Survival and the Sex Ratio in Trisomy 17-18

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TRISOMY 17-18 was first recognized in 1960 (Edwards *et al.*, 1960; Smith *et al.*, 1960), and a variation in the sex ratio (M/F) from that in the general population was noted in 1962 (Ferguson-Smith, 1962). In the general population, there is a small preponderance of males, while in trisomy 17-18 there is a marked excess of females. This difference might be due to factors which operate prior to conception or to those which are unfavorable to the male during development *in utero* or after birth.

Vital statistics for the general population show that males are subject to greater risk of death at each age (F. Nelson, personal communication). This is especially true during the first few months of life. Most deaths in infants with trisomy 17-18 occur before the age of six months (Weber *et al.*, 1964). This report examines the survival of 42 males and 150 females with cytologically proven trisomy 17-18 in order to determine whether the excess of females is present at birth or arises during early life.

RECORDS

Records of mortality and survival on cases of trisomy 17-18 were obtained from published sources (Weber *et al.*, 1964; Holman *et al.*, 1963; Levkoff *et al.*, 1964; Lewis, 1964; Taylor and Polani, 1964; Turner *et al.*, 1964; Wagshall-Ives and Berman, 1963; Yunis *et al.*, 1964) and through personal communications. The 42 male (Appendix I) and 150 female (Appendix II) cases included in this study were all established to have trisomy 17-18 by cytological study. All cases with similar clinical syndromes which had cytological evidence of mosaicism or translocation were excluded.

RESULTS

Survival

Males with trisomy 17-18 usually do not survive as long as females. The difference in the mortality between males and females in this series is not significant at the 5% level ($\chi^2_{(1)}=3.5$) (see Table 1). However, when the survival data are expressed in the form of survivorship tables (Merrell and Shulman, 1955), the case fatality rate for males during the first few weeks of life is obviously higher than for females (Tables 2 and 3). Only one male sur-

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TABLE 1. TRISOMY 17-18: CHI-SQUARE TEST OF MORTALITY DIFFERENCE BETWEEN MALES AND FEMALES

	Males	Females	Totals
Nonsurvivors	37	109	146
Survivors	5	41	46
TOTAL	42	150	192

$\chi^{2}_{(1)} = 3.5$, $P > 0.05$.

vived longer than one year, while 21 females survived at least this long. Five of the 42 males and 41 of the 150 females were surviving when the cases were indexed.

Examination of the age-specific fatality rates by sex (Tables 2 and 3, column *e*) shows that these rates are high at all ages. Comparisons show that the fatality rates are highest for males at the youngest ages and are higher for males than for females through 14 days. The probability of survival from birth to specific ages is also given (column *g*). The probability of survival for males to any specified age is less than for females, especially during the first few weeks of life.

Sex Ratio

The sex ratio at or near birth is needed to establish whether the excess of females observed among all cases noted is present at birth. In fact, the cases diagnosed during the first few days of life are too few to establish the sex ratio at birth. Some of the cases were not diagnosed until at least a year of age, and the majority were not diagnosed until two months of age. By two months of age, the excess male fatality has already affected the sex ratio. Therefore, the 1/3 ratio of males to females obtained from all cases noted probably does not represent the ratio at birth.

From the data available, it may be possible to obtain a better estimate of the sex ratio near birth for trisomy 17-18 if the difference in mortality of the sexes is considered. If one could group all cases according to the age of ascertainment, the sex ratio of the youngest group observed would most closely approximate the sex ratio at birth. However, this cannot be done, since the age of ascertainment is not available for most of the cases noted. If, instead of considering all cases, one considers only the cases which died and groups these nonsurvivors according to their length of survival, the sex ratio of the group which survived for the shortest period after birth will most closely approximate the sex ratio at birth. In Table 4, the nonsurviving cases are arranged by sex according to length of survival. The sex ratio for all cases in the groups which survived more than three months is 0.33–0.35, which is similar to the ratio for all cases indexed (0.28). On the other hand, the sex ratio for the groups which survived for two months or less increases from 0.40 at two months to 0.55 at 14 days.

TABLE 2. SURVIVORSHIP TABLE FOR MALES WITH TRISOMY 17-18

Life Interval	During the Interval						
	No. alive at beginning	No. dying	No. withdrawn	Average no. observed $d=a-\frac{1}{2}c$	Mortality rate $e=b/d$	Probability of survival $(1-e)$	Probability of survival from birth to beginning of the interval $\pi(1-e_i)$
	a	*b*	*c*	*d*	*e*	*f*	*g*
Through 14 days	42	12	1	41.5	0.289	0.711	1.000
15 days through one month	29	3	0	29	0.103	0.897	0.711
Second month	26	9	2	25	0.360	0.640	0.638
Third month	15	3	0	15	0.200	0.800	0.408
Fourth month	12	3	0	12	0.250	0.750	0.326
Fifth month	9	1	0	9	0.111	0.889	0.244
6 through 12 months	8	5	2	7	0.714	0.286	0.217
13 through 24 months	1	0	0	1	0.000	1.000	0.062
25 through 36 months	1	1	0	1	1.000	0.000	0.062
TOTAL		37	5				

TABLE 3. SURVIVORSHIP TABLE FOR FEMALES WITH TRISOMY 17-18

Life Interval	During the Interval						
	No. alive at beginning	No. dying	No. withdrawn	Average no. observed $d=a-\frac{1}{2}c$	Mortality rate $e=b/d$	Probability of survival $(1-e)$	Probability of survival from birth to beginning of the interval $\pi(1-e_i)$
	a	*b*	*c*	*d*	*e*	*f*	*g*
Through 14 days	150	22	3	148.5	0.148	0.852	1.000
15 days through one month	125	12	2	124	0.097	0.903	0.852
Second month	111	26	4	109	0.238	0.762	0.769
Third month	81	17	5	78.5	0.216	0.784	0.590
Fourth month	59	9	4	57	0.158	0.842	0.462
Fifth month	46	9	2	45	0.200	0.800	0.389
6 through 12 months	35	9	5	32.5	0.277	0.723	0.311
13 through 24 months	21	4	6	18	0.222	0.778	0.225
25 through 36 months	11	0	4	9	0.000	1.000	0.175
37 through 48 months	7	0	2	6	0.000	1.000	0.175
49 through 60 months	5	1	1	4.5	0.222	0.778	0.175
61 through 120 months	3	0	2	2	0.000	1.000	0.136
121 months and beyond	1	0	1	0.5	0.000	1.000	0.136
TOTAL		109	41				

TABLE 4. LENGTH OF SURVIVAL IN NONSURVIVORS WITH TRISOMY 17-18

The number of nonsurviving males at each specified time is taken from Table 2, column *b*. All 37 males who died had died by 36 months after birth, 36 had died by 12 months after birth, 31 had died by five months after birth, and so on. The number of nonsurviving females at each specified time is taken from Table 3, column b.

Time after birth (months)	At the end of the interval: Number of nonsurviving males	At the end of the interval: Number of nonsurviving females	Totals	Sex ratio (males/females)
60	37	109	146	0.34
48	37	108	145	0.34
36	37	108	145	0.34
24	36	108	144	0.33
12	36	104	140	0.35
5	31	95	126	0.33
4	30	86	116	0.35
3	27	77	104	0.35
2	24	60	84	0.40
1	15	34	49	0.44
14 days	12	22	34	0.55

DISCUSSION

The sex ratio of the 20 cases presented in the report by Ferguson-Smith (1962) is 0.42. He found no difference in the average length of survival of males and females to account for the unusual sex ratio. The sex ratio calculated for all cases included in the present report is 0.28, and males appear to die at a greater rate than females, especially during the first few weeks after birth.

Since all patients included in this report were cytologically diagnosed, they had to live long enough for such studies to be done. Therefore, the true fatality rates during the period shortly after birth probably are greater than the estimates given in Tables 2 and 3. Furthermore, in view of the greater mortality of males during this critical period, relatively more males with trisomy 17-18 than females escape detection. Therefore, the true sex ratio at birth is also probably greater than at two weeks of age.

The sex ratio as estimated from nonsurviving cases of trisomy 17-18 appears to increase as the time elapsed after birth decreases. Since an increase in the sex ratio for nonsurvivors is also observed in the general population, the increase observed in trisomy 17-18 seems reasonable.

SUMMARY

1. Survivorship data on 192 cases of trisomy 17-18 have been evaluated. The

data suggest that males have a greater fatality rate than females, especially during the first few weeks after birth.

2. The sex ratio (M/F) estimated from nonsurviving cases of trisomy 17-18 is affected by the difference in male and female fatality rates. It decreases from a value of 0.55 at 14 days to 0.35 at three months after birth, but does not change appreciably afterward.

3. The difference in mortality between males and females during the first few weeks after birth may account for part of the excess of females noted among all cases of trisomy 17-18.

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APPENDIX I

SOURCE MATERIAL ON MORTALITY AND SURVIVAL IN 42 MALE CASES OF TRISOMY 17-18 VERIFIED BY CYTOLOGICAL STUDY

Source	No. of cases	Age if alive	Age at death
Bray	1	2 months	
Finley	2		8 weeks
			21 weeks
France *	3		4 days
			8 days
			31 days
Gerald *	3	204 days	84 days
			229 days
German *	1		37 days
Gottleib *	1		5.5 months
Gruber *	3	40 days	25 days
			59 days
Hayman *	1	10 days	
Harris	1	11 months	
Holman	2		2 days
			12 days
Hustinx	1		265 days
Kadjii and Oikawa	1		47 days
Koenig *	1		6 weeks
Lele	1		5 weeks
Lewis	1		4 days
Morishima *	1		4 months
Palmer *	1		68 days
Root *	1		4 hours
Rosenfield *	1		4 months
Smith *	4		56 days
			1 month
			2.5 months
			3.75 months
Townes *	2		13 days
			14 days
Uchida *	3		2 hours
			8 days
			32 months
Voorhess *	2		7 weeks
			5 months
Warkany	1		2 days
Wilton	1		6 months
Zellweger	1		21 days
Zetterqvist	1		7 days

* The references for these survival data are cited in an earlier report (Weber *et al.*, 1964).

Appendix II

Source Material on Mortality and Survival in 150 Female Cases of Trisomy 17-18 Verified by Cytological Study

Source	No. of cases	Age if alive	Age at death
Bishop	2	19 months	
		4 years	
Brandt	1	70 months	
Bray	2	6 months	6 months
Carr	4	3 8/12 years	23 days
			5 weeks
			8 weeks
Chamberlin	2	4½ months	
		6 months	
Crawfurd *	1		60 days
Dallaire	3		84 days
			109 days
			135 days
Delhanty *	2		34 days
			60 days
Edwards *	2		47 days
			4.5 months
Finley	1		3 days
France *	5		9 days
			18 days
			22 days
			31 days
			49 days
Gerald *	10	45 days	4 days
		109 days	42 days
		1½ years	71 days
			89 days
			110 days
			122 days
			428 days
German *	1		149 days
Goodman	1		2 months
Gottleib *	2		75 days
			102 days
Gruber *	5	59 days	1 day
			2 days
			6 days
			92 days
Hansen *	1		6.5 months
Haycock *	1		6 weeks

* The references for these survival data are cited in an earlier report (Weber *et al.*, 1964).

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APPENDIX II. (CONTINUED)

Source	No. of cases	Age if alive	Age at death
Hayman *	1	18 months	
Haskin	1		228 days
Hecht *	6	2.5 months	34 days
		4 months	62 days
			141 days
			203 days
Hirschhorn and Firschein	4	5 days	
		6 days	
		28 days	
		49 days	
Hofnagel	1	90 days	
Hooft	2	4½ months	1 month
Hurwitz	1		11.5 months
Hustinx	3		2 days
			41 days
			144 days
Kadjii and Oikawa	2	2 months	51 days
Kamoshita	1		87 days
Koenig *	1		3 months
Lejeune and LaFourcade *	3		10 days
			12 days
			158 days
Levkoff	1		12 weeks
Lewis	1		6.5 weeks
Luzzatti	1		53 days
Matsui	2	1 7/12 years	29 days
Morishima *	4	10 weeks	15 days
		1 month	
		10 months	
Naujoks	1		4½ months
Palmer *	5	14 months	2 months
			3 months
			5 months
			1 6/12 years
Porter	2		49 days
			50 days
Root *	1		10 days
Smith *	8	35 months	4 hours
			1 month
			42 days
			70 days
			84 days
			140 days
			448 days

* The references for these data are cited in an earlier report (Weber *et al.*, 1964).

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APPENDIX II. (CONTINUED)

Source	No. of cases	Age if alive	Age at death
Steinberg and Jackson *	1		3.5 months
Taylor and Polani	5		5 days
			11 days
			30 days
			42 days
			60 days
Townes *	5	4 months	2 days
		23 months	3 days
			13 months
Turner	1	10 days	
Uchida *	9	120 days	26 hours
		29 months	2 days
			4 weeks
			6 weeks
			2.75 months
			7 months
			50 months
Versluys	1	6 3/12 years	
Voorhess *	4		14½ hours
			1 month
			2 months
			4 months
Wagshall-Ives	4		20 days
			51 days
			66 days
			201 days
Warkany	8	3 months	4 days
		3 months	3 months
		2 years	3½ months
		2 4/12 years	3¾ months
Weber *	3	123 months	11 weeks
			6 months
Weiss	2	43 months	2.5 months
Wilton	1		4 weeks
Wright	4		1 day
			2 days
			2 days
			2 months
Yunis	1	7 months	
Zellweger	3	7 months	3 months
			4 months

* The references for these survival data are cited in an earlier report (Weber *et al.*, 1964).