Pyloric stenosis in the Oxford Record Linkage Study Area

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Summary. The files of the Oxford Record Linkage Study were employed to identify 220 infants presenting with infantile hypertrophic pyloric stenosis (IHPS) in the 6-year period 1966 to 1971. Information on these infants was obtained from birth certificates and maternity notes. The overall incidence was 2.5 per 1000 live-births. There was a distinct seasonal variation, with highest incidence to infants born in the third quarter of the year as well as variation in incidence with area: the cities had much lower rates of IHPS than the adjacent rural or small urban areas. It was shown that the rates in the south and east of the area studied were far greater than in the north and west.

In the present study there was no excess of primiparae, the peak maternal age group was 20 to 24; there was a slight excess of parents of social classes I and II; and a significant association with mothers who were Rhesus negative. The rate of IHPS among sibs was 85 per 1000. Though there was the usual correlation with the male sex (M:F ratio = 5.5:1), there was no variation with birthweight and only among the females was an association found with prolonged gestation. There appeared to be an inverse relation between gestation and age on admission to hospital.

The disease of infantile hypertrophic pyloric stenosis (IHPS) has become so amenable to present methods of treatment that there have been relatively few studies designed to elucidate the causes of the disorder. One of the major drawbacks to any study of this kind is that the condition generally manifests itself after discharge from maternity hospital. Thus any information on factors connected with the relevant pregnancy and social background must either be obtained from retrospective inquiry of the mother or from a procedure of linking with the records from the relevant maternity hospital or domiciliary midwife. The problem, too, of obtaining an unbiased control population can often be extremely time consuming. The present study has the advantage of employing the data banks of the Oxford Record Linkage Study and in a sense may be considered to be prospective.

Pyloric stenosis had been described in the medical reports of the 18th century (Blair, 1717; Weber,

1758; Armstrong, 1777), but was first recognized as a clinical syndrome after a description of 5 cases by Hirschsprung (1888) in Copenhagen. At the turn of the century several types of surgical procedure were attempted with varying degrees of success, until in 1912 Rammstedt developed a very simple procedure which has remained one of the most satisfactory surgical operations to this day, with an extremely low associated mortality. Nevertheless there are a few paediatricians who still prefer management by medical means.

The incidence within the British Isles has generally been reported as of the order of 2 to 3 per 1000 livebirths (Table I). The only other European areas recorded as having incidences of over 1 per 1000 are Gothenburg in Sweden and Budapest in Hungary. The rate in the southern countries of Europe is apparently very low. The one study from Malta (Cachia and Fenech, 1966) suggested that the rate there was as high as 0.9 because of the intermingling of races resulting from the presence of British servicemen on the island. In the middle-

TABLE I
REPORTED INCIDENCES OF PYLORIC STENOSIS

Author	Area	Years Studied	Total Births	Pylorics	
				No.	Inc. ‰
<i>British Isles</i>					
Davison (1946)	Newcastle upon Tyne	1939-42	17 457	49	2.8
MacMahon <i>et al</i> (1951)	Birmingham	1940-49	194 216	578	3.0
Lawson (1951)	Dundee	1940-46	21 288	32	1.5
McLean (1956)	Aberdeen	1938-53	110 394	369	3.3
Smith (1960)	Edinburgh	1950-58	66 966	205	3.0
Dodge (1970)	Belfast	1957-69	107 244	289	2.6
<i>Rest of Europe</i>					
Wallgren (1941)	Gothenburg	1934-40	25 642	102	4.0
Wallgren (1960)	Gothenburg	1950-59	58 231	116	2.0
Czeizel (1972)	Budapest	1962-67	108 966	159	1.5
Cachia and Fenech (1966)	Malta	1952-64	100 655	89	0.9
<i>Rest of world</i>					
Field (1951)	Malaya			0	0.0
Gharib (1964)	Iran	1956-62	39 875	3	0.1
Laron (1955)	Israel				0.5
Center for Disease Control (1974)	Atlanta, USA (White)	1968-72	NS	150	1.5
Laron and Horne (1957)	Pittsburg, USA (White)	1945-55	127 029	153	1.2
	(Black)		22 809	11	0.5

NS = not stated.

east, both Iran (Gharib, 1964) and Turkey (Eckstein, 1940) report extremely low rates.

In the United States there are very clear racial differences: in Pittsburgh, Laron and Horne (1957) found the incidence among white infants to be 1.2 compared to 0.5 among black infants. Similar figures from Metropolitan Atlanta for 1968-72 are even more extreme at 1.5 and 0.2 (Center for Disease Control, December 1974). A study of 13 000 Negro infants in Nashville, Tennessee, however, produced an incidence as high as 0.9 (Hara *et al*, 1966). In Hawaii a study by Shim *et al* (1970) over the years 1942 to 1966 showed that whereas the incidence among Caucasians was 1.9, that among those of Japanese origin was 0.5, and among 11 000 Chinese infants there were no cases at all. Unfortunately there are no studies on the incidence of the lesion in the countries of the British Commonwealth, though there is a report that it is extremely rare among children of Australian aborigines (Watson, 1956).

There are varying reports as to the secular variation of the disease. In Gothenburg (Wallgren, 1941, 1960) there appears to have been a halving of the incidence from 1934 to 1959, and a decrease in incidence from 3.1 to 2.2 was shown in Belfast over the years 1957 to 1969. In Birmingham, however, MacMahon *et al* (1951) showed an increase from 2.5 in the years 1940-1944 to 3.4 in the years 1945 to 1949. A similar increase was shown in Aberdeen (McLean, 1956), with incidences of 2.3, 2.7, 3.6, and

4.5 in each 4-year period from 1938 to 1953. More recently Murfin (1974) has reported a pronounced increase in the small island of Barbados.

As well as the well-substantiated excess of males with the lesion, apparent in all countries and all races, it had been generally assumed by physicians that IHPS was predominantly a disease of the first-born. It was Still in 1927 who first attempted to test this assumption with 400 cases admitted to Great Ormond Street Hospital. After inspecting various control groups, he came to the conclusion that there was indeed an excess of first-births in his series. This finding was substantiated by Cockayne and Penrose (1943); by Ford *et al* (1941) in Toronto; McQuaid and Porrit (1950) in Oxford; McKeown *et al* (1951a) in Birmingham; Shim *et al* (1970) in Hawaii; Dodge (1970) in Belfast; and Danis (1957) in Brussels. Lack of a positive association has, however, been reported in an almost equal number of studies: Delprat and Pflueger (1948) and Benson and Warden (1957) in the USA; Dougall (1969) in Glasgow; Czeizel (1972) in Budapest, and Huguenard and Sharples (1972) also in the USA. This last study was of interest in that the authors analysed some 55 completed sibships identified by the presence of at least 1 case of pyloric stenosis. They concluded that the position of affected cases within the sibships did not differ from that expected by chance.

One of the major effects noted in epidemiological studies has been the increased risk of recurrence

within families. This topic is examined in the present study only for sibs born within the period 1965 to 1972. Record linkage techniques were employed to examine whether the index infants, their sibs, or their mothers showed an increased risk of hospital admission or death from any other cause.

Subjects and methods

The Oxford Record Linkage Study (Acheson, 1967; Baldwin, 1972) was started in 1962 and from 1966 to 1971 the area covered included Oxfordshire and that part of Berkshire within the Oxford Regional Hospital Board area. The two cities of Oxford and Reading are included, but the rest of the area is largely rural with several town centres, and a total population of some 800 000.

The following data are collected: (a) information on all deliveries in the area. (In the case of hospital births, detailed description of pregnancy and delivery, of any abnormality or illness in the baby, and certain social factors, are abstracted by trained clerks from the hospital notes onto set forms. For domiciliary deliveries the same information is abstracted from the midwife's notes.) (b) Birth certificates of *all* deliveries to women resident in the area. (c) Death certificates of all persons resident in the area. (d) Details of all general and psychiatric hospital admissions in the area.

The present study began by considering all infant admissions for pyloric stenosis in the period 1966 to 1971.

Some infants were admitted with an initial diagnosis of vomiting, diarrhoea, or wasting, though after treatment the diagnosis was revised to pyloric stenosis. For this reason the discharge diagnoses were also checked. All the codes and the patient's ages were checked and, where necessary, the original notes referred to.

Any cases for whom a birth certificate had not been received (i.e. were not infants of mothers normally resident in the area) were then excluded. There were then 220 confirmed cases with only two infants being treated medically, the rest undergoing Rammstedt's pyloromyotomy. Eight of these cases had in fact been delivered outside the area and only appear in our series when data solely abstracted from birth certificates are considered.

For the initial analyses the index cases were compared with the total population at risk, but for more detailed assessment of factors such as type of pregnancy, delivery, and neonatal morbidity each of the 212 cases for which maternity data were available was matched with 3 livebirth controls of the same social class, parity, maternal age, place of delivery, legitimacy, and year of delivery. In the event there were 7 index cases for which no matched controls were available as parity or maternal age was unknown, leaving a control series of 615 (205 × 3) maternities.

From the identifying characteristics of the mothers (names, date of birth, etc), it was possible to find details of all other deliveries to those women in the period 1965 to 1972. In this way a group of sibs was identified. The files of hospital admissions and deaths were then

scanned to identify any admissions to the index cases, controls, their mothers, and their sibs.

Results

Incidence

Over the 6-year period 1966 to 1971 there were 88 658 livebirths delivered to women whose home address was in the area, giving an overall incidence of 2.48 per 1000 livebirths. Considering only those deliveries which actually took place within the area, the rate is 2.56 per 1000 livebirths (222/82761).

Of the 220 cases 186 were male and 34 female, giving a male to female ratio of 5.47:1. In terms of the population at risk this gives an incidence of 4.1 per 1000 male livebirths and only 0.8 per 1000 female livebirths.

In all there were 7 pairs of twins involving 8 index infants: i.e. 1 in 28 of the series was a twin. This is almost twice as many as would be expected from the proportion of population livebirths which were twins (1 in 52), but the difference is not significant.

Variation with place of residence

As can be seen from Table II there is some variation in incidence with the type of area in which the mother resides, in that there is a lower rate of IHPS if the infant resides in a city compared with the rest of the area. When looked at according to the new reorganized local authority areas (Fig. 1) the incidences to the south-east are much higher than those in the north-west, but the two cities still have incidences much lower than the surrounding areas, the incidence in the city of Oxford being exceptionally low. The highest incidence was found in the small town of Wallingford with 6 cases in 642 births (i.e. 9.3 per 1000).

TABLE II
VARIATION IN INCIDENCE ACCORDING TO PLACE
OF RESIDENCE OF MOTHER

Area of Residence	No. Index Cases	Total Livebirths	Incidence
City	47	23 749	1.98
Small town	49	16 762	2.92
Rural areas	124	48 147	2.58
All	220	88 658	2.48

(0.25 < P < 0.1)

Variation with time

Table III shows the significant seasonal variation in month of birth with a peak incidence of IHPS in late July. This effect is even more extreme among the small number of females in the series.

FIG. 1. Incidence of IHPS by local authority area; (a) West Oxfordshire, (b) Cherwell, (c) Vale of the White Horse, (d) Wallingford, (e) Newbury, (f) Wokingham, (x) Oxford County Borough, (y) Reading County Borough.

TABLE III
QUARTER OF BIRTH OF CASES OF PYLORIC STENOSIS

Date of Birth	No. Index Cases*	Incidence
January-March	43 (6)	1.87
April-June	50 (8)	2.12
July-September	74 (14)	3.33
October-December	53 (6)	2.56
Total	220 (34)	2.48

$\chi^2 = 11.3$; d.f. = 3; $P < 0.02$.

Edward's test (1961) for seasonality: $\chi^2 = 6.4$; d.f. = 2 $P < 0.05$.

$\sigma = 42^\circ$ i.e. minimum is end of January, maximum is end of July.

* No. of females in parentheses.

TABLE IV
YEAR OF BIRTH OF CASES OF IHPS

Year	No. Livebirths at risk	No. of Cases IHPS*	M:F ratio	Incidence
1965	15 286	8 (0)	—	—
1966	15 131	36 (4)	8.0:1	2.40
1967	14 804	46 (9)	4.1:1	3.11
1968	14 889	31 (1)	30.0:1	2.08
1969	14 640	40 (6)	5.7:1	2.73
1970	14 667	32 (6)	4.3:1	2.18
1971	14 527	27 (8)	2.4:1	—

*No. of females in parentheses.

The method by which the cases were ascertained (i.e. the hospital admissions over the years 1966-71) results in the identification of a few infants born in 1965 and incomplete ascertainment in 1971 (Table IV). Omitting these two years there is a certain amount of year-to-year variation, but this is not statistically significant. Note the more erratic variation in the number of female affected cases.

A test for clustering in date of birth and area of residence proved negative using both the method of Knox (1963, 1964) applied to small local authority areas, and that of Ederer, Myers, and Mantel (1964).

Hospital of delivery

From Table V it can be seen that there is a striking variation with the size of the hospital in which the infant had been delivered. There is a higher incidence in domiciliary than hospital deliveries, but the incidence in the small hospitals (i.e. those without a consultant obstetrician on the staff) closely resembles that of the domiciliary deliveries. This effect is independent of the variation in incidence with the place of residence of the mother.

TABLE V
SIZE OF HOSPITAL IN WHICH INDEX INFANT WAS DELIVERED

Place of Delivery	No. Cases IHPS	Total Livebirths	Incidence
Large maternity hospital	109	53 199	2.05
Small hospital	67	18 361	3.65
All hospital	176	71 560	2.46
Domiciliary	36	11 182	3.22

$\chi^2 = 17.43$ d.f. = 1.
 $P < 0.001$.

Maternal age and parity

Fig. 2 shows the estimated incidence according to parity (defined as the number of previous pregnancies exceeding 28 weeks' gestation). Though two recent papers by Huguenard and Sharples (1972) from the University of Michigan have shown that this type of approach may give misleading results when dealing with incomplete family sizes, most reports to date have used this method, and have concluded that the greatest risk is to the firstborn infant. It is, therefore, interesting to note that in the present series the highest incidence is in the second birth place. The risk to the third born infant is lower than to the second but still higher than to the firstborn. The most striking finding, however, is the relative absence of affected infants in the higher parities.

FIG. 2. Variation in incidence with parity.

Similarly, in Fig. 3 it can be seen that the incidence is highest at maternal ages 20 to 24 with a significant fall thereafter as age increases. An analysis of age and parity together adds little of note (Table VI).

FIG. 3. Variation in incidence with maternal age.

Social class

In 1910 Rommel found a high proportion of children of physicians in his series and concluded that IHPS was a disease of the intellectual classes. Dodge (1970) in Belfast also described what he considered to be a high proportion of doctor's infants as well as an excess of children of policemen. He concluded that it was a disease of children whose fathers were in stressful occupations.

In the present series we have an excess of infants of fathers of upper social classes, but no clear trend is apparent in Table VII. There were only 2 children of physicians and no cases recorded as having a policeman for a father!

TABLE VII
INCIDENCE OF IHPS BY SOCIAL CLASS

Social Class	No. Cases IHPS	Incidence
I	18	2.47
II	40	3.56
III	89	2.32
IV	32	2.92
V	10	2.11
Armed Forces	12	2.69
Students	2	2.78
Not known	9	1.63
Total	212	2.54

Maternal blood group

Dodge (1974) reported a striking excess of index mothers of blood groups O and B in Belfast, but in the present study (Table VIII) we find no significant variation in the distribution of ABO blood groups compared with the whole maternity population. In contrast there is a consistent excess of women who were Rhesus negative ($P < 0.02$).

Legitimacy

Only 9 of the 220 (4.8%) index cases were recorded on the birth certificate as being illegitimate.

TABLE VI
DISTRIBUTION OF PYLORIC CASES BY MATERNAL AGE AND PARITY

Age (y)	Parity						Total	
	No.	Rate*	No.	Rate	No.	Rate	No.	Rate
≤19	11	1.85	3	2.07	—	—	14	1.83
20-24	44	3.03	33	3.18	15	4.54	95	3.22
25-29	15	2.05	32	3.05	8	1.54	65	2.47
30-34	4	1.88	7	1.89	11	2.98	27	2.06
35+	—	—	3	2.22	3	1.83	8	1.20
NK	1	()	1	()	—	—	3	2.11
Total	75	2.45	79	2.88	37	2.64	18	1.68
							3	5.32
							212	2.54

* Rates per 1000 estimated livebirths (estimated livebirths at risk = 1968 livebirths × 6).

TABLE VIII
INCIDENCE BY MATERNAL BLOOD GROUPS

ABO Group	Rhesus +ve	Rhesus -ve	All Known
A	2.60 (73)	2.97 (17)	2.66
B	1.51 (9)	5.09 (6)	2.10
AB	2.99 (6)	2.30 (1)	2.87
O	2.08 (61)	3.61 (22)	2.34
All known	2.28 (149)	3.42 (46)	2.53

No. of cases in parentheses.

This compares with 7% of all births on our files, and while not statistically of significance, clearly suggests that IHPS is not among the many conditions which have an increased incidence among illegitimate births.

For the remaining analyses we employ for comparison the control series described earlier.

Maternal religion and maternal origin

Dodge (1970) reported an excess of births to Protestants in his Belfast study, but in the present series, with controls matched for parity, there is no demonstrable variation with religion (Table IX).

Similarly, with data on maternal origin (Table X) there is no clear pattern—though the excess of index

TABLE IX
MATERNAL RELIGION IN CASES AND CONTROLS

Maternal Religion	Index Cases	Controls	Relative Risk
Church of England	151	434	1.04
Roman Catholic	25	77	0.97
Non-conformist	12	45	0.80
Muslim	1	3	1.00
Buddhist	—	—	
Jewish	1	—	
Other	2	5	
'None'	1	3	0.82
Not Stated	12	44	
Total	205	615	1.00

TABLE X
MATERNAL PLACE OF BIRTH IN CASES AND CONTROLS

Maternal Place of Birth	Index Cases	Controls	Relative Risk
Oxford Record Linkage Area	72	216	1.00
Greater London	32	58	1.66
Rest of England	63	186	1.02
Scotland, Ireland, Wales	18	54	1.00
West Indies	1	11	0.27
India and Pakistan	3	10	0.90
Europe	5	15	1.00
Rest of world	1	13	0.23
Not Stated	10	52	0.57
Total	205	615	1.00

mothers who were born in Greater London is statistically significant ($P < 0.025$).

History of pregnancy and delivery

A comparison of case with control mothers revealed that 134 (65%) index pregnancies were recorded as being perfectly normal compared with 397 (65%) of controls. Only 1 index and 1 control mother were noted to have excessive vomiting throughout pregnancy, 2 cases in both series had hydramnios, and only 13 (6%) of index pregnancies were complicated by pre-eclamptic toxæmia compared with 56 (9%) of controls.

The proportion of cases receiving artificial induction of labour was similar in both series; lengths of labour were identical. The mode of delivery was unremarkable, the only factor of note being the 4 cases delivered before arrival at maternity hospital (compared with 3 controls). As to position on delivery, again there was no difference between the cases and their controls.

Abnormality in infant

Only 10 of the 205 index infants with matched controls (4.9%) had any type of congenital defect noted at birth: all were relatively trivial (4 had small birth marks, 1 extra digit on each hand, 1 extra ear lobe, 1 pilonidal sinus, 1 bilateral hydrocele, and penis with a long tight prepuce). This compared with 27 control infants (4.4%) with defects noted at birth of which 5 were major malformations (1 Down's syndrome, 2 spina bifida, 1 hare lip and cleft palate, and 1 bilateral cleft palate). A further 2 index cases were noted at subsequent admission to have congenital defects (1 congenital heart, 1 bat ear), compared with 6 controls (1 microcephaly, 1 malrotation of gut, 1 ventricular septal defect, 1 syndactyly, 1 congenital dislocation of hip, 1 deformed finger).

Not only was the proportion of defects in the index series unremarkable, there was also a lack of significant morbidity in the neonatal period, though it might be worth noting that 3 index infants had systolic murmurs (1 control), only 2 had jaundice (18 controls) and 5 began vomiting while at the maternity hospital (3 controls). Only 3 index infants were diagnosed as having a pyloric tumour before discharge from maternity hospital.

Apart from the index admission, there were 48 other admissions to infants who had had pyloric stenosis compared with 82 to controls. The excess was mainly the result of the increased number of index cases with tonsil and adenoid problems, otitis media or hernias (Table XI). Four control infants

TABLE XI

CAUSES OF HOSPITAL ADMISSION OF INDEX CASES AND CONTROLS

Cause of Hospital Admission	Index Case (N = 205)	Control (N = 615)
Accidents	7	8
Hernias	10	15
Tonsils and adenoids	7	8
Respiratory disease	5	10
Otitis media	3	2
Urinary tract infections	0	0
Gastrointestinal infections	0	5
Feeding problems	2	1
Poisoning	3	9
Other	11	24
Total infants admitted	48	82

died after the neonatal period, 2 of severe malformations, but all index cases survived this period.

Birthweight and gestation

In the Hawaii study (Shim *et al*, 1970), birthweight was positively correlated with pyloric stenosis ($P < 0.001$). Czeizel in Budapest (1972) found a significant excess of affected males with birthweight more than 3500 g, but no difference in the distribution of gestation. Other series (Dougall, 1969; Dodge, 1970) failed to find any association. Table XII shows the gestational distributions of the cases and controls. There is little of note.

TABLE XII

GESTATION DISTRIBUTION OF CASES AND CONTROLS

Gestation (w)	No. Cases	No. Controls	Relative Risk
< 37	9	40	0.90
37-38	27	72	1.13
39-41	127	394	0.97
42+	18	45	1.20
Not known	24	64	1.13
Total	205	615	1.00

In the tables thus far the controls have been control mothers, matched with mothers of pyloric infants. For a full investigation of possible birthweight or gestation differences, it is necessary to match the mothers on one further variable: the sex of the infant to which they gave birth. Only 146 male cases could be matched in this way (out of 173), and 29 female cases (out of 32).

The mean gestation for the index males was 40 weeks 1 day, and for their matched controls 39 weeks 5 days, the difference being clearly not significant (Table XIII). In the case of the females, however, using a *t*-test on the paired differences, there does seem to be a lack of premature pyloric girl infants ($0.025 > P > 0.01$). The mean length of

TABLE XIII

Matched pairs of same sex

Difference between gestations:

case-control $\pm$ SE of differencemales: 2.16 days $\pm$ 1.8 ($t = 1.2$)females: 10.35 days $\pm$ 4.0 ($t = 2.6$)*

Difference between birthweights:

males: 52 g $\pm$ 57 g ($t = 0.9$)females: -31 g $\pm$ 120 g ($t = -0.3$)* $P < 0.025$.

gestation for these index females was 40 weeks 4 days and for their matched controls, 39 weeks 1 day.

When considering the birthweight of these infants, the female cases were no heavier than their controls, the mean birthweights being 3.2 kg and 3.3 kg, respectively. The mean birthweight of 3.4 kg was the same for both index males and their controls.

Age at admission

As can be seen from Fig. 4 the majority of infants were admitted between the 3rd and 7th week of life, with a mode at 5 weeks and median at 6 weeks. From Table XIV, however, it can be seen that the

FIG. 4. Distribution of cases by age on admission.

TABLE XIV

AGE AT ADMISSION AND GESTATION

Gestation (w)	No.	Age at Admission	
		Median	Mean
< 37	17	7 w	51.9 d
38-40	117	6 w	39.8 d
41+	50	5 w	37.3 d

age at admission (and, presumably, the age at onset of symptoms) appears to vary with the gestation of the infant, in that the longer the infant spent *in utero* the earlier does his tumour tend to present.

McKeown *et al* (1952) had also reported that domiciliary births tend to present earlier than infants delivered in hospital, but there was no evidence of such a finding in the present study; nor was there any sex difference in age at admission.

Morbidity and other pregnancies in the mothers

As can be seen from Table XV there was little difference between index and control mothers in respect of reasons for hospital admission. Indeed the only factor in which an excess was found was in cysts and benign tumours in the female reproductive systems (6 cases, 5 controls).

As regards pregnancy spacing, the index infant was not conceived after a particularly long or short interval of time measured since the preceding delivery. The sibs of controls were, however, more likely to be perinatal deaths ($22/336 = 6.5\%$) than the sibs of the index cases ($0/129$).

TABLE XV
CAUSES OF HOSPITAL ADMISSION TO MOTHERS
OF INDEX CASES AND CONTROLS

Cause of Admission	Index Mothers (N = 205)	Control Mothers (N = 615)
Abortion	10	45
Cervicitis, vaginal bleeding, etc.	5	24
Menstrual disorder	4	8
Cysts in ovary, uterus, tube, or vagina	4	5
Urinary tract infection	1	3
Cholecystitis	4	9
Overdose	3	7
Anxiety/depression	0	3
Appendectomy	2	6
Accidents	0	5
Benign neoplasms	2	2
Malignant neoplasms	0	3
Tonsils and adenoids	0	5
Otitis media	1	1
Thyrototoxicosis	1	1
Other	7	22

Sibs

In all, apart from the twins, there were 127 sibs of index cases delivered in the period 1965 to 1972. The sex ratio among these sibs was unremarkable (Table XVI), and pyloric stenosis was confirmed in 9 (a rate of 71 per 1000). Of the 7 pairs of twins, 1 pair (MM) was concordant, and in 1 (FF) pair the cotwin was stillborn. If these data are added to those of Table XVI, one finds that 11 sibs were affected out of 134 at risk (where the concordant

TABLE XVI
SIBS OF INDEX SERIES (EXCLUDING CO-TWINS
OF INDEX CASES)

Sibs	Index Case		All
	Male	Female	
<i>Prior to index</i>			
Male	26 (4)	3 (0)	29 (4)
Female	23 (1)	3 (0)	26 (1)
<i>Subsequent to index</i>			
Male	32 (4)	6 (0)	38 (4)
Female	29 (0)	5 (0)	34 (0)
<i>All sibs</i>			
Male	58 (8)	9 (0)	67 (8)
Female	52 (1)	8 (0)	60 (1)

In parentheses are numbers of sibs with pyloric stenosis.

twins each contributed one sib). This gives a rate of 82 per 1000, some 30 times that of the population as a whole.

Apart from the excess of sibs with IHPS, the other causes of hospital admission seem unremarkable when compared with the sibs of controls (Table XVII). Six of the index sibs had congenital defects compared with 17 controls. There were two postneonatal deaths in each series. There were no hospital admissions to the unaffected co-twins.

TABLE XVII
CAUSES OF HOSPITAL ADMISSION OF SIBS OF
INDEX CASES AND CONTROLS

Cause of Hospital Admission	Sibs of Index Cases	Sibs of Controls
Accident	3	5
Hernias	2	3
Tonsils and adenoids	3	2
Respiratory infections	1	4
Otitis media	2	1
Urinary tract infections	2	1
Gastrointestinal infections	1	1
Feeding problems	2	1
Accidental poisoning, foreign body, etc.	0	8
Pyloric stenosis	9	1
Other	1	13
Total infants	127	320

Discussion

Although several authors are agreed that there is a strong genetic component in the development of IHPS, it is generally admitted that there must also be a strong 'environmental' factor (Knox, 1958; Carter, 1972; McKeown *et al*, 1952) responsible for much of the variation. The only person to produce a cogent theory as to the identity of this environmental factor has been Dodge (1970). On the basis of his findings in Belfast, and by analogy with

duodenal ulcer where the male preponderance is similar to that found in IHPS, Dodge has suggested that maternal stress together with the maternal genetic make-up (especially determined by the presence of blood groups O and B) has resulted in an excessive production of gastrin during late pregnancy. Gastrin has been shown to cross the placenta and could be responsible for irritating the fetal duodenum.

Certainly an association has been reported between pyloric stenosis and evidence of healed duodenal ulcer in some children. Lee (1967) suggested a process of high acid secretion producing duodenitis, in turn giving rise to superficial duodenal ulceration, this resulting in a reflex protective pylorospasm which, it is suggested, produces hypertrophy of the pyloric muscle and hence protection of the duodenum with the result that the ulcer heals.

Dodge's hypothesis has received some support from experiments in which pregnant bitches have been injected with pentagastrin and their puppies found to have duodenal ulcers and pyloric hypertrophy (Karim *et al*, 1974).

Thomson (1925) produced a theory with a slightly different mode of action. He suggested that the hypertrophy results from a primary incoordination of autonomic impulses resulting in overaction and hence hypertrophy. There was no suggestion of any environmental influence however.

The present study has involved the type of population hitherto neglected in epidemiological analyses of IHPS because of the relatively large geographical area with many different centres of medical care. Most previous studies have only considered cases occurring in large cities. This could be why our findings fail to substantiate those of others, notably Dodge.

Certainly the major findings of the present study: seasonal variation in time of birth, area variation, and the lack of cases delivered in large hospitals, have not been reported previously. However, an analysis of available data from the Center for Disease Control in Atlanta does appear to show a similar seasonal picture to that which we reported.

Although we have looked for evidence of abnormal stress in our index mothers, there was nothing to suggest that they were other than a completely 'normal' group of women. Nor does the blood group data of the present study support Dodge's hypothesis. We suggest that while we obviously cannot refute the possibility of maternal stress and related gastrin production being implicated, there must be some other 'environmental' agent responsible for the findings we report.

We are extremely grateful to Professor Sir Richard Doll and Dr J. A. Baldwin for helpful advice, and to Mrs Bettine Sutton, Mrs Valerie Hazell, and Mrs Jean Lawrie for clerical and secretarial assistance.

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