An analysis of perinatal mortality for male twins and female twins in the same pregnancies is reported. The fetal death rates were not different, but the neonatal rate was significantly higher for the males.

PERINATAL MORTALITY IN TWINS BY SEX

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It appears that from the moment of conception, the male of the species is at a physical disadvantage when compared with the female. Birth and mortality data, as well as the more recent genetic investigations of early pregnancy terminations, point in this direction.

The comparison, by sex, is very difficult to control. Each pregnancy varies from every other in many ways. Therefore, we have chosen to look at differential mortality by sex, using twin gestations in which the infants were of different sex. This permits us to disregard many variables such as age, parity, race, and complications surrounding a particular pregnancy. All these factors may be related to the outcome of a particular pregnancy. Thus, by using only twin pregnancies which result in one male and one female, we have a population of females and a population of males quite well controlled because each has had the same mother in the same pregnancy. Most perinatal mortality studies by sex ignore the abundance of variables. It is always hoped that large numbers will counteract or erase this problem. However, it is possible that the pregnancy course of mothers of male singletons or male-male twin sets may differ from that of mothers of female singletons or female-female twin sets. Also, it is possible that the mothers themselves differ at the start of the pregnancy. If either of these situations does exist, increasing the number of births under study will only make more evident the bias present in the ensuing analyses.

Any differences observed for a group of unlike sex twins will be between a male sharing the same uterus with a female and a female sharing a uterus with the male. Such differences may not carry over to the general population of males and females. However, this possibility seems less important than the advantage to be gained by having the same mother, at the same time, in the same hospital, with the same complications.

To estimate perinatal mortality rates for females and males it is necessary to use the data from all the twins. Contributions to the difference between these estimates will come only from the subset of those unlike sex twin pregnancies where the outcome was not the same for the two fetuses; and so this subset will be of special interest.

Method of Obtaining Data

This type of study is relatively easy for us to accomplish on data furnished by the Obstetrical Statistical Cooperative. This voluntary organization includes obstetrical departments of teaching hospitals which code their deliveries on the same code sheet. The data are then punched on IBM cards. Twin deliveries result in two cards which are alike except for the punches concerning the babies. Duplicates

Table 1—Total Deliveries and Sets of Twins in Hospitals of Obstetrical Statistical Cooperative

Hospital	Period	Total Deliveries	Twin Sets
Baltimore City	1956-1957	7,269	89
Beth-El	1954-1959	18,949	178
Boston Lying-In	1957-1959	12,612	147
Grace New Haven	1955-1959	23,972	272
Kings County	1951-1959	43,823	573
Long Island Jewish	1956-1959	6,891	70
Maimonides	1956-1960	21,409	220
Mount Sinai of New York	1953-1959	30,236	340
Pennsylvania	1957-1958	6,747	76
Sinai of Baltimore	1950-1959	28,803	256
University of Colorado	1952-1957	6,024	50
University of Maryland	1950-1959	31,437	370
Total		238,172	2,641

of these cards are sent to a central office where they are available for study. From 1950, when the Cooperative was first organized with three hospitals, through 1960, there had accumulated a pool of 238,172 deliveries. The hospitals whose data were utilized for this study and their periods of participation in the Obstetrical Statistical Cooperative, as well as the number of twin sets available from each hospital, are detailed in Table 1. The only conditions for inclusion in this twin study are that each fetus weigh at least 400 grams.

Before carrying out a detailed analysis in the controlled method to be used here, we wanted to be certain that our over-all perinatal mortality rate was in keeping with those found by others.

Table 2 gives the breakdown for the 5,282 babies (2,641 twin sets) by outcome for sex and order combinations. A few definitions are in order. *Outcome* has three possibilities: discharged alive (later referred to simply as "live"); fetal death; and neonatal death. The last grouping refers to infants born alive, but who died before 28 days of age. All our data are hospital data. Should an infant be discharged alive and die outside the hospital before 28 days of life, he would have entered our data as live, not as a neonatal death. However, the rate of such occurrences is estimated by us to be very low from actual checking of death records from the New York City Health Department for Kings County Hospital and Beth-El Hospital deliveries for three years.

Table 3 gives previous data reported by others. We add our results for comparison, although such comparisons are fraught with statistical pitfalls. Frequently, the populations are not comparable. The lower limit of weight of the fetus to be included in the study is a very important factor when comparisons are contemplated. The perinatal mortality rates will be much higher for those series that include the very small fetuses which have only a slight chance of survival. Another factor is the year when the delivery took place. The length of time that the child has been observed after birth is also important in determining the perinatal mortality rate. Some studies may have stopped prior to the 28th day of life and others may go on for longer periods of time. As indicated above, in addition to these statistical problems, the

Table 2—Obstetrical Statistical Cooperative

A—Outcome for Twins by Sex and Order

	Discharged Alive	Fetal Death	Neonatal Death	Total
First and female	1,209	49	84	1,342
First and male	1,134	50	102	1,286
Second and female	1,151	40	105	1,296
Second and male	1,115	62	155	1,332
Sex and/or order unknown	11	8	7	26
Total	4,620	209	453	5,282

B—Twin Rates for Comparison with Previous Studies

$$\text{Total perinatal mortality} = \frac{209+453}{5{,}282} = 125 \text{ per 1,000 total births}$$

$$\text{Total fetal death rate} = \frac{209}{5{,}282} = 40 \text{ per 1,000 total births}$$

$$\text{Total neonatal death rate} = \frac{453}{4{,}620+453} = 89 \text{ per 1,000 live births}$$

problems of maternal age, socioeconomic status, and pregnancy complication also exert an influence.

Bearing in mind these difficulties, we nevertheless make the comparison. In our opinion, perinatal mortality rates in the current study are not unduly divergent from those reported in other studies.

One of the factors involved in the comparisons mentioned above, the time period or year in which the deliveries occur, affects not only the total perinatal mortality rate, but may also affect sex differences. Loewe and McKeown[7] give fetal death rates in single pregnancies for males and females separately for a 20-year period (Table 4). The male fetal death rate declined from 43.2 per 1,000 to 26.8; the female from 36.8 to 24.3. What is of greater interest in our sex-outcome discussion is that the difference between male and female changed in the period from 6.4 per 1,000 for 1928-1929 to 2.5 for 1946-1947.

Table 3—Perinatal Results from Literature (per 1,000)

Author	Years of Analysis	No. Twins (Infants)	Fetal Death Rate	Neonatal Death Rate
Kurtz[6]	1947-1953	1,000	28	70
Bender[3]	1946-1950	944	40	70
Donnelly[4]	1953-1954	2,798	32	86
Potter[8]	1941-1947	502	58	82
Stone[9]	1949-1955	384	26	115
Anderson[1]	1948-1952	360	39	111
Guttmacher[5]	1950-1956	2,654	46	87
Current study	1950-1960	5,282	40	89

Table 4—Sex Specific Stillbirth Rates—Single Pregnancies* (per 1,000)

England and Wales 1928-1947			
	Male	Female	Difference Male-Female
1928-1929	43.2	36.8	6.4
1930-1931	44.1	37.4	6.7
1932-1933	44.0	38.7	5.3
1934-1935	42.8	38.3	4.5
1936-1937	41.6	37.0	4.6
1938-1939	40.0	36.2	3.8
1940-1941	37.8	34.1	3.7
1942-1943	32.8	30.4	2.4
1944-1945	28.8	26.4	2.4
1946-1947	26.8	24.3	2.5

* From Loewe and McKeown, Reference 7.

Comparative Studies

Similar studies, which have analyzed perinatal twin mortality by birth order, invariably show a higher rate for the second baby. This is also true in our series. Kurtz gives perinatal mortality rates by sex and order combinations. In Table 5 we have compared our rates with his. The flow of perinatal mortality rates from the low for the first and female to a high for the second and male is present in both series. For the group as a whole and for most of the sex-order subgroups our material shows a higher perinatal mortality rate than that of Kurtz. This may well be due to the fact that our series has a lower weight limit of 800 grams for two babies while Kurtz's series has a lower weight limit of 1,500 grams for two babies.

Most previous studies have demonstrated a higher fetal mortality rate, as well as a higher neonatal mortality rate for males. This well-accepted "fact" was recognized in a previous communication from the Obstetrical Statistical Cooperative (Guttmacher and Kohl).[5] They apologized for finding an increased fetal loss rate for females by stating, "Our higher rate, for females in the fetal death group, must be due to a sampling error, since it is counter to the published findings of larger samples." This finding was one of the stimulants for the present investigation.

The fetal and neonatal mortality rates by sex and order combinations are recorded in Table 6. For the fetal rates, there seems to be some effect of sex and/or order (male rates are higher than female) but the variation is not significant ($X_3^2=4.57$, $P>20$ per cent). For the neonatal rates, the variation is significant ($P<0.1$ per cent). So far, we have used all our twins to estimate rates; we have not yet looked at the controlled sets: one male and one female in the same pregnancy.

Prior to proceeding with that analysis, we wish to point out certain facts about our data. All deliveries over 400 grams birthweight are coded by hospitals in the Obstetrical Statistical Cooperative, and all deliveries satisfying this prestated condition are automatically included. The total number of sets of twins, therefore, was listed long before our study was planned, and so we were unable to unwittingly select material with bias. A weakness in these data (corrected as of January 1, 1961) is that males were designated by a specific punch in column 68 while females were designated by the absence of such a punch. Therefore, it

Table 5—Perinatal Mortality Rates for Twins by Sex and Order (per 100)

	Kurtz*	Current Study
First and female	6.2	9.9
First and male	7.3	11.8
Second and female	11.2	11.2
Second and male	13.9	16.3
Total perinatal rate	9.8	12.3
Total number of babies	1,000	5,256†

* See Reference Number 6.
† Note: 13 sets (26 babies) for whom we do not have both sex and order information have been deducted from our total of 5,282 babies.

is possible that sex was simply not coded, but that our interpretation would have been that the infant was a female. Since in most studies sex is not of prime interest, we might expect some undercoding of males. Unfortunately, we seem to get this. Our series, in the preliminary stage of this study, showed 51.5 per cent females; this is out of line with the sex ratio reported by others. Therefore, it was necessary for us to verify sex before our detailed analysis could be undertaken.

Since our purpose was to take steps to counteract the tendency not to code male as male, deliveries coded as male did not require verification. The ideal action would have been to recheck actual hospital birth notes for every set of twins which was coded either as two females or as one male and one female (some 1,800 sets). This would have given us a correct estimate of fetal and neonatal rates for males and females, as well as the difference in these rates between male and female. Only the 277 unlike outcome sets contribute to this sex difference in rates, and for these 174 unlike outcome sets (except, of course, the 103 two-male sets) it was imperative that the hospital records be checked for sex.

Actually, we compromised between the essential minimum and ideal maximum. In addition to the former, we checked 1,030 like-outcome sets which were readily available to our staff. This checking of approximately two-thirds (1,200 of maximum of 1,800 sets) changed our percentage of females from 51.5 per cent to 50.1 per cent. It seems apparent that further sex checking of the like-outcome sets would reduce this percentage to the more usual slight excess of males.

In Table 7 the 2,641 sets of twins are classified by sex, outcome, and order of birth. The horizontal heading shows sex and order simultaneously: female-male, meaning the first baby female, the second male. The vertical heading details the outcome and order simultaneously. The number in each cell are sets of twins, not numbers of babies. For example, there were 354 sets in which the female was first, the male was second, and both babies were discharged alive.

Up to this point, all the 2,641 sets of twins have been utilized in mortality rates. We now limit ourselves to the 840 unlike-sex sets to take advantage of the superior control offered by having 840 females and 840 males resulting from the one set of 840 pregnancies. Their data is presented in Tables 8 and 9. The fetal and neonatal rates for the males are estimated by $\frac{(A+C)}{(A+B+C+D)}$; for the females by $\frac{(C+D)}{(A+B+C+D)}$.

The significance of the difference between

Table 6—Obstetrical Statistical Cooperative

Fetal and Neonatal Mortality Rates for Twins, by Sex and Order Combinations (per cent)

	Fetal	Total No. of Babies	Neonatal	Total No. of Babies Born Alive
First and female	3.7	1,342	6.5	1,293
First and male	3.9	1,286	8.3	1,236
Second and female	3.1	1,296	8.4	1,256
Second and male	4.7	1,332	12.2	1,270
Total	3.8	5,256	8.8	5,055

Table 7—Obstetrical Statistical Cooperative

Sets of Twins by Sex, Order and Outcome

	Female Male	Male Female	Female Female	Male Male	Sex Unknown	Total
Like Outcome—Total	375	367	829	792	1	2,364
Both alive	354	345	770	716	0	2,185
Both fetal death	4	4	16	21	1	46
Both neonatal death	17	18	43	55	0	133
Unlike Outcome—Total	68	30	71	103	5	277
A live, B fetal death	8	9	10	21	4	52
B live, A fetal death	7	3	12	15	1	38
A live, B neonatal death	39	10	28	33	0	110
B live, A neonatal death	7	6	15	16	0	44
A neonatal death, B fetal death	2	1	0	6	0	9
B neonatal death, A fetal death	5	1	5	6	0	17
One live, one neonatal death (order unknown)	0	0	1	5	0	6
One neonatal death, one fetal death (order unknown)	0	0	0	1	0	1
Total	443	397	900	895	6	2,641

the male and female rates is evaluated by $X_1^2 = \frac{[\,|A-D|\,-1]^2}{A+D}$ (McNemar test for correlated samples). The former, estimation of rates, involves all columns and may not be completely correct, since we did not pursue the checking of hospital records to the maximum. However, the evaluation of significance of sex difference involves only columns A and D, the 98 unlike-outcome sets among the 840 unlike-sex sets. These have been completely validated. The only possible addition to them from all the 2,641 sets is the five unlike-outcome sets where the

Table 8—Obstetrical Statistical Cooperative

Fetal Death Rates for Twins from Controlled* Sets

	Sets by Joint Outcome					Fetal Rates (Per cent)		
	A Female Live† Male Fetal Death	B Both Born Live	C Both Fetal Death	D Male Live† Female Fetal Death	Total Sets	Female	Male	Result of McNemar Test
Female first/male second	10	417	4	12	443	3.61	3.16	not sign. diff.
Male first/ female second	4	379	4	10	397	3.52	2.02	not sign. diff.
Both combined	14	796	8	22	840	3.57	2.62	not sign. diff.

* Twin pregnancies resulting in one male and one female.
† Born alive.

sex of the fetal death is unknown. And so, evaluating these sets will give us well-controlled, completely checked conclusions for differences in fetal and neonatal mortality for males and females.

Table 8 lifts from Table 7 the 840 unlike-sex sets (controlled sets) for the examination of difference in fetal rates for males and females, given perfect control in the pregnancy. Table 9 does the same for neonatal rates. The tables give the analysis separately for the male-first/female-second, and female-first/male-second groups and both groups combined.

Possible Variables

We argue there is no need to keep the two groups separate; that there is no difference for our analysis between the twin set I (where the first baby born was female and discharged alive, the second baby a fetal death and male) and twin set II (where the first baby was male and fetal death and the second female and discharged alive). In other words, of the three variables (sex, outcome, and order of birth), only three associations of two variables at a time are theoretically possible: sex and outcome, outcome and order of birth, sex and order of birth. Sex and outcome is the one we are testing here. If the sex and order of birth can be shown to be independent, the established relationship of order of birth and outcome can be used by us to sharpen our analysis. A priori reasoning certainly argues that sex and order of birth, given the same outcome, are independent. Furthermore, among the 840 unlike-sex sets (Table 7), 742 have the same outcome. Independence would lead us to expect 371 where the male was first and 371 where the female was first. Our observed results are 367 and 375. For those still unconvinced, separate analysis is given in Tables 8 and 9.

For the fetal death comparison, in columns A and D (one fetal death, one live birth) we have 14 sets where the male suffered the fetal death and 22 the female. Although there were more twin sets where the fetal death was the female, these results could easily have arisen by chance. We have no evidence of significant difference in fetal death rates between males and females from our controlled data.

When we consider the five sets where the sex of the fetal death could not be ascertained, we find the live birth to have been male in four of them and female in one. To enter the unlike-sex analysis, the fetal deaths would have to have been of

Table 9—Obstetrical Statistical Cooperative

Neonatal Death Rates for Twins from Controlled* Sets

	Sets by Joint Outcome					Neonatal Rates (Per cent)		
	A Female Live† Male Neonatal Death	B Both† Live	C Both Neonatal Death	D Male Live† Female Neonatal Death	Total Sets	Female	Male	Result of McNemar Test
Female first/ male second	39	354	17	7	417	5.76	13.43	sign. diff. at 1% level
Male first/ female second	6	345	18	10	379	7.39	6.33	not sign. diff.
Both combined	45	699	35	17	796	6.53	10.05	sign. diff. at 1% level

* Twin pregnancies resulting in one male and one female.
† Discharged alive.

the opposite sex. This would mean, at most, one male fetal death and four female fetal deaths. Adding them to the above, our result would have been 15 male fetal death sets and 26 female death sets. Our conclusions would remain the same: higher observed fetal death rates for the female, but not ruled out by chance. We have no evidence of an association between sex and fetal death.

For the neonatal death rates, we find 45 sets where the male suffered the neonatal death and 17 where the female did. This is highly significant ($X_1^2=11.8$) and would not happen by chance once in a thousand trials.

Discussion

We believe that this "controlled set" method of investigation has provided verification of a greater tendency of the male to neonatal death, but not for fetal death. It is disturbing that our negative finding for the fetal deaths come from a total of only 41 sets of twins. Out of a total of 2,641 sets of twins collected over a ten-year period, we have only 41 sets where one baby lived and one baby suffered a fetal death and their sexes were not the same. We are, of course, planning to continue this type of analysis. We have attempted to increase our population by examining vital statistics records of the New York City Health Department. The problem here is that the sex of fetal deaths is very frequently coded as "unknown." Over a two-year period we identified 62 sets where one baby lived and one was a fetal death and possibly were of unlike sex. However, 29 of these listed the fetal death as of unknown sex.

In searching for data tabulated in a similar fashion so that we might compare our results, we were fortunate enough to find a classification of all legitimate twin births for England and Wales in 1949-1950 and followed for a year of life (Barr and Stevenson).[2] In this series of 17,169 sets of twins, there was a total of 4,973 different sex but like outcome sets and 1,148 unlike sex and unlike outcome sets. These 1,148 may be classified as follows:

413 sets—female discharged alive, male neonatal/infant death

226 sets—female born alive, male fetal death

296 sets—male discharged alive, female neonatal/infant death

213 sets—male born alive, female fetal death

Analysis of these data gives precisely the same result as that gained by our own unlike sex, unlike outcome sets. Both our data and that of Barr and Stevenson, when submitted to statistical analysis, demonstrate that the male suffers a higher neonatal death rate, but is not subjected to a higher fetal death rate than his female companion in the same pregnancy.

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