleft. Congenital malformations of the circulatory system were responsible for a major portion of deaths due to congenital malformations; this was true for each type of cleft.

Only 30 percent of the deaths of children with Pierre Robin syndrome were attributed to the causes specified in Table 6. The remaining 33 cases died from poorly defined congenital malformations of the digestive system, genito-urinary system, bone and joint, or other unspecified malformations. As might be expected, deaths from cause 755, cleft palate and harelip, were proportionately more frequent for children born with cleft palate with or without cleft lip than for isolated cleft lip. The child born with a cleft palate is very susceptible to infection and is likely to have complications due to the presence of associated malformations (4).

TABLE 6. Deaths due to congenital malformations by type of cleft of deceased children born with clefts, 1956–1965.

ICD code number, seventh revision	*cause of death*	*total deaths*		*type of cleft*			
		number	*rate**	*cleft lip*	*cleft lip and palate*	*cleft palate*	*Pierre Robin syndrome*
750–759	congenital malformations	1,140	90.8	132	491	470	47
750	monstrosity	53	4.2	10	24	18	1
751	spina bifida	44	3.5	5	20	17	2
752	hydrocephalus	71	5.7	10	33	28	—
753	other central nervous system	84	6.7	10	47	26	1
754	circulatory	345	27.5	50	143	145	7
755	cleft palate and harelip	129	10.3	9	61	56	3
756–759	other congenital malformations	414	33.0	38	163	180	33

* Rate per 1,000 births with clefts.

AUTOPSY. Medical certification of the underlying cause of death is based upon the best information, including findings of autopsy, available to the physician. Table 7 shows that roughly half of the deaths in this study were followed by autopsy. These figures are higher than those reported by Arthaud (1) who estimated that an average of 20–25 percent of deaths in the United States are followed by autopsy. Autopsy was performed most often following deaths due to congenital malformations of the circulatory system.

Both Shorting (15) and McIntosh, et al. (12) point out the difficulty of comparing their data on neonatal deaths which included findings of autopsy with those of other studies in which the proportions of deaths that were followed by autopsy differ, or in which these data are not indicated. The identification of associated malformations, as well as causes of death, would be affected by whether autopsy was done.

TABLE 7. Deaths with autopsy by cause of death of deceased children born with clefts, 1956–1965.

ICD code number, seventh revision	*selected cause of death*	*total deaths*	*with autopsy*	
			number	*percentage*
	all deaths	1,838	950	52
754	congenital malformation of circulatory system	345	235	68
750–759 (X754)	other congenital malformations	795	364	46
760–773	certain diseases of early infancy	329	166	50
774–776	prematurity	114	28	25
810–985	accidents	27	12	44
	all other causes	228	145	64

TABLE 8. Births, deaths, and death rates by birthweight and age at death of children born with clefts, 1956–1965.

birthweight in grams	*total*		*age at death*					
	births	*deaths*	*under 28 days*		*1–11 months*		*1 year or more*	
			deaths	*rate**	*deaths*	*rate**	*deaths*	*rate**
all birthweights.....	12,553	1,838	1,314	104.7	429	34.1	95	7.6
2,500 grams or less....	2,015	947	764	379.2	161	79.9	22	10.9
2,501–4,000 grams.....	9,594	781	480	50.0	239	24.9	62	6.5
4,001 grams or more..	892	69	31	34.8	28	31.4	10	11.2
unknown.....	69	41	39	565.2	1	14.5	1	14.5

* Rate per 1,000 births with clefts.

BIRTHWEIGHT. Premature birth is a factor of great importance in considering mortality among the newborn. Ivy (9), Wallace, et al. (18), and Potter (14) refer to increased deaths among infants of low birthweight with malformations. Whereas about eight percent of all babies in the United States weigh 2,500 grams or less at birth, about two-thirds of all neonatal deaths occur among babies in that low weight group (16). In the present study babies of low birthweight comprised 16 percent of all births with clefts and 58 percent of the neonatal deaths.

Table 8 shows the death rate for neonatal, other infant, and children's deaths according to their weight at birth. The death rates are high for infants of low birthweight who died before their first birthdays. It is likely that most of the 69 babies whose birthweights were not recorded were small and were rushed without weighing into special care. If this supposition is true, it is not surprising that their neonatal death rate was high. The relatively low death rates for children with cleft lip and the higher death rates for children with cleft palate remain unchanged by introducing the factor of birthweight.

PARENTAL AGE. Maternal and paternal ages at the time of birth of the

TABLE 9. Births, deaths, and death rates by age of mother and type of cleft of children born with clefts, 1956–1965.

type of cleft	*under 35 years*			*35 years and older*		
	births	*deaths*	*death rate**	*births*	*deaths*	*death rate**
all clefts.....	11,029	1,509	136.8	1,516	329	217.0
isolated cleft lip.....	3,046	195	64.0	332	44	132.5
cleft lip and palate.....	4,640	636	137.1	685	164	239.4
isolated cleft palate.....	3,175	633	199.4	468	107	228.6
Pierre Robin syndrome...	168	45	267.9	31	14	451.6

* Rates per 1,000 births with clefts. Births exclude 8 mothers: age unknown.

TABLE 10. Births, deaths, and death rates by age of father and type of cleft of children born with clefts, 1956–1965.

type of cleft	*under 40 years*			*40 years and older*		
	births	*deaths*	*death rate**	*births*	*deaths*	*death rate**
all clefts	10,868	1,507	138.7	1,271	267	210.1
isolated cleft lip	2,968	190	64.0	302	39	129.1
cleft lip and palate	4,605	636	138.1	557	135	242.4
isolated cleft palate	3,123	631	202.0	391	85	217.4
Pierre Robin syndrome	172	50	290.7	21	8	381.0

* Rates per 1,000 births with clefts. Births exclude 414 fathers: age unknown. Deaths exclude 64 fathers: age unknown.

infants with facial clefts were arranged into four groups: mothers under 35 years, mothers 35 years and older; fathers under 40 years, and fathers 40 years and older. Tables 9 and 10 show that death rates were higher both for older mothers and for older fathers. This relationship was evident for each type of cleft, although clefts involving the lip reflected greater differences than did isolated cleft palate.

Loretz, et al. (11) also observed an increase in deaths of children with clefts whose mothers were 35 years or older. In a previous study based upon several years of the births from which the present population originated, older parental age was observed to be related more to clefts occurring with other malformations than to those occurring as single malformations (6). In the present study multiple and single malformations were examined for each parental age group. Table 11 reveals that the percentage of multiple malformations in children of parents in the older age groups exceeded the percentage of multiple malformations found in children of younger parents. Advanced age of both mothers and fathers was associated most often with children born with isolated cleft lip. There was also a substantial increase in the percentage of multiple malformations among children with Pierre Robin syndrome born to older mothers, although the numbers involved may have been too small to be more than an interesting observation.

Comparisons of Survivors and Decedents. Table 12 summarizes the birth characteristics previously discussed that are descriptive of the surviving and the deceased children born with clefts. Compared with deceased children, the sex distribution of survivors was more predominantly male for children with clefts of the lip, with or without cleft palate, whereas the proportion of surviving males with isolated cleft palate and Pierre Robin syndrome was very slightly lower. More survivors than deceased children were white, had a birthweight greater than 2,500 grams, were born to mothers younger than 35 years, and fathers younger than 40 years. It is apparent that studies based on populations of survivors, as

TABLE 11. Percentage of multiple malformations by parental age and type of cleft of deceased children born with clefts, 1956–1965.

type of cleft	age of mother								
	total			under 35 years			35 years and older		
	total	multiple	percentage	total	multiple	percentage	total	multiple	percentage
all clefts	1,838	1,439	78.3	1,509	1,167	77.3	329	272	82.7
isolated cleft lip	239	178	74.5	195	141	72.3	44	37	84.1
cleft lip and palate	800	615	76.9	636	482	75.8	164	133	81.1
isolated cleft palate	740	604	81.6	633	514	81.2	107	90	84.1
Pierre Robin syndrome	59	42	71.2	45	30	66.7	14	12	85.7
	age of father								
	total*			under 40 years			40 years and older		
	total	multiple	percentage	total	multiple	percentage	total	multiple	percentage
all clefts	1,774	1,397	78.7	1,507	1,178	78.2	267	219	82.0
isolated cleft lip	229	172	75.1	190	139	73.2	39	33	84.6
cleft lip and palate	771	598	77.6	636	491	77.2	135	107	79.3
isolated cleft palate	716	586	81.8	631	513	81.3	85	73	85.9
Pierre Robin syndrome	58	41	70.7	50	35	70.0	8	6	75.0

* Excludes 64 fathers: age unknown.

TABLE 12. Summary of characteristics describing surviving and deceased children born with clefts, 1956–1965.

characteristic	percentage	
	surviving children	deceased children
male sex		
isolated cleft lip	62	54
cleft lip and palate	67	59
isolated cleft palate	48	50
Pierre Robin syndrome	46	51
race other than white	8	11
birthweight		
2,500 grams or less	10	52
2,501–4,000 grams	82	43
4,001 grams or more	8	4
mothers 35 years or older	11	18
fathers 40 years or older	10	15

found in cleft palate clinics or surgery clinics are not representative of all children born with clefts.

Summary

Death records were searched to find those that matched birth certificates of 12,553 children who were born with a cleft lip or palate between 1956–1965 in thirty birth registration areas of the United States. The search revealed that death occurred to 1,838 children. An analysis of their records showed that the death rate for infants born with clefts was five times that for the general population of infants in the United States. Moreover, infants with clefts died at an earlier age than infants in the general population.

A greater number of deaths among children born with clefts was attributed to congenital malformations than to any other cause, a finding compatible with the presence of a high proportion of multiple malformations (78%) among the deceased children who were born with clefts. Deaths occurred more often to males than to females when the type of cleft was isolated cleft palate or Pierre Robin syndrome, and more often to females when the cleft involved the lip. Babies weighing 2,500 grams or less at birth presented a greater risk of mortality than did babies of heavier birthweight. There was a higher risk of mortality to children with clefts if the mother was 35 years or older or if the father was 40 years or older at the time of birth. Older maternal and paternal ages were also accompanied by increases in the number of deceased children having multiple malformations.

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APPENDIX 1. Follow-up studies of children born with cleft lip and palate.

investigator	*source of data*	*follow-up period from birth*	*births*	*deaths*	
				number	*percent*
Bardanouve (*2*)	birth certificates, 1955–1965, case records, death certificates	10 years	363	42	11.5
British Columbia Registry (*3*)	birth and death records, various agencies, 1952–1964	1–12 years	770	115	15.0
Gentry (*5*)	death certificates, 1948–1955, birth certificates	5 years	1,414	143	10.0
Ivy (*9*)	birth certificates, 1954, 1955, death certificates	1 year	303* 267*	31 32	10.0 12.0
Lending, et al. (*10*)	birth certificates, 1955, death certificates	1 year	123	20	16.3
Loretz, et al. (*11*)	birth and death certificates, 1955	6 months	368	57	15.5
McKeown and Record (*13*)	birth records, 1950–1952, death records	5 years	105	33	31.4
Shorting (*15*)	registry cases, 1952 thru 1958, hospital and physicians records	1–7 years	455	77	16.9
Wallace, et al. (*18*)	birth and death certificates, public health nurse, 1953	36 days	135	15	11.0
present study	birth certificates, 1956–1965, death certificates	1–11 years	12,553	1,838	14.6

* Born in 1954.
† Born in 1955.

APPENDIX 2. Reporting areas participating in the cleft lip and palate mortality study, by year.

reporting area participating	*years*									
	56	*57*	*58*	*59*	*60*	*61*	*62*	*63*	*64*	*65*
Alabama							×	×	×	×
Alaska							×	×	×	×
Arizona							×	×	×	×
Arkansas							×	×	×	×
California	×	×	×	×	×	×	×	×	×	×
Colorado							×	×	×	×
Hawaii	×	×	×	×	×	×	×	×	×	×
Iowa							×	×	×	×
Kentucky							×	×	×	×
Louisiana							×	×	×	×
Michigan							×	×	×	×
Missouri								×	×	×
Montana							×	×	×	×
Nebraska							×	×	×	×
Nevada							×	×	×	×
New Mexico							×	×	×	×
Oregon							×	×	×	×
Rhode Island							×	×	×	×
South Carolina							×	×	×	×
South Dakota							×	×	×	×
Tennessee							×	×	×	×
Texas							×	×	×	×
Utah							×	×	×	×
Virginia							×	×	×	×
Washington							×	×	×	×
West Virginia							×	×	×	×
Wisconsin	×	×	×	×	×	×	×	×	×	×
Wyoming							×	×	×	×
Baltimore							×	×	×	×
New York City								×	×	×

×—participating year.

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