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SEASONAL VARIATION IN CONGENITAL ABNORMALITIES

PRELIMINARY REPORT OF A SURVEY CONDUCTED BY THE RESEARCH COMMITTEE OF COUNCIL OF THE COLLEGE OF GENERAL PRACTITIONERS

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Seasonal variation in the frequency of births of infants with a particular congenital defect is important evidence of an environmental factor in its aetiology. McKeown and Record (1951) observed that anencephalic stillbirths occurred more frequently in winter than in summer, but since then comparatively few defects have been examined in a similar manner. The reason has probably been that without a system of notification it is difficult to collect a sufficiently large series of any given abnormality for analysis. Seasonal variation seemed a suitable subject for the College of General Practitioners to study as its members could readily provide the dates of birth of infants born with defects in their practices. In 1958, the Epidemic Observation Unit of the College therefore began to collect information on this subject as part of a general investigation of prenatal influences in foetal development. The main object was to study the seasonal and regional distribution of abnormalities and to form a register of children, live or stillborn, with defects. It was intended that the register should be available to other research workers for more detailed studies; those interested would be put in touch with the patients' practitioners.

Because of the difficulty in achieving complete ascertainment of defects in any population and in establishing the appropriate number of births for use in the denominator, it was decided to base the study on the distribution rather than on the absolute incidence of the various defects by season. The validity of this approach depended on doctors being equally likely to report abnormalities in births occurring at all times of the year. This seemed to be a reasonable expectation but, even if there were any bias, it would probably affect all types of abnormality and comparison between diagnostic groups could still be made. Thus it was accepted that doctors participating in the survey might not be representative of all doctors and that all cases from a practice need not be reported.

MATERIALS AND METHODS

After completion of a small pilot study, a personal letter was sent at the end of 1960 to all members and associates of the College in the United Kingdom and Eire, asking for their co-operation in providing brief details about infants with congenital defects born between 1954 and 1960. The information asked for included patient's name, place and date of birth, and a description of all abnormalities present. It was made clear to the practitioners that, even if they were unable to make a thorough search of their records, every case which they reported could be used for our purpose. Letters were posted to 4,000 practitioners in all and 1,373 of these replied. In addition, eleven medical officers of health who heard of the investigation volunteered to give information about cases which had come to their notice, an offer which was gladly accepted.

Reports for over 10,000 children born during the 7-year period were received, but a check of the

separate notifications from practitioners and public health departments led to the exclusion of 58 duplicate reports. Some further cases were omitted because they were described inadequately or because the abnormality was not accepted as a congenital defect. This left for analysis a total of 9,951 children with 12,900 defects; 7,705 (77 per cent.) of cases had one abnormality, and 2,246 (2 per cent.) had two or more. Differences of opinion regarding the definition of congenital abnormality gave rise to some difficulty and it was our policy to include rather than exclude doubtful categories.

Details from the notification forms were transferred to index cards which will eventually form the Register. Each case was allocated as many cards as there were defects listed for that individual so that the cards could be filed by diagnosis. Punch cards are now being prepared from the available information for full analysis at the College Records and Statistical Unit. This will include detailed study of seasonal and secular variations, association of defects, geographical differences, and inter-related questions.

Before embarking on the full analysis it was decided to sort the index cards for each defect by year and month. This initial study was made to test the diagnostic classification we had devised and to obtain some preliminary information on seasonal distribution prior to the detailed analysis. The diagnostic classification had been evolved by trial and error to cover all the defects notified in the best way for our purposes. We were unable to find any published classification which exactly met our requirements, but the eight main categories do correspond fairly closely to the International Classification of Diseases and Injuries (WHO, 1957). The list originally comprised 155 headings grouped under eight different body systems, but any diagnostic category which contained less than 25 cards was added to an appropriate miscellaneous category which reduced the total number of headings to 83.

In this paper dates of birth for infants with a given defect were analysed without regard for any other defects which might also be present in the same individual. With our present very limited knowledge of the clinical syndromes of congenital disease, there seemed to be no alternative method. It was realized that as a given defect, associated or not with other defects, might be caused in different ways there might be conflicting seasonal patterns within a category that would be missed. Any seasonal effect observed, on the other hand, might well be due to a much larger variation in an aetiologically related section of the group.

Findings

The notified defects considered as a whole were equally distributed by date of birth between the four quarters of the year. This is shown in Table I, where the number of diagnoses are expressed as proportions of all births in England and Wales by quarter for the 7-year period, 1954–60, during which the defective children were born.

The quarterly distribution of notified defects in the 83 diagnostic categories is shown in Table II (opposite). These figures were examined for seasonal variation by dividing the year into half in two ways: (1) to compare the first half with the second half, and (2) to compare the two summer quarters with the two winter quarters. χ^2 values were calculated for deviations from the distribution that would be expected if there were no seasonal variation. The use of statistical tests of significance has been questioned in studies of this kind which are made in a search for clues rather than for the examination of well-defined hypotheses. The χ^2 values may be found helpful nevertheless, though it must be borne in mind that in 166 tests about eight would be expected to reach the 5 per cent. level of significance by chance. In fact, probabilities of 0·05 or less were found in seventeen analyses, and of 0·01 or less in five. Eleven of the seventeen significant results and all five least likely to be due to chance were found in the winter-summer comparison.

The strongest evidence for a winter excess was found in cataract, anencephaly, spina bifida, oesophageal atresia, and congenital dislocation of

TABLE I

SEASONAL DISTRIBUTION OF CONGENITAL DEFECTS AS A PROPORTION OF ALL BIRTHS IN ENGLAND AND WALES, 1954–60

Quarters	1st	2nd	3rd	4th	Total
Total Births in England and Wales, 1954–60	1,311,892	1,330,641	1,275,870	1,234,053	5,152,456
Defects from College Survey	3,201	3,182	3,082	3,137	12,900*
No. of Defects per 1,000 Births	2·44	2·39	2·42	2·54	2·50

* Including 298 in which the month of birth was not given.

TABLE II
SEASONAL DISTRIBUTION OF BIRTHS WITH CONGENITAL DEFECTS, 1954–60

	Defects	Total	Quarter				Probability from χ^2 Test	
			1st	2nd	3rd	4th	1st and 2nd 3rd and 4th	4th and 1st 2nd and 3rd
I. Special Senses (530)	Cataract	106	34	19	22	31	1·00	*·02*
	Squint	65	26	11	18	10	·92	·39
	Blindness or other eye defects	204	43	59	52	50	1·00	·21
	Deafness or defects of internal ear	155	41	41	33	40	·47	·57
II. Nervous System (4,262)	Anencephaly	739	180	189	149	221	·92	*·02*
	Microcephaly	131	42	34	29	26	·07	·66
	Hydrocephaly	761	191	181	180	209	·54	·16
	Spina bifida	1,076	282	244	255	295	·47	*·02*
	Cerebral palsy	311	72	89	74	76	·53	·40
	Encephalocoele	42	8	11	9	14	·54	·76
	Mongolism	656	161	174	156	165	·58	·89
	Other mental defects	384	92	96	87	109	·68	·36
	Epilepsy and fits	62	19	11	17	15	·81	·45
	Neuromuscular defects	44	9	7	14	14	·07	·76
	Other Central Nervous System defects	56	13	12	17	14	·42	·79
III. Cardiovascular System (1,665)	Patent ductus arteriosus	153	31	39	36	47	·29	·81
	Fallot's tetralogy or Eisenmenger's complex	102	25	34	22	21	·11	·32
	Dextrocardia	28	9	11	4	4	*·02*	·71
	Coarctation of aorta	34	6	8	9	11	·29	1·00
	Aortic stenosis	33	8	11	10	4	·38	·12
	Pulmonary stenosis	71	15	17	27	12	·41	*·04*
	Transposition of great vessels	38	9	8	11	10	·52	1·00
	Atrial septal defects	93	22	21	26	24	·47	·92
	Ventricular septal defects	297	84	75	78	60	·22	·60
	Septal defects (type unspecified)	67	16	19	13	19	·72	·72
	Other or unspecified congenital heart disease	706	174	169	179	184	·45	·71
	Other vascular or lymphatic defects	43	6	16	15	6	·89	*<·01*
IV. Digestive or Respiratory System (2,124)	Hare lip	430	114	118	108	90	·10	·29
	Cleft palate	495	133	129	125	108	·19	·56
	Branchial cleft abnormalities	34	14	10	5	5	*·02*	·49
	Branchial cleft abnormalities	34	14	10	5	5	*·02*	·49
	Oesophageal atresia	86	29	16	14	27	·66	*<·01*
	Tracheo-oesophageal fistula	46	15	12	10	9	·24	·76
	Abnormality of larynx or trachea	26	8	7	5	6	·44	·70
	Lung defects	28	10	7	6	5	·25	·71
	Pyloric stenosis	607	145	155	156	151	·78	·54
	Abnormality of hepatic system	40	10	9	11	10	·75	1·00
	Abnormality of small intestine	72	24	22	11	15	*·02*	·48
	Megacolon	33	9	7	9	8	·86	·86
	Rectal or anal atresia	102	22	26	36	18	·55	*·03*

Continued overleaf

TABLE II—*continued*
SEASONAL DISTRIBUTION OF BIRTHS WITH CONGENITAL DEFECTS, 1954–60

	Defects	Total	Quarter				Probability from χ^2 Test	
			1st	2nd	3rd	4th	1st and 2nd 3rd and 4th	4th and 1st 2nd and 3rd
continued IV. Digestive or Respiratory System (2,124)	Other ano-rectal abnormalities	33	6	9	10	8	·60	·38
	Other or unspecified intestinal abnormality	35	5	10	16	4	·40	*< ·01*
	Other digestive or respiratory defects	57	14	18	9	16	·35	·69
V. Musculo-skeletal System (2,651)	Absent or vestigial limb(s)	25	5	8	5	7	·84	·84
	Partial absence of upper limb	61	14	22	16	9	·16	*·05*
	Partial absence of lower limb	26	5	9	8	4	·70	·11
	Absent digits only	64	15	17	18	14	1·00	·45
	Polydactyly	168	46	47	36	39	·17	·89
	Syndactyly	154	31	33	44	46	*·04*	1·00
	Congenital dislocation of hip	271	86	57	56	72	·36	*< ·01*
	Talipes	795	210	190	200	195	·86	·60
	Achondroplasia	42	9	11	12	10	·76	·54
	Other abnormal forms of upper limbs	127	30	34	36	27	·92	·25
	Other abnormal forms of lower limbs	126	17	33	44	32	*·02*	*·01*
	Abnormalities of mandible	46	10	11	12	13	·55	1·00
	Abnormalities of skull	138	36	38	26	38	·40	·40
	Defects of ribs or chest wall	53	15	10	18	10	·68	·68
	Hiatus hernia	45	13	9	8	15	·89	·10
	Diaphragmatic hernia	74	18	18	16	22	·82	·48
	Exomphalos	98	28	22	29	19	·84	·69
	Umbilical hernia	66	14	18	19	15	·81	·33
	Inguinal or femoral hernias	84	18	23	24	19	·82	·27
	Deformities of spine	86	21	21	27	17	·82	·27
	Other musculo skeletal defects	102	29	29	26	18	·17	·43
VI. Genito-urinary System (568)	Polycystic kidney	39	15	10	7	7	·08	·42
	Other kidney malformations	74	22	18	14	20	·48	·25
	Renal pelvis and ureter abnormalities	58	18	16	10	14	·19	·43
	Ectopia vesicae or epispadias	39	12	11	9	7	·25	·86
	Hypospadias or other urethral abnormalities	236	66	57	53	60	·52	·29
	Other malformations of genitalia	110	27	30	26	27	·71	·84
	Other defects of genito-urinary system	12	2	4	3	3	1·00	·57
VII. Skin (376)	Haemangiomata or "birth marks"	171	46	43	43	39	·59	·92
	Ichthyosis	42	11	7	15	9	·35	·76
	Infantile eczema	26	6	8	8	4	·70	·24
	Extra ear or lobe	38	6	11	11	10	·52	·33
	Absent or malformed external ear	58	17	21	8	12	*·02*	1·00
	Other skin defects	41	6	10	13	12	·16	·44
VIII. Miscellaneous (426)	Cretinism	32	9	11	7	5	·16	·48
	Fibroycystic disease	138	29	44	35	30	·50	·09
	Other metabolic defects	78	22	20	19	17	·50	1·00

Continued

TABLE II—*continued*

SEASONAL DISTRIBUTION OF BIRTHS WITH CONGENITAL DEFECTS, 1954–60

Defects		Total	Quarter				Probability from χ^2 Test	
			1st	2nd	3rd	4th	1st and 2nd 3rd and 4th	4th and 1st 2nd and 3rd
continued VIII. Miscellaneous (426)	Disease due to rhesus incompatibility ..	31	5	9	8	9	·59	·59
	Gross foetal abnormality	70	17	13	23	17	·24	·81
	Tumours	61	13	15	13	20	·52	·52
	Other abnormalities	16	6	3	4	3	·62	·62
Grand Total of All Defects		12,602	3,201	3,182	3,082	3,137		

the hip; there was a suggestion of a similar trend in hydrocephaly. In anencephaly this apparent winter excess was due to the difference between the high proportion in the fourth quarter and low proportion in the third. A summer excess was present in pulmonary stenosis, possible aortic stenosis, and in a composite group of 43 children with other vascular or lymphatic defects. Of the 43, 23 had abnormalities of the aortic and pulmonary arches and fourteen of these were born in summer. Among the remainder the summer excess was greater but the group was mixed and the number small. A majority of children with partial absence or certain other malformations of upper or lower limbs were also born in the summer. This unexpected finding was fairly consistently shown by the four relevant categories and contrasted with the lack of similar seasonal variation in polydactyly, syndactyly and in those with absent or vestigial limbs. A third series of defects with a summer excess was rectal or anal atresia, other ano-rectal abnormalities, and other or unspecified intestinal abnormalities. Of the 35 children in the last-mentioned group, eighteen had absence or atresia of the large gut and twelve of these were born in summer. There was thus a general tendency for children with malformations of the lower part of the alimentary tract to be born in the summer. The magnitude of the seasonal differences which have been described above are illustrated in the Figure (overleaf).

There were six diseases in which the χ^2 test suggested that the unequal distribution of births between the first and second halves of the year might not be due to chance. In four of these—dextrocardia, branchial cleft abnormalities, abnormality of the small intestine, and absent or malformed external ear—more of the births were in the first half of the year, but the largest number available for analysis in any of these groups was 72. The two remaining categories were syndactyly, in which ninety of the 154 children (58 per cent.) were born in the second half of the year, and certain other abnormal forms of the lower limbs, in which a summer excess already described was a more obvious feature.

Table II shows that seasonal differences were the exception; in most diagnostic groups the births were distributed evenly. More detailed study may reveal other trends which cannot be seen in the present crude analysis. Seasonal and other variations in time may well have been lost by the amalgamation of data from all parts of the country for the whole 7-year period. For this reason it is probably unwise to draw negative conclusions at this stage of our analysis, particularly as diagnostic categories large enough to be least affected by chance fluctuations are those in which later detailed study may be most fruitful. With this reservation it can be said that there was little or no evidence in Table II of any seasonal influence in such large groups as cerebral palsy, mongolism, other mental defects, most congenital heart disease, pyloric stenosis, and talipes.

DISCUSSION

It is reassuring that some of the positive findings from this analysis have previously been demonstrated by others. McKeown and Record (1951) showed that the incidence of anencephaly in Birmingham from 1940–47, and in Scotland from 1939–46, was higher in October to March than in April to September. No similar variation was noted in spina bifida or hydrocephalus. Using more extensive Scottish still-birth records, these findings were confirmed and studied in greater detail by Edwards (1958) and Record (1961). From their studies it appeared that the peak incidence was from November to January, implying that the seasonal factor responsible was probably strongest between March and July.

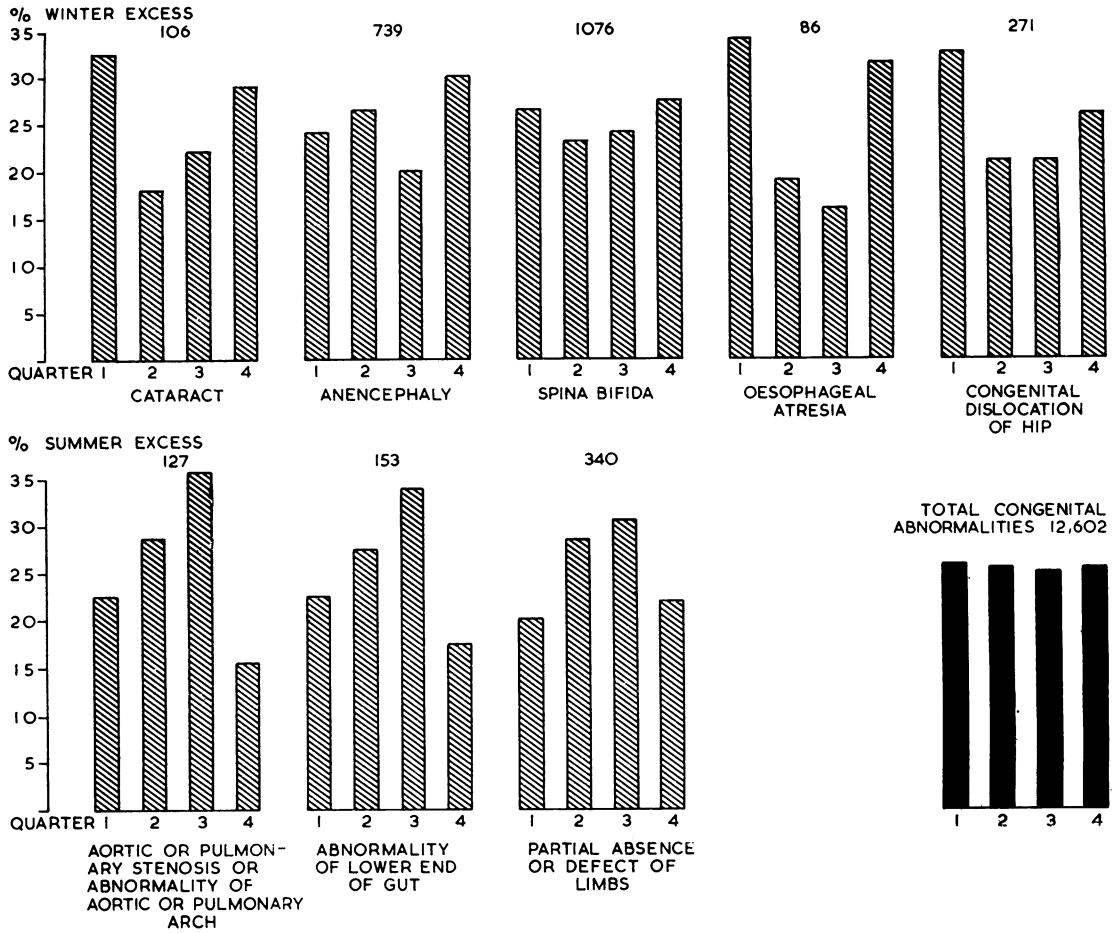

FIGURE.—Quarterly distribution of births of infants with certain defects.

MacMahon, Pugh, and Ingalls (1953) found no seasonal fluctuation for anencephaly, spina bifida, or hydrocephaly in Rhode Island. While the findings on anencephaly in the College survey were in general agreement with British reports, a winter excess for spina bifida was equally apparent. Guthkelch (1962) reported a similar seasonal trend for spina bifida in Manchester Children's Hospital, 1949–58.

The evidence presented here of a winter excess of births of children with congenital dislocation of the hip confirms the findings of Record and Edwards (1958). The quarterly distribution in our series is similar to theirs with a peak in the first quarter. They thought that the winter prevalence was probably due to influences in the postnatal, rather than the prenatal, environment. In cataract there was a winter excess which may reflect its association with rubella, an infection prevalent in spring and early summer. There was little evidence of this relationship in the seasonal distribution of patent ductus arteriosus and deafness, presumably because a smaller proportion of these defects is due to rubella.

Quite unexpected was the finding of a summer excess among children born with partial absence or certain other malformations of the upper or lower limbs. There was no suggestion of a similar trend in the small group of children with absent or vestigial limbs.

The summer predominance of pulmonary stenosis and to a lesser extent aortic stenosis contrasted with the general lack of seasonal variation in the births of children with other and unspecified congenital heart

disease. Had it been possible to break down the large group of other and unspecified heart disease the analysis might have been less negative. In studies of persistent ductus (Polani and Campbell, 1960), of coarctation of the aorta (Campbell and Polani, 1961), and of pulmonary stenosis (Campbell, 1962), differences between boys and girls were found in the seasonal pattern which were obscured when the sexes were taken together. A comparison of these findings with those from the College survey must await the detailed analysis.

In a study of congenital oesophageal atresia and tracheo-oesophageal fistula, Knox (1959) concluded that clustering of cases occurred and that this might be due to some infective process; however, no seasonal variation in incidence was noted. In our series a winter excess of oesophageal atresia, but not of tracheo-oesophageal fistula was found, and it is perhaps relevant that hiatus hernia, where there is shortening of the oesophagus, showed a similar trend. In contrast there was a summer excess for abnormalities of the lower gut.

SUMMARY

Brief details concerning 9,951 children born with congenital defects in 1954–60 were provided by 1,373 general practitioners and eleven public health departments to the Epidemic Observation Unit of the College of General Practitioners. The number of defects in these children was 12,900; 23 per cent. had two or more defects. A Register has been prepared from this information and will be made available to other research workers at the discretion of the College Council.

In preparation for detailed statistical analysis of this material, a preliminary study has been made of the quarterly distribution of births in 83 diagnostic categories. In most of these there was little evidence of seasonal variation, but in certain groups the difference between summer and winter seemed to be greater than could be attributed to chance. A winter excess was seen in cataract, anencephaly, spina bifida, oesophageal atresia, and congenital dislocation of the hip; a summer excess was seen in partial absence or certain other defects of upper and lower limbs, pulmonary stenosis, and atresia or other abnormalities of the lower alimentary tract.

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