4. *Incidence of Clefts in the World*

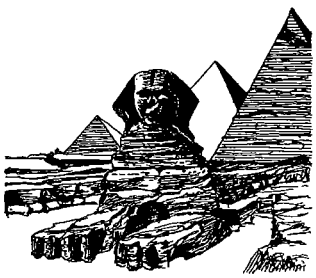
Date	Source	Location	Incidence	Ratio to Normal Births
4000–2000 B.C.	mummies	Egypt	1:1,000	1:1,000
A.D. 1864	Fröbelius	Russia	118:180,000	1:1,525
1908	Rischbieth	London	39:67,945	1:1,742
1924	Davis	Baltimore	24:28,085	1:1,170
1929	Peron	Paris	106:100,889	1:952
1931	Schröder	Münster, Germany	28:34,000	1:1,214
1931	Gunther	Leipzig, Germany	102:102,834	1:1,008
1933	Sanders	Leiden, Holland	16:15,270	1:954
1934	Grothkopf	Hamburg, Germany	74:47,200	1:638
1934	Faltin	Finland		1:950
1934	Sanvenero-Roselli	Italy		1:1,000
1939	Edberg	Göteberg, Sweden	28:27,000	1:964
1939	Fogh-Andersen	Copenhagen	193:128,306	1:665
1940	Conway	New York	32:22,513	1:704
1940	Henderson	Hawaii	35:18,024	1:515
1942	Grace	Pennsylvania	250:202,501	1:810
1944	Mueller	Wisconsin	736:567,504	1:771
1946	Hanhart	Switzerland		1:1,250
1947	Phair	Wisconsin		1:770
1949	Oldfield	England		1:600
1949	Hixon	Ontario	695:655,332	1:943
1950	Ivy	Pennsylvania	766:583,690	1:762
1953	MacMahon	Birmingham	285:218,693	1:767
1953	Wallace	New York		1:1,202
1954	Douglas	Tennessee		1:1,694
1955	Lending	New York		1:1,342
1955	Lutz	California	70:72,107	1:1,030
1955	Lorenz	California		1:851
1958	Kung and Chu	China		1:1,000
1958	Pleydell	Northamptonshire, England		1:637
1960	Sesgin and Stark	New York	21:27,087	1:1,290
1960	Rank and Thompson	Tasmania	160:96,510	1:603
1960	Broadbent	Utah	89:59,000	1:663
1961	Tretsven	Montana	229:123,114	1:538
1961	Simkiss and Lowe	Africa	3:2,068	1:689
1961	Curtis	Canada		1:936
1963	Robinson	Trinidad		1:857
1963	Knox	Northumberland, England	574:404,124	1:704
1964	Conway	New York	1,457:1,823,244	1:1,251
1965	Longenecker	New Orleans	154:199,109	1:1,293
1965	Millard and McNeill	Jamaica	30:56,256	1:1,887
1966	Niswander	Phoenix	50:25,340	1:507
1969	Gupta	Nigeria		1:1,055
1972	Carlisle	Phoenix	32:16,495	1:515

If all the microforms could be included, then undoubtedly these percentages would be altered.

METHODS OF RECORDING

The discrepancies in the incidence of clefts in the different countries may be due in some part to the methods of recording. In Denmark, the fact that all of these defects must be reported to the National Institute of Speech Defects accounts for the accuracy of Danish statistics. In Finland, 99 percent of clefts are operated on at the Finnish Red Cross Hospital. In Pennsylvania, U.S.A., all defects must be recorded on the birth certificate, and yet Ivy showed that in spite of this regulation only 83.3 percent of cleft lip and palate deformity were recorded. Imagine the discrepancies elsewhere!

INCIDENCE



In all the ancient tombs of Egypt only one mummy with a cleft palate has been dug up, suggesting an incidence of about 1:1,000 during the years 4000 to 2000 B.C. But not just anybody could get pickled and swathed, so this probably eliminates the lower income population and reduces the recorded incidence. If, on the other hand, the ingenious Egyptians made a special effort to mummify clefts, the apparent incidence may be too high.

THERE IS A DIFFERENCE IN RACIAL INCIDENCE

Caucasian

Date	Author	Incidence	Ratio to Normal Births
1926	Davis	17:15,565	1:916
1956	Fogh-Andersen	644:393,457	1:611
1957	Rank and Thompson	160:96,510	1:603
1961	Ivy	311:242,128	1:779
1963	Woolf	90:59,650	1:663
1965	Longenecker	51:22,092	1:433
1967	Chung	30:16,385	1:546
1971	Fogh-Andersen	150:75,000	1:500

In countries where the population is of Caucasian origin, the incidence is now generally between 1:500 and 1:600.

African

Date	Author	Incidence	Ratio to Normal Births
1961	Simkiss and Lowe	3:2,068	1:689
1969	Gupta		1:1,055

Although there are very few studies from Africa in those series reported, the incidence of cleft lip and palate seems less common. The practice of infanticide in many uncivilized tribes of Africa would certainly tend to reduce the incidence. Oluwasanmi reported 128 cases from Ibadan in Nigeria, but in general it is difficult to get records with infanticide in progress and with the unwillingness of the family to give a history of a cleft because of the stigma attached thereto.

New World Negroes

Date	Author	Country	Incidence	Ratio to Normal Births
1924	Davis	America	7:12,520	1:1,789
1961	Ivy	America	11:43,032	1:3,912
1963	Altemus	America	36:79,842	1:2,218
1963	Robinson	Trinidad		1:1,888
1965	Longenecker	America	112:173,936	1:1,553
1965	Millard and McNeill	Jamaica	30:56,000	1:1,887
1967	Chung	America	14:16,959	1:1,211

The low incidence of cleft lip and palate in the American Negro has often been noted. In 1924 in Baltimore, John Staige Davis reported an overall incidence of 1:1,170, crediting the low incidence on the large number of Negroes in his area. He showed a much lower incidence in the Negro (1:1,790) than in the Caucasian (1:915). In 1965 Longenecker in New Orleans corroborated Davis' findings with an incidence of 1:1,553 in Negroes compared with 1:692 in Caucasians. Altemus reported 1:2,218 in Negroes.

Caribbean islands

Date	Author	Country	Incidence	Ratio to Normal Births
1963	Robinson	Trinidad		1:1,888
1965	Millard and McNeill	Jamaica	30:56,000	1:1,887

Robinson's Trinidad is composed of 54 percent Negro-mixed and 36 percent East Asian Indian. Although the total incidence of cleft lip and palate was 1:857, the East Asian Indian incidence was 1:500 and the Negro-mixed was 1:1,888.

McNeill and I studied the percentage of clefts in the 56,256 births at Victoria Jubilee Maternity Hospital in Kingston, Jamaica, from 1960 through 1963. At least 90 percent of these births were Negro or Negro-mixed, and the incidence over these four years is of interest: lip only, 1:6,250; palate only, 1:9,091; lip and palate, 1:3,704; all types combined, 1:1,875.

Logical reasons for low incidence in New World Negroes

INFANTICIDE. It has been suggested that in the uncivilized tribes of Africa the practice of destroying all deformed newborns would have a discouraging effect on the propagation of clefts.

SELECTIVE SPECIMENS. The reduced incidence of cleft lip and palate has been demonstrated only in the Negroes of North America, Trinidad and Jamaica. These are a selective group, having been chosen originally as excellent physical specimens to bring a good price in the slave market. It is unlikely that the avaricious slave traders would have taken up the space in their ships to transport cleft lip and palate slaves who would be certain to demand a lower sales value.

SURVIVAL OF THE FITTEST. Infants with the more severe cleft deformities, particularly as seen in the bilateral type, have great difficulty with breast feeding. In uncivilized areas or even in underdeveloped countries where breast feeding is the only source of food for the newborn, the chance of survival for infants with such clefts is slim. Even in Jamaica, when a child with a severe cleft is seen at the initial visit at Kingston Public Hospital, he is extremely malnourished. This infant is usually one of a large poor family, and if the cleft is not closed early the child often does not survive.

Confirmation in reverse

As will be noted later, in the New World Negro the entity cleft palate alone is relatively more common than in the Caucasian. This finding can be explained by the same logic in reverse. A

simple palate cleft unnoticed at birth would spare the infant's life, unnoticed in the slave mart would not affect the sale and if not severe would allow enough breast feeding for survival.

Japanese

Date	Author	Incidence	Ratio to Normal Births
1958	Neel	171:63,796	1:373

In 1958 Neel reported the high incidence of 1:373 in Japanese.

American Indian

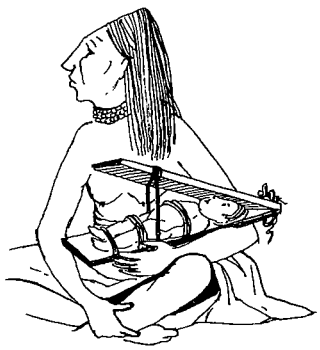
Date	Author	Incidence	Ratio to Normal Births
1963	Miller	31:12,337	1:398
1963	Tretsven	27:7,461	1:276
		14:4,499	1:321
1966	Niswander	50:25,340	1:507
1972	Carlisle	32:16,495	1:515

In 1963 Miller reported that the incidence in American Indians in British Columbia is nearly as high as among the Japanese. Tretsven reported an even higher incidence of 1:276 in Montana Indians.

The high incidence among American Indians has been attributed by Jaffe to the traditional life style of these poor people, who suffer from infectious diseases and widespread malnutrition. There is also considerable inbreeding as marriage outside the tribe is discouraged.

Carlisle in Phoenix noted that the incidence of clefts varied greatly in the different Indian tribes in the southwestern U.S.A.

Date	Author	Tribe	Incidence	Ratio to Normal Births
1963	Tretsven	Flathead	6:921	1:154
1970	Jaffe	Navajo	70:28,000	1:400
		Montana	27:7,461	1:276
1972	Carlisle	White Mountain Apache	9:2,948	1:328
		San Carlos Apache	10:2,727	1:273
		Pima	6:4,590	1:765
		Papago	5:2,930	1:586
		Hopi	2:3,300	1:1,650



In the Flathead tribe of Montana there is a very high—1:154—incidence of clefts. Any group bearing such a name and producing clefts at that rate naturally stimulated our curiosity. H. Wolfgang Losken of Pietermaritzburg, South Africa, during his Maytag-McCahill Fellowship in Miami, assisted in compiling these data on cleft incidence and on his way home stopped off at the Museum of North Arizona in Flagstaff to trace the origin of the name Flathead. According to Catlin, it was the custom of the Chinook to flatten the head of the papoose with a wicker cradle head-board, and the squashed result was considered a mark of distinction and superiority. It was disappointing, however, to find that the people listed in the official reports as Flatheads never practice artificial head flattening. It would be too much anyway to have both a flat head and such a good chance for a cleft!

SPLIT UVULA. Jaffe examined 944 Navajo school children and found an incredible 1:9 (106 cases) incidence of split uvula. He reported a 65 percent one-fourth cleft, 25 percent one-half cleft and 10 percent three-quarter and total clefts of the uvula.

Shapiro and Cervenka reported a 1:10 bifid uvula in American Indian school children having at least five-sixteenths Chippewa ancestry. A striking positive relationship between prevalence of bifid uvula and percentage of Indian ancestry was observed. In children having thirteen-sixteenths to full-blooded Chippewa ancestry, a remarkable 1:5 incidence of bifid uvula was recorded.

Hawaii

Date	Author	Nationality	Incidence	Ratio to Normal Births
1940	Henderson	Hawaiian	35:18,024	1:515
1946	Krantz	Chinese		1:1,000
1958	Kung and Chu	Chinese		1:1,000
1963	Robinson	East Indian		1:500
1966	Krantz	Filipino	15:4,249	1:283
		Caucasian blends	16:3,834	1:240
		Hawaiian blends	27:7,748	1:287

An incidence of 1:1,000 was reported in the Chinese. Krantz and Henderson in Hawaii found a high incidence of clefts in

Filipinos, Caucasian blends and Hawaiian blends. It was felt that mixed races have a higher incidence than pure races.

Indonesia

Anthony Pelly of Sydney, Australia, passed by Miami in 1973 after a plastic surgical sojourn with the Javanese of Indonesia. He had some interesting statistics. Six babies with clefts are born every hour in Indonesia or 360 clefts in 2½ days. This is the total number of clefts produced in Australia in one year where the ratio of clefts to normal births is 1:600. At Tjipto Hospital, Jakarta, he found the ratio of clefts to be 85 percent CL, 2 percent CLP and 13 percent CP. This again suggests high perinatal mortality in total clefts causing selection by survival of the fittest.

RACIAL INCIDENCE OF CLEFT LIP WITH OR WITHOUT CLEFT PALATE

There is considerable evidence to support the genetic independence of cleft lip, with or without cleft palate, as a distinct entity from cleft palate alone (Fogh-Andersen, 1943; Woolf and Broadbent, 1963; Clark Fraser of Canada, 1955; Metrakos, 1943; as well as Tor Goran and Henriksson of Sweden and Palmi Moller of Iceland).

Ivy and Stark feel that cleft lip, cleft palate and cleft lip and palate should be studied separately.

Cleft lip with or without cleft palate is very rare in New World Negroes (Millard, 1:2,344; Altemus, 1:4,696). Robert Ivy stated that cleft lip is six times more common in whites than non-whites.

The percentage of cleft lip in most Caucasian series of clefts is 25 percent, CLP 50 percent and CP 25 percent.

CLEFT PALATE

Fogh-Andersen reported that 25 percent of clefts in Denmark were cleft palate alone. A similar figure is found in most series consisting of only Caucasians. In the American Negro cleft palate alone is relatively more common. Fifty percent was reported by

Chung and Myrianthopoulos and 47 percent by Altemus. Fogh-Andersen reported a 76 percent cleft palate incidence among clefts on the Faroe Islands and 82 percent among Eskimos in Greenland.

GENERALIZATION OF INCIDENCE

A concise guide to the pertinent and approximate facts on the incidence of clefts has been compiled by Lazarus and Ryan of Tulane University School of Medicine in their programmed instruction text on cleft lip and cleft palate.

Cleft lip and cleft palate together occur 1:1,289 live births.

Cleft lip alone occurs 1:1,000 live births, more commonly in the male sex and three times as frequently as cleft palate alone.

Cleft palate alone occurs 1:2,500 live births, with a higher incidence in the female sex.

According to Sesgin and Stark in 1961, the incidence of cleft lip–cleft palate as compared to the frequency of the 10 most common congenital anomalies (and least wanted) is low on the list.

1. Foot deformities
2. Hydrocele
3. Hypospadias
4. Mongolism
5. Cryptorchidism
6. Congenital heart disease
7. Polydactyly
8. Hemangioma
9. Cleft lip and cleft palate
10. Hydrocephalus

CLEFTS ARE ON THE INCREASE

Recent studies show an increasing incidence, particularly over the last century, to 1:500. Poul Fogh-Andersen in 1963 stated that the frequency in the population had doubled in the past 50 years and trebled in the last 100 years. His accurate records in the kingdom of Denmark over the last 30 years have shown a definite rising trend. In 1941 the incidence was 1:770 and in 1971 it was 1:500.

Date	Author	Country	Ratio to Normal Births
1941	Fogh-Andersen	Denmark	1:770
1946			1:730
1951			1:685
1956			1:610
1961			1:549
1971			1:500

REASONS FOR INCREASE

1. *Falling perinatal mortality.*

2. *Decreased operative mortality.* Peron quoted a 13 percent mortality rate in the first 10 days of life, and Fogh-Andersen quoted a similar figure. In 1954 Ivy reported that 10 percent died within the first year of life—nearly all had multiple congenital anomalies. In 1962 Lewin reported that of the 5,000 infants with clefts born in Russia in one year, one-third die. Fogh-Andersen reported a reduction to 0.4 percent mortality (3 deaths in 900).

3. *Attendant increase in fertility.* Molsted Pedersen (1964) reported a 1:170 (5 in 853) incidence of clefts in children born of diabetic mothers. Many who not so long ago would have died of grave illnesses like diabetes now have children.

4. *Importance of intermarriage.* Consanguineous marriages may account for rising incidence in small countries such as Denmark, Finland, Greenland and Tasmania. Small communities where marriage outside the tribe is frowned upon may account for the high incidence in American Indians.

5. *Steadily improving operative results.* Books like this, devoted to the study of the evolution of corrective surgery of these anomalies, suggest definite improvement of the methods and their results. This, of course, continues more and more to prevent a cleft from interfering with marriage and possible cleft propagation. As 30 to 40 percent of patients demonstrate heredity for the defect, it is not surprising that the incidence is increasing.

It is probable that the contraceptive pill may take part in the reduction of cleft incidence. Yet, until the geneticists find the true causes of cleft, prevention will remain out of reach. In the meantime, we must accept our part of the blame for the increase and get on with improvements until having a child born with a cleft is of no more concern to a family than having a child with an inguinal hernia.

THE INFLUENCE OF GENETICS

Clarke Fraser

F. Clarke Fraser, Professor of Human Genetics, McGill University, and Director, Department of Medical Genetics, The Montreal Children's Hospital, always liked mathematics and then, during the first genetics lecture he attended, something clicked. He was halfway through medical school when the argument on the relative importance of heredity and environment grew hot. As the pendulum seemed to be swinging too far toward environment and he felt it was actually a combination of both, he leapt to the defense of genetics. His hypothesis was that environmental agents fired at animals of different constitutions would produce different frequencies of malformations. Hamilton Baxter got him some cortisone with which he produced cleft palates in mice and confirmed his theory when he did, indeed, produce strain differences!

In the Grabb, Rosenstein, and Bzoch's 1971 book *Cleft Lip and Palate,* Fraser outlined in a tout sheet the chances of parents having children with clefts, assuming that known genetic and chromosomal syndromes had been excluded. Noting the frequency of the defect in the general population to be 0.1% for CL ± CP and 0.04% for CP, he correlated various situations with estimated percentages.

If *both parents are unaffected* and they have *an affected child,* the probability that their next baby will have the same condition if,

they have *no affected relatives:* 4% in CL ± CP, 2% in CP
they have *an affected relative:* 4% in CL ± CP, 7% in CP
they are related to each other: same as general population
the *affected child has another malformation:* 2% in CL ± CP, 2% in CP

If *unaffected parents* have *two affected children,* the probability that their next baby will have the same condition is 9% in CL ± CP and 1% in CP.

If *one parent is affected* and they have *no affected children,* the probability of the next baby being affected is 4% in CL ± CP and 6% in CP.

If *one parent is affected* and they have *an affected child,* the probability that their next baby will be affected is 17% in CL ± CP and 15% in CP.

If *both parents are affected,* Fraser estimated, assuming a heritability of 80%, the risk for the offspring would be about 60%. Their having one or two affected children increases the risk only slightly above this, presumably because the two affected parents contribute about all the "susceptibility" genes there are.

Distant relatives

It is interesting that affected relatives; outside the parents and siblings, have been found unrelated by Fraser. My cases of unilateral CL ± CP revealed a 20% positive family history. Fraser explains:

> 20 percent positive family histories is about par for the course and means that you did not go out into the fourteenth cousins (in which case it might have been a 100%) or stopped at first degree relatives (when it might have been about 7 or 8%).

Other malformations

It is puzzling that when there is another major malformation which is not part of a genetic syndrome, the risk becomes smaller for recurrence of the cleft anomaly.

The degree of cleft

According to Carter, the more severe the patient's defect, the higher the recurrence risk with 2.5 percent for unilateral cleft lip to 5–7 percent for bilateral cleft lip and palate.

A feminist trend

Both Carter and Woolf concur that the rate of recurrence is a little higher for females than males.