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# Differences in the Reported Frequencies of Cleft Lip Plus Cleft Lip and Palate in Asians Born in Hawaii and the Continental United States[1] (41474)

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*Abstract.* The etiology of cleft lip with or without cleft palate (CL/CP) is not known but present evidence suggests that both genetic and environmental factors act to determine susceptibility. Race has been reported to exert a strong influence on the incidence of CL/CP; e.g., the frequency of CL/CP is nearly twice as high among Japanese born in Japan or Hawaii as it is among Caucasians in Hawaii, Western Europe, and North America, and the risk in American blacks is one-half that in Caucasians. This notwithstanding, a survey of Los Angeles Hospitals and Clinics for families with facial clefting revealed no Orientals despite the fact that this group constitutes 6% of the population. To investigate the possibility that the rate of clefting had declined in Orientals' data was obtained from birth certificates from Hawaii, California, and New York, and from the USPHS Birth Defects Monitoring Program. The results suggest that the frequency of CL/CP but not isolated CP may be significantly lower among Japanese and other Orientals born in California and New York than among those born in Japan or Hawaii. This implies that environmental factors play a major role in determining the frequency of CL/CP in this racial group in the Orient and Hawaii.

Isolated cleft palate (CP) and cleft lip with or without cleft palate (CL/CP) are congenital malformations of unknown etiology. Both anomalies tend to recur in families and also to vary in incidence with season and year of conception, and parental social class, age, parity, ethnic origin, and place of residence during pregnancy (1–4). It is not clear whether the variations in the frequency of CP and CL/CP observed among populations and races are predominantly genetic or environmental in origin, because in past studies most of the groups compared differed in both respects.

The influence of race on the incidence of CP and CL/CP appears to be especially strong (5). The frequency of cleft lip with or without cleft palate has been reported to be nearly twice as high among Japanese born in Japan or Hawaii as it is among Caucasians born in Hawaii, Europe, or North America (6, 7) and the frequency of CP in blacks is approximately one-half that in American Caucasians (1). This notwithstanding, a survey of Los Angeles Hospitals and Clinics for families with facial clefting revealed no Orientals even though this group constitutes 6% of the population. It was concluded that either Oriental patients were going to private physicians not affiliated with mainstream medical institutions or the incidence of clefting was low.

In an effort to determine if the frequency of facial clefting in the Oriental population in California had truly declined, data from birth certificates were obtained from the States of Hawaii, California, and New York, and hospital discharge diagnoses were secured from the USPHS Birth Defects Monitoring Program. The results suggest that the frequency of CL/CP but not CP may be significantly lower among Japanese and other Orientals born in California and New York than among those born in Japan or Hawaii. This implies that environmental factors play a major role in

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determining the frequency of CL/CP in this racial group in the Orient and Hawaii.

**Methods.** Computer printouts giving total live births, and the number of isolated cleft palates, cleft lips, and cleft lips plus cleft palates with the race of the mother and father were obtained from the Departments of Health of the States of Hawaii, California, and New York. In addition, data were obtained from the Birth Defects Monitoring Program, USPHS Center for Disease Control, Atlanta, Georgia. The data from the USPHS CDC do not contain information on the race of mother or father, and all Orientals are recorded as "Asians." Approximately 20% of all "Asian" births were reported from the State of Hawaii.

Isolated cleft palate and cleft lip with or without cleft palate are considered to have distinct genetic and environmental etiologies (1, 7). Because ascertainment varies between studies, comparisons of frequencies of CP and CL/CP were made between races within each study only. It is assumed that nonascertainment within a study will be equally distributed over racial subgroups of the population as was the case in Hawaii as reported by Ching and Chung (7). With the exception of the data from the Birth Defects Monitoring Program the information reported is derived from incrosses only.

Statistical analyses were done by Leslie Bernstein, Ph.D. The Mantel–Haenszel test (8) was used to test the hypothesis of equal incidence (risk ratio = 1) among Caucasians and Japanese or Asians.

**Results.** *Isolated cleft palate among Caucasians and Japanese born in Hawaii or California (Table I).* The frequencies of isolated cleft palate among Japanese in Hawaii and California were consistently lower than those found among Caucasians; however, the differences were not statistically significant.

*Cleft lip and cleft lip plus cleft palate among Caucasians and Japanese born in Hawaii or California (Table I).* The relative risk of Japanese in Hawaii producing progeny with CL/CP was 1.85 to 2.41 times higher than that in Caucasians; however, in

TABLE I. ISOLATED CLEFT PALATE (CP) AND CLEFT LIP PLUS CLEFT PALATE (CL/CP) AMONG CAUCASIANS AND JAPANESE BORN IN HAWAII OR CALIFORNIA

| | Caucasian | | Japanese | | CP | Caucasian | Japanese | CL/CP |
|---|---|---|---|---|---|---|---|---|
| | Number of live births | CP per 1000 births | Number of live births | CP per 1000 births | Relative risk | CL/CP per 1000 births | CL/CP per 1000 births | Relative risk |
| Hawaii | | | | | | | | |
| 1948–1966[a] | 77,013 | 0.43 | 67,608 | 0.65 | 1.51 | 0.98 | 1.82 | 1.85* |
| 1974–1976[b] | 11,914 | 0.67 | 4,650 | 0.00 | — | 0.58 | 1.50 | 2.41* |
| California | | | | | | | | |
| 1968–1973[c] | 2,807,851 | 0.27 | 28,238 | 0.18 | 0.63 | 0.58 | 0.46 | 0.79 |
| 1974–1977[c] | 1,081,126 | 0.33 | 5,463 | 0.00 | — | 0.67 | 0.55 | 0.82 |

[a] Ref. (7).
[b] Data from birth certificates supplied by the Department of Health, State of Hawaii.
[c] Data from birth certificates supplied by the Department of Health, State of California.
* $P < 0.05$.

California during roughly the same period the risk was essentially the same.

*Isolated cleft palate among Caucasians and Asians born in Hawaii or in the United States (Table II).* The relative risk of Chinese, Japanese, or Filipinos, either as individual races where those data were available or as "Asians," producing progeny with CP in Hawaii, California, New York or in other areas of the United States was consistently but not significantly below that of Caucasians.

*Cleft lip and cleft lip plus cleft palate among Caucasians and Asians born in Hawaii or in the United States (Table II).* The relative risk of CL/CP was higher in all Asian racial groups in Hawaii (1.53 to 2.41, individual data not shown), but in California and New York the frequencies were somewhat lower than that of Caucasians. The relative risk of CL/CP in Asians (1.20) from the USPHS data (1970–1979) was not significantly higher than that of Caucasians even though approximately 20% of the Asian births were reported from Hawaii. (From this one would reason that the risk among Asians born in the continental USA is lower than 1.20.)

**Discussion.** Opinions differ on whether the variations in the frequencies of facial clefting between racial groups are due primarily to differences in the environment (9) or in the population frequency of particular combinations of genes which influence development (5). The findings presented here support the view that the variations in frequencies of CL/CP noted between Caucasians and Japanese and other Orientals born in Hawaii and the United States are secondary to environmental changes.

The few studies which have reported differences in the frequency of clefts among races agree that clefts are seen much less frequently among blacks than among Caucasians from the same geographic area. It has been reported that only seven cleft cases were observed among 12,520 black births (0.55/1000) at Johns Hopkins Hospital. During the same period there were 17 cases among 15,656 Caucasian births (1.06/1000) (10). Other studies based on

TABLE II. ISOLATED CLEFT PALATE AND CLEFT LIP AND CLEFT LIP PLUS CLEFT PALATE AMONG CAUCASIANS AND ASIANS BORN IN HAWAII OR IN THE UNITED STATES

| | Caucasian | | Asian[a] | | CP | | Caucasian | Asian | CL/CP | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Number of live births | CP per 1000 | Number of live births | CP per 1000 | Relative risk | $\chi^2$ | CL/CP per 1000 births | CL/CP per 1000 births | Relative risk | $\chi^2$ |
| Hawaii, 1974–1976 | 11,914 | 0.67 | 10,858 | 0.09 | 0.13 | 3.50 | 0.58 | 1.19 | 2.05 | 3.14 |
| California, 1974–1977 | 1,081,126 | 0.33 | 29,844 | 0.20 | 0.60 | 1.92 | 0.66 | 0.50 | 0.76 | 1.00 |
| USPHS,[b] 1970–1979 | 7,334,169 | 0.54 | 58,822 | 0.57 | 1.05 | 1.22 | 1.01 | 1.22 | 1.20 | 2.21 |
| New York State,[c] 1975–1979 | 843,190 | 0.21 | 11,355 | 0.26 | 1.25 | 0.03 | 0.53 | 0.35 | 0.66 | 0.63 |

[a] Japanese, Chinese, and Filipino.
[b] Data from the USPHS Birth Defects Monitoring Program.
[c] Data from birth certificates supplied by the Department of Health, State of New York.

birth certificate data have reported consistently lower attack rates of facial clefting among American blacks than among Caucasians (11–13) and this relationship is maintained despite geographic and cultural change (2). Although these studies strongly suggest that genetic differences primarily account for the variations in attack rates for CP and CL/CP between Blacks and Caucasians, as with all studies of this type the differences may be caused by unrecognized variations in ascertainment, local environment, racial classification, or diagnostic criteria. Some of the problems associated with the use of birth certificates in the epidemiologic assessment of facial clefts are addressed in Refs. 16 and 17.

Ching and Chung (7) reported that the Caucasian incidence of oral clefts in Hawaii was approximately the median value found among other Caucasoid populations studied (14) and that the incidence of CL/CP for Japanese was significantly higher and intermediate between the incidences estimated by Neel (5), Koguchi (6), and Kobayashi (15) for Japanese in Japan suggesting that the racial frequencies were not altered significantly by the migration of the Japanese and Caucasians to Hawaii (the frequency of CP among Japanese born in Hawaii was slightly higher than that estimated for Japanese in Japan). The data presented here support those findings but suggest strongly that when the Japanese and perhaps other Asians migrate to California, New York, or other areas of mainland United States the frequency of CL/CP but not CP decreases to approximate that noted in Caucasians.

There are three explanations for the differences observed in the frequency of CL/CP among the Japanese living in Hawaii or California and among other Asians living in Hawaii and the United States. There may be cultural differences in the reporting frequency (16, 17), migration to the mainland may not be representative of the entire population or there may have been a true decrease in the occurrence of this anomaly in these racial groups as a function of time or assimilation into a different culture and environment. At present there is no evidence in support of the first two possibilities but observations exist which support the concept that attack rates for facial clefting in certain racial groups do vary with geography and environment (1, 2, 4). Prominent among changes which occur with migration is diet. Oriental and Hawaiian diets tend to be lower in fat and animal protein and higher in fish, vegetables and vitamin A than does the average western diet (18, 19). This may be of specific interest because it is known that high dietary levels of vitamin A increase susceptibility to cleft palate in mice bearing H-2D$^b$ alleles in their major histocompatibility complex (20).

Finally, the observation that the frequency of isolated cleft palate among the Japanese did not vary with time and place as did that of CL/CP tends to support the view that these anomalies have distinct etiologies.

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