CONGENITAL MALFORMATIONS AND OTHER DISORDERS--
THE INFLUENCE OF GENETIC AND NONGENETIC FACTORS

MASTER

Final Report

for Period January 1, 1974 to June 30, 1975

Charles M. Woolf
Arizona State University
Tempe, Arizona
85281

PREPARED FOR THE U. S. ENERGY RESEARCH AND DEVELOPMENT
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Final Report Submitted to
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INSTITUTION:	Arizona State University Tempe, Arizona 85281
DEPARTMENT:	Department of Zoology
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ABSTRACT

During the years 1960-1975, research has been carried out at the University of Utah and Arizona State University by the Principal Investigator to determine the importance of genetic and nongenetic factors for specific congenital malformations in man. This work has been supported by the U. S. Atomic Energy Commission and the U. S. Energy Research and Development Administration. Before the etiologic role of mutation can be evaluated for congenital malformations, it is necessary to obtain this information.

A total of 20 papers have been published as a result of this research program. Two papers have been accepted for publication and a manuscript has been submitted for publication. Other papers are being written at the present time. It is anticipated that the data generated by this research program will serve as the basis for many future research projects. The Principal Investigator is thankful for the support given by the U. S. Atomic Energy Commission and the U. S. Energy Research and Development Administration.

INTRODUCTION

This research program on congenital malformations was supported by the United States Atomic Energy Commission and the United States Energy Research and Development Administration during the periods 1960-1966 and 1969-1975. The objective was to investigate the etiological role of genetic and specific nongenetic factors for certain congenital malformations in man. Before the etiological role of mutation can be evaluated for congenital malformations, it is necessary to obtain this information. Mutagenic agents such as radiation are of minor importance if the malformation in question is maintained in the population for some reason other than a balance between mutation rate and selection pressure, or if nongenetic factors are of etiological importance.

The following papers have come from this research program:

- (1) Woolf, C. M. and R. B. Grant. Albinism among the Hope Indians in Arizona. Am. J. Human Genetics 14:391-400, 1962.
- (2) Woolf, C. M., R. M. Woolf and T. R. Broadbent. A genetic study of cleft lip and palate in Utah. Am. J. Human Genetics 15:209-215, 1963.
- (3) Woolf, C. M., R. M. Woolf and T. R. Broadbent. Genetic and nongenetic variables related to cleft lip and palate. Plast. Reconstr. Surg. 32:65-74, 1963.
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- (5) Woolf, C. M., R. M. Woolf and R. R. Broadbent. Cleft lip and heredity. Plast. Reconstr. Surg. 34:11-14, 1964.

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- (7) Woolf, C. M., R. M. Woolf and T. R. Broadbent. Lateral incisor anomalies: Microforms of cleft lip and palate? Plast. Reconstr. Surg. 35:543-547, 1965.
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- (15) Reid, R. L., and C. M. Woolf. A genetic and karyotype study of complete or incomplete paraxial radial hemimelia in Arizona - Implications for genetic counseling. Ariz. Med. 27:6-11, 1970.
- (16) Woolf, C. M. Congenital cleft lip: A genetic study of 496 propositi. J. Med. Genetics 8:65-83, 1971.
- (17) Woolf, C. M. Congenital hip disease: Implications for genetic counseling. Social Biology. 18:10-17, 1971.
- (18) Woolf, C. M. Missing maxillary lateral incisors: A genetic study. Am. J. Human Genetics. 23:289-296, 1971.

- (19) Woolf, C. M., and N. C. Myrianthopoulos. Polydactyly in American Negroes and Whites. Amer. J. Human Genetics. 25:397-404, 1973.

- (20) Woolf, C. M. A genetic study of syndactyly in Utah. Social Biology. 20:335-346, 1973.

A paper on spina bifida cystica has been accepted for publication in Social Biology. A copy of that paper is included with this report.

- (21) Woolf, C. M. A genetic study of spina bifida cystica in Utah. Social Biology. (in press)

Another paper on dermatoglyphics and cleft lip has been submitted for publication in The American Journal of Human Genetics. A copy of that paper is also included with this report.

- (22) Woolf, C. M., and Ann D. Gianas. Congenital cleft lip and fluctuating dermatoglyphic asymmetry. Amer. J. Human Genetics. (submitted)

A paper with a title of Albinism has been accepted for publication in Handbook of North American Indians (published by the Smithsonian Institute). A copy is included with this report.

- (23) Woolf, C. M. Albinism. Handbook of North American Indians. (in press).

Research on the genetic aspects of specific malformations since 1960 has resulted in a collection of a large quantity of data and pedigrees that lend themselves to various types of analyses. These data and pedigrees contain answers to many questions concerning the etiology of congenital malformations. Even though the contract period is concluded, additional papers will be published. In each case the United States Energy Research and Development Administration will be acknowledged for its support of the research. Summaries of the subject matter of these future papers are presented in this report.

The following subject matter on the problem of sex ratio in cases of syndactyly type 1 will be the basis of a future paper submitted for publication.

THE PROBLEM OF SEX RATIO IN CASES OF SYNDACTYLY TYPE I

Because of the dominant mode of inheritance of many types and the conspicuous nature of digital anomalies, syndactyly is a prime congenital malformation for family history studies. A genetic study of syndactyly in Utah has been made by the Principal Investigator (Woolf, in press). Propositi were selected from medical records in hospitals in the larger cities of Utah (Salt Lake City, Ogden, and Provo). Large kindreds were encountered with Type I Syndactyly (Zygodactyly) and Type II Syndactyly (Synpolydactyly). Of interest is the strong sex ratio favoring males which occurs in the Utah kindreds with members showing Type I syndactyly. The reasons for this distorted sex ratio remain enigmatic. Two different hypotheses present themselves: (1) The aberrant sex ratio results from lower penetrance in females than males; (2) The aberrant sex ratio results from segregation distortion in males involving the Y chromosome and the autosome which carries the dominant mutant gene. In order to test these hypotheses an attempt was made to obtain a large number of pedigrees. Thirty five pedigrees of Syndactyly Type I were located by searching the world literature. Sixteen were added from the study of syndactyly in Utah. The 51 pedigrees have been divided into two sub-groups: Syndactyly Type Ia includes kindreds in which affected members have webbing only between the second and third toes. Syndactyly Type Ib includes kindreds in which affected members have webbing between the third and fourth fingers and/or the second and third toes with occasional involvement of other digits.

The data from 26 pedigrees of Syndactyly Type Ia are presented in Table 1. In these pedigrees there are 175 affected individuals; 109 are males (62%) and 66 are females (38%). The data do not support the hypothesis that the aberrant sex ratio is due to lower penetrance in females than males. Such a hypothesis would predict that "skips" in pedigrees would occur more frequently in females than males. In the 26 pedigrees under study, nine heterozygous individuals who were free of the trait transmitted the dominant gene to one or more offspring. Eight were males; one was a female.

In the pedigrees, affected fathers produced 187 offspring, of which 104 (55.6%) were affected. This value does not deviate significantly from the expected Mendelian value of 50% ($\chi^2 = 2.14$, $.2 > P > .1$). Yet, 77.4% of the sons and 34.8% of the daughters were affected. Each of these two values do differ significantly from the expected Mendelian value of 50% ($\chi^2 = 26.9$, $\chi^2 = 7.9$, respectively). Such a severe distortion of frequency values is not observed among the progeny of affected females. A total of 63 offspring were produced by these females. Of this number, 27 (42.9%) had Syndactyly Ia. This frequency value does not deviate significantly from the expected Mendelian value of 50% ($\chi^2 = 1.0$, $.5 > P > .3$). However, 53.1% of their sons were affected and only 32.3% of their daughters were affected. Neither of these frequency values deviates significantly from 50% ($\chi^2 = .03$, $.9 > P > .8$; $\chi^2 = 3.2$, $.1 > P > .05$, respectively). Since the sex ratio of progeny (95 sons: 92 daughters) of affected fathers is normal, a type of differential sperm dysfunction seems to be ruled out where the favored

sperm is one with the Y chromosome and the dominant gene for syndactyly. However, the data are compatible with the hypothesis of segregation distortion where at the first meiotic division, the dominant gene tends to go to the same pole as the Y chromosome. Tending to negate this hypothesis, however, is the troublesome low frequency value of affected daughters (32.3%) of affected mothers. Even though this value does not deviate significantly from 50%, it is nevertheless of the same magnitude as the frequency of daughters (34.8%) of affected fathers. It is possible that this low frequency value is merely an example of sampling error; however, it may also manifest some other phenomenon.

Analyses of published pedigrees can often lead to erroneous conclusions. Pedigrees that appear in the literature may have been submitted for publication solely because they show many affected individuals. Furthermore, there may be a tendency to omit normal sibs from such pedigrees. Accordingly, in these pedigrees, the frequency of affected offspring produced by affected parents may tend to be high. It is apparent that more kindreds of Syndactyly Type Ia are needed before a definitive statement can be made about the inheritance of this anomaly.

The distorted data for Syndactyly Type Ia become even more meaningful when a comparison is made with the data for Syndactyly Type Ib. The data for the latter anomaly, resulting from an analysis of 25 pedigrees, are given in Table 2. There are 195 affected members of these pedigrees; 90 (46%) are females and 105 (54%) are males. The sex ratio data fit a

1:1 ratio ($\chi^2 = 1.01; .5 > P > .3$). All data are compatible with the hypothesis of autosomal dominant inheritance with reduced penetrance in females and males. In these pedigrees there were 27 skips; 15 of these were females and 12 were males. There is no significant difference in the frequency of affected sons of affected fathers and the frequency of affected sons of affected mothers. The high proportion of affected sons of fathers heterozygous for Syndactyly Type Ia is not observed in the sons of fathers heterozygous for Syndactyly Type Ib.

TABLE 1

Offspring of parents heterozygous for Syndactyly Type Ia

Parentage	Sex	Total	Normal	Affected	"Skipped"	Percent Affected	Transmission Frequency*
Heterozygous Fathers	Sons	95	18	72	3	77.42	80.65
	Daughters	92	59	32	1	34.78	35.87
	Total	187	77	104	4	55.61	57.75
Heterozygous Mothers	Sons	32	14	17	1	53.13	56.25
	Daughters	31	21	10	0	32.26	32.26
	Total	63	35	27	1	42.86	44.44

* Transmission Frequency: Frequency of heterozygotes in the offspring of heterozygotes

TABLE 2

Offspring of parents heterozygous for Syndactyly Type Ib

Parentage	Sex	Total	Normal	Affected	"Skipped"	Percent Affected	Transmission Frequency*
Heterozygous Fathers	Sons	111	56	49	4	44.55	48.18
	Daughters	93	51	37	4	40.22	44.57
	Total	204	107	86	8	42.16	46.08
Heterozygous Mothers	Sons	108	59	40	8	37.04	44.44
	Daughters	111	65	35	11	31.53	41.44
	Total	219	124	75	19	34.25	42.92

* Transmission Frequency: Frequency of heterozygotes in the offspring of heterozygotes

The following subject matter on congenital hip in the Apache Indians will be the basis of a future paper submitted for publication.

CONGENITAL HIP IN THE APACHE INDIANS

Etiologic heterogeneity exists for congenital hip disease (acetabular dysplasia and hip subluxation, or dislocation). Both genetic and nongenetic factors influence the probability that this anomaly will occur. Carter and Wilkinson (1964) proposed that congenital hip disease (symbolized by CHD) has at least two genetic components. They proposed that the depth of the joint socket is determined by polygenes, and generalized joint laxity is probably due to a dominant gene. Woolf (1971) concluded that genetic factors play an important etiological role, but a definitive statement could not be made as to the nature of the genetic mechanism. Nongenetic factors which are known to influence the risk of CHD include season of birth, order of birth, and breech malposition at birth. These exogenous factors seem to play a more important role in females than males in determining whether CHD will occur; hence, this disorder is more heritable in males than females.

The incidence of CHD varies among populations. High incidence values have been reported for Navajo and Apache Indian populations living in Arizona. A prevalence rate of 38/1000 was reported by Rabin et. al (1965) for the Navajo Indians living at Many Farms, Arizona. Kraus and Schwartzmann (1957) observed a minimum incidence of 30.5/1000 among the Fort Apache Indians living at Whiteriver, Arizona. Both the Navajo and Apache Indians are members of the Athabascan linguistic stock.

There are two Apache Indian populations in Arizona: the White River population (n = 6000) and the San Carlos population (n = 4500). Preliminary

investigations have indicated that the incidence of CHD is much higher among the Fort Apache Indians than the San Carlos Indians. An investigation has been initiated to explore this suggestion. Specific aims of this study are (1) to determine the incidence of CHD in these two Apache Indian populations; (2) to do a genetic analysis of CHD in these populations; (3) to estimate the coefficient of inbreeding in these two populations; and (4) to investigate the importance of certain nongenetic factors such as birth order, breech malposition and season of birth.

Two incidence values for CHD have been obtained for the San Carlos Indian population. Names of all Apache Indian children born between January, 1960 and December, 1972 were obtained from the fifth revision of the 1970 census record. This record attempts to assess the lineage of each individual in the population. It was possible, therefore, to exclude children who were mixtures of San Carlos Apache and some other tribe (or race) from the study. The medical record of each full-blood child was reviewed at the Public Health Service hospital in San Carlos. Complete medical histories were recorded for children affected with CHD. A total of 1108 medical records were surveyed. Eight children (all females) were noted to have either provisional, probable, or confirmed congenital hip dislocation or dysplasia. This procedure leads to an incidence value of 7.22/1000 in the San Carlos population.

A second incidence value was obtained by using a hospital list of births occurring between January, 1963 and January, 1970. This list records the

names of children born at the hospital or those born at home and brought into the hospital shortly after birth. There is no distinction between full and mixed blood children on this list; all children on the list were included in the study. The medical record of each child was reviewed. Of the 1128 children whose medical records were surveyed, six (all females) were diagnosed as having provisional, probable or confirmed congenital hip dislocation or dysplasia. This gives a prevalence value of 5.32/1000.

Figures that are derived from similar ascertainment methods are needed for the White River Apache population. The incidence value for the Fort Apache population reported by Kraus and Schwartzmann (1956) represents minimum prevalence. The authors estimate that not more than 50 per cent of the total cases had been located, and cases of dysplasia and subluxation were not included in the study. Because of a delay in obtaining approval from the Fort Apache Tribal Council, it has not yet been possible to obtain incidence data for the White River Apache population. U. S. Public Health Hospital authorities have requested that this research should be carried out during the winter months when the demands on their medical records are minimal by outside research teams. Accordingly, work requiring medical records at White River has been postponed until a later time.

It seems apparent, however, that a difference in prevalence values between the San Carlos and White River Apache populations does exist.

Epidemiologic and inbreeding studies will be carried out to gain insight into the reasons for this difference.

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A Genetic Study of *Spina Bifida Cystica* in Utah

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Numerous studies have been carried out during the past decade to determine if spina bifida cystica has a genetic component (Williamson, 1965; Carter, David, and Laurence, 1968; Richards, McIntosh, and Sweenine, 1972; Carter and Evans, 1973). The results of these studies indicate the complexity of the situation. Although the frequency of the malformation is increased in the sibs of propositi as compared with newborn frequency values in the general population, a genetic interpretation is obscured by exogenous factors of etiologic importance that may be present in the home environment. It is also generally agreed that genetic and nongenetic factors causing spina bifida cystica also lead to anencephaly. Both malformations are increased in frequency in the sibs of propositi with either disorder. Based on their own studies and data found in the literature, Carter and Evans (1973) suggest that both of these malformations of the central nervous system are influenced by a genetic predisposition depending on variation at several loci and additional environmental factors. Renwick (1972) presents the intriguing hypothesis that an unidentified substance in certain potato tubers is a major teratogenic agent. Carter and Evans (1973) obtained heritability estimates of 0.60, 0.65, 0.70, for South Wales, Glasgow, and London populations, respectively, where spina bifida cystica and anencephaly occur at a relatively high frequency.

In 1960, studies were initiated by the present author in the state of Utah to determine the etiological importance of genetic factors for various congenital malformations. The results of several of these studies have been published (Woolf, Woolf, and Broadbent, 1963a, 1963b, 1964, 1965; Woolf, 1963, 1971a, 1971b; Woolf, Koehn, and Coleman, 1968; Woolf and Woolf, 1970, 1973). Spina bifida cystica and anencephaly have a relatively low incidence in Utah (Woolf and Turner, 1969). Assuming a polygenic mode of inheritance, the frequency of a congenital malformation in the sibs of probands with the disorder should be a reflection of the incidence in the general population (Edwards, 1969; Falconer, 1965). The frequency in the sibs of probands from a low incidence population (such as Utah) should be lower than the frequency in sibs of probands from a high incidence population (such as Great Britain). Such a phenomenon is not expected for single gene inheritance.

The objective of the present study in Utah was to determine the incidence of spina bifida cystica in the sibs of probands with this congenital malformation; the purpose was to gain further evidence for or against a polygenic mode of inheritance and to obtain an empiric risk value that would be useful for genetic counseling in Utah.

METHODS

Because spina bifida cystica is relatively infrequent in Utah

and the total population of Utah is only about a million, it was not feasible to obtain a large number of *propositi* for this study.

A total of 107 cases (45 males, 62 females) of *spina bifida cystica* were obtained from hospital records in Salt Lake City, Utah.

Upon receiving the names of these *propositi* and their parents, current addresses were obtained from telephone books, city directories, or church records. The homes were visited by field workers who attempted to obtain information of epidemiologic interest. Special attention was given to the occurrence of an anomaly of the central nervous system in the sibs of these *propositi*. An attempt was made to verify these anomalies in the sibs by utilizing hospital records. Since etiological factors leading to a defect of the central nervous system often lead to fetal wastage, an attempt was also made to obtain information on stillbirths and miscarriages resulting from the pregnancies of the mothers of the *propositi*.

Control data were obtained from obstetrical records in Salt Lake City, Utah and Phoenix, Arizona. The objective was to determine if mothers who have produced a child with *spina bifida cystica* show an increased propensity for stillbirths and miscarriages. Control females were matched with the mothers of the *propositi* on the basis of total number of live births. For example, if the mother of a *propositus* had six live births (including the *propositus*), the first female encountered in the obstetrical records with six live births was used as the control.

RESULTS

Spina bifida cystica in sibs: Experience demonstrated that medical records and stillbirth records in the state of Utah do not yield reliable data on specific anomalies present in stillbirths. Information was not available to determine the frequency of anencephaly in the relatives of the propositi. For this reason, the data presented in this study only concern spina bifida cystica in live births.

The propositi had a total of 317 live born sibs. Of this number, 151 were born subsequently to the propositi. Three (0.95%) of the 317 sibs were born with spina bifida cystica. Two of these affected sibs were born subsequently to the propositi, giving a frequency of 2 in 151, or 1.32%. The overall frequency of 0.95% would not be appropriate for genetic counseling since there is a tendency for some parents to terminate the sibship after the birth of a child with spina bifida cystica. Any such tendency results in empirical risk values that are biased downwards; for example, if all sibships were terminated after the birth of an affected child (propositus), the empirical risk value would be zero. For this important reason, the frequency of spina bifida cystica in sibs born subsequently to the propositi is the proper risk value for genetic counseling.

Woolf and Turner (1969) presented data on the incidence of

major malformations among live births in Utah based on nursery records available in the Latter-day Saints Hospital in Salt Lake City, Utah. During the 1951-1961 period there were 59,561 live births in this hospital. Twenty were born with spina bifida cystica. An additional 10 had multiple malformations including spina bifida cystica, giving a total frequency of 30 in 59,561, or 0.05%. Using the population incidence and the risk in sibs, Falconer (1965) developed a method for determining the heritability of anomalies showing polygenic inheritance. Genetic and nongenetic variation exists between affected and nonaffected individuals. In the absence of nonadditive genetic variance, heritability (h^2) is defined as the proportion of the total variance due to genetic differences between affected individuals. Using a population incidence of 0.05% and a sib frequency of 1.32% gives an heritability value of 0.60. It is of interest that a similar heritability value was obtained for South Wales where the incidence of spina bifida cystica is relatively high (Carter and Evans, 1973).

Fetal loss among sibs: The mothers of the probands had a total of 500 pregnancies. Thirteen (2.6%) ended in stillbirths and 66 (13.2%) in miscarriages, giving a total fetal loss of 15.8%. The control females from Salt Lake City had a total of 504 pregnancies. Of this number, 16.5% resulted in either a stillbirth (1.0%) or a miscarriage (15.5%). The percentage values for the control females

from Phoenix were 1.0% stillbirths and 13.1% miscarriages, giving a total fetal loss of 14.1%. Since the total percentage values (15.8%, 16.5%, and 14.1%) are quite similar, these results are compatible with the hypothesis that females who have produced a child with spina bifida cystica do not show an increased tendency for pregnancies to terminate in a loss of the fetus. This conclusion is not unexpected because of the results of other studies (Williamson, 1965) and the relatively small number of mothers included in the study. It is of interest, however, that the mothers of the propositi had 2.6% stillbirths, as compared with 1.0% in control females from Salt Lake City and Phoenix. Because of the inadequacy of the records, it could not be determined if the increase in the mothers of the propositi was due to anomalies of the central nervous system.

DISCUSSION

In Great Britain, the risk of spina bifida cystica in sibs born subsequently to propositi with this disorder is over 5% (Carter and Evans, 1973). Even though only 107 families were included in this study in Utah, and therefore the reliability of the estimates may be questioned, the frequency of sibs with spina bifida cystica is of the order of magnitude expected if the genetic predisposition has a polygenic mode of inheritance. For example, using the average of the

heritability values calculated for Great Britain, i. e., 0.65, by Carter and Evans (1973) and the population incidence of 0.05% obtained for Utah (Woolf and Turner, 1969), the expected frequency of spina bifida among the sibs is 1.64%. This expected value is remarkably similar to the observed value of 1.32% among sibs born subsequently to the propositi. If the actual frequency of affected sibs had been over 5%, which is observed in the sibs of propositi in Great Britain, the polygenic model would be negated because of the low incidence in the Utah population, unless the heritability was much higher in the Utah population.

The population of Utah is predominantly Caucasian. Mormon pioneers began arriving in 1847. The area soon became a "genetic melting pot". Between 1847 and the coming of the railroad in 1869, 80,000 members of the Mormon Church from the United States and Europe emigrated to the area. From 1850 to 1900, over 30,000 converts emigrated to Utah from the Scandinavian countries (Mulder, 1955), and from 1850 to 1929, over 52,000 emigrated from Great Britain (Evans, 1937). Converts arrived in smaller numbers from Germany, Holland, Austria, France, Switzerland, and elsewhere. In 1880, twenty-five different nationalities were represented (Mulder, 1956). Although Mormon communities were established in many locations in the intermountain west and many of these relatively isolated communities were colonized

by groups of families, the rate of inbreeding never went as high as might have been expected. A study of the frequency of consanguineous marriages among the Mormon people and their relatives living in Utah revealed that inbreeding has been minimal when compared with populations in other parts of the world (Woolf et al, 1956). The Mormon people in Utah, especially those residing in cities, are highly outbred, a situation resulting from the continual flow of emigrants to Utah and the social pressure, especially in recent years, against the marriage of closely related individuals. The composite and outbred nature of the population dictates that congenital anomalies resulting from rare autosomal recessive genes and polygenes should be relatively infrequent.

Hewitt (1965) noted that the geographical variation in the incidence of spina bifida cystica in the United States during the period 1950-1955 is both large and credible, with the lowest values occurring in the western part of the United States. He proposed that this geographical variation is due to greater outbreeding in the western part of the United States. Renwick (1972) proposes, alternately, that this geographical variation is correlated with the severity of the late-blight (Phytophthora infestans) attack of potatoes. Potatoes grown in the western part of the United States, such as in Idaho and Utah, tend not to have blight because the low atmospheric humidity does not promote

the sporulation and spread of the fungus. The true reason for the geographic variation is unknown. An exogenous agent may be the principal cause; however, if so, it is of interest that it leads to frequency data mimicking polygenic inheritance. It is likely that exogenous agents and a polygenic predisposition interact to give spina bifida cystica. The importance of a genetic predisposition is shown by racial differences; spina bifida and anencephaly occur at a low incidence in Negroes living in various different geographical regions (Carter and Evans, 1973).

SUMMARY

A genetic study of spina bifida cystica was carried out in Utah using 107 probands with this congenital malformation. The frequency of sibs with this disorder born subsequently to the probands was 1.32%. This relatively low frequency is compatible with the hypothesis of polygenic inheritance because of the low incidence of this disorder in the general population. The heritability estimate based on the risk in subsequent sibs and the population incidence is 0.60, which corresponds to values obtained in Great Britain where this malformation of the central nervous system occurs at a relatively high frequency. A genetic predisposition and unknown environmental factors probably interact to give spina bifida cystica.

Total fetal loss due to miscarriage and stillbirths was not increased in frequency in the pregnancies of the mothers of the propositi when compared with control females from Salt Lake City, Utah and Phoenix, Arizona. However, the stillbirth frequency was increased in the pregnancies of the mothers of the propositi when compared with the control females. It is not known if this increase is attributable to malformations of the central nervous system.

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CONGENITAL CLEFT LIP AND FLUCTUATING
DERMATOGLYPHIC ASYMMETRY

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It has been well established that the close relatives of propositi with cleft lip with or without cleft palate (CL(P)) have a significantly increased frequency of CL(P), but not of isolated cleft palate (CP), while the close relatives of propositi with CP have a significantly increased frequency of CP but not of CL(P) (1-3). Furthermore, when concordance is present in parent-child combinations, the type of cleft appearing in a parent, i.e., CL(P) or CP, is the type usually found in his child (4). Although exceptions do occur, such as the Van Der Woude (lip pit) syndrome (5), and related syndromes (6), these results indicate that, in general, the genetic mechanism giving rise to CL(P) is separate from the one giving rise to CP.

Because it has a higher incidence value and therefore propositi are more prevalent, CL(P) has been the subject of more genetic studies than CP. Etiologic heterogeneity is present for CL(P). Even though the bulk of the cases may have a polygenic mode of inheritance (4), a certain proportion result from chromosomal aberrations (7), rare mutant genes (6), and unknown exogenous factors. The heritability of CL(P) is estimated to be about 0.76 (8-9). Data are also compatible with the hypothesis that unilateral and bilateral CL(P) are part of a genetic continuum, with more genes being required, on the average, to give the bilateral condition (9).

One type of evidence for etiologic heterogeneity is the observation that CL(P) occurs at a lower frequency in the close relatives of propositi with associated malformations than in the close relatives of propositi without associated malformations (9), and that parents and children concordant for CL(P) tend not to have associated malformations

(4). One interpretation is that polygenic cases of CL(P) do not in general have associated malformations while those cases of CL(P) with associated malformations tend to occur for other reasons. Further suggested evidence for etiologic heterogeneity for CL(P) comes from the interesting observation made by Adams and Niswander (10) that propositi with CL(P) who have a family history of this disorder demonstrate increased fluctuating asymmetry of their dermatoglyphics and molar teeth, but propositi with CL(P) who lack a family history of this disorder do not show this type of asymmetry. Based upon the models developed by other (11-13), Adams and Niswander (10) conclude that polygenic systems buffer the development of an organism against environmental influences; the substitution of genes in one of these systems lowers developmental stability and thereby increases the probability of the occurrence of CL(P) and, concomitantly, increased fluctuating asymmetry.

The results of Adams and Niswander (10) suggested the need for a study of the close relatives of propositi with CL(P). If their conclusions are correct, the close relatives of CL(P) propositi with a familial history of this congenital malformation may also show a tendency for increased fluctuating asymmetry. A study was designed to examine the palmar dermatoglyphics of the normal sibs and parents of CL(P) propositi with and without a family history of this congenital malformation. The objective of this paper is to present the results of this study.

MATERIAL AND METHODS

Propositi over five years of age were obtained from the Crippled Children's Hospital, Phoenix, Arizona, and from a group of CL(P) propoiti previously encountered in a genetic study carried out in Utah by the senior author (9). The latter were used to increase the number of propoiti with a family history of CL(P). Attempts were made to obtain the dermal prints of the propoiti and their normal sibs and parents. Normal parents attending the meetings of the Arizona Cleft Lip/Palate Association were also included in this study even though their CL(P) children might not have been available for printing, or were under five years of age, and therefore did not serve as propoiti. The controls included 83 children (5-17 years old) and 83 adults (18-50 years old). These children were from church schools or were participating in summer recreational programs in Phoenix or Tempe, Arizona. The adult controls were students, faculty, and staff at Arizona State University. Permanent dermal prints were obtained from 721 individuals using the technique of Aase and Lyons (14). The propoiti and controls were all Caucasian.

The dermatoglyphic measurement used in this study was the atd angle. This angle was found by drawing a line on the print from the a and d triradius to the t triradius. The angle was measured and recorded to the nearest whole number. The difference between the angle for the right and left hands was then determined. Absolute values were used in the calculation of the variance of these differences (intra-pair variance). An F value was obtained by dividing the intra-pair variance for the propoiti, normal sibs, and normal parents by the intra-

pair variance for the controls. A propositus was categorized as a familial case if CL(P) had occurred in a relative with a coefficient of relationship greater than $r = 1/32$.

Following the procedures of Adams and Niswander (10), individuals were removed from the study if a landmark such as an a triradius or a t triradius was missing. Individuals were also excluded from the study who exhibited asymmetrical hypothecar patterns.

RESULTS AND DISCUSSION

The results of this investigation (see Table 1) confirm the observations of Adams and Niswander (10) that familial cases of CL(P), but not sporadic cases of CL(P), have increased fluctuating asymmetry for the atd angle. The results also show that the normal sibs and normal parents of the familial and sporadic cases are similar to the controls for this type of asymmetry. The similarity between the close relatives of the familial cases of CL(P) and the controls does not negate the hypothesis that the substitution of genes in a given polygenic system lowers developmental stability and thereby increases the probability of occurrence of CL(P) and increased fluctuating asymmetry. This hypothesis may still be correct. The majority of familial cases of CL(P) fall within the range of the controls for the difference measurement (see Table 2) signifying that the biological effect is a small one. Because of this strong overlap and the fact that segregation would diminish the effect in relatives, it is perhaps predictable that the close relatives of familial cases could not be distinguished from the controls for this measurement by using small or even

moderately large samples. Support for the hypothesis comes from the observation that in two different studies propoiti with a family history of CL(P) demonstrate increased fluctuating asymmetry. The observation that sporadic cases are similar to the controls emphasizes that it is not the developmental error per se leading to CL(P) that produces the asymmetry. Other types of congenital malformations purported to have a polygenic mode of inheritance should be investigated in this manner. It would be of biological interest if individuals born with certain other types of malformations, such as congenital dislocation of the hip and spina bifida cystica, only show increased fluctuating asymmetry if they have a family history of the malformation.

SUMMARY

Fluctuating asymmetry for the palmar atd angle was studied in propoiti born with CL(P) and their normal parents and sibs. The propoiti with a family history of this congenital malformation were significantly different from the controls for this type of asymmetry. The propoiti without a family history and the normal parents and sibs of both types of propoiti were similar to the controls. The difference between the two types of propoiti suggests that in some individuals a genetic mechanism may account for CL(P) and increased fluctuating asymmetry for this dermatoglyphic trait.

TABLE 1

ANALYSIS OF THE atd ANGLE IN RIGHT AND LEFT HANDS

Individuals	n	Intra-pair variance	F value
Family History of CL(P)			
a) propositi-----	47	12.9	2.39**
b) normal sibs-----	81	6.7	1.24
c) normal parents-----	96	4.2	0.78
No Family History of CL(P)			
a) propositi-----	42	6.0	1.11
b) normal sibs-----	77	5.1	0.94
c) normal parents-----	95	6.9	1.28
Controls-----	166	5.4	

** Significant at the 0.01 level

TABLE 2
COMPARISON OF THE CONTROLS AND PROPOSITI WITH A FAMILY
HISTORY OF CL(P) FOR ASYMMETRY OF THE atd ANGLE

		<u>Difference between the atd angles in the right and left hands</u>			
Individuals	No.	0	1 - 5	6 - 9	≥ 10
Controls-----	166	22.3%	69.9%	6.6%	1.2%
Propositi-----	47	10.6%	70.2%	12.8%	6.4%

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ALBINISM

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Generalized oculocutaneous albinism, abbreviated here as albinism, is an inborn error of metabolism with a world-wide distribution. The overall incidence of albinism in European populations is about 1 in 20,000, with estimates varying from 1 in 10,000 in Norway to 1 in 29,000 in Italy (Pearson et al. 1911-1913). Higher incidence values have been recorded in other populations. A prevalence value greater than 1 in 3750 occurs among the Navajo Indians in southwestern United States (Woolf 1965). Among school children in the township of Lagos, in southwestern Nigeria, a prevalence of 1 in 2858 was reported by Barnicot (1952). Prevalence values of about 1 in 200 occur among the Cuna Indians of San Blas Province, Lower Panama (Keeler 1964), Jemez and Zuni Indians of New Mexico, and the Hopi Indians of Arizona (Woolf 1965; Woolf and Grant 1962; Woolf and Dukepoo 1969). One of the highest prevalence values occurs among the Brandywine tri-racial (Negro, Caucasian, Amerindian) isolate of Maryland. In this isolate of about 5000 individuals, the prevalence of albinism is about 1 in 85 (Witkop et al. 1966).

Witkop et al. (1970) have shown that both tyrosinase-positive (ty-pos) and tyrosinase-negative (ty-neg) types of albinism occur in man. Each type may show recessive autosomal inheritance. The offspring of marriages between ty-pos and ty-neg albinos are normal, indicating that different autosomal loci are involved (Trevor-Roper 1952; Witkop et al. 1970). Although there is some overlap, especially in younger individuals, phenotypic differences exist between the two types. Ty-neg albinos have white hair, pink skin, translucent gray blue irides and severe nystagmus and photophobia. Ty-pos albinos are characterized by gradual accumulation with age of pigment in the eyes, skin, and hair, and in general exhibit only

moderate nystagmus and photophobia. In North Carolina ty-pos albinism is about twice as frequent as ty-neg albinism among Negroes; these frequency values are approximately reversed among Caucasians (Witkop et al. 1970). Albinos occurring in the Cuna and Zuni Indians and members of the triracial Brandywine isolate in Maryland are ty-pos (Witkop et al. 1970). It is assumed that this is the type of albinism occurring in the Hopi, Jemez, Navajo and other southwestern Indians. The phenotype of these albinos, with their flaxen hair, supports this hypothesis.

The detrimental nature of albinism is well documented (Keeler, 1964) with metastatic skin cancer being a common disease among those who are not protected from the sun. Neel et al. (1949) conclude that in past generations the relative reproductive (Darwinian) fitness (W) of albinos was about 0.4 to 0.5. A relative fitness of 0.4 implies that albinos leave 40 functional offspring for every 100 left by nonalbinos. When a deleterious trait is due to an autosomal recessive gene (c), and when carriers (Cc) and noncarriers (CC) have the same relative fitness ($W=1$), the frequency of affected individuals (cc) in a large population is a function of both the mutation rate (μ) and the selection coefficient ($s = 1 - W$) against affected individuals. The frequency of affected individuals at equilibrium is $R = \mu/s$. The mutation rate at the ty-pos albino locus is unknown, but if a value of 1/50,000 is assumed (that is, there is one gamete containing the mutant gene among 50,000 produced), and the relative fitness of these albinos is given the value of 0.4, the frequency of ty-pos albinos at equilibrium in a large population would be $R = \mu/s = (1/50,000)/(0.6) = 1/30,000$. Mutation pressure and selection against albinos probably accounts for the frequency of individuals with this inborn error of metabolism in most world populations. The occurrence of populations with a

high frequency of ty-pos albinos, such as 1 in 200, indicates that some force other than mutation pressure and natural selection has been operating in past generations.

Hrdlička (1908) visited the Hopis in 1900 and described eleven albinos from ten sibships. Based on an estimated population size of about 2000, the reported prevalence was 1 in 182. Hrdlička missed three albinos living on the reservation at that time (Woolf and Dukepoo 1969). His estimate of the population size may also have been in error. A pilot study (Woolf and Grant 1962) verified Hrdlička's observation that albinos are common in the Hopi population. The observed frequency in 1962 was about 1 in 227. The Hopi reservation is located in northwestern Arizona where it is completely surrounded by the Navajo reservation. Eleven of the twelve existing Hopi villages are located on the top or at the base of three mesas, known as First, Second, and Third Mesa. One village (Moenkopi) is located on the western range of the Navajo reservation but is actually an offshoot of the Third Mesa population. One of the three villages on First Mesa was established by Tewa emigrants from the Rio Grande area in New Mexico, in about 1700, following the Pueblo revolt against Spanish authority during the latter part of the seventeenth century (Dozier 1954). The Hopi and Tewa Indians on First Mesa have intermarried extensively so that First Mesa should be considered as a Hopi-Tewa gene pool. Further investigations (Woolf 1965; Woolf and Dukepoo 1969) of albinism on the Hopi reservation revealed that generalized oculocutaneous albinism is restricted to the Second and Third Mesa populations. In 1968, there were 26 living albinos. Based on an estimated population size of 5000 for Second and Third Mesa, this observed number of albinos gives a frequency value of about 1 in 192. First Mesa is devoid of any individual with generalized

oculocutaneous albinism. No living Hopi remembers any albino of this type being born at First Mesa; furthermore, there is no recorded evidence for such an event. However, a gene causing partial albinism and subtotal nerve deafness is present in the First Mesa population (Woolf 1965; Woolf, Dolowitz and Aldous 1965). The gene giving this syndrome may be located in the X chromosome or an autosome. Two brothers were born in 1952 and 1956 with the syndrome. No other case occurs in the Hopi population. However, Bourke (1884:343), in a narration of his journey to the Hopi reservation in 1881, described a young Hopi boy with the physical features of this syndrome, suggesting that the gene has been segregating in members of this population in past generations.

Stephenson (1904) documented the presence of albinos among the Zunis. This reference plus personal reports of the occurrence of albinos in other Indian populations in Arizona and New Mexico were the catalyst for a study by the present author to determine which Indian populations in these states have a high prevalence of albinos (Woolf 1965). The Indian populations surveyed and the results of the survey are given in Table 1. The majority of the Indian populations in Arizona and New Mexico have no living albinos; three stand out as high prevalence populations: Hopi Indians (1 in 227) in Arizona and the Zuni (1 in 247) and Jemez Indians (1 in 140) in New Mexico. Albinism occurs at lower prevalence values in the Laguna (1 in 2000) and San Juan Indians (1 in 500) in New Mexico, and the Navajo Indians (1 in 3750) in Arizona, New Mexico, Colorado, and Utah. Albinism in the Laguna and San Juan Indians can be attributed to gene flow among the New Mexico pueblo Indians. The presence of the albino gene in the Navajo population is explainable by the close proximity of the Navajo reservation to the Hopi and

Zuni reservations and by Navajo raids in the past on the Hopis and Zunis for the purpose of obtaining food, women, livestock and other booty. Several of the Navajo families with albinos reside near the Hopi reservation.

What is the explanation for the high frequency of ty-pos albinos in the Hopi, Jemez and Zuni Indians? Possible explanations are the founder principle, genetic drift, selection for the heterozygote, some type of cultural selection, or a combination of one or two of these forces. It is evident that the reason for a high frequency in one of these populations may not be the same reason for a high frequency in another population.

FOUNDER PRINCIPLE AND GENETIC DRIFT

A gene may be common in a population if one or more of the few early founders carried the gene. Witkop et al. (1966) conclude that the frequency of albinos in the Brandywine triracial isolate in Maryland is due to the founder principle. All albinos in this inbred population trace their ancestry to a single pair of individuals who were among the founders of the present population. Jones (1965) prepared pedigrees of the albinos in the Jemez population and suggested that the high frequency of albinism in this population can at least partly be attributed to migration. A number of the albinos or heterozygotes are of Pecos descent. While the Pecos Pueblo in New Mexico was at one time a flourishing community of over 2000 individuals, it was reduced to 17 individuals in 1838 by Commanche raids and diseases introduced by Europeans. These 17 individuals migrated to Jemez and helped found the present Jemez population. Jones proposes that these migrants either introduced the albino gene into the small Jemez gene pool or sub-

stantially increased the frequency of the albino gene in this pool. Whether the founder principle is the total explanation for the high frequency of albinism at Jemez or in any other southwestern Indian population has yet to be determined; however, it is a hypothesis that has merit.

Indian populations in the southwest have been plagued by epidemics, periodic starvation conditions and raids by hostile groups. As a consequence, these populations have often consisted of a small number of individuals and the number has remained small over many generations. If the albino gene were present in one of these small populations, the frequency of the gene would be expected to fluctuate from generation to generation by chance segregation and recombination. The recessive gene for albinism may well have reached a high frequency in one or more Indian populations by this force of genetic drift. Stern (1960:271) gives genetic drift as one possible explanation for the high frequency of albinism among the Cuha Indians in Panama.

If the chance process of genetic drift or the founder principle is the explanation for the high frequency of albinism in the Hopi, Jemez, or Zuni Indians, what is the origin of the mutant gene? The ty-pos albino gene in these three different Indian populations is likely "identical by descent" since gene flow has occurred among the Pueblo Indians of Arizona and New Mexico in historic and prehistoric times (see Woolf 1965). The presence of ty-pos albinism in the remote Cuna Indians of Lower Panama suggests further that the mutant gene is not of recent origin and draws attention to Central America as the possible site of origin. There were many albinos in Montezuma's royal household at the time of the conquest. Albinos along with malformed individuals were considered by the Aztecs

as wards of the state. In Prescott's account (p. 320) of Montezuma's royal household at the time of the conquest of Mexico, the following is found:

I must not omit to notice a strange collection of human monsters, dwarfs, and other unfortunate persons, in whose organization Nature had capriciously deviated from her regular laws. Such hideous anomalies were regarded by the Aztecs as a suitable appendage of state. It is even said, they were in some cases the results of artificial means, employed by unnatural parents desirous to secure a provision for their offspring by thus qualifying them for a place in the royal museum.

Numbered in quantity among the unfortunate persons under Montezuma's protection were albinos (Orazco y Berra 1880:381):

There was in this house a room in which there were men, women and children, white at birth in the face, body, hair, eyebrows and eyelashes.

The extent of the practice of protecting malformed children in Central America before the coming of Cortez is unknown. The protection of albinos by the early Aztecs could have served as the catalyst for the propagation of the albino gene at an increased frequency in certain segments of the population and its dissemination by migration to various regions in Central America and the southwestern part of the United States.

SELECTION FOR THE HETEROZYGOTE

A slight discontent is associated with the conclusion that ty-pos albinism reached a high frequency in four different Indian populations (Cuna, Hopi, Jemez, and Auni) by only the chance processes of the founder principle or genetic drift. For this reason other mechanisms should be considered that could act by themselves or in conjunction with a chance force. One such mechanism is selection for the heterozygote.

A deleterious recessive gene will be maintained in a population at an increased frequency if the heterozygotes has a reproductive advantage. For example, if the relative reproductive fitness values (W) of heterozygotes (Cc) and albinos (cc) were 1.00 and 0.5, respectively, the relative fitness of non-carriers (CC) would only have to be 0.962 in order to maintain an albino frequency of $R = 1/200$ in a large population. This slight advantage of the heterozygote, which would be difficult to measure in a practical situation might manifest itself by increased fertility, vigor, maturation rate, or resistance to a disease. An argument against the heterozygote advantage hypothesis for albinism is that environmental conditions are not too different at the present time among the various Indian Pueblo groups in Northern Arizona and New Mexico, even though large differences exist in the frequency of the albino gene in these groups. A heterozygote advantage in one population should be found in all other populations with similar environmental conditions. Yet, it is clear that relative fitness values can be influenced by genetic background (Woolf and Knowles 1964). In the presence of a specific homozygous background produced by genetic drift and many generations of inbreeding, heterozygosity for certain mutant genes might

increase reproductive fitness. A corollary would also be that the advantage ceases with the advent of genetic variability. The presence of albinism at a high frequency in some populations and not others would imply that the latter lacked the proper genetic background or the allele had not been introduced by migration or mutation. Reed (1965) has speculated that the advantage of the heterozygote may be due to genes adjacent to the albino locus rather than at the albino locus.

Some type of advantage of the heterozygote cannot be ruled out as the explanation for the high frequency of albinism in various Indian populations. This hypothesis has bearing on the suggestion of Jones (1965) that the albino gene was introduced into the Jemez population by the 17 Pecos Indians who survived Comanche raids and diseases introduced by Europeans. If this was the origin of the albino gene in the Jemez population, was it merely chance that the gene was present in some of these survivors, or did heterozygosity for the gene increase the probability of surviving a disease introduced by Europeans?

CULTURAL SELECTION

If an Indian population acquired a high frequency of the deleterious typos albino gene by either genetic drift or the founder principle, natural selection should be instrumental in decreasing the frequency from generation to generation. Natural selection against the gene would be more effective in the hot desert populations of southern Arizona than in the more temperate climates of northern Arizona and New Mexico. Pueblo dwellings which afford protection from the sun would lessen the effectiveness of natural selection. An interesting question is whether the impact of natural selection could have been further lessened at any

given time in any pueblo population by cultural attitudes or practices with the consequence that the gene was maintained at a high frequency, or even increased in frequency in at least a segment of the population. This possibility was explored carefully for the Hopi Indians (Woolf and Dukepoo, 1969).

Traditional Hopis reflect only a positive attitude towards albinos and state there is complete acceptance of them in their society. Albinos perform in ceremonies along with other Hopis, and several have been influential chiefs and priests. They are considered as part of the Hopi heritage on Second and Third Mesa (Woolf and Dukepoo 1969). Marriage is important in the life of a Hopi. It is extremely rare to find an adult, especially a woman, who has never been married. The fact that many albinos have remained unmarried contradicts the attitude of complete acceptance in the traditional Hopi society. One albino male stated he was unable to work in the fields and therefore could not grow corn for a wife and family. Although the inability to provide for a family is the excuse usually given for males, the reason is not obvious for females. The acceptance by Hopis of this Hopi heritage apparently stops at marriage. Females should reject males who cannot work in the fields. However, any real or subconscious bias towards marrying an albino apparently does not manifest itself in the selection of a temporary sex partner. Hopis for centuries have made their living by farming. Men and boys would leave the mesa tops and go to the fields, often many miles from the mesas. It is commonly known among the inhabitants of Second and Third Mesa that albino males were not expected to labor in the fields. They remained in the villages and performed tasks such as weaving. In the villages they were protected from the sun and hostile nomads, and most importantly, albino males had ample time and

often the opportunity to engage in sexual activity. One albino male is especially legendary for this activity:

I knew that old man. Some say
he had about twelve kids; others say about
fifteen.

He never married.

They say he was always around trading
with the ladies. He would make babies with
them.

He was real funny, and knew a lot of
good stories. Everyone liked him.

If the high frequency of albinism in the Hopi population were initially due to genetic drift or the founder principle, it is certain that the acceptance and protection of albinos by the Hopis would reduce the effectiveness of natural selection in reducing the frequency of this deleterious gene. Furthermore, in a small population, a sexually active male will have an imposing effect on gene frequencies in subsequent generations. This effect has been described by Neel (1970:817-818) for the Yanomama Indians of southern Venezuela and northern Brazil, where the award for male achievement is extra wives. It was noted that a greatly disproportionate number of grandchildren were born to a few males. The sexual activity of some albino males during the daytime in the villages on top of the mesas may have given the gene frequency a thrust upward in segments of the population during certain periods of time. Whether a similar phenomenon could have influenced gene

frequencies in the Jemez and Zuni populations in past generations is unknown. The Jemez and Zuni Indians are similar to the Hopi Indians regarding the acceptance and protection of albinos (Woolf 1965:28-29). Jemez and Zuni albinos also tend not to marry. However, it is expected that cultural practices regarding albinos might differ among populations and at different times within a population. For example, the frequency of albinism is high among the Cuna Indians of Panama in spite of apparent cultural selection against albinos in some of the Cuna towns, including infanticide (Keeler, 1964). This suggests that the gene frequency in the Cuna population is decreasing each generation from a high value caused by genetic drift or the founder principle, or is being maintained by selection for the heterozygote.

CONCLUSION

The recessive gene for albinism is spread widely through Indian populations of Central America and the southwestern part of the United States. The gene is at a high frequency among the Cuna Indians of San Blas Province, Lower Panama, the Jemez and Zuni Indians of New Mexico, and the Hopi Indians of Arizona. The protection of albinos by the early Aztecs may have served as a catalyst for the propagation of the gene at an increased frequency in certain segments of the population and its eventual dissemination to various regions by migration.

Because of the detrimental nature of this inborn error of metabolism, the existence of Indian populations with a high prevalence of albinos presents an intriguing problem in population genetics. Although selection for the heterozygote could be the major reason for the high frequency of the gene in these populations, other hypotheses may be more tenable. A hypothesis to explain the high frequency

among the Hopi Indians of Arizona involves an interaction of the chance process of genetic drift or the founder principle with a form of cultural selection. The reason for a high frequency in one Indian population may not be the same reason for a high frequency in another population.

A study of the Hopi, Jernez and Zuni Indians in the southwestern part of the United States indicates that time will soon erase albinism as a heritage of these people. Modern transportation facilities, schools on and off the reservation where members of different ethnic groups associate, and growing populations forcing young people to seek employment off the reservation all promote outbreeding, reduce the frequency of the albino gene, and decrease the probability of homozygosity for this gene. The frequency of albinism in these populations will decrease rapidly with the decline of their cultures.

Table 1. Prevalence of Albinism in Southwest Indian Populations in 1967

Population	Estimated population size	Number of albinos	Estimated prevalence
Acoma, New Mexico	2,400	0	
Apache (Jicarilla), New Mexico	1,400	0	
Apache (Mescalero), New Mexico	1,500	0	
Apache, Arizona	11,000	0	
Cochiti, New Mexico	600	0	
Hopi, Arizona	5,000	22	1 in 227
Islets, New Mexico	2,000	0	
Jemez, New Mexico	1,400	10	1 in 140
Laguna, New Mexico	4,000	2	1 in 2,000
Navajo, Arizona, New Mexico, Colorado, Utah	90,000	24	1 in 3,750
Papago, Arizona	9,000	0	
Picuris, New Mexico	150	0	
Pima, Arizona	7,000	0	
San Felipe, New Mexico	1,300	0	
San Ildefonso, New Mexico	290	0	
San Juan, New Mexico	1,000	2	1 in 500
Sandia, New Mexico	200	0	

Santa Ana, New Mexico	400	0	
Santa Clara, New Mexico	800	0	
Santo Domingo, New Mexico	1,900	0	
Taos, New Mexico	1,300	0	
Zia, New Mexico	425	0	
Zuñi, New Mexico	4,200	17	1 in 247

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