# An Epidemiologic Survey of Twins in a Large, Prospectively Studied Population

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Most epidemiologic studies of twins exclude pairs with no liveborn members, thus underestimating to a varying degree the incidence rate of twinning. The mortality rate of twins is more severely underestimated because abortions or fetuses below a a certain weight, even when known, are not considered among twin deaths. Both of these shortcomings are minimized in the present survey of twin births which occurred in the Collaborative Study of Cerebral Palsy, Mental Retardation, and Other Neurological and Sensory Disorders of Infancy and Childhood. This is a cooperative effort on the part of 14 institutions throughout the United States and the National Institute of Neurological Diseases and Stroke of the National Institutes of Health to observe and study events which affect the parents before and during pregnancy and to relate them to the outcome of pregnancy. To this end, approximately 60,000 pregnant women are being followed from the first months of their pregnancy, through labor and delivery, and up to the seventh year of the Study child's life. The Study population is about 45% white, 47% Negro, 7% Puerto Rican, and the rest a variety of other ethnic groups. The collection of information, medical examinations, and laboratory tests are done in uniform fashion and according to preestablished protocol. The prospective nature of the Study makes possible the recording of observations with high accuracy and the avoidance of biases inherent in other types of investigations. These advantages should also be reflected in the collection and evaluation of the twin data.

## BIRTH INCIDENCE AND ZYGOSITY

Table 1 gives a summary of the twins born to Study mothers. In all, 615 pairs of twins were born among 56,249 pregnancies with known outcome, or 1 in 91.5 births. Among whites there were 259 twin births in 25,991 pregnancies, or 1 in 100.3 births; among Negroes there were 331 twin births in 26,080 pregnancies, or 1 in 78.8 births; and among the Other group, consisting mostly of Puerto Ricans, there were 25 twin births in 4,178 pregnancies, or 1 in 167.1 births.

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The twin birth incidence for all maternal ages was higher among Negroes than among whites, and agrees with previous findings (Strandskov 1945; Enders and Stern 1948; Shipley et al. 1967; U.S. Department of HEW 1967). This, as it will be seen later, is due mostly to an increase in dizygotic (DZ) twin births, but also to a slight increase in monozygotic (MZ) twin births. The twin birth incidence among the Other group was considerably lower, but this does not appear to be due to the small size of the sample. The HEW report gives a twinning rate of 10.4 per 1,000 deliveries (with at least one live birth) for the Other group in the United States in 1964, which is comparable with the overall rate of 10.1 per 1,000 deliveries. Shipley et al., however, in a survey of twins in California between 1905 and 1959, found that the Other group, consisting mostly of Japanese and Chinese, had a twinning rate of 6.8 per 1,000 deliveries, which is comparable with our rate of 6.0 per 1,000 deliveries. It is possible, therefore, that Puerto Ricans, as well as Orientals, have a low twinning rate.

TABLE 1

TWINS IN THE COLLABORATIVE STUDY

| Twins | White | | Negro | | Other | | Total | |
|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % |
| Like-sexed, monozygotic pairs | 71 | 27.4 | 101 | 30.5 | 10 | 40.0 | 182 | 29.6 |
| Like-sexed, dizygotic pairs | 51 | 19.7 | 55 | 16.6 | 6 | 24.0 | 112 | 18.2 |
| Unlike-sexed, dizygotic pairs | 84 | 32.4 | 115 | 34.8 | 5 | 20.0 | 204 | 33.2 |
| Like-sexed pairs, zygosity undetermined | 51 | 19.7 | 52 | 15.7 | 4 | 16.0 | 107 | 17.4 |
| Pairs, sex unknown | 2 | 0.8 | 8 | 2.4 | ..... | ..... | 10 | 1.6 |
| Totals | 259 | 100.0 | 331 | 100.0 | 25 | 100.0 | 615 | 100.0 |
| All cases with known outcome | 25,991 | ..... | 26,080 | ..... | 4,178 | ..... | 56,249 | ..... |
| Birth incidence of twins | 1/100.3 | ..... | 1/78.8 | ..... | 1/167.1 | ..... | 1/91.5 | ..... |
| Incidence per 1,000 births | 10.0 | ..... | 12.3 | ..... | 6.0 | ..... | 10.9 | ..... |

The zygosity of 508 pairs of twins was established by comparison of sex, blood types using nine systems (ABO, MNS, Rh, P, Kell, Lewis, Lutheran, Duffy, and Kidd), and gross and microscopic examination of the placenta. Finger and palm prints were were collected for 113 like-sexed pairs, but in no case were they solely deciding in establishing zygosity. As shown in table 1, 182 pairs were like-sexed MZ, 112 pairs were like-sexed DZ, and 204 pairs were unlike-sexed DZ. In 107 like-sexed pairs the zygosity could not be determined. In 78 of these pairs one or both twins died early, before zygosity tests could be done, and placental examinations were not available or were not deciding. The 29 remaining pairs were lost to the Study either because they were delivered outside a Study hospital or because their families withdrew their cooperation. In 10 pairs, the sex of one or both twins could not be determined. Some were early abortions, some ectopic pregnancies, and in two cases a fetus papyraceous was found on the placenta after delivery of a presumed singleton.

An estimate of the zygosity of a large sample of twins can, of course, be made using Weinberg's difference method. The method is based on the assumptions that

the sex ratio is 1:1 and that the sex distribution of DZ twins occurs according to chance frequencies. On this basis the number of all DZ twins is twice that of unlike-sexed twins; the number of MZ twins, therefore, can be obtained by subtracting the number of DZ twins from all twins.

The equality-of-sex ratio holds in our material. Table 2 shows the sex distribution of 605 pairs of twins of known sex. While there is a very slight preponderance of males over females, the sex ratio of 1.01 is actually closer to equality than is usually observed. By the Weinberg method, then, the overall proportions of MZ and DZ pairs, 32.6% and 67.4% (table 3), accordingly are in agreement with expectation. In Negroes the proportion of DZ pairs is much higher than in whites, 71.2% to 65.4%, again in agreement with previous findings (Strandskov and Edelen 1946; Enders and Stern

TABLE 2

SEX RATIO OF TWINS IN THE COLLABORATIVE STUDY

| Sex | No. of Pairs | Males | Females |
|---|---|---|---|
| Like-sexed | 401 | 404 | 398 |
| Unlike-sexed | 204 | 204 | 204 |
| Total | 605 | 608 | 602 |

NOTE.—Sex ratio, 1.01.

TABLE 3

ESTIMATED ZYGOSITY OF TWINS IN THE COLLABORATIVE STUDY (WEINBERG DIFFERENCE METHOD)

| Zygosity | White | | Negro | | Other | | All Twins | |
|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % |
| Monozygotic | 89 | 34.6 | 93 | 28.8 | 15 | 60.0 | 197 | 32.6 |
| Dizygotic | 168 | 65.4 | 230 | 71.2 | 10 | 40.0 | 408 | 67.4 |

1948; Bulmer 1960; Shipley et al. 1967; U.S. Department of HEW 1967). Among twins in the Other group the estimate is for a higher proportion of MZ than DZ twins. The HEW report estimates an MZ twinning rate of 5.1 and a DZ twinning rate of 5.3 per 1,000 deliveries for the Other group, but our figures of 3.6 and 2.4 per 1,000 deliveries for this group agree very closely with those of Shipley et al., who estimated a MZ twinning rate of 4.7 and a DZ twinning rate of 2.2 per 1,000 deliveries in the Japanese and Chinese population of California. It is reasonable, then, to assume that the higher proportion of MZ twins in our Other group is not the result of sampling variation.

It should be pointed out that the Weinberg method for estimating zygosity in a large sample of twins is not very accurate, and at best provides a working approximation of the frequencies of MZ and DZ twins. In our material, for example, the 101 pairs of Negro twins whose zygosity was determined by placental examination and comparison of blood groups exceeds the 93 estimated. In the same theoretical context

it is interesting to note that according to Hellin's law, 6.2 sets of triplets would be expected to be born in the Collaborative Study population. Six sets of triplets were actually born—obviously a very good agreement.

Age of mother is a very important parameter known to influence the rate of twinning. Figure 1 shows the percentage of twin births, by race, out of all births by age of mother. The findings agree, in the main, with those of previous reports. The curve for all twins shows a sharp increase with age up to the 30–34 age group, then a decline, and again an increase after the 35–39 age group. The number in the last two age groups is 66. The curves for whites and Negroes show the same pattern but with a higher overall twin rate for Negroes in all age groups.

When examined by zygosity (fig. 2), the MZ twinning rate appears to be rather stable until about the age of 39 years and then to increase sharply. This trend accounts entirely for the increase in all twins in this age group, observed earlier. The MZ twinning rate is slightly higher in Negroes than in whites, except in the last two age

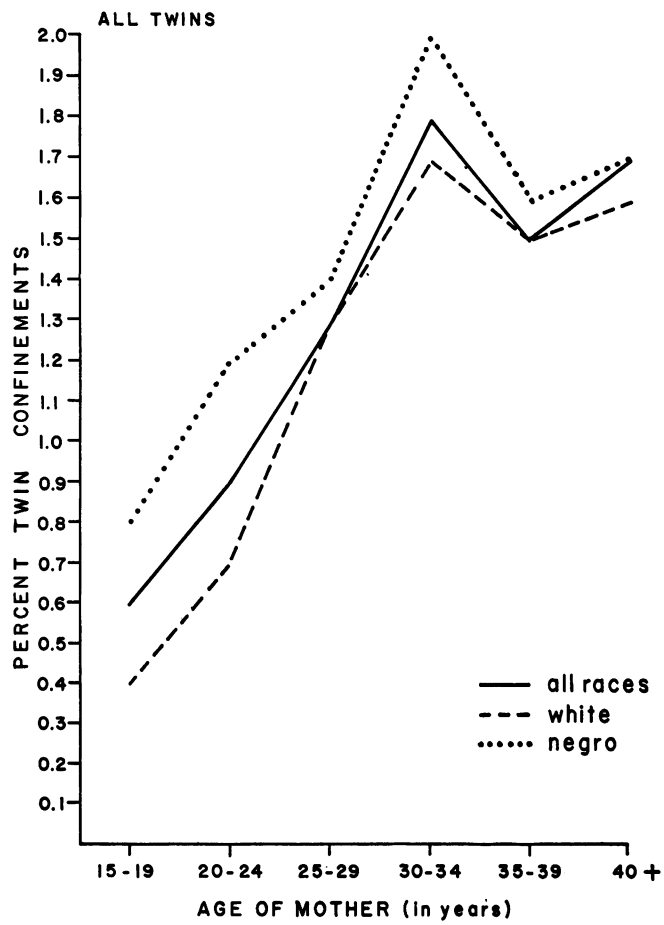


FIG. 1.—Frequency of twin births, by race, in relation to age of mother

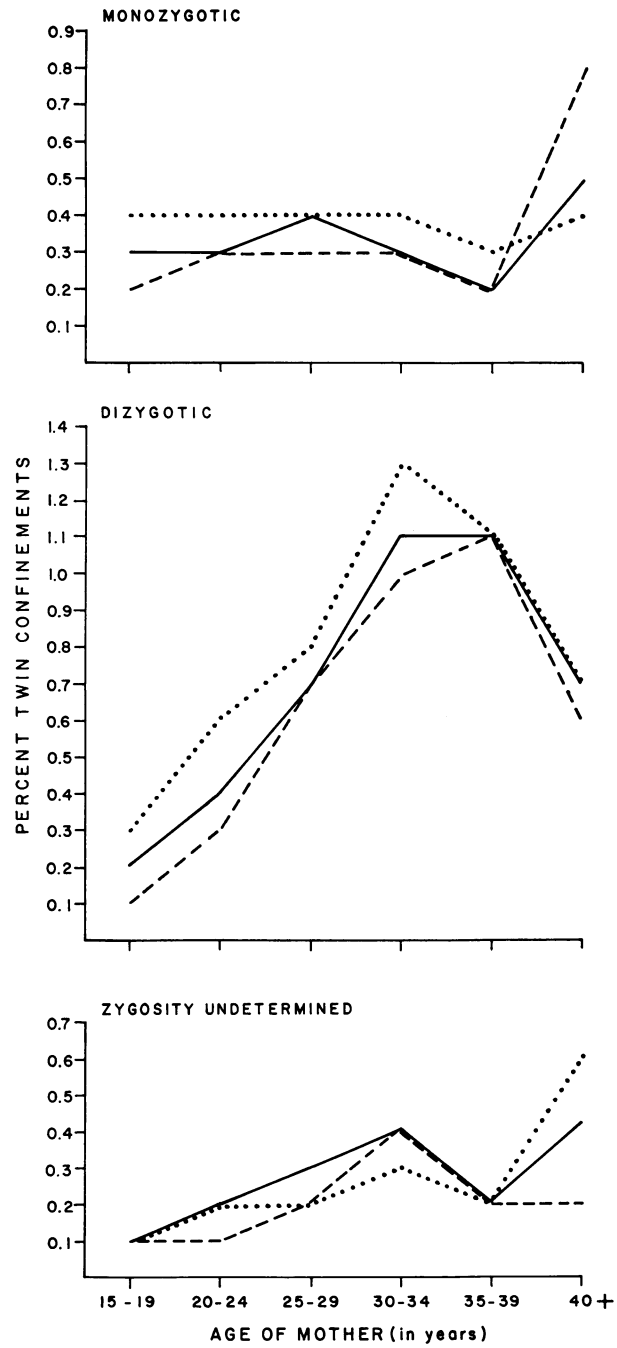


FIG. 2.—Frequency of twin births in relation to age of mother by race and zygosity. Solid line = all races, dashed line = white, dotted line = Negro.

groups. The increase in MZ twinning among whites seems to be sharper than that in Negroes, but the numbers in the last age groups are small, seven for whites and six for Negroes.

DZ twinning increases with age up to the 30–34 age group in Negroes and the 35–39 age group in whites, and then declines dramatically. The DZ twinning rate is considerably higher in Negroes than in whites, and is in line with previous observations. The curves for twins of undetermined zygosity show the increase and decline characteristic of DZ twins up to the 30–34 age group and then the sharp increase after age 39 which is characteristic of MZ twins. This increase, however, is confined to Negro twins though, again, the numbers here are small.

TABLE 4

TWINS BY SEX, ZYGOSITY, AND PLACENTAL FORM

| Sex | Zygosity | Placental Form | No. of Pairs | % |
|---|---|---|---|---|
| Like-sexed | Monozygotic | MA-MC | 9 | 1.5 |
| Like-sexed | Monozygotic | DA-MC | 102 | 16.6 |
| Like-sexed | Monozygotic | DA-DC | 48 | 7.8 |
| Like-sexed | Monozygotic | Unknown | 23 | 3.7 |
| Subtotal | ..... | ..... | (182) | ..... |
| Like-sexed | Dizygotic | DA-DC | 93 | 15.1 |
| Like-sexed | Dizygotic | Unknown | 19 | 3.1 |
| Subtotal | ..... | ..... | (112) | ..... |
| Like-sexed | Undetermined | DA-DC | 74 | 12.0 |
| Like-sexed | Undetermined | Unknown | 33 | 5.4 |
| Subtotal | ..... | ..... | (107) | ..... |
| Unlike-sexed | Dizygotic | DA-DC | 204 | 33.2 |
| Unknown | Undetermined | Unknown | 10 | 1.6 |
| Subtotal | ..... | ..... | (214) | ..... |
| Total | ..... | ..... | 615 | 100.0 |

NOTE.—MA = monoamniotic, MC = monochorionic; DA = diamniotic, DC = dichorionic.

Table 4 describes the distribution of the placental type of the twins. Usable information about the placenta was available for 530 pairs. Of these, nine pairs or 1.7% (1.5% of all twins) were monoamniotic, the rest were diamniotic. The occurrence of a single amnion is, indeed, infrequent, but not as rare as Potter (1963) reported. In her material she found only one monoamniotic placenta in 548 which she examined. Of the 159 MZ pairs for whom placental information was available, 48, or 30.2%, were diamniotic-dichorionic and their zygosity could not have been determined without the aid of blood types and other tests. But in this survey, the zygosity of over half of the twin pairs could have been determined on the basis of sex and placental type alone. Careful examination of the fetal membranes, therefore, when these are available, can be a very useful adjunct in the determination of twin zygosity.

### SOCIOECONOMIC BACKGROUND

There is a little information in the literature concerning the socioeconomic background of families in which twins are born. A socioeconomic index utilizing scores for education, occupation, and family income was developed to describe the population of the Collaborative Study (Myrianthopoulos and French 1968), using the methodology of the U.S. Bureau of the Census (1963). Figure 3 shows the distribution of the twins by socioeconomic index, compared with that of the Study population. The scores for the socioeconomic index are given on a scale from zero (low) to 10 (high). The fit is very good except at the extreme right, where there is an increase of twins in the 6.0–9.9 socioeconomic range. This seems to imply that mothers in the higher socioeconomic categories have more twins. This is not a small sample effect, for the number in these socioeconomic categories is 152, or one-fourth of the twin population. The use of an oral contraceptive can also be ruled out as a cause of the increase in twinning rate. The curve for whites shows a pronounced increase in the same socioeconomic categories and bimodality is evident. The number in these categories is 109. The fit of the curve for Negro twins is excellent, but again the increase in the 6.0–9.9 socioeconomic categories is evident. The number here is 37. In all instances the increase is statistically highly significant ($P<.005$). When plotted by zygosity (fig. 4), the same picture is again obtained. In the higher socioeconomic categories there is a highly significant increase in MZ and DZ twins, as well as in the twins of unknown zygosity ($P<.005$).

In order to assess socioeconomic effects when maternal age effects on twinning frequency are taken into account, logit transforms of the proportions, using three socioeconomic levels (0–2.9; 3.0–6.9;$\geq$ 7.0), were subjected to regression analysis and consequent $\chi^2$ analysis of variance. A computer program written by Dr. Alfred Naylor was utilized for these analyses. Within each racial or zygosity grouping of data, maximum likelihood fitting of constants of the following two equations was carried out:

$$T_i = a + bx + cx^2 \ , \tag{1}$$

$$T_{ii} = A + D_1y + D_2z + Bx + Cx^2 \ , \tag{2}$$

where $T$'s are predicted transforms and $x$ is coded maternal age. Constants $b$ and $c$ in equation (1) relate to linear and parabolic effects of maternal age (preliminary calculations indicated that a parabolic term was needed). In equation (2), $y = 1$ if the socioeconomic level was intermediate; otherwise, $y = 0$. Similarly, $z = 1$ if the socioeconomic level was high; otherwise $z = 0$. Thus, $D_1$ and $D_2$ are adjustments from lowest socioeconomic level $A$ to intermediate and high levels, respectively.

The results of $\chi^2$ analysis of variance are summarized in table 5. Each $\chi^2$ in the first column represents the difference between maternal age $\chi^2$ (second column) from fitting equation (1) and the regression $\chi^2$ from fitting equation (2). The residual $\chi^2$ (column three) shows the goodness of fit of the four-constant model. The table shows that after adjustments for maternal age are applied, the $\chi^2$ with 2 df for socioeconomic differences is highly significant in the DZ group and borderline in the Negro group. The residual differences among maternal age–socioeconomic combinations is negligible

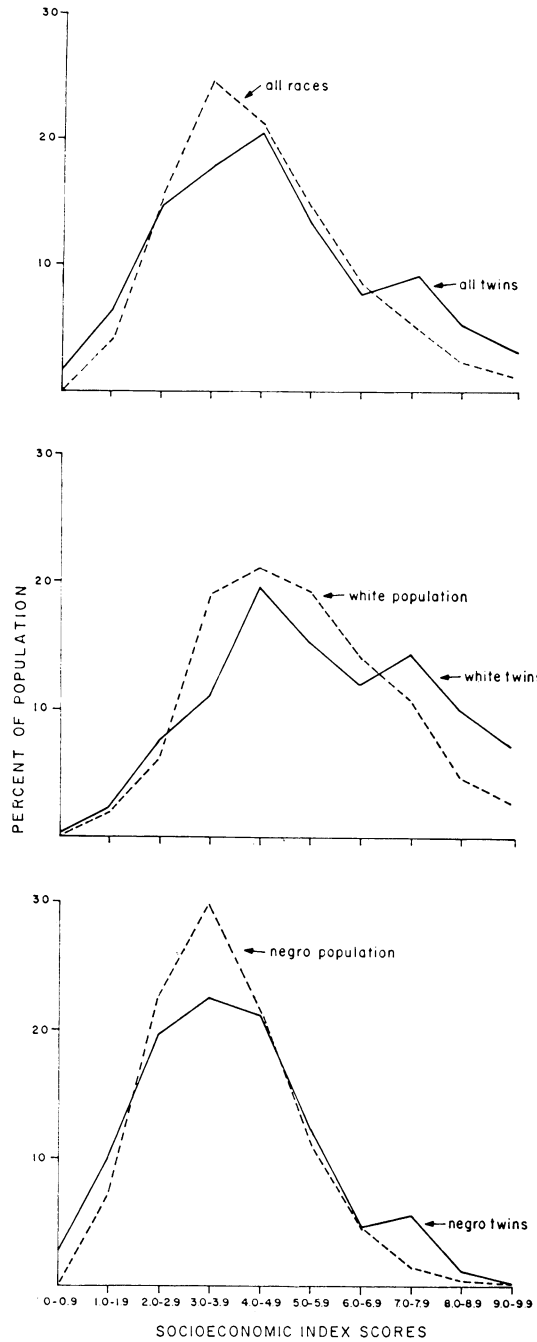


FIG. 3.—Distribution of socioeconomic index scores of mothers of twins, by race, compared with that of the Study population.

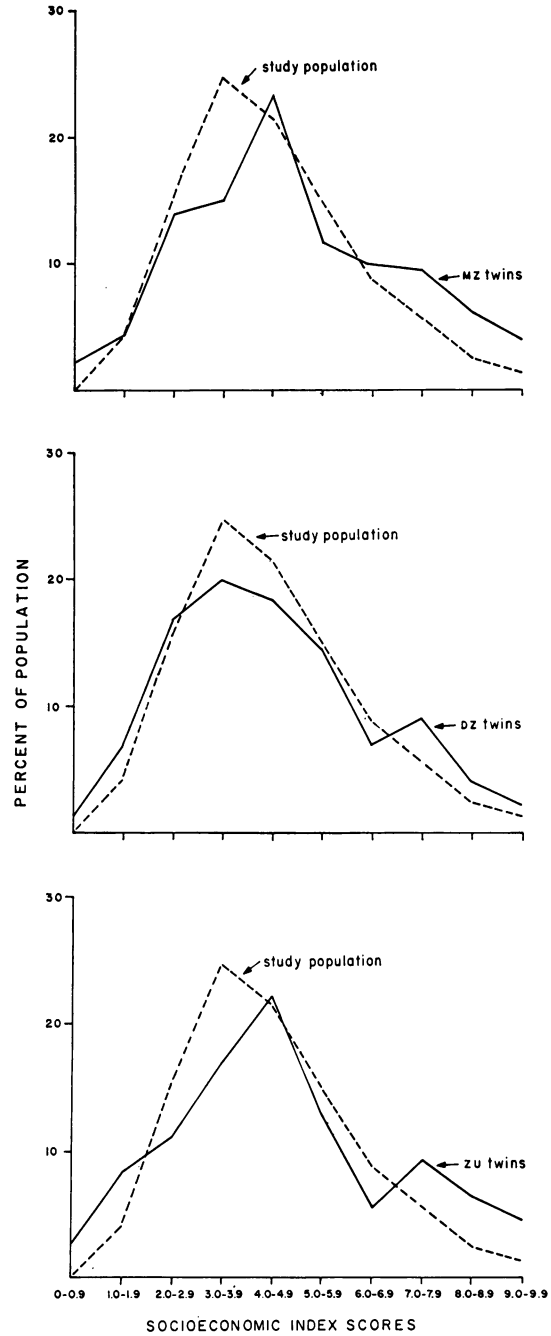


FIG. 4.—Distribution of socioeconomic index scores of mothers of twins, by zygosity of twins, compared with that of the Study population.

in all but the Negro group. A further complete analysis of the Negro data into main effects and interactions was carried out in order to resolve the apparent difficulty. This analysis showed that among Negroes both maternal age and socioeconomic effects and interactions between them were operative. Thus, it appears that the increase in DZ twinning frequency in the higher socioeconomic groups is independent of age of mother, and that the increase in Negro twins is a product of interaction between maternal age and socioeconomic effects.

Variation of twinning rate with socioeconomic status was previously observed by Lilienfeld and Pasamanick (1955) who, using the Weinberg method, found an increase of MZ twins only in the upper socioeconomic groups of the white but not the Negro population of Baltimore. They suggested that the difference might reflect higher abortion rates in the lower socioeconomic groups, resulting in lower frequency of MZ

TABLE 5

$\chi^2$ ANALYSIS OF SOCIOECONOMIC EFFECT AFTER PARABOLIC ADJUSTMENT FOR MATERNAL AGE

| Twins | Socioeconomic Category $\chi^2_{(2)}$ | Maternal Age $\chi^2_{(2)}$ | Residual $\chi^2_{(7)}$ |
|---|---|---|---|
| White and Negro | 4.6 | 53.7* | 10.3 |
| White | 0.4 | 34.7* | 6.1 |
| Negro | 5.3 | 26.0* | 25.2* |
| Monozygotic | 0.0 | 1.2 | 3.5 |
| Dizygotic | 12.7* | 64.5* | 8.5 |

* $P < .01$.

twins. This does not seem to be the case in our population. Their results are not quite the same as those of the present study, but the methods of determination of twin frequencies and level of socioeconomic background also differ.

Erickson and Fellman (1967) found that in Scandinavian populations the rate of twinning was significantly higher in illegitimate maternities than in legitimate ones. These investigators suggested that unwed mothers may have a tendency to polyovulation, thus producing an excess of DZ twins, and also have better physical qualifications to complete a multiple pregnancy. In our study, 82 illegitimate pregnancies resulted in twin births, 11 among white, 69 among Negro and two among Other mothers. Table 6 shows that the proportion of both white and Negro single mothers of twins is somewhat lower than the proportion of single mothers of singletons. When examined by age of mother, however, the percentage of illegitimate twin births out of all births is slightly but consistently higher than the legitimate ones for all age groups (table 7). The same is true for DZ twins taken alone. None of these differences is significant by conventional $\chi^2$ test on individual $2 \times 2$ tables except for that of DZ twins in the 20–24 age group.

Adjustment for both race and maternal age would not be very meaningful because of the small number (11) of illegitimate twin births among white mothers. Therefore, further analysis of maternal age effects on the rate of twinning of illegitimate maternities was performed by regression analysis on logit transforms of the proportions,

using Dr. Naylor's program mentioned earlier. Parabolic adjustment of the maternal age effect was necessary and proved adequate. The regression of the legitimacy code (1 for legitimate, 2 for illegitimate) for all twins was 0.110081, which was 1.75 times its standard error, 0.063038. The regression of the legitimacy code for DZ twins was 0.170695, or 1.92 times its standard error, 0.088816. Both of these values are borderline significance at the 5% level in two-tail tests. Considering, however, that our data showed a consistent difference in the same direction as that of the Scandinavian data, the regressions would be significant when referred to a one-tail test which is appropriate for these data. Our results, therefore, can be interpreted as confirming the observations of Erickson and Fellman.

## MORTALITY

It is well known that the vast majority of twin deaths occurs during the first four weeks of life. The proportion of twins in the population changes little after the age of one month and is practically constant after the first year (Allen 1955). In this survey, the neonatal period (up to age 28 days) is used as the most crucial and representative period of twin mortality.

Fetal and neonatal deaths in our material amounted to 17.3% and were significantly higher among like-sexed than among unlike-sexed pairs (table 8). While female

TABLE 6

TWINS BORN TO SINGLE MOTHERS

| RACE | NO. OF TWIN PAIRS | PERCENTAGE OF SINGLE MOTHERS | |
|---|---|---|---|
| | | Twins | Study Population |
| White | 11 | 4.2 | 5.2 |
| Negro | 69 | 20.8 | 27.0 |
| Other | 2 | 8.0 | 7.6 |
| Total | 82 | 13.5 | 15.6 |

TABLE 7

PERCENTAGE TWIN LEGITIMATE AND ILLEGITIMATE MATERNITIES BY AGE OF MOTHER

| AGE OF MOTHER | ALL TWINS | | DIZYGOTIC TWINS | |
|---|---|---|---|---|
| | Legitimate | Illegitimate | Legitimate | Illegitimate |
| ≤15–19 | 0.6 | 0.7 | 0.2 | 0.2 |
| 20–24 | 0.9 | 1.1 | 0.4 | 0.7 |
| 25–29 | 1.3 | 1.5 | 0.7 | 0.8 |
| 30–34 | 1.9 | 2.7 | 1.2 | 2.0 |
| ≥35 | 1.5 | 3.2 | 1.0 | 1.9 |

deaths were slightly higher in like-sexed than in unlike-sexed pairs, the difference is not significant. It is the male deaths which were responsible for the higher frequency of deaths in like-sexed pairs and the difference here is highly significant. Table 9 shows fetal and neonatal deaths by type of death and race. The death rate of Negro twins, 17.5%, was about the same as that of white twins, 17.8%. The death rate of twins in the Other group was much lower, only 10.0%, but the numbers here are small. The fetal and neonatal death rates in the total Collaborative Study population are 5.6% for whites, 5.0% for Negroes, and 5.7% for other races, with an overall rate of 5.4%. Fetal deaths in whites and Negroes were twice as high as those of the Study

TABLE 8

FETAL AND NEONATAL MORTALITY OF TWINS BY SEX

| Sex | No. Born | No. of Deaths | Deaths (%) |
|---|---|---|---|
| Both: | | | |
| Like-sexed pairs | 802 | 149 | 18.6 |
| Unlike-sexed pairs | 408 | 47 | 11.5 |
| Sex unknown | 20 | 17 | 85.0 |
| Total | 1,230 | 213 | 17.3 ($P<.003$) |
| Males: | | | |
| Like-sexed pairs | 404 | 93 | 23.0 |
| Unlike-sexed pairs | 204 | 23 | 11.3 |
| Total | 608 | 116 | 19.1 ($P<.001$) |
| Females: | | | |
| Like-sexed pairs | 398 | 56 | 14.1 |
| Unlike-sexed pairs | 204 | 24 | 11.7 |
| Total | 602 | 80 | 13.3 ($P>.3$) |

TABLE 9

FETAL AND NEONATAL MORTALITY OF TWINS AND OF THE COLLABORATIVE STUDY POPULATION BY RACE AND TYPE OF DEATH

| Race | Twins | | | | | | | Collaborative Study Population | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. Born | Fetal Deaths | | Neonatal Deaths | | Total Deaths | | Fetal Deaths (%) | Neonatal Deaths (%) | Total Deaths (%) |
| | | No. | % | No. | % | No. | % | | | |
| White | 518 | 43 | 8.3 | 49 | 9.5 | 92 | 17.8 | 4.4 | 1.2 | 5.6 |
| Negro | 662 | 53 | 8.0 | 63 | 9.5 | 116 | 17.5 | 3.2 | 1.8 | 5.0 |
| Other | 50 | 4 | 8.0 | 1 | 2.0 | 5 | 10.0 | 3.9 | 1.8 | 5.7 |
| Total | 1230 | 100 | 8.1 | 113 | 9.2 | 213 | 17.3 | 3.8 | 1.6 | 5.4 |

population, but neonatal deaths were more than five times as high as those of the Study population. The numbers for the Other group are too small to admit comparison.

The fetal and neonatal twin deaths in this study were considerably higher than those observed in other studies, which range from 10% to 14% (table 10). It is evident that the difference is not in the neonatal deaths but in the fetal deaths which are much higher in Collaborative Study twins than in previously reported studies. The period for which deaths are reported in these studies is not uniform and, further, there is considerable confusion in the use of the terms "perinatal" (time surrounding birth or up to the discharge of the infant from the hospital) and "neonatal" (the first four weeks of life). In some studies these terms are used interchangeably (Potter 1963). The main bias, however, is due to variability in ascertainment of twin deaths.

Kurtz et al. excluded all twin pairs whose combined weight fell below 1,500 grams; Donnelly's study was done retrospectively from birth and death certificates, and the inaccuracies of this type of investigation are well known; Potter included only

TABLE 10

TWIN MORTALITY FROM REPORTS IN THE LITERATURE

| Investigator | Area Surveyed | No. of Twins | Fetal Deaths (%) | Neonatal Deaths (%) | Total Deaths (%) |
|---|---|---|---|---|---|
| Bender 1952 | Liverpool | 944 | 4.0 | 7.0 | 11.0 |
| Kurtz et al. 1955 | Jersey City | 1,000 | 2.8 | 7.0 | 9.8 |
| Donnelly 1956 | Iowa | 2,798 | 3.2 | 8.6 | 11.8 |
| Potter 1963 | Chicago | 1,134 | 3.1 | 7.5 | 10.6 |
| Robertson 1964 | Edinburgh | 900 | 4.4 | 9.2 | 13.6 |
| Donaldson and Kohl 1965 | United States | 5,282 | 4.0 | 8.9 | 12.9 |
| Hendricks 1966 | Cleveland | 758 | ..... | ..... | 14.0 |
| Present study | United States | 1,230 | 8.1 | 9.2 | 17.3 |

pregnancies which terminated in the birth of two "reportable" infants, that is, weighing over 400 grams; Robertson reviewed the records of 450 women who delivered twins after the twenty-eighth week of gestation, or before if one or both infants were born alive, but excluded 46 gravidae who aborted twin fetuses during the period of his study—if these abortions were included in the fetal deaths, then the proportion of fetal deaths in his study would be 13.2%, that of neonatal deaths 8.4%, and that of all deaths 21.6%; Donaldson and Kohl included only fetuses weighing at least 400 grams each; Hendricks excluded twins born prior to 20 weeks of gestation and twin sets with one ovum blighted.

Table 11 shows fetal and neonatal deaths by sex of twins, sex of pairs, and placental type. It is of interest that over half of the monoamniotic twins died, and that four of the five deaths were fetal deaths. The relationship of placental types to mortality in the twins of the Collaborative Study will be treated in more detail in another report.

Yerushalmy and Sheerar (1940), Barr and Stevenson (1961), Potter (1963), and others found an impressive loss of like-sexed twins, which they attributed to excessive mortality of MZ twins. In the first two studies the investigators estimated mortality

rates indirectly and were able to show that MZ pairs have higher mortality than DZ pairs, with male higher than female. In 293 of 567 pairs of her twin sample whose zygosity was determined by comparison of blood types, Potter found an 11.2% fetal and neonatal mortality in the definitely monozygotic pairs as against 3.5% in the definitely dizygotic. Our data support these findings although our figures are higher than those of Potter.

Table 12 shows the observed and estimated fetal and neonatal deaths of our twins by zygosity. The mortality of MZ pairs, 14.8%, was about double that of the DZ, 7.6%. The mortality of the large number of pairs of undetermined zygosity, however, which amounted to 44%, casts doubt on the accuracy of these figures. It should be remembered that the twins of undetermined zygosity were all like-sexed, and should contain a large number of DZ pairs. An estimate of twin mortality by zygosity can be made, using the Weinberg method for distribution of the twin pairs of undetermined zygosity between MZ and DZ pairs, assuming equal mortality among like-

TABLE 11

FETAL AND NEONATAL DEATHS OF TWINS BY SEX OF TWINS, SEX OF PAIRS, AND PLACENTAL TYPE

| Twins | No. | Fetal Deaths | | Neonatal Deaths | | Total | |
|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % |
| Males | 608 | 56 | 9.2 | 59 | 9.7 | 115 | 18.9 |
| Females | 602 | 32 | 5.3 | 49 | 8.1 | 81 | 13.4 |
| Male pairs | 202 | 43 | 10.7 | 49 | 12.1 | 92 | 22.8 |
| Female pairs | 199 | 21 | 5.3 | 36 | 9.0 | 57 | 14.3 |
| Unlike-sexed pairs | 204 | 24 | 5.9 | 23 | 5.6 | 47 | 11.5 |
| MA-MC pairs | 9 | 4 | 22.2 | 1 | 5.6 | 5 | 27.8 |
| DA-MC pairs | 102 | 18 | 8.8 | 28 | 13.7 | 46 | 22.5 |
| DA-DC pairs | 419 | 33 | 3.9 | 59 | 7.0 | 92 | 10.9 |
| Unknown pairs | 85 | 49 | 28.8 | 21 | 12.3 | 70 | 41.1 |

NOTE.—MA = monoamniotic, MC = monochorionic; DA = diamniotic, DC = dichorionic.

TABLE 12

OBSERVED AND ESTIMATED FETAL AND NEONATAL DEATHS OF TWINS BY ZYGOSITY

| Zygosity | No. | Fetal Deaths | | Neonatal Deaths | | Total | |
|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % |
| Observed: | | | | | | | |
| Monozygotic pairs | 182 | 23 | 6.3 | 31 | 8.5 | 54 | 14.8 |
| Dizygotic pairs | 316 | 24 | 3.8 | 24 | 3.8 | 48 | 7.6 |
| Undetermined pairs | 107 | 41 | 19.1 | 53 | 24.8 | 94 | 43.9 |
| Estimated: | | | | | | | |
| Monozygotic pairs | 197 | 40 | 10.2 | 62 | 15.7 | 102 | 25.9 |
| Dizygotic pairs | 408 | 48 | 5.9 | 46 | 5.6 | 94 | 11.5 |

and unlike-sexed DZ twins. The results show the same trend, with overall mortality of MZ twins more than double that of DZ twins.

Table 13 shows the mortality of one or both twins of a pair by zygosity. The proportion of pairs with two deaths, 13.2%, was much higher than that with one death, 8.3%, and the difference is significant. The table, however, is somewhat misleading because of the large number of twins of undetermined zygosity. For example, the table shows that among MZ pairs the proportion of pairs with one and two deaths was the same, 9.9%, a very dubious finding; and that in DZ pairs, deaths occurred almost exclusively among unlike-sexed twins.

A much more instructive way of examining the mortality of one or both twins of a pair is by sex distribution, as shown in table 14. Here, the proportion of like-sexed pairs with two deaths, 14.2%, was significantly higher than that of pairs with one death, 8.7%. The difference was contributed entirely by the male pairs, whose proportion with two deaths was 18.8% while that with one death was 8.4%. In the female like-sexed pairs there was no appreciable difference between pairs with one and two deaths, the proportions being 9.0% and 9.5%, respectively. It is also worth noting that while the proportion of like-sexed male pairs with two deaths was

TABLE 13

MORTALITY IN ONE OR BOTH TWINS OF A PAIR BY ZYGOSITY

| Zygosity | No. of Pairs | Pairs with One Death | | Pairs with Two Deaths | | Pairs, Both Survived | | No. of Deaths |
|---|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % | |
| Monozygotic | 182 | 18 | 9.9 | 18 | 9.9 | 146 | 80.2 | 54 |
| Dizygotic: | | | | | | | | |
| Like-sexed | 112 | 1 | 0.1 | ..... | ..... | 111 | 99.9 | 1 |
| Unlike-sexed | 204 | 13 | 6.4 | 17 | 8.3 | 174 | 85.3 | 47 |
| Zygosity undetermined | 117 | 19 | 16.2 | 46 | 39.3 | 52 | 44.5 | 111 |
| Total | 615 | 51 | 8.3 | 81 | 13.2 | 483 | 78.5 | 213 |

TABLE 14

MORTALITY IN ONE OR BOTH TWINS OF A PAIR BY SEX

| Sex | No. of Pairs | Pairs with One Death | | | Pairs with Two Deaths | | | Pairs, Both Survived | | No. of Deaths |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. | % | | No. | % | | No. | % | |
| Like-sexed (MM) | 202 | 17 | 8.4 | 8.7 | 38 | 18.8 | 14.2 | 147 | 72.8 | 93 |
| Like-sexed (FF) | 199 | 18 | 9.0 | | 19 | 9.5 | | 162 | 81.5 | 56 |
| Unlike-sexed | 204 | 13 | 6.4 | | 17 | 8.3 | | 174 | 85.3 | 47 |
| (Male death) | ..... | (6) | ..... | | ..... | ..... | | ..... | ..... | (23) |
| (Female death) | ..... | (7) | ..... | | ..... | ..... | | ..... | ..... | (24) |
| Sex unknown | 10 | 3 | 30.0 | | 7 | 70.0 | | 0 | 0 | 17 |
| Total | 615 | 51 | 8.3 | | 81 | 13.2 | | 483 | 78.5 | 213 |

more than double that of the female like-sexed pairs with two deaths, that with one death was about the same. Among unlike-sexed pairs there was a preponderance of pairs with two deaths, but the proportion of pairs with one and two deaths was well below that of like-sexed pairs.

The excess mortality in male like-sexed pairs, whether MZ or DZ, is indeed impressive. Our data agree with the finding of Yerushalmy and Sheerar (1940) that nearly all the excess mortality in like-sexed pairs can be accounted for by deaths of both members of pairs, and those of Barr and Stevenson (1961) that the proportions of like- and unlike-sexed pairs with one and two deaths are not significantly different ($\chi^2 = 0.9$, $P > .3$).

Much has been written about the mortality of the firstborn versus the second-born twin. Most investigators agree that the second-born twin has a somewhat higher mortality risk than the first (Potter 1963; Wyshak and White 1963; Robertson 1964).

TABLE 15

FETAL AND NEONATAL MORTALITY BY BIRTH ORDER AND SEX

| Sex | Fetal Deaths | | | | | Neonatal Deaths | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Delivered First | | Delivered Second | | Total | Delivered First | | Delivered Second | | Total |
| | No. | % | No. | % | | No. | % | No. | % | |
| Male | 10 | 34.5 | 19 | 65.5 | 29 | 31 | 51.7 | 29 | 48.3 | 60 |
| Female | 7 | 41.2 | 10 | 58.8 | 17 | 25 | 49.0 | 26 | 51.0 | 51 |
| Total | 17 | 36.9 | 29 | 63.1 | 46 | 56 | 50.4 | 55 | 49.6 | 111 |

In our material, among 46 fetal deaths with known sex which occurred immediately before or during the birth process (table 15), 17 occurred in the firstborn and 29 in the second-born twin. The differences in the total as well as by sex are not significant but they are consistent, confirming previous findings. Among the 111 neonatal deaths, however, 56 occurred in the firstborn and 55 in the second-born twin. Obviously there is no difference in mortality during the neonatal period between firstborn and second-born twins who were born alive.

### CAUSES OF DEATH

The causes of fetal and neonatal twin deaths, as far as they could be determined, are given in table 16. Highest on the list of fetal death is abortion. In the strictest sense, abortion should not be considered as a cause of death, but it is listed here in order to separate it from deaths which occurred after 28 weeks of gestation, for which the cause is sometimes known or can be inferred with some degree of certainty. The most common cause of neonatal deaths was respiratory distress syndrome (hyaline membrane disease), a disease of prematurity. It accounted for 34.6 of neonatal deaths or 17.4% of all deaths. In Potter's data (1963) it was listed as a cause of death in 18.8% of neonatal deaths, or 13.2% of all twin deaths. It is difficult to

account for this discrepancy. A possible explanation might be that the criteria used for the diagnosis of respiratory distress syndrome in the Collaborative Study were more liberal than those for Potter's study. Malformations were responsible for 3.8% of fetal deaths and 9.3% of neonatal deaths, or for 6.6% of all deaths. These figures are not too different from those of Potter (1963), who reported 5.9% for fetal deaths and 10.7% for perinatal deaths. Hendricks (1966) also reported that in a study of 438 multiple pregnancies in Cleveland, 8.4% of twins who died had malformations, but did not state whether or not these malformations were considered as a cause of death. Extensive data on malformations as a cause of death in twins were given by Barr and Stevenson (1961), but in that study the analysis included twins dying during the first year of life from congenital malformations, and comparison with our material would not be entirely appropriate.

TABLE 16

FETAL AND NEONATAL TWIN DEATHS

| Cause of Death | Fetal Deaths | | Neonatal Deaths | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| Abortion | 44 | 41.5 | ..... | ..... | 44 | 20.7 |
| Respiratory distress syndrome | ..... | ..... | 37 | 34.6 | 37 | 17.4 |
| Anoxia, asphyxia | 8 | 7.5 | 8 | 7.5 | 16 | 7.5 |
| Malformation | 4 | 3.8 | 10 | 9.3 | 14 | 6.6 |
| Trauma, hemorrhage | 6 | 5.7 | 7 | 6.5 | 13 | 6.1 |
| Other | 15 | 14.1 | 40 | 37.4 | 55 | 25.8 |
| Unknown | 29 | 27.4 | 5 | 4.7 | 34 | 15.9 |
| Total | 106 | 100.0 | 107 | 100.0 | 213 | 100.0 |

Table 17 gives the causes of death in twins by zygosity. It is not surprising that abortion accounted for 32.4% of deaths in twins of undetermined zygosity. Among twins of known zygosity, abortion as a cause of death was low in MZ twins, 3.7%, compared with 12.5% in DZ twins. Anoxia was higher in MZ twins, 11.2%, than in DZ twins, 6.3%. Malformation was also significantly higher in MZ twins, 9.2%, than in DZ, 2.1%. Respiratory distress syndrome and trauma were about the same in the two groups, although both were lower in the group of undetermined zygosity. The sex differences (table 18) do not seem to be great for abortion and respiratory distress syndrome. Males, however, seem to have had higher mortality from anoxia, while females suffered more from malformation and trauma. Trauma as a more frequent cause of death in females is rather difficult to explain, especially when male infants are generally heavier and more prone to trauma during birth. The numbers, however, are small and the difference may well be due to sampling variation. The material on malformations in these twins will be presented in detail elsewhere.

## SUMMARY

In the population of the Collaborative Study of Cerebral Palsy, Mental Retardation, and Other Neurological and Sensory Disorders of Infancy and Childhood, 615

pairs of twins were born among 56,249 maternities. Zygosity was determined by comparison of blood groups, finger- and palm prints, and examination of fetal membranes. Among white twins 34.6% were MZ and 65.4% DZ; among Negro twins 28.8% were MZ and 71.2% DZ; and among twins in the Other group, consisting mostly of Puerto Ricans, 60.0% were MZ and 40.0% DZ.

The frequency of DZ twinning in both whites and Negroes increased steadily to ages 35–39 and then fell sharply. The frequency of MZ twinning was stable to age 39, then showed an increasing trend, slight for Negroes, striking for whites. There was an apparent increase in the frequency of twinning in higher socioeconomic groups which was found to be independent of age of mother in DZ twins, and a product of interaction between maternal age and socioeconomic effects in Negro twins. Although our data do not provide statistical proof, they can be interpreted as confirming the recent report that twinning rate is higher in illegitimate maternities than in legitimate ones.

TABLE 17

CAUSES OF FETAL AND NEONATAL TWIN DEATHS BY ZYGOSITY

| Cause of Death | Monozygotic | | | | Dizygotic | | | | Zygosity Undetermined | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | FD | NND | Total | % | FD | NND | Total | % | FD | NND | Total | % |
| Abortion | 2 | ..... | 2 | 3.7 | 6 | ..... | 6 | 12.5 | 36 | ..... | 36 | 32.4 |
| Respiratory distress syndrome | ..... | 13 | 13 | 24.1 | ..... | 12 | 12 | 25.0 | ..... | 12 | 12 | 10.8 |
| Anoxia, asphyxia | 1 | 5 | 6 | 11.2 | 2 | 1 | 3 | 6.3 | 5 | 2 | 7 | 6.3 |
| Malformation | 3 | 2 | 5 | 9.2 | ..... | 1 | 1 | 2.1 | 1 | 7 | 8 | 7.2 |
| Trauma, hemorrhage | 3 | 1 | 4 | 7.4 | 3 | 1 | 4 | 8.3 | ..... | 5 | 5 | 4.6 |
| Other | 3 | 9 | 12 | 22.2 | 7 | 9 | 16 | 33.3 | 5 | 22 | 27 | 24.3 |
| Unknown | 11 | 1 | 12 | 22.2 | 6 | ..... | 6 | 12.5 | 12 | 4 | 16 | 14.4 |
| Total | 23 | 31 | 54 | 100.0 | 24 | 24 | 48 | 100.0 | 59 | 52 | 111 | 100.0 |

NOTE.—FD = fetal death; NND = neonatal death.

TABLE 18

CAUSES OF FETAL AND NEONATAL TWIN DEATHS BY SEX*

| Cause of Death | Male | | | | Female | | | |
|---|---|---|---|---|---|---|---|---|
| | FD | NND | Total | % | FD | NND | Total | % |
| Abortion | 22 | ..... | 22 | 18.8 | 14 | ..... | 14 | 16.9 |
| Respiratory distress syndrome | ..... | 21 | 21 | 17.9 | ..... | 16 | 16 | 19.3 |
| Anoxia, asphyxia | 6 | 6 | 12 | 10.3 | 2 | 2 | 4 | 4.9 |
| Malformation | 1 | 5 | 6 | 5.1 | 3 | 5 | 8 | 9.6 |
| Trauma, hemorrhage | 4 | 1 | 5 | 4.3 | 2 | 6 | 8 | 9.6 |
| Other | 9 | 20 | 29 | 24.8 | 5 | 20 | 25 | 30.1 |
| Unknown | 18 | 4 | 22 | 18.8 | 7 | 1 | 8 | 9.6 |
| Total | 60 | 57 | 117 | 100.0 | 33 | 50 | 83 | 100.0 |

NOTE.—FD = fetal death; NND = neonatal death.

* Excluding 8 abortions, 1 other, and 4 unknown deaths of unknown sex.

Fetal and neonatal deaths amounted to 17.3% and were significantly higher among like-sexed than unlike-sexed pairs. The difference was contributed almost entirely by deaths in male pairs. In the majority of cases both members of a pair died. There was no difference in neonatal deaths between firstborn and second-born twins.

The most common cause of neonatal twin deaths was respiratory distress syndrome. Malformation was responsible for 6.6% of all deaths and was significantly higher in MZ than in DZ twins.

## REFERENCES


ALLEN, G. 1955. Comments on the analysis of twin samples. *Acta Genet. Med.* (Roma) **4**:143–159.

BARR, A., and STEVENSON, A. C. 1961. Stillbirths and infant mortality in twins. *Ann. Hum. Genet.* **25**:131–140.

BENDER, S. 1952. Twin pregnancy. A review of 472 cases. *J. Obst. Gynaec. Brit. Emp.* **59**:510–517.

BULMER, M. G. 1960. The twinning rate in Europe and Africa. *Ann. Hum. Genet.* **24**:121–125.

DONALDSON, R. S., and KOHL, S. G. 1965. Perinatal mortality in twins by sex. *Amer. J. Public Health* **55**:1411–1418.

DONNELLY, M. M. 1956. The influence of multiple births on perinatal loss. *Amer. J. Obstet. Gynec.* **72**:998–1003.

ENDERS, T., and STERN, C. 1948. The frequencies of twins, relative to age of mothers, in American populations. *Genetics* **33**:263–272.

ERICKSON, A. W., and FELLMAN, J. 1967. Twinning in relation to the marital status of the mother. *Acta Genet.* **17**:385–398.

HENDRICKS, C. H. 1966. Twinning in relation to birth weight, mortality, and congenital anomalies. *Obstet. Gynec.* **27**:47–53.

KURTZ, G. R.; KEATING, W. J.; and LOFTUS, J. B. 1955. Twin pregnancy and delivery. *Obstet. Gynec.* **6**:370–378.

LILIENFELD, A. M., and PASAMANICK, B. 1955. A study of variations in the frequency of twin births by race and socio-economic status. *Amer. J. Hum. Genet.* **7**:204–217.

MYRIANTHOPOULOS, N. C., and FRENCH, K. S. 1968. An application of the U.S. Bureau of the Census socioeconomic index to a large, diversified patient population. *Soc. Sci. Med.* **2**:283–299.

POTTER, E. L. 1963. Twin zygosity and placental form in relation to the outcome of pregnancy. *Amer. J. Obstet. Gynec.* **87**:566–577.

ROBERTSON, J. G. 1964. Twin pregnancy: morbidity and fetal mortality. *Obstet. Gynec.* **23**:330–337.

SHIPLEY, P. W.; WRAY, J. A.; HECHTER, H. H.; ARELLANO, M. G.; and BORHANI, N. O. 1967. Frequency of twinning in California. *Amer. J. Epidem.* **85**:147–156.

STRANDSKOV, H. H. 1945. Plural birth frequencies in the total, the "white" and the "colored" U.S. populations. *Amer. J. Phys. Anthrop.* **3**:49–55.

STRANDSKOV, H. H., and EDELEN, E. W. 1946. Monozygotic and dizygotic twin birth frequencies in the "white " and the "colored" U.S. populations. *Genetics* **31**:438–446.

U.S. BUREAU OF THE CENSUS. 1963. Methodology and scores of socioeconomic status. Working Paper 15. Government Printing Office, Washington, D.C.

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE. 1967. Multiple births, United States—1964. Public Health Service Publ. 1000, ser. 21, no. 14. Government Printing Office, Washington, D.C.

WYSHAK, G., and WHITE, C. 1963. Birth hazard of the second twin. *J. Amer. Med. Ass.* **186**:109–110.

YERUSHALMY, J., and SHEERAR, S. E. 1940. Studies on twins. II. On the early mortality of like-sexed and unlike-sexed twins. *Hum. Biol.* **12**:247–263.