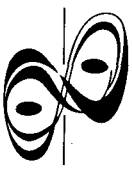

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Congenital Anomalies in Twins in Northern Ireland I: Anomalies in General and Specific Anomalies Other Than Neural Tube Defects and of the Cardiovascular System, 1974-1979

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Abstract. Data are presented from a large-scale population-based study in Northern Ireland, in which multiple sources of ascertainment were used. As found in other studies, the overall prevalence at birth of congenital anomalies amogst twins (285.4/10,000) was somewhat higher than the rate amongst singletons (241.8/10,000). Unlike in other studies, however, the rate amongst twins of like sex (287.8/10,000) was not markedly higher than that amongst twins of unlike sex (252.3/10,000). Problems of comparison between series are discussed.

Key words: Congenital anomalies, Twins, Ascertainment, Discordance, Gastrointestinal malformations, Genital malformations, Syndactyly, Down syndrome

INTRODUCTION

In the past few decades, the perinatal mortality rate of twins has improved [18,20]. Nevertheless, in Western countries, approximately one in ten perinatal deaths occur in multiple births [13,15]. There are four main causes of perinatal mortality in twins: complications of prematurity, uteroplacental insufficiency, delivery trauma and congenital anomalies. The recent improvement in perinatal outcome is considered to be due to improvements in obstetric intervention which have affected the first three categories, and especially in the management of twins weighing less than 1500 g at birth [3]. The fourth category – congenital anomalies – has not shared in

the improvement. Extrapolating from trends that have occurred in the outcome of singleton pregnancy, congenital anomalies are becoming relatively more important in the list of perinatal problems encountered by twins.

Not only mortality, but also morbidity in twins due to congenital anomalies is important. Congenital anomalies in multiple births present a wider range of problems than those in singleton births. When both twins are affected, parents have to care for more than one handicapped child. More commonly, however, only one child is affected, and parents have to cope with bringing up children of the same age but with different mental and physical needs [2].

In general, there is consistent evidence that anomalies are more common amongst twins than singletons [9]. The pattern is less clear for specific anomalies other than those unique to twins. The anomalies unique to twins represent only a small proportion of congenital malformation in twins. At least in part, this lack of clarity is due to methodological problems. In particular, there have been few large population-based studies with ascertainment beyond the neonatal period. In this paper, we present data from a large-scale population-based study in Northern Ireland, in which two sources of ascertainment, covering a period up to the end of the second month, were used. Elsewhere, associations between twinning and (1) neural tube defects [11] and (2) anomalies of the cardiovascular system [12] in this population are described and discussed.

METHODS

Data on births (live and still) delivered in Northern Ireland during the period 1974-1979 were obtained from the Child Health System, which includes statutory notification of birth and information collected by the Health Visitor during the first effective visit after birth. Individual birth records coded as twins were linked in pairs by computerised comparison of variables such as district and date of birth, maternal and paternal age, previous medical history of the parents: where possible, doubtful matches were checked with the appropriate Health and Social Service Board. From 3,367 records of multiple births, 57 (1.7%) were identified as triplets and 3,294 (97.8%) as twins. There were 157,068 births identified as singletons and 245 births of unknown multiplicity. The present study relates to identified twins and singletons only.

For purposes of comparison with other studies, and constrained by the recording of diagnostic information in some of the sources of ascertainment, congenital anomalies were defined to include the generally accepted conditions included in Section XIV of the eighth revision of the International Classification of Diseases [22] togheter with neoplasia, inborn errors of the endocrine system, of metabolism and of the blood and blood-forming organs, "mental retardation" for which a prenatal etiology could not be excluded, certain neurological disorders, hernia and pilonidal cyst and sinus.

During the study period, special arrangements were made for the ascertainment of births with anomalies of the cardiovascular system and for births with Down syndrome.

Births with anomalies other than Down syndrome and of the cardiovascular system were identified from records of two sources whose remit is early infancy. Firstly, the Child Health System includes data from the notification (live or still) required by law within 36 hours of delivery, and from the first effective visit by the Health Visitor after birth in the case of domiciliary confinements or discharge in the case of hospital confinements. Returns on congenital anomalies have to be made no less than six and no more than eight weeks after the birth of the individual to whom they relate. Thus, the data may include conditions which are not manifest until after the perinatal period. Secondly, the Registrar General's Congenital Malformation Notification is a voluntary system whereby doctors or other Community Health Staff notify the occurrence of congenital anomalies they encounter in the course of their practice in a period between four and eight weeks after birth.

Data on births with Down syndrome were collected from several sources – the two sources operating in the perinatal period, records of the genetic counselling clinics and of the only cytogenetics laboratory in the province, autopsy records, death certificates, and in-patient and out-patient records of the three hospitals with units specialising in diseases of childhood.

Diagnostic Discrepancies

Clearly, when multiple sources of ascertainment are involved, discrepancies in diagnosis between sources can arise. In the case of Down syndrome, a hierarchy of information was established, and the final diagnosis was agreed with a medical geneticist. For the other anomalies, the information from the two sources was regard as equally valid and was merged.

Analysis

Following Hook's recommendation [5] the results for live and stillbirths have been analysed separately.

RESULTS

The composition of the study population is summarized in Table 1.

The overall prevalence at birth of congenital anomalies amongst twins was 285.4/10,000, somewhat higher (RR = 1.2, $P > 0.10$) than the rate of 241.8/10,000 amongst singletons (Table 2).

The rate amongst twins of like sex was slightly higher than amongst twins of unlike sex. There were only ten stillborn twins; nine of these had anomalies of the nervous system and one had anomalies affecting multiple systems. The stillbirths

are therefore excluded from all subsequent analysis except that relating to anomalies of the central nervous system.

Table 1 - Births in Northern Ireland, 1974-1979, by outcome and multiplicity

Multiplicity	Outcome		
	Livebirth	Stillbirth	Total
Singleton	155,370	1,698	157,068
Multiple	3,262	105	3,367
Twin	3,193	101	3,294
from like-sex pair	2,139	85	2,224
from unlike-sex pair	1,054	16	1,070
Triplet	54	3	57
Multiple, unspecified	15	1	16
Unknown	233	12	245
Total	158,865	1,815	160,680

Table 2 - Births with anomalies in Northern Ireland, 1974-1979, by outcome and multiplicity

Outcome	Singletons		RR	Twins						RR
				Total		Like sex		Unlike sex		
	N	Rate per 10,000	T:S	N	Rate per 10,000	N	Rate per 10,000	N	Rate per 10,000	L:U
Livebirth	3,322	213.8	1.2	84[a]	263.1	57	266.5	25	237.2	1.1
Stillbirth	476	2,803.3	0.4	10[b]	990.1	7	823.5	2	1,250.0	0.7
All births	3,798	241.8	1.2	94[a,b]	285.4	64	287.8	27	252.3	1.1

RR, T:S = Ratio of rate of anomalies in twins to that in singletons.
RR, L:U = Ratio of rate of anomalies in twins of like sex to that of twins of unlike sex.
[a] There were two liveborn twins with anomalies from pairs of unknown sex type.
[b] There was one affected stillborn twin from a pair of unknown sex type.

There was a marked excess of anomalies of the central nervous system other than neural tube defects amongst twins (Table 3). This was consistent for hydrocephalus and microcephalus, but numbers are small. For this group of anomalies, the prevalence at birth among twins of like sex was slightly lower than among those of unlike sex.

Table 3 - Anomalies of the nervous system, other than neural tube defects, in Northern Ireland, 1974-1979, by multiplicity

Type of anomaly	Singletons		RR	Twins						RR
				Total		Like sex		Unlike sex		
	N (n stillborn)	Rate per 10,000	T:S	N (n stillborn)	Rate per 10,000	N (n stillborn)	Rate per 10,000	N (n stillborn)	Rate per 10,000	L:U
Hydrocephalus[a]	106 (46)	6.7	2.7	6 (5)	18.2	3 (3)	13.5	3 (2)	28.0	0.5
Microcephalus	40 (6)	2.5	3.6	3 (0)	9.1	3 (0)	13.5	0 (0)	0.0	0.0
Other	15 (3)	9.6	0.3	1 (1)	3.0	1 (1)	4.5	0 (0)	0.0	0.0
Total	159 (55)	10.1	3.0	10 (6)	30.4	7 (4)	31.5	3 (2)	28.0	1.1

RR, T:S = Ratio of rate of anomalies in twins to that in singletons.
RR, L:U = Ratio of rate of anomalies in twins of like sex to that in twins of unlike sex.
[a] Excludes cases with spina bifida.

In spite of the association between unlike sex twinning and maternal age, the rate of Down syndrome in twins (N = 3, rate per 10,000 livebirths = 9.4) was lower than that in singletons (N = 259, rate per 10,000 livebirths = 16.7). Two of the cases were from like sex pairs, the third from a pair of unknown sex type.

Again amongst livebirths, there were significantly higher risks of anomalies of the digestive and genital system, and of anomalies in the category "other isolated" in twins than in singletons (Table 4).

Twins of like sex were at increased risk of orofacial cleft and other anomalies of the upper alimentary tract and digestive system as compared to twins of unlike sex, and there was also a suggestion of an increased risk for anomalies of the muscoloskeletal system.

Numbers are too small to permit drawing definitive conclusions about differences in the sex distribuition of twins and singletons with different types of anomalies. The observed pattern is that where the male proportion is greater than 0.50 in affected singletons, the male proportion is higher still for affected twins (Table 4). This is particularly pronounced for anomalies of the digestive system. The male proportion for anomalies of the musculoskeletal system is also higher in twins (0.60) than in singletons (0.45).

Again, numbers are too small for clear conclusions to be reached about any association between birth order in multiple delivery and malformation. The general pattern is for anomalies to be more common in the second-born twin; this is particularly pronounced for anomalies of the musculoskeletal system (Table 4).

Rates of specific anomalies which occurred in twins are compared between twins and singletons in Table 5. The excess risk of anomalies of the digestive system in twins is largely due to pyloric stenosis, whereas that for the genital system was observed for all of the specific anomalies involved. As far as other specific anomalies are concerned, either no marked difference in rate as compared to twins was observed, or the number of cases of twins were too small to permit clear conclusions to be drawn. The frequency of births with anomalies of multiple systems was virtually identical in twins (28.2/10,000 livebirths) and singletons (27.7/10,000 livebirths).

Sociodemographic Variables

Because of problems of small numbers of twins with specific anomalies, we have restricted analysis by sociodemographic variables to livebirths with any type of anomaly.

There are clear excess risks to twins who were born in the Eastern and Northern areas of the province, who were born in 1976 and 1979, who were male, who were delivered to women aged less than 25 and whose mothers were primiparae. Rates of anomaly were substantially lower in twins delivered in the West of the province, who were delivered in 1978, whose fathers worked in an occupation classifiable to Social Class 1, whose mothers were aged 40 or more at birth, and who were delivered preterm.

Table 4 - Anomalies other than of the central nervous and cardiovascular systems, and other than Down syndrome, in livebirths in Northern Ireland, 1974-1979, by multiplicity

Organ, system affected or type of anomaly	Singletons		RR	Twins						RR	Birth order		Male proportion	
	N	Rate per 10,000	T:S	Total		Like sex		Unlike sex		L:U	I	II	Singletons	Twins
				N	Rate per 10,000	MM	FF	MM	FF					
Eye	35	2.3	0.0	0	0.0	0	0	0	0	U			0.37	U
Ear, face and neck	67	4.3	0.0	0	0.0	0	0	0	0	U			0.34	U
Respiratory	38	2.4	1.3	1	3.1	0	0	1	0	0.0	0	1	0.66	1.00
Cleft lip and/or cleft palate	209	13.5	1.4	6	18.8	3	2	1	0	2.5	2	4	0.57	0.67
Digestive	213	13.7	1.8	8	25.1	6	1	1	0	3.4	3	5	0.57	0.88
Genital	197	12.7	2.7	11	34.5	7	0	4	0	0.9	5	6	0.90	1.00
Urinary	52	3.3	0.9	1	3.1	0	0	1	0	0.0	0	1	0.77	1.00
Musculoskeletal	1,508	97.1	1.0	30[a]	94.0	15	7	3	4	1.5	11	19	0.45	0.60
Teguments	156	10.0	0.3	1	3.1	0	0	0	1	0.0	0	1	0.37	0.00
Other isolated	20	1.3	2.4	1	3.1	0	1	0	0	0.0	0	1	0.55	0.00
Multiple systems other than Down syndrome	99	6.4	1.5	3	9.4	1	1	0	1	1.0	1	2	0.44	0.33
Inborn errors of metabolism	29	1.9	0.0	0	0.0	0	0	0	0	U			0.41	0.33
Neoplasia	12	0.8	0.0	0	0.0	0	0	0	0	U			0.58	U

RR, T:S = Ratio of rate of anomalies in twins to that in singletons.
RR, L:U = Ratio of rate of anomalies in twins of like sex to that in twins of unlike sex.
U = undefined.
[a] One male baby was from a pair of unknown sex type.

Table 5 - Specific anomalies, other than Down syndrome and other than of the central nervous and cardiovascular systems, in livebirths in Northern Ireland, 1974-1979, by multiplicity

Anomaly	Singletons		RR	Twins	
	N	Rate per 10,000	T:S	N	Rate per 10,000
Anomaly of lung other than agenesis or congenital cystic lung	12	0.8	3.9	1	3.1
Isolated cleft lip	46	3.0	3.1	3	9.4
Isolated cleft palate	63	4.1	0.0	0	0.0
Cleft lip and palate	100	6.4	1.5	3	9.4
Pyloric stenosis	26	1.7	7.4	4	12.5
Tracheo-esophageal fistula, atresia or stenosis	60	3.9	0.8	1	3.1
Atresia and stenosis of rectum and anal canal	49	3.2	2.0	2	6.3
Anomaly of intestinal fixation	2	0.1	31.0	1	3.1
Undescended testis	9	0.6	5.2	1	3.1
Hypospadias	136	8.8	2.5	7	21.9
Epispadias	1	0.1	31.0	1	3.1
Other specified anomaly of genital organs	15	1.0	6.3	2	6.3
Renal agenesis	16	1.0	3.1	1	3.1
Clubfoot	672	43.3	0.9	12	37.6
Syndactyly	82	5.3	2.4	4	12.5
Reduction deformity of upper limb	58	3.7	1.7	2	6.3
Other anomaly of upper limb	53	3.4	4.6	5	15.7
Congenital dislocation of hip	435	28.0	0.9	8	25.1
Other anomaly of lower limb	145	9.3	1.3	4	12.5
Other & unspeciefied anomaly of unspecified limb	9	0.6	5.2	1	3.1
Anomaly of skull and faces bones	32	2.1	1.5	1	3.1
Anomaly of spine	45	2.9	1.1	1	3.1
Other anomaly of rib and sternum	5	0.3	10.3	1	3.1
Other specified anomaly of muscle, tendon and fascia	60	3.9	0.8	1	3.1
Unspecified anomaly of musculoskeletal system	7	0.5	6.2	1	3.1
Pilonidal sinus	14	0.9	3.4	1	3.1
Unspecified congenital anomaly	5	0.3	10.3	1	3.1
Conjoined twins[a]				2	6.3
Turner's syndrome	8	0.5	6.2	1	3.1

[a] Liveborn pair: no other anomaly detected. There was also a stillbirth with an autosomal anomaly from a conjoined pair: there is no record of any abnormality in the liveborn cotwin.

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Concordance

Four pairs were completety concordant; these pairs were all of like sex.

Anomaly	Number of concordant pairs	Concordance rate (%)	
		Overall	Like-sex pairs
Hydrocephalus	1	20.0	50.0
Pyloric stenosis	1	33.3	33.3
Hypospadias	2	40.0	100.0

Three pairs had anomalies affecting the same anatomical system; again these pairs were all of the same sex.

	Twin A	Twin B
1.	Isolated cleft lip	Cleft lip and palate
2.	Congenital dislocation of the hip	Congenital dislocation of the hip, clubfoot and anomaly of the spine.
3.	Clubfoot, other anomaly of upper limb and other anomaly of lower limb	Reduction deformity of upper limb, other anomaly of rib and sternum and other specified anomaly of genital organs.

Further concordance rates may therefore be derived as follows:

Anomaly group	Number of concordant pairs	Concordance rate (%)	
		Overall	Like-sex pairs
Cleft lip and/or cleft palate	1	20.0	25.0
Musculoskeletal	2	7.1	10.0

In one instance, both members of a pair had a congenital anomaly, but different anatomical systems were involved; one twin had congenital dislocation of the hip, the other had isolated spina bifida.

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DISCUSSION

Apart from the data on Down syndrome, the methods of ascertainment employed in the present study are less than ideal. There is a lack of follow-up from pediatric in-patient and out-patient records, and there are no data from death certificates or records of autopsy. However, most series in the literature are restricted to neonatal records [9] and only four previous surveys relate to geographic populations [7,8,14,21]. A further limitation is that no direct determination of zygosity was undertaken.

The general finding of a moderate excess risk in twins as compared to singletons is confirmed. However, in contrast to an earlier study in Belfast [19] and to what is generally accepted, there was no clear excess in twins of like sex as compared to twins of unlike sex. Review of the literature shows that virtually all evidence of an excess of anomalies of all types in twins of like sex is derived from the WHO Collaborative Study [19]. Without exception, the studies in each of the areas involved were based on hospital series, and therefore the possibility of bias of detection of anomalies in like sex twins cannot be excluded. As twins of like sex tend to have a higher frequency of perinatal problems in general [1] the opportunity for detecting anomalies in twins of like sex must be greater. The only other studies to report an excess in twins of like sex are those of Layde et al [8] and Windhan and Bjerkedal [21]. The latter study is based on neonatal records only, and the excess is moderate. The study of Layde et al [8], in which the excess is marked, is based on multiple sources and follow up of the child to one year of age. Apart from differences in methods of ascertainment, comparisons of overall rates of malformation between studies are difficult to interpret because of differences in the ranges of anomalies considered, differences in the definition of stillbirth and differences in the maternal age distributions. In the study of Windham and Bjerkedal [21], for example, fetal deaths from 16 weeks gestation are included, whereas in the present study data were available only for stillbirths of 28 weeks gestation or more.

Possible bias of ascertainment poses one important difficulty of interpretation in comparing prevalences of anomalies at birth between twins and singletons. Following Hook et al [6], the possibility that delivery of twins may prompt more intensive examination for anomalies than delivery of singletons has been considered by comparing the rates of "minor" anomalies recorded in the study, between twins, stillborn singletons, liveborn singletons of low birthweight, liveborn singletons of long gestation and liveborn singleton term infants (Table 6).

Compared with liveborn singleton infants delivered at term, an excess of microcephalus and anomalies of the external genitalia is observed in all other groups. In general, no excess is observed in liveborn singletons of long gestation, and amongst the remaining groups, any excess of "minor" malformations is least marked for twins. We therefore do not confirm the findings of the Madison study of Hook et al [6], but it must be noted that the opportunity for recording minor anomalies is restricted as compared to the Madison study.

There are relatively few published reports with which the prevalence at birth of specific anomalies, or groups of anomalies, in twins and singletons estimated in

the present study can be compared.

The excess risk of hydrocephalus in all births (live and still) is consistent with other studies, although not all of these include stillbirths [4,7,8,14,16].

Table 6 - Pregnancy outcome status[a] associated with some specific minor anomalies. Northern Ireland, 1974-1979 - CHS and RG only[b]

Anomalies	Twins	Singletons			
		Stillborn	Liveborn		
			Low birthweight	Long gestation	Term
Microcephalus	3 (9.1)	6 (35.3)	14 (19.5)	1 (2.4)	13 (0.9)
Squint or buphthalmos	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Tongue	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	21 (1.5)
Genital	9 (27.3)	3 (17.7)	21 (29.2)	4 (9.8)	111 (8.0)
Hip and foot	19 (57.7)	24 (141.3)	69 (95.9)	26 (63.4)	955 (68.8)
Poly- & syndactyly	4 (12.1)	5 (29.4)	13 (18.1)	2 (4.9)	116 (8.4)
Hernia	0 (0.0)	9 (53.0)	10 (13.9)	1 (2.4)	30 (2.2)
Skin	0 (0.0)	0 (0.0)	0 (0.0)	3 (7.3)	36 (2.6)
Branchial cleft	0 (0.0)	0 (0.0)	1 (1.4)	0 (0.0)	5 (0.4)
Population	3,294	1,698	7,196	4,098	138,782

[a] Rates per 10,000 births in parentheses.

[b] CHS = Child Health System; RG = Registrar General's Congenital Malformation Notification.

As noted by Kallen [7], we found markedly higher rates of hydrocephalus in infants with birthweights of less than 2500 g (4.37‰in singletons; 2.80‰in twins) than in infants with higher birthweights (0.43‰in singletons; 1.12‰in twins). As the frequency of preterm delivery is higher in twins than in singletons, the excess of hydrocephalus in twins could be secondary to the positive association between postnatal hydrocephalus and prematurity attributed to delivery damage. However, as also noted by Kallen [7], the excess in twins is confined to infants weighing over 2500 g at birth (< 2500 g, RR = 0.6; 2500 g + RR = 2.6). Moreover, in Northern Ireland, only one of the twins with hydrocephalus was born alive.

For other group of anomalies, the only large scale studies potentially permiting comparison are those of Myrianthopoulos [16,17] Layde et al [8], Windham and Bjerkedal [21] and Kallen [7]. We are reluctant to make comparison between the present study and the NCPP study [16,17] because the methods of ascertainment and diagnostic criteria differ substantially. It is difficult to make direct comparisons with the results of the Swedish study [7] as figures are presented only for the specific anomalies found in twins. As in the Swedish study, the rates of cardiovascular malformations, anal atresia, severe kidney malformations and limb reduction deformities were higher in twins than in singletons, but unlike in the Swedish data, the rate of spine defects and esophageal atresia, the other two components of the "VACTERL syndrome", were similar in twins and singletons (Table 5). It is stressed that

the number of cases from Northern Ireland with any of the above specific anomalies did not exceed two. In contrast to the findings from the present study, there was no excess of anomalies of the urogenital system in twins in Sweden, or of pyloric stenosis (included in "other gut malformations" in Kallen's paper). Comparisons have been made with the other two studies using the ranges of codes specified in these two studies and including stillbirths in the comparison with the study of Windham and Bjerkdal [21] but not that of Layde et al [8]. As compared to the Norwegian study (Table 7), the overall excess of anomalies of the central nervous system, and the deficit of anomalies of the hip, are not confirmed.

Table 7 - Comparison of congenital anomalies other than of the cardiovascular system in singletons and twins between Northern Ireland, 1974-1979 (present study) and Norway [21]

Category of anomalies[a]	Northern Ireland 1974-1979					Norway 1967-1979				
	Singletons		RR	Twins		Singletons		RR	Twins	
	N	Rate per 10,000	T:S	N	Rate per 10,000	N	Rate per 10,000	T:S	N	Rate per 10,000
Hernia	57	3.6	0.0	0	0.0	568	7.3	1.2	14	9.1
CNS	1,048	66.7	1.1	24	72.9	1,147	14.8	1.8	41	26.8
EEFN	99	6.3	0.0	0	0.0	424	5.5	0.9	8	5.2
CL/P	226	14.4	1.3	6	18.2	1,430	18.4	1.2	33	21.5
Resp/Dg	235	15.0	1.8	9	27.3	632	8.2	0.9	11	7.2
G-U	251	16.0	2.3	12	36.4	2,813	36.3	1.0	58	37.9
Limb	976	62.1	1.1	22	66.8	6,472	83.5	1.0	130	84.8
Hip	459	29.2	0.8	8	24.3	7,117	91.8	0.4	59	38.5
Other	256	16.3	0.9	5	15.2	866	11.2	1.1	19	12.4
Multiple	120	7.6	1.6	4	12.1	423	5.5	1.3	11	7.2
Down	230	14.6	0.4	2	6.1	780	10.1	0.8	12	7.8
Individuals	3,798	241.8	1.2	94	285.4	23,424	302.1	0.9	426	278.1
Population	157,068			3,294		775,405			15,320	

RR, T:S = Ratio of rate of anomalies in twins to that in singletons.
[a] CNS = Central nervous system; EEFN = Eye, ear, face and nose; CL/P = Cleft lip and/or palate; Resp/Dg = Respiratory/Digestive system; G-U = Genitourinary system.

Moreover, no anomalies of the eye, ear, face or nose and no hernias, were observed amongst the twins in Northern Ireland. Also unlike in the Norwegian data, marked excesses of anomalies of the respiratory and digestive, and genitourinary systems, were found. In addition, the excess of cases with anomalies affecting multiple systems and the reduced frequency of Down syndrome, are more pronounced in the data from Nothern Ireland. With the exception of Down syndrome and other

anomalies affecting multiple systems, the discrepancies are found for the groups of anomalies whose rates in singletons differ substantially between the populations. In the case of anomalies of the central nervous system, it is generally accepted that there is a biological difference. Some of the other anomalies are internal, and the different methods of ascertainment are likely to be important. The others are rare, and chance is the likeliest explanation.

As compared to the white population of Metropolitan Atlanta, the rates of virtually all anomalies in singletons in Northern Ireland (with the notable exception of Down syndrome on which a special study was carried out) are lower (Table 8). The differences were twofold or more for anomalies of the central nervous system other than neural tube defects or hydrocephaly, of the eye, head, ear, nose and throat, lung, jaw, tongue, for pyloric stenosis, and other anomalies of the digestive system, for polydactyly, for anomalies of the skin, hair and spleen, for hernias, metabolic anomalies, angiomata, neoplasms and TORCH infections. The converse applied only for miscellaneous limb anomalies and congenital dislocation of the hip.

The differences almost certainly reflect the different methods of ascertainment and it is not surprising that there should be so little consistency in the ratios of the rates in twins to those in singletons between the studies. However, there is a consistent excess risk in twins of anomalies of the lower gastrointestinal tract, of anomalies of the genitalia, and of syndactyly, and the reduced risk of Down syndrome is also consistent between the studies.

As also noted by Kallen [7], chance is the likeliest explanation for any differences is the sex distribution of twins and singletons with different types of anomalies. The indication of a raised male proportion in twins with anomalies of the digestive or musculoskeletal system found in the present study (Table 4) does not apper to be borne out by the Swedish data [7], the male proportions in twins being 0.52 (13 of 25) and 0.42 (84 of 199), respectively. However, data on the male proportions in singletons in this series are not presented.

The general pattern for anomalies to be more common in the second-born twin (Table 4) in the present sudy contrasts with Kallen's [7] finding that just over half (406 of 785 - 52%) of the malformed twins were first-born. When considered in isolation, this evidence suggests that there may have been bias of ascertainment in the present study. Second-born twins tend to have more perinatal problems than first-born twins [2], and therefore may tend to stay in hospital longer after delivery. In consequence, the opportunity to make a diagnosis of congenital anomaly may be greater in the second-born than in the first-born twin. However, if this were true, a greater excess of "minor" malformations in twins than is apparent in the data presented in Table 6 might have been expected, and multiplicity would have been expected to influence the relative probability of ascertainment in the analysis of Little and Carr-Hill [10]. Kallen [7] found that positional foot defects were markedly more common in twin 1 (44 out of 68), which he attributed to chance variation as many malformations were studied. In the present study, these defects were also more common in twin 1 (7 out of 12), in contrast to the pattern for musculoskeletal defects in general. It would be helpful to have information from other studies on this issue.

Table 8 - Comparison of congenital anomalies other than NTDs and other than of the cardiovascular system, in liveborn singletons and twins between Northern Ireland, 1974-1979 (present study) and the white population of Metropolitan Atlanta, 1969-1976 [8]

Anomalies[a]	Singletons				Twins				RR, T:S	
	NI[b]		MA[c]		NI[b]		MA[c]		NI[b]	MA[c]
	N	Rate	N	Rate	N	Rate	N	Rate		
Hydrocephaly	60	3.86	77	5.52	1	3.13	4	16.39	0.8	3.0
Other CNS (non-NTD)	39	2.51	93	6.67	3	9.40	2	8.20	3.7	1.2
Eye	33	2.12	139	9.97	0	0.00	2	8.20	0.0	0.8
Miscellaneous HEENT	61	3.93	438	31.41	0	0.00	5	20.49	0.0	0.7
Lung	15	0.97	34	2.44	1	3.13	4	16.39	3.2	6.7
Cleft palate	63	4.05	93	6.67	0	0.00	2	8.20	0.0	1.2
Cleft lip/palate	146	9.40	173	12.41	6	18.79	6	24.59	2.0	2.0
Jaw, tongue	25	1.61	141	10.11	0	0.00	2	8.20	0.0	0.8
Pyloric stenosis	26	1.67	292	20.94	4	12.53	2	8.20	7.5	0.4
Lower GI	76	4.89	171	12.26	3	9.40	11	45.08	1.9	3.7
Miscellaneous gut	12	0.77	27	1.94	0	0.00	3	12.30	0.0	6.3
Genital	197	12.68	673	48.26	11	34.45	23	94.26	2.7	2.0
Ureter	52	3.35	58	4.16	1	3.13	3	12.30	0.9	3.0
Clubfoot	672	43.25	682	48.91	12	37.58	7	28.69	0.9	0.6
Polydactyly	70	4.51	165	11.83	0	0.00	4	26.39	0.0	1.4
Syndactyly	82	5.28	118	8.46	4	12.53	5	20.49	2.4	2.4
Miscellaneous limb	157	10.10	13	0.93	4	12.53	2	8.20	1.2	8.8
Congenital hip	435	28.00	175	12.55	8	25.05	3	12.30	0.9	1.0
Skin, hair	65	4.18	279	20.01	0	0.00	4	16.39	0.0	0.8
Spleen	2	0.13	15	1.08	0	0.00	1	4.10	0.0	3.8
Conjoined twins				...	3	9.40	7	28.69		
Down syndrome[d]	259	16.70	147	10.54	3	9.40	1	4.10	0.6	0.4
Other autosomal defects	20	1.29	21	1.51	0	0.00	0		0.0	0.0
Hernias	27	1.82	164	11.76	0	0.00	5	20.49	0.0	1.7
Omphalocele/ gastroschisis	31	2.00	50	3.59	0	0.00	4	16.39	0.0	4.6
Metabolic	29	1.87	58	4.16	0	0.00	1	4.10	0.0	1.0
Angiomata	38	1.45	260	18.65	0	0.00	6	24.59	0.0	1.3
Neoplasms	12	0.77	38	2.73	0	0.00	1	4.10	0.0	1.5
TORCH infections	3	0.19	23	1.65	0	0.00	0	...	0.0	0.0
Total livebirths	155,370		139,440		3,193		2,440			

Rates per 10,000 livebirths.
RR, T:S = Ratio of rate of anomalies in twins to that in singletons.
[a] HEENT = Ear, face and neck; GI = Gastrointestinal; TORCH = Toxoplasmosis, rubella, cytomegalovirus, herpes virus.
[b] NI = Northern Ireland.
[c] MA = Metropolitan Atlanta.
[d] Data for Northern Ireland from special study.

CONCLUSION

The results of the present study confirm previous findings that anomalies are more common amongst twins than singletons, but do not confirm previous reports of a marked excess in twins of like sex.

Few large series have been published with which comparison can be made for other types of anomalies but the available evidence suggests that twins are at higher risk of anomalies of the lower gastrointestinal tract, of anomalies of the genitalia and of syndactyly. Evidence of a reduced risk of Down syndrome in twins is also consistent between studies.

As in previous studies, discordance was found to be the norm.

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