OBSERVATIONS

Incidence and Prevalence of Cleft Lip and Palate: What We Think We Know

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The descriptive epidemiology of the spectrum of orofacial cleft disorders has many methodologic problems, including (1) casefinding using data sources such as birth certificates, fetal death certificates, and hospital records that often produce ascertainment bias, selection bias, or both and (2) the multiple comparisons problem (i.e., the chance occurrence of statistically significant findings). The resultant incidence and prevalence rates from studies with inadequate designs or inadequate data are limited and may be misleading. A variety of reasons is advanced to explain the wide discrepancies in reported statistics on orofacial clefting from different geographic areas, ethnic groups, and time periods. Specific recommendations are offered for producing better epidemiologic data. An example of how higher quality descriptive statistics can be used for future hypothesis testing is also provided.

KEY WORDS: orofacial clefts, cleft lip, cleft palate, epidemiology, incidence, prevalence, epidemiologic methods, bias

The literature on the descriptive epidemiology of the spectrum of orofacial clefts provides many statistics on the incidence and prevalence of these conditions (Habib, 1978a and 1978b; McWilliams et al, 1984; Byrd, 1987; Hodges and Salyer, 1987). Although the rates for cleft lip and palate are frequently cited, their validity remains in doubt.

In the literature, there are examples of the misuse of epidemiologic terminology (Taylor, 1972; Schendel and Gorlin, 1974; Åbyholm, 1978a), which indicates some lack of understanding about the concepts of incidence and prevalence. Incidence and prevalence are both rates, but they are neither equivalent nor interchangeable (Lilienfeld and Lilienfeld, 1980; Mausner and Kramer, 1985).

Incidence means the new occurrence of orofacial clefts in a defined population over a specified period of time. Incidence rates for any condition are usually cohort-specific. They refer to one or more groups in the population, such as "all products of conception" or "all live births" in a given year. Incidence reflects etiologic factors. To be counted, newly diagnosed cases must come to medical attention. Therefore, their impact on families and on the health system is another factor influencing case ascertainment rates.

Prevalence refers to the total number of existing cleft cases of all, or particular ages in a defined population at a given point in time or during a specified, delimited period. Prevalence rates are cross-sectional in nature and therefore cover all existing birth cohorts in the defined population during the specified time. Prevalence provides a picture of the cumulative personal and societal burdens of clefts or their sequelae. Prevalence data may also include some unknown fraction of current cases with unmet needs for care, as well as surgically repaired cases.

METHODOLOGIC CONCERNS

Epidemiologic investigations of cleft lip and palate that have been conducted to date tend to be limited by case ascertainment bias, selection bias, or both. Multiple sources exist for case finding, including statistics such as birth registration records, death certificates, and fetal death certificates; hospital diagnostic and treatment records; office or clinic case records of private surgeons, orthodontists, speech pathologists, and other specialists; and case registries operated by health departments or clinical study centers (Emanuel et al, 1973). Studies of orofacial clefts have frequently relied on birth certificates and clinical records of treated or hospitalized cases as adequate sources of information, which has led to the underreporting of both incidence and prevalence (Åbyholm, 1978a).

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Relatively few population-based studies have been conducted in which deaths of fetuses with orofacial cleft conditions were counted along with liveborn cleft lip and/or palate cases (Nishimura, 1970; Iizuka, 1973; Nishimura, 1975; Nishimura and Okamoto, 1976; Koguchi, 1980; Melnick et al, 1980). Fetal death certificates may not record these anomalies, either because of the difficulty of recognizing and diagnosing them (Kraus et al, 1963) or because they may not have been the sole, principal, or even contributory cause of death. The underreporting of cleftassociated deaths in all conceptuses produces a distorted picture of the true incidence of these anomalies.

Reliance on birth certificate data is also prone to ascertainment bias (Ivy, 1957; Milham, 1963; Conway and Wagner, 1966; Meskin and Pruzansky, 1967; Conway et al, 1968; Bardanouve, 1969; Czeizel and Tusnadi, 1971; Burdi et al, 1972; Emanuel et al, 1973; Åbyholm, 1978a; Green et al, 1979). For example, a 14.5 percent underreporting error was found for cleft lip and palate patients' birth registration in Norway when compared with subsequent surgery records (Åbyholm, 1978b). A 16 percent error in underreporting of orofacial clefts and other anomalies was found in Pennsylvania's birth certificates (Ivy, 1957). New York underreported 30 percent of all congenital malformations (Conway and Wagner, 1966), and 35 percent of Arkansas' facial cleft cases were not recorded as such on their birth certificates (Green et al, 1979). Many cases that are reported have been misclassified (Meskin and Pruzansky, 1967). For example, 52 percent of all facial cleft malformations in Arkansas (Green et al, 1979) were reported incorrectly. Birth registration data are therefore inadequate for studying not only clefts, but also associated anomalies. The probability of recording congenital anomalies has also been shown to vary directly with the gravity of the condition (Gittelsohn and Milham, 1965; Meskin and Pruzansky, 1967; Ross and Johnston, 1978; Green et al, 1979), although other factors may also contribute. Facial clefts occurring in females, for instance, are more likely to be registered than are those in males (Meskin and Pruzansky, 1967).

Although underreporting characterizes birth certificate data, it has not been found to produce bias in secular trend analyses such as for birth month of cleft children (Hay, 1967). Presumably, all rates are lower than they should be, but their overall pattern in relationship to each other is preserved.

Hospital birth records have been thought to have greater accuracy than have birth certificate records (Schurter and Letterman, 1966). However, two studies contradict that prevailing thought. Emanuel et al (1973) examined the quality of hospital newborn records as a data source for orofacial clefts in King County, Washington for the years 1956 to 1965. The records permitted ascertainment of 98.5 percent of the total cleft cases found through all sources combined, but only 68.4 percent had been coded as such on the discharge abstract. The hospital records were also found to be unreliable for ascertaining associated anomalies. In another study, Myrianthopoulos and Chang (1974) found that diagnosing congenital malformations at the hospital of birth identifies only about one-third (32.1 percent) of those conditions detectable by the end of the first year of life.

Birth certificate, fetal death certificate, and hospital rec-

ord data all reflect the difficulty of, and frequent failure in, documenting milder expressions of clefting when enumerating phenotypic cases in newborns, stillbirths, and abortuses (Kraus et al, 1963; Porterfield and Trabue, 1965; Porterfield et al, 1976). A clinical consequence of early failure to recognize anomalies is their late treatment, as may occur with submucous cleft palate (Weatherley-White et al, 1972; Lowry et al, 1973; Bagatin, 1985). An adverse impact on incidence and prevalence statistics also occurs whenever their data source lacks necessary documentation.

Many epidemiologic studies have not drawn populationbased samples in their casefinding for orofacial clefts. They have relied instead upon treated series of cases, the information for which is contained in hospital or clinic records (Millard and McNeill, 1965; Altemus, 1966; Azaz and Koyoumdjisky-Kay, 1967; Borchakan, 1969; Oluwasanmi and Adekunle, 1970; Robinson and Shepherd, 1970; Åbyholm, 1978b; Siegel, 1979; Iregbulem, 1982; Shin et al, 1985). This approach introduces bias in favor of selecting the more severe surviving cleft cases and/or those associated congenital malformations (Oka, 1979). Further, an institution may serve only a segment of the general population (Oka, 1979). Consequently, selection bias is inherent in the study of this one segment, often the only type likely to come to medical attention because of higher socioeconomic and educational status and racial or other barriers to access. The culture of poverty, which may operate to denv or delay care to lower-income persons in need, may also favor those very environmental factors (inadequate nutritional status and higher maternal infection rates) that may predispose them to higher rates of clefting (Alternus, 1966; Tolarova, 1987). Data derived from biased and/or inadequate samples of the population cannot provide accurate clues to the epidemiologist, geneticist, or teratologist seeking to identify and analyze the causes of cleft lip and/or palate.

An additional methodologic problem, often overlooked in the literature, is that statistically significant correlations can occur by chance when multiple comparisons are made during analysis of any large data set (Mantel and Haenszel, 1959). An illustration of this is Saxen's (1975) replication study of her own earlier investigation of orofacial clefts (Saxen, 1974). She examined a second sample of cases from the Finnish Register of Congenital Malformations. The original findings of clefting were significantly associated with parental age, social factors, emotional stress, and seasonal variation, and they were not reproduced in the later investigation, although the association with prematurity remained.

To summarize, methodologic inadequacies in the descriptive epidemiology of orofacial clefts have caused most existing incidence and prevalence data to be limited or misleading. The failure to take into account fetal wastage and underascertainment have biased incidence statistics. The frequent failure to diagnose and report mild expressions of orofacial clefts, such as submucous cleft palate, and selection bias in study samples have invalidated many prevalence statistics. Nevertheless, it remains important to obtain high quality epidemiologic data on cleft lip and palate for several reasons. Incidence rates can stimulate genetic and epidemiologic investigations of heritable and environmental factors (Chung et al, 1974, 1980). Prevalence rates can document current clinical care needs and are useful to project future caseloads.

REASONS FOR DISCREPANCIES IN RATES OF OROFACIAL CLEFTS

Reported rates for clefts vary widely both within and between geographic areas and for different racial or ethnic groups (Schurter and Letterman, 1966; Beckman and Myrberg, 1972; Ching and Chung, 1974; Leck, 1976; Åbyholm, 1978a; Oka, 1979; Koguchi, 1980). The differences in rates may be either spurious or real. No study has as yet adequately distinguished all of the differing explanations for the observed rate differences among sites.

Spurious differences in the reported rates for orofacial clefts may be attributable to several different factors. One is the use of differing diagnostic criteria (Chung et al, 1968; Bagatin, 1985). Another factor is the limitation imposed by inadequacies in the classification systems employed for cleft phenotypes, including inappropriate lumping of categories (Gordon et al, 1969). A third factor that may be responsible for apparent differences in reported rates is reliance on inaccurate sources (Emanuel et al, 1973) such as birth certificates, hospital records, and clinic records, with failure to correct for their underascertainment bias. The underrecognition of less severe expressions of clefts, such as submucous cleft palate, may occur (Bagatin, 1985), regardless of the source of data. Underrecognition of repaired cleft defects may also occur if cases are surveyed when older. Last, a change of many birth mothers' places of residence between conception and delivery may markedly alter the comparison of clefting rates between one geographic area and another (35.5 percent did so in an unpublished study by Flynt in Atlanta from 1969–1971, as reported without elaboration by Emanuel et al, 1973).

Additional reasons for spurious rate differences across various studies result from the employment of different sampling methods (Chung et al, 1968). Using a case series, for instance, does not necessarily yield representative samples, whereas employing random or properly constituted systematic samples is much likelier to do so. Treating perinatal deaths and/or stillbirths as exclusions from some populations studied (as in Brogan and Murphy, 1979), but not from others may result in significantly biased statistics if one fails to take sample design differences into account. Potential counting problems become particularly important when sex differences in the prenatal lethality of fetal malformations occur (Niswander et al, 1972; Oka, 1979; Bixler, 1981). Rate differences can also be created by sampling from different types of populations. A clinic sample, for example, has an inherent selection bias (Biggerstaff, 1969; Oka, 1979) compared with a general population sample. Comparisons of population rate statistics can also be influenced adversely if the sampled populations differ significantly in their racial, ethnic, socioeconomic status, or other subgroup composition. Finally, spurious rate differences can occur if unequal sampling fractions are employed to estimate incidence or prevalence rates in different populations (Chung and Myrianthopoulos, 1975) and if measurement error or instability in these rates is overlooked in comparing them.

Actual rate differences for cleft lip and palate are attributable to underlying variation in the populations from which the different samples have been drawn. These differences may be based on a number of factors. One is variation in genetic susceptibility. There are variations between ethnic groups (Burdi et al, 1972; Leck, 1972) and basic differences in facial width among the races (Lynch and Kimberling, 1981). The different proportions of susceptible genotypes between races may be caused by their different rates of survivorship and reproduction or by the effects of migration (Lynch and Kimberling, 1981). There may also be differences attributable to allelic restriction in the ancestors of various populations (Melnick and Shields, 1976; Bixler, 1981). Another factor contributing to true population rate differences in orofacial clefts is variation in environmental exposure(s). Different populations may be exposed to teratogenic influences that differ in nature, dose, or duration. Selective subpopulation exposure rates may exist, such as those caused by sex differentials in the timing of palatogenesis in developing embryos (Bixler, 1981).

The factors mentioned above that account for discrepancies in orofacial cleft rates can also confound reported secular trends in incidence and prevalence (Charlton, 1966; Ivy, 1968; Tünte, 1969; Stark et al, 1970; Brogan and Murphy, 1978; Rintala and Stegars, 1982). Thus, rates of congenital lip and palate anomalies may be influenced by lack of statistical adjustment for such factors as the changing proportions of susceptible genotypes (Lynch and Kimberling, 1981), racial compositions (Conway and Wagner, 1966), or exposures to teratogenic factors (Lynch and Kimberling, 1981) in the same population during different referent time periods. Secular trends in rates may also be affected by changes in case ascertainment methodology over time, such as improved diagnosis of cleft variants and better reporting in general (Fogh-Andersen, 1980). Consequently, few of the secular trend observations reported in the literature can be interpreted as either spurious or real.

RECOMMENDATIONS FOR PRODUCING BETTER DESCRIPTIVE STATISTICS

Based on the critical review of the literature as noted above, the following recommendations are offered with respect to the accuracy of incidence and prevalence rates for orofacial clefts.

Multiple sources of ascertainment from population-based samples should be used for incidence statistics (Klaskova-Burianova, 1973), and complete censuses or representative samples should be employed for prevalence statistics. These constitute the best approaches available for preparing accurate rate estimates, because no single data source has sufficient reliability (Czeizel and Tusnadi, 1971). Incidence and prevalence rates should also be corrected for underascertainment before publishing or comparing with other statistics. For this purpose, the method of Ching and Chung (1974) is recommended.

In preparing incidence data to support genetic and other etiologic studies, all abortuses and stillbirths should be included or appropriate adjustments made. Similarly, the effects of differential prenatal and postnatal death rates on the apparent sex ratios for clefts should be documented. All degrees of cleft expression should be diagnosed to prevent underascertainment. Last, in interpreting the relationship of prevalence to incidence data, the influence of anomalyspecific survivorship should not be ignored, either on each separate condition or on overall statistics.

All epidemiologic and genetic statistics should be presented by specific cleft type whenever possible (Fogh-Andersen, 1942; Fraser, 1970; Melnick and Bixler, 1981; Khourly et al, 1983). Each cleft type should be subdivided by the presence or absence of associated congenital malformations (Emanuel et al, 1973; Spry and Nugent, 1975). The syndromic cleft cases should be separated from nonsyndromic ones (Bixler, 1981). Incidence statistics for clefts will further benefit risk factor studies if they are tallied separately for familial and sporadic cases (Burdi et al, 1972; Melnick et al, 1980; Bixler, 1981; Shields et al, 1981), whose genetic and environmental risk factors may differ, and then by syndromic versus nonsyndromic status within these categories (Melnick et al, 1980). Since the major cleft phenotypes are actually heterogeneous entities (Melnick and Shields, 1976; Bixler, 1981), disaggregating them for statistical purposes may aid the investigation of unitary disease categories.

Incidence and prevalence rates need further investigation. Incidence studies by time, place, and person (e.g., by month of birth, residence at conception, cleft laterality, and other factors) should be repeated, avoiding underdiagnosis, misdiagnosis, faulty sampling, and the other strategic errors that have been described in this paper.

In comparing different countries and evaluating secular trends in clefting rates (Emanuel et al, 1973), all incidence and prevalence rates should be adjusted for racial composition of the population. Either the standard direct or indirect method of adjustment may be used (Mausner and Kramer, 1985). Last, incidence rates should be adequately studied in suspected high risk population subgroups, such as specific parental gentotypes or phenotypes, older parents, multiparous mothers, medicated mothers, mothers with certain chronic diseases, and parents from lower socioeconomic classes.

EXAMPLE OF HYPOTHESIS TESTING WITH DESCRIPTIVE EPIDEMIOLOGIC DATA

The hypothesis of a continuum of reproductive casualty postulates that the more severely affected the fetus, the greater the chance of abortion or stillbirth (Lilienfeld and Pasamanick, 1954; Pasamanick et al, 1956; Porter and Hook, 1979). This is known as the lethal component. Survivors then contribute to infant mortality rates in direct proportion to the severity of their defects, particularly in the neonatal period (the sublethal component of the postulated continuum) (Lilienfeld et al, 1955). The least impaired in gross anatomic terms might show only subtle mental or emotional deficits (Pasamanick et al, 1956). Data on cerebral palsy (Lilienfeld and Pasamanick, 1955), epilepsy (Lilienfeld and Pasamanick, 1954; Pasamanick and Lilienfeld, 1955a), mental deficiency (Pasamanick and Lilienfeld, 1955b), and behavior disorder (Pasamanick et al, 1956) consistent with this conceptual framework were already presented by its originators to enhance the biologic plausibility of their hypothesis. In modern genetic terms, chromosomal anomalies affect the expression of many genes and hence are usually more severe in their effects than are conditions involving only single gene deficits.

Additional epidemiologic statistics lend further support to the continuum of reproductive casualty, although their consistency with it still does not provide definitive proof. These findings include (1) a high frequency of orofacial clefting and of other malformations in abortuses (Kraus et al, 1963; Nishimura, 1970; Iizuka, 1973; Nishimura, 1975; Nishimura and Okamoto, 1976; Dronamraju and Bixler, 1983); (2) a stillbirth rate for cleft malformations twice as great as the live birth rate in the same population (Åbyholm, 1978a); and (3) mental retardation as the most common cleftassociated condition in some studies (Weatherley-White et al, 1972; Åbyholm, 1978b). In all of these findings, the clefting may be part of a syndrome rather than an isolated condition. The finding of median facial clefts as predictors of brain malformation and functional derangement and dysfunctional outcomes proportional to cleft severity (DeMyer, 1975) are also consistent with the hypothesis of a continuum of reproductive casualty, but etiologic evidence remains weak.

A more refined examination of this hypothesis would involve cross-classifying cleft cases by (1) familial or sporadic and (2) syndromic or nonsyndromic. Each of the four subgroups so created should then be tallied by specific type of cleft case. Analyses should explore the multiplicity and severity of all fetal malformations and other effects within each subgroup (i.e., familial syndromic, familial nonsyndromic, sporadic syndromic, and sporadic nonsyndromic). In this way, additional correlational findings can be adduced to help substantiate the hypothesis of a continuum of reproductive casualty by studying differential survivorship among the population of all conceptuses. The recommendations for hypothesis testing in no way are meant to preclude application of the more direct approaches of analytic epidemiology, such as case-control studies or prospective research designs (Lilienfeld and Lilienfeld, 1980; Mausner and Bahn, 1985).

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Commentary

Every few years or so, a review article on the incidence of cleft lip and palate appears in the literature. If one were to estimate the frequency of these articles, one every five years with a variance of 2 years would be a safe guess. All of these articles attempt to clarify variables associated with the clefting phenomena. In the end, however, only a few variables associated with cleft lip and palate have remained consistent within all of these reports, as follows:

- 1. A distinct racial gradient in the incidence of cleft lip and palate (Orientals with the highest incidence, blacks the lowest, and whites intermediate). For isolated cleft palate, the gradient is not as dramatic, although the trend remains the same as with cleft lip and palate.
- Difference in the incidence of congenital clefts by sex. More males are born with cleft lip or a combination of cleft lip and palate. For combined clefts of the lip and palate, both male and female, males are affected more severely. More females are affected with isolated clefts of the palate.
- 3. A higher incidence of isolated cleft lip or cleft lip and palate occurs on the left side, but cleft palate is more often associated with bilateral than with unilateral cleft of the lip.
- 4. Clefts are often associated with other congenital anomalies and are frequently a part of a distinct syndrome.

The other variables described in the article by Sayetta et al, such as seasonal variation and secular trends, remain obscure. All of this is not new. Those who have been in the field of craniofacial disorders for any length of time will find the four phenomena associated with congenital clefts of the lip and palate to be old news. And so they are. But, this conclusion leaves us with only two directions to follow. One is to conclude that, because there are so many unknown factors associated with the etiology of congenital clefts, it is best to save time and money and concentrate our resources on improving treatment. The second alternative is not to abandon these epidemiologic studies and to continue to gather population data using improved standardized methods. The former direction is not appealing to most of us, especially if we are epidemiologists or geneticists. The path to the latter direction is a more interesting and potentially more satisfying one. It is to this path that Dr. Sayetta and her colleagues are trying to direct us.

To those of us who have been balancing ascertainment bias and incomplete ascertainment, the recommendations proposed by the authors to help us "produce better epidemiologic data" are redundant. We should, however, realize that all of us are not trained epidemiologists, and it is to the nonepidemiologists among us as well as to the newcomers to the field that this article will find its mark. In orienting us to this "correct" path, however, the guidelines should be clearly described.

Sayetta et al point out that measures of frequency of congenital clefts have been misused. This can lead to confusion when comparing different studies from other places and times. It is, therefore, essential that rates of congenital clefts are made in terms that will allow comparison between populations or between subgroups within a population (MacMahon and Pugh, 1982). A clear distinction is made between incidence and prevalence of a condition in the article by Dr. Sayetta and her co-workers. We now know that they are both rates, and that incidence is the number of new cases over a specified period of time. Prevalence, however, is quite different. It measures the total number of cases of a condition "of all, or particular, ages in a defined population at a given point in time or during a specified delimited period."

Although we are left with a clearer notion of incidence and prevalence and now recognize that they are "neither equivalent nor interchangeable," we are still not sure what we can do with these rates. Incidence of a condition is obviously useful in determining changes or trends over a period of time, within and between populations. Beyond that there appears to be little more that we can do with these rates. What is important between incidence and prevalence is that, although they are not interchangeable, they are nevertheless interrelated. Prevalence varies as the product of incidence and duration (MacMahon and Pugh, 1982), or stated mathematically,

$Prevalence = Incidence \times Duration$

This interrelationship is obviously of more importance to infectious and acute diseases than it is to congenital disorders. For the former we can determine the onset of the disease, average duration, and the termination, all measured within the time units specified for incidence. Because congenital cleft lip and palate occur prenatally, onset is obviously measured at birth. Incidence is then measured as the number occurring in all live births. We will exclude fetal death in this discussion. Because the duration for a cleft, whether repaired or not, is for life, duration is conveniently eliminated or given a value of one. Eliminating one value of the relationship or given a value of one. Eliminating one value of the relationship because duration is assumed unity (birth to death) simplifies the relationship. However, it may also obscure some interesting clues related to the developmental biology of clefts. For example, the average age of death of individuals born with a cleft has not been investigated. Because orofacial clefts are usually fusion problems, specifically the lack of fusion that leads to a cleft, it would be of interest to determine the average life span, major cause of death, and other health-related factors associated with mortality of those born with a cleft.

Ascertainment bias and incomplete ascertainment are systematically reviewed and are major concerns of the authors. Nothing less than complete ascertainment appears to be their goal in order to attain the "true" incidence and prevalence of clefts. A commendable stance, but one that is philosophically and economically unsatisfactory. "Philosophically unsatisfactory" because, no matter how completely one thinks that all of the possible cases have been included in the study, there will still remain uncertainty as to whether complete ascertainment has been achieved. It is also "economically unsatisfactory" because it would require an enormous amount of resources in time and money to attempt complete ascertainment of all cases of congenital clefts.

Rather than adhering stringently to eliminating ascertainment bias and incomplete ascertainment, it would be much more cost-effective, more realistic, and more productive to develop strategies to estimate bias and completeness of ascertainment and then to make the appropriate corrections. Some of the methods are available through estimates of underreporting discovered by several authors. Others can be developed through the use of sampling techniques used in population genetics (Li, 1961) to analyze familial aggregate of rare diseases (Morton, 1982), which are free of bias because of incomplete ascertainment (Burdette, 1962). This approach is at once both old and new. It is old because population geneticists have long dealt with the simple inheritance of rare traits and have developed elegant methods to determine frequencies and familial patterns of these traits. It is new because, with the combining of techniques of both epidemiology and population genetics, a new discipline has emerged—genetic epidemiology.

A prime mover of this discipline is Newton Morton, who published the first book on genetic epidemiology (Morton, 1982). In the introduction, he describes genetic epidemiology as "A science that deals with etiology, distribution, and control of disease in groups of relatives and with inherited causes of disease in populations" (Morton, 1982, pp. 1–2). A broader definition of "inherited" is meant in this description, and includes "both biological and cultural inheritance. The set of relatives may be as close as twins or extended as an ethnic group" (Morton, 1982, p. 1).

Because clefts of the lip and palate are for the most part discrete, classifiable, and fairly common entities, and because clefting also tends to occur in families as family specific cleft types (Oka, 1979), genetic epidemiology as defined above promises to provide us with another more refined approach to uncovering the causal factors of congenital clefts.

Another more easily attained approach that will fulfill the requirements of epidemiology, population genetics, and genetic epidemiology is the sharing of clinical data. Clinical as well as population data on cleft lip and palate from several centers throughout the world will greatly advance the knowledge of etiology as well as improved treatment methods for clefts of the lip and palate. Acquisition, storage, processing, and transfer of data, and subsequently the sharing of information, is possible now at high speeds and low expense that were only dreamt of just a decade ago. The power of microcomputers has grown at a phenomenal rate, and at the same time their costs have decreased. Now is the time to become serious about standardizing data files and to develop cooperative research projects through active sharing of clinical data. It is only through the pooling of data that some of the vexing questions remaining about the etiologic factors associated with clefting will have a chance to be answered. It is obvious, by looking at all of the previous studies examined by Dr. Sayetta and colleagues, that no single center or study has been able to gather sufficient data to analyze and test hypotheses satisfactorily on etiologic factors or to define better treatment techniques for clefts of the lip and palate.

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