

# CONGENITAL MALFORMATIONS IN TWINS

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*Among 1195 twins born in the Collaborative Perinatal Project, for whom information was available, 219 (18.33%) were found to have malformations, 179 (14.98%) single and 40 (3.35%) multiple. The frequency of malformations among twins was significantly higher than that among singletons from the same population, but the difference was entirely contributed by MZ twins. This holds true for both major and minor malformations. The frequency among Negro twins was higher than among white, and among male twins higher than among female. Twins had more malformations of the central nervous, musculo-skeletal, ear, respiratory, cardiovascular, and alimentary systems and fewer malformations of the genitourinary and integumentary systems than singletons. In a significant number of cases when one twin of a pair had a malformation, the cotwin also had a malformation though not necessarily the same as that of the first twin.*

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This report is based on data from twins born in the Collaborative Perinatal Project of the United States. As mentioned in a previous paper, this is a prospective study of factors which affect the parents before and during pregnancy and their relation to the outcome of pregnancy.

Among 56,249 pregnancies with known outcomes 615 pairs of twins were born, 259 pairs to white mothers, 331 pairs to Negro mothers, and 25 pairs to mothers of "Other" ethnic groups, mostly Puerto Rican. The zygosity of 508 pairs was established by comparison of sex, blood types utilizing nine systems and gross and microscopic examination of the placenta (Myriantopoulos 1970). In most pairs of undetermined zygosity one or both twins died either in utero or soon after birth. Twins about whom we had doubtful or no information were excluded from the study. This left us with 1195 twin individuals at risk for malformation, including fetal and neonatal deaths on whom an autopsy was performed.

The definitions, classification and criteria for diagnosis of congenital malformations in the Collaborative Perinatal Project have been given in detail elsewhere (Myriantopoulos and Chung 1974). To summarize, a congenital malformation is defined as a gross physical or anatomical developmental anomaly which was present at birth or was detected during the first year of life. Malformations were divided into major and minor categories on the basis of their severity, threat to life and cosmetic significance.

Table 1 shows the distribution of malformations in the twins in comparison to that in singletons from the same population. Among 1195 twins, 219 (18.33%) were found to have malformations, 179 (14.98%) single and 40 (3.35%) multiple. The total number of malformations was 294, 115 of which were found in association with some other malformation. The frequency of twins with malformations was significantly higher than that of singletons whose frequency was 15.56%, 12.97% with single and 2.59% with multiple malformations. This finding agrees with previously published reports, some

Table 1. *Distribution of malformations in twins and singletons.* (Numbers in parentheses are multiple malformations)

	Twins	Singletons
Total number of malformations	294 (115)	10,480 (3,574)
Total number of malformed cases	219 (40)	8,288 (1,382)
Total number of individuals	1,195	53,257
Frequency (mean number) of malformations	0.246	0.197
Frequency of malformed cases (%)	18.33	15.56
Frequency of multiple malformations among all malformations (%)	39.12	34.10
Frequency of multiply malformed cases among all malformed cases (%)	18.26	16.67

of which give an even higher increase of malformations in twins over singletons (Guttmacher and Kohl 1958, Hendricks 1966).

These are, undoubtedly, among the highest malformation rates ever reported for both twins and singletons. The high frequency is, of course, easily explained on the basis of the period of time through which the malformations were observed and the conditions which made almost complete ascertainment possible. In this context it is important to note that of malformations observed through the first year of life only about one third was detected at birth.

It is evident from Table 2 that the increase of malformations in twins is contributed mainly by MZ twins while DZ twins show about the same malformation frequency as singletons. The increased frequency of MZ twins with malformations has been observed by several investigators (see Bulmer 1970). The twins of unknown zygosity have a higher frequency of malformations than singletons but that is understandable since they represent a mixture of MZ and DZ like-sexed twins.

The increase in frequency of MZ twins with malformations holds true for both major and minor malformations (Table 3). The frequency of MZ twins is increased over that of singletons in all three malformation categories, major only, major and minor, and minor only, while the frequency of DZ twins is about the same in the major only, and major and minor categories, and substantially decreased

Table 2. *Distribution of malformations in twins by zygosity, and singletons.* (Numbers in parentheses are multiple malformations)

	Twins			Singletons
	MZ	DZ	ZU	
Total number of malformations	119 (44)	112 (36)	63 (35)	10,480 (3,574)
Total number of malformed cases	90 (15)	91 (15)	38 (10)	8,288 (1,382)
Total number of individuals	373	617	205	53,257
Frequency (mean number) of malformations	0.319	0.181	0.307	0.197
Frequency of malformed cases (%)	24.13	14.75	18.54	15.56
Frequency of multiple malformations among all malformations (%)	36.97	32.14	55.56	34.10
Frequency of multiply malformed cases among all malformed cases (%)	16.67	16.48	26.32	16.67

Table 3. *Distribution of twins and singletons by major and minor malformations, and percentages*

	Twins			Singletons
	MZ	DZ	ZU	
Major	40 10.72	48 7.78	25 12.20	3,781 7.10
Major & Minor	9 2.41	9 1.46	4 1.95	641 1.20
Minor	41 10.99	34 5.51	9 4.39	3,866 7.26
Total number of individuals	373	617	205	53,257

in the minor only category. Twins of unknown zygosity have the highest frequency in the major only category and the lowest in the minor only category. This is not surprising for most twins of unknown zygosity are fetal deaths and have a high rate of major malformations which are probably the cause of death.

Table 4 shows the frequency of twins with malformations by race and sex, compared to that of singletons. Negro twins are more frequently malformed than white twins. This is true of singletons also but the proportion of Negro malformed twins is much higher than that of Negro singletons when compared to white twins and singletons. The high frequency of malformations in Negro twins is almost totally due to the high frequency in Negroes in general of a few minor malformations such as polydactyly and branchial cleft anomalies. Male twins are more frequently malformed than female, following the pattern of singletons. There is a slight overall increase of multiple malformations in all twins over singletons, which is totally contributed by female twins.

Table 5 shows the distribution of malformations by system in twins and singletons. The most impressive feature of the comparison is the more than two-fold increase in twins of cardiovascular and alimentary tract malformations and to a lesser degree of central nervous system and related skeletal malformations. These are practically all major malformations. Significantly increased are also ear malformations and malformations of the upper respiratory tract and mouth, which constitute a mixture of major and minor malformations. Genitourinary and skin malformations, on the other hand, are slightly decreased in twins.

Table 4. *Frequency of twins with malformations compared with that of singletons, by race and sex (%)*

	Twins		Singletons	
	With at least one malformation	With multiple malformations	With at least one malformation	With multiple malformations
White	15.69	3.42	14.73	2.60
Negro	20.59	3.43	16.80	2.63
Other	15.79	1.75	12.79	2.29
Male	20.37	3.03	17.03	3.17
Female	16.31	3.66	14.04	1.99
Total	18.33	3.35	15.56	2.59