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INFANTILE HYPERTROPHIC PYLORIC STENOSIS: DATA ON 81 PAIRS OF TWINS

by

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Until recently it was thought that when infantile pyloric stenosis occurs in one twin, the other twin is almost invariably affected if the pair is monozygous, and rarely affected if it is dizygous (Sheldon, 1938). It has been necessary to modify this conclusion to some extent in the light of a number of recent exceptions. Using cases reported in the literature, Laubscher & Smith (1947) found 11 examples of concordance in 13 monozygous pairs, and 1 in 23 dizygous pairs. Powell & Carter (1951) added 4 pairs of their own to others previously published, and noted that both twins were affected in 12 of 17 monozygous pairs, and in 3 of 29 dizygous pairs; corresponding figures reported by Metrakos (1953) were 12 in 18 and 1 in 29 respectively. The impression remains that the incidence of concordance is substantially greater in monozygous than in dizygous twins.

With the exception of Sheldon's series, which included only one undoubtedly monozygous pair, all of the series upon which this conclusion is based were composed largely of published cases, which can by no means be accepted as representative. The problem evidently requires examination of a substantial number of unselected twins with at least one affected member.

An opportunity to assemble such a series was provided by an enquiry in which the hospital records of 3,982 children with pyloric stenosis were examined; 87 of them were twins. Direct evidence of zygosity was not available, and in assessing the incidence of concordance in monozygous and dizygous pairs we have relied on examination of the sex distribution of the twin pairs, a method used by Record and McKeown (1951) in investistigation of malformations of the central nervous system.

The 87 affected twins were obtained as follows. There were 12 among the 489 propositi born in Birmingham in the years 1940-49, of which details were previously published (McKeown, MacMahon and Record, 1951a). By inspection of records of all children treated for pyloric stenosis at the Birmingham Children's Hospital in the years 1938-54, 24 were added: 5 in the period 1940-49 (born outside Birmingham, and therefore not included in the earlier series) and 19 from years earlier than 1940 and later than 1949. Notes of patients with pyloric stenosis were also examined in hospitals in Liverpool, Manchester, Newcastle-on-Tyne and Sheffield, and a further 51 affected twins were obtained. Attention was confined to years in which all records were available, and the data are believed to include all twins in what is in effect an unselected series of 3,982 patients. The number of pairs from each source is shown in Table 1. The data are given in full in the apendix.

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Table 1 - Sources of records of twins with pyloric stenosis

Source	Years	No. of records of patients with pyloric stenosis	No. of affected twins	No. of twin pairs
Birmingham Children's Hospital	1938-54	1482	36	33
Records for Newcastle-on-Tyne kept by Dr. George Davison	1928-50	1100	22	19
Newcastle General Hospital	1951-54	275	7	7
Royal Manchester Children's Hospital	1948-54	272	1	1
Duchess of York Hospital for Babies, Manchester	1948-54	251	3	3
Alder Hey Children's Hospital, Liverpool	1945-54	227	6	6
Sheffield Children's Hospital	1947-54	186	5	5
Royal Liverpool Children's Hospital	1948-54	147	3	3
Booth Hall Hospital, Manchester	1949-54	112	4	4
Total		3982	87	81

Incidence of Pyloric Stenosis in Twins

The proportion of twins among affected was 1 in 46 (87 in 3,982), about the same as in the general population of births (1 in 42). This result supports the conclusion of Powell and Carter (1951), based on four series of cases from the literature, that the incidence of pyloric stenosis is approximately the same in twins as in single births.

Before assessing the risk of pyloric stenosis in the partner of an affected twin we exclude 11 of the 81 pairs. In 10 the second twin was unaffected, but died during the first three months of life, before the end of the period of risk of the condition. In the other excluded set (MM) the diagnosis was considered uncertain: one twin had pyloric stenosis which was confirmed at operation; the twin partner had identical clinical signs (projectile vomiting, visible peristalsis and palpable tumour) but no tumour was found at operation.

In 6 of the 70 remaining pairs, both were affected. The incidence in partners of affected twins (8.6 per cent) is much higher than in the general population of births (0.3; MacMahon, Record and McKeown, 1951), but is only a little higher than in sibs born after a child with pyloric stenosis (5.8; McKeown et al. 1951 a). This conclusion is supported by examination of data from the literature; the twins shown in Table 2 were observed in consecutive series of cases of pyloric stenosis. (Reports of isolated cases were

not included). In 6 of the 64 pairs both members were affected. This incidence (9.4 per cent) is about the same as that obtained from our own data; the estimate obtained by combining the two series is 9.0 per cent).

Table 2 - Proportion of twin pairs in which both members were affected. Data from the literature

Source	Nº of pairs	
	Total	With both twins affected
Thomson (1921)	1	9
Monrad (1927)	3	0
Sheldon (1938)	23	1
Rinvik (1940)	2	0
Ford et al. (1941)	12	2
Cockayne & Penrose (1943)	11	2
Shaefer & Erbes (1948)	7	0
Grimes et al. (1950)	3	1
Ward-McQuaid & Porritt (1950)	2	0
Total	64	6

Pyloric Stenosis in Monozygous and Dizygous Twins

Although we have no direct evidence of the type of twinning for our own data, an estimate of the relative incidence of concordance in monozygous and dizygous pairs can be obtained from (i) the relative frequency with which both twins are affected in like and unlike sex pairs, and (ii) a comparison of the observed incidence of concordance in like sexed pairs with the expected incidence of monozygous pairs. Table 3 gives the distribution accordin according to sex of the 56 pairs for which data were complete. (In 5 of the 70 cases, sex of the unaffected twin was unknown).

(i) In examining the frequency of concordance in like and unlike sexed pairs we confine attention to 54 pairs with at least 1 affected male member. There were 31 MM pairs of which 4 (13 per cent) were concordant, and 23 MF pairs with 2 (9 per cent) concordant. The incidence of concordance is apparently no higher in like sexed pairs, of which a proportion are monozygotic, than in unlike sexed pairs, all of which are dizygotic. Moreover, since pyloric stenosis is much more common in males than in females (sex ratio for single affected births is approximately 80 per cent male) the expected incidence in the male partner of an affected male is in any case considerably higher than in the female twin of an affected male. Numbers are of course rather small, and the result depends on the presence of 2 MF pairs with both affected, of which there were no examples among the 64 pairs selected from the literature.

(ii) The expected proportion of monozygotic twins among like sexed pairs is 44 per

cent in a general population (using Waterhouse's estimate (1950) of 28.6 per cent as the proportion of twins which are monozygotic). In the present context a correction is necessary because of the low birth order, and hence low maternal age, at which children with pyloric stenosis are born. Correction by application of the age specific twin incidences given by Waterhouse to the distribution of 478 Birmingham cases (previously described by McKeown, MacMahon and Record, 1951 b) changes the expected proportion of monozygous pairs among all twins to 29.1 per cent, and among like sexed twins to 45 per cent. (The sex incidence of pyloric stenosis does not of course affect the proportion of monozygous pairs among like sexed twins, since the differential rates apply to both types of like sexed twins).

Table 3 - Distribution of twin pairs according to sex

Sex	Affected	Number
MM	One	27
	Both	4
FF	One	8
	Both	0
MF	Male	21
	Female	3
	Both	2
Total	One	59
	Both	6
	Total	65

Of the 39 like sexed pairs, 18 (45 per cent) might therefore be expected to be mo no zygous. There were 4 concordant pairs. Even if we assume that all of them were monozygotic (and there are several recorded examples of concordant dizygous pairs) the proportion is much below the expected incidence. It seems probable that a substantial number of the 35 like sexed pairs with only one affected member were monozygotic.

Table 4 - Observed and expected distribution by sex of a series of twins with pyloric stenosis

Sex of set	Expected distribution		Observed distribution
	Proportion	Numbers	
MM	0.517	33.6	31
FF	0.129	8.4	8
MF	0.354	23.0	26
Total	1.000	65.0	65

$x^2 = 0.61$, $n = 2$, $0.7 < p < 0.8$

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Finally, it can be shown that the distribution of MM, FF and MF pairs among the 65 pairs corresponds closely to the distribution expected in a twin universe which contains the usual proportions of monozygotic and dizygotic twin pairs. The sex distribution of a series of twins born at the maternal ages at which patients with pyloric stenosis are born can readily be calculated from the proportion of twins which are monozygous. As noted above, from data of Waterhouse (1950), this proportion is estimated as 29.1 per cent. The corresponding percentage frequencies of MM, FF and MF sets respectively are 32.3, 32.3 and 35.4, and the frequencies with which such sets will contain at least one affected member are $1 - (1 - a)^2$, $1 - (1 - b)^2$ and $1 - (1 - a)(1 - b)$, where a and b are the incidences of pyloric stenosis in males and females. Substituting for a and b the figures of 0.006 and 0.0015 previously recorded (MacMahon et al., 1951), and applying these rates to the above percentage frequencies of MM, FF and MF sets, we obtain the expected distribution noted in Table 4. Correspondence between observed and expected distributions is close, which suggests that this sample is drawn from a universe of twins containing the usual proportion of monozygous pairs.

Summary

87 affected twins (in 81 pairs) were identified among 3,982 children with pyloric stenosis. The proportion of twins among affected (1 in 46) is about the same as in the general population of births. The incidence of pyloric stenosis in partners of affected twins is 8.6 per cent, considerably higher than in the general population of births (0.3 per cent) but only slightly higher than in subsequent sibs (5.8 per cent).

The frequency of concordance is about the same in MM (4 of 31) and MF (2 of 23) pairs. Of 39 like sexed pairs 4 were concordant; the expected number of monozygotic pairs is 18 (assuming the usual proportion of monozygotic pairs), which suggests that the frequency of concordance among them is not greater than 4 in 18. It is shown that the distribution of MM, FF and MF pairs in the series corresponds closely to the distribution expected in a twin universe which contains the usual proportions of monozygotic and dizygotic twin pairs.

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APPENDIX

Details of 81 pairs of twins in which at least one member had pyloric stenosis

1 - Pairs with one affected member

N.	Source of record	Date of birth	Birth rank	Sex of unaffected	Sex of affected	Method of diagnosis	Remarks
1	BC	20- 4-39	1	♂	♂	Operation	
2*	BC	12- 4-40	4	♂	♂	Operation & autopsy	Affected died
3	BC	9- 9-41	1	♂	♂	Operation	Affected died
4*	BC	25- 4-44	3	♂	♂	Tumor palpated	Affected died aged 12 months – tuberculosis
5*	BC	19- 2-45	3	♂	♂	Operation	
6*	BC	23-12-45	3	♂	♂	Operation	Eldest sibling operated for pyloric stenosis
7*	BC	7- 5-48	3	♂	♂	Operation	
8	BC	18- 2-48	1	♂	♂	Operation	
9*	BC	8- 9-49	1	♂	♂	Operation	
10*	BC	11- 9-49	3	♂	♂	Tumor palpated	
11	BC	5-11-51	2	♂	♂	Operation	
12	BC	2- 6-53	2	♂	♂	Operation	
13	BC	28- 4-54	3	♂	♂	Operation	
14	AH	21-10-53	2	♂	♂	Operation	
15	BH	8- 8-51	2	♂	♂	Operation	
16	RMC	24- 2-50	7	♂	♂	Operation	
17	NG	8- 1-52	3	♂	♂	Operation	
18	NG	21- 6-53	2	♂	♂	Operation	
19	NG	8-11-53	?	♂	♂	Operation	
20	NG	30- 6-54	2	♂	♂	Operation	
21	SC	27-11-52	2	♂	♂	Operation	
22	GD	2- 9-37	3	♂	♂	Operation	
23	GD	6- 4-42	3	♂	♂	Operation	
24	GD	6-11-42	2	♂	♂	Operation	
25	GD	19- 3-44	?	♂	♂	Operation	
26	GD	10- 9-46	2	♂	♂	Operation	
27	GD	25-11-50	1	♂	♂	Operation	
28	BC	?- 7-41	1	♀	♂	Operation	Illegitimate
29*	BC	5-10-47	1	♀	♂	Operation & autopsy	Affected died
30*	BC	6-12-47	1	♀	♂	Operation	
31	BC	13-11-51	3	♀	♂	Operation	
32	BC	19- 7-51	2	♀	♂	Operation	
33	BC	11-12-51	1	♀	♂	Operation	
34	BC	1- 1-52	4	♀	♂	Operation	
35	BC	9- 4-54	3	♀	♂	Operation	
36	AH	27-12-53	2	♀	♂	Operation	
37	RLC	20- 5-51	3	♀	♂	Operation	

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N.	Source of record	Date of birth	Birth rank	Sex of unaffected	Sex of affected	Method of diagnosis	Remarks
38	RLC	8- 2-54	?	♀	♂	Operation	
39	BH	31- 8-52	1	♀♀	♂♂	Operation	
40	DY	25- 5-54	4	♀♀♀	♂♂♂	Operation	
41	NG	28- 2-51	1	♀♀♀	♂♂♂	Operation	Affected died
42	NG	11- 4-53	2	♀♀♀	♂♂♂	Operation	
43	SC	?- 9-48	?	♀♀♀	♂♂♂	Operation	
44	SC	19- 4-51	2	♀♀♀	♂♂♂	Operation	
45	GD	29- 1-39	3	♀♀♀	♂♂♂	Operation	
46	GD	23- 7-39	5	♀♀♀	♂♂♂	Operation	
47	GD	9-10-46	1	♀♀♀	♂♂♂	Operation	Illegitimate
48	GD	16- 6-49	5	♀♀♀	♂♂♂	Operation	
49	BC	23-11-46	1	?	♂♂♂	Operation	
50	AH	30-12-48	5	?	♂♂♂	Operation	
51	AH	26-10-44	8	?	♂♂♂	Operation	
52	GD	1- 1-33	?	?	♂♂♂	Tumor palpated	
53*	BC	22- 3-48	1	♀	♀♀♀	Operation	Affected died
54*	BC	23- 3-49	1	♀♀	♀♀♀	Autopsy	Affected died
55	BC	7- 1-54	1	♀♀♀	♀♀♀	Tumor palpated	Illegitimate
56	RLC	19- 6-51	4	♀♀♀	♀♀♀	Operation	
57	BH	11-11-52	3	♀♀♀	♀♀♀	Operation	
58	DY	31- 5-53	2	♀♀♀	♀♀♀	Operation	
59	DY	3-11-50	2	♀♀♀	♀♀♀	Operation	Elder sibling operated for pyloric stenosis
60	SC	17- 4-51	1	♀	♀♀	Operation	
61	BC	31- 1-52	5	♂♂♂	♀♀	Operation	
62	AH	20-10-49	1	♂♂	♀♀♀	Operation	
63	GD	1928	4	♂♂	♀♀♀	Tumor palpated	
64	AH	22- 5-51	4	?	♀♀♀	Operation	An elder sibling operated for pyloric stenosis

2 - Pairs with two affected members

N.	Source of record	Date of birth	Birth rank	Twin A		Twin B		Remarks
				Sex	Method of diagnosis	Sex	Method of diagnosis	
65	BC	17- 6-37	1	♂	Operation	♂	Autopsy	
66	BC	12- 4-45	1	♂♂	Operation	♂♂	Autopsy	Illegitimate
67	GD	24- 9-47	1	♂♂	Operation	♂♂	Operation	
68	GD	26-12-48	2	♂♂	Operation	♂♂	Operation	
69	BC	12-11-51	4	♂	Operation	♀	Operation & autopsy	
70	GD	10- 8-37	1	♂	Operation	♀	Operation	

3 - Pairs with one affected member in which the condition of the second member is unknown

N.	Source of record	Date of birth	Birth rank	Affected twin		Unaffected twin	
				Sex	Method of diagnosis	Sex	Fate
71	BC	27- 2-49	1	♂	Operation	♂	Operation, no tumor found (see text)
72	BC	14-12-37	1	♂	Operation	♂	Died age 2 months – gastroenteritis and pneumonia
73	BC	31-10-50	?	♂	Operation	?	Died age 4 weeks – atelectasis
74	BH	24- 5-51	2	♂	Operation	♀	Died age 24 hours – spina bifida
75	GD	16- 2-39	3	♂	Operation	?	Died. Cause not stated
76	GD	19- 9-41	1	♂	Operation	♂	Stillborn
77	GD	10- 8-48	2	♂	Operation	?	Stillborn
78	BC	23- 2-51	5	♀	Operation	♀	Died age 4 weeks – gastroenteritis
79	NG	31- 8-54	1	♀	Operation	♀	Died age 3 weeks – neonatal infection and pulmonary haemorrhage
80	SC	26-11-52	?	♀	Operation	?	Died age 2 days – cerebral haemorrhage
81	GD	4- 4-43	?	♀	Operation	?	Died age 16 days – cause not stated

Source of record

BC	Birmingham Children's Hospital.
RLC	Royal Liverpool Children's Hospital.
AH	Alder Hey Children's Hospital, Liverpool.
RMC	Royal Manchester Children's Hospital.
DY	Duchess of York Hospital for Babies, Manchester.
BH	Booth Hall Hospital, Manchester.
NG	Newcastle General Hospital.
SC	Sheffield Children's Hospital.
GD	Dr. George Davison.

[1] Numbers asterisked were included in a previous series and were given in an appendix (McKeown et al, 1951 a).

RIASSUNTO

87 gemelli colpiti (su 81 coppie) sono stati identificati fra 3.982 bambini affetti da stenosi pilorica. La proporzione dei gemelli fra i colpiti (1 su 46) è circa la stessa che nella popolazione generale delle nascite. L'incidenza della stenosi pilorica nei cogemelli di individui affetti è 8,6 per cento, considerevolmente più alta che nella popolazione generale delle nascite (0,3 per cento), ma solo leggermente più alta che nei fratelli successivi (5,8 per cento).

La frequenza della concordanza è circa la stessa nelle coppie MM (4 su 31) ed MF (2 su 23). Di 39 coppie dello stesso sesso 4 erano concordanti; il numero previsto di coppie monozigotiche è 18 (supponendo la proporzione usuale di coppie monozigotiche), il che suggerisce che la frequenza della concordanza fra di essi non sia superiore a 4 su 18. Viene dimostrato che la distribuzione di coppie MM, FF ed MF nella serie, corrisponde da vicino alla distribuzione prevista in una popolazione gemellare che contenga la consueta proporzione di coppie gemellari monozigotiche e dizigotiche.

RÉSUMÉ

87 jumeaux atteints (sur 81 couples) on été identifiés sur 3.982 enfants malades de sténose pilorique. La proportion des jumeaux parmi les malades (1 sur 46) est environ la même que dans la population générale des naissances. L'incidence de la sténose pilorique dans les co-jumeaux d'individus affectés est de 8,6 pour cent, considérablement plus élevée que dans la population générale des naissances (0,3 pour cent), mais seulement légèrement plus élevée que dans les frères successifs (5,8 pour cent).

La fréquence de la concordance est environ la même dans les couples MM (4 sur 31) et MF (2 sur 23). Sur 39 couples du même sexe, 4 étaient concordants; le nombre prévu de couples MZ est 18 (en supposant la proportion habituelle de couples MZ), ce qui suggère que la fréquence de la concordance entre eux n'est pas supérieure à 4 sur 18. Il est en effet démontré que la distribution de couples MM, FF et MF dans la série, correspond de près à la distribution prévue dans une population gémellaire qui renferme la proportion habituelle de couples gémellaires MZ et DZ.

ZUSAMMENFASSUNG

Von 3,982 mit Pylorusstenose behafteten Kindern waren 87 Zwillinge (von 81 Zwillingspaaren). Die Proportion von Zwillingen bei den Kindern mit Pylorusstenose ist 1 in 46, was ungefähr der Proportion von Zwillingsgeburten bei den Gesammtgeburten entspricht. Das Vorkommen von Pylorusstenose in Partnern von Zwillingen mit Pylorusstenose ist 8.6%, also bedeutend grösser als das Vorkommen von Pylorusstenose bei den Gesammtgeburten (0.3%), aber nur ein wenig grösser als dasselbe bei später geborenen Geschwistern (5.8%).

Die Häufigkeit der konkordanten Zwillingspaare ist ungefähr dieselbe in MM (4 von 31) und MF (2 von 23) Paaren. Von 39 Paaren des gleichen Geschlechtes waren 4 Paare konkordante; die zu erwartende Zahl von eineiigen Paaren ist 18 (die gewöhnliche Proportion von eineiigen Paaren angenommen), was bedeuted, dass die Häufigkeit von konkordanten Zwillingspaaren innerhalb eineiiger Paare nicht grösser als 4 in 18 ist. Es wird gezeigt, dass die Verteilung von MM, FF und MF Paaren in den Daten dieses Werkes ähnlich ist der Verteilung, die man in einer Gruppe von Zwillingen, welche die gewöhnliche Proportion von eineiigen und zweieinigen Zwillingspaaren enthält, erwartet.