CONGENITAL MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM

I—A SURVEY OF 930 CASES*

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INTRODUCTION

Of the causes of stillbirths and infant mortality which have not shared in the general improvement during the last fifty years easily the most important are the congenital malformations. At the beginning of the present century, when ideas about their aetiology were turning from mysticism to morbid anatomy, their investigation could have been regarded as an interesting academic exercise, which might add something to knowledge of the intra-uterine environment or of human genetics, but could make no considerable contribution to the accountancy of preventable deaths. This is not the position to-day. The intervening years have added little to our knowledge of the aetiology of the malformations, but the effectiveness of preventive measures against other causes of infant death before and after birth has enormously altered their relative contribution to the total deaths. In the white population of New Zealand, for example, they recently accounted for nearly one-fifth of the deaths under one year (Leitch, 1944), and these figures are being approached in this country, where infant mortality attributed to malformations has shown a slight absolute and a large relative increase (Table I). Scottish data for stillbirths and first-year deaths show that in the six years to 1945, 10 per cent. of all foetuses that reached viable age were born dead or died in the first year of life; more than 10 per cent. of these deaths were ascribed to congenital malformations (Table II, overleaf). Expressed differently, 1 per cent. of all foetuses alive in the 28th week of pregnancy died from congenital malformations before the first birthday.

CAUSATION.—The subject has been reviewed extensively (Warkany, 1947; Gruenwald, 1947), and it will suffice to recall the results of the main lines of enquiry. In lower animals, where the

embryos are in intimate contact with a changing environment, it was readily demonstrated that external factors can modify the course of embryonic development. Unspecific physical agents, such as *x* rays, ultra-violet light, mechanical shaking or temperature changes, and a large number of chemical agents which inhibit growth, gave rise in a variety of species to congenital deformities. The application of some of this work to the more uniform uterine environment of mammals is doubtful, but there is also evidence from the animal laboratory that the mammalian foetus may be deformed by external influences. On the other hand, certain malformations in animals are undoubtedly genetically determined, though some of them bear little resemblance to the common human deformities.

It is difficult to assess the relevance of this evidence, much of it on invertebrates and lower vertebrates, to the corresponding problem in man. The

TABLE I†
QUINQUENNIAL INFANT MORTALITY RATES FOR ENGLAND AND WALES (1901-1945)

Period	Infant Deaths per 1,000 Live Births		Rates expressed as a percentage of those from 1901 to 1905	
	From Congenital Malformations	From all Causes	From Congenital Malformations	From all Causes
1901-05	4.33	138	100	100
1906-10	4.94	117	114	85
1911-15	3.85	110	89	80
1916-20	4.04	90	93	65
1921-25	4.32	76	100	55
1926-30	4.94	68	114	49
1931-35	5.85	62	135	45
1936-40	6.11	55	141	40
1941-45	5.97	50	138	36

* This research was assisted by a grant from the Birmingham University Students' Social Service Fund.

† Martin, W. J. (1949). *Brit. med. J.*, 1, 438.

TABLE II*
STILLBIRTH AND INFANT MORTALITY RATES FOR SCOTLAND (1939-1945)

Year	Stillbirths per 1,000 Total Births		Infant Deaths per 1,000 Live Births		Combined Stillbirths and Infant Deaths per 1,000 Total Births		Contribution of Malformations to Total Deaths
	From all Causes	From Foetal Defects	From all Causes	From Congenital Malformations	From all Causes	From Congenital Malformations	%
1939	42.2	5.83	68.5	6.35	107.9	11.9	11.0
1940	42.1	6.09	78.3	6.05	117.1	11.9	10.1
1941	39.6	6.53	82.7	6.81	119.0	13.1	11.0
1942	38.2	5.71	69.3	7.12	104.8	12.6	12.0
1943	35.6	6.07	65.2	6.21	98.5	12.1	12.3
1944	32.5	5.93	65.0	5.96	95.4	11.7	12.3
1945	33.0	6.65	56.2	5.56	87.2	12.0	13.8
1939-1945	37.5	6.11	69.3	6.30	104.2	12.2	11.7

* Annual Reports of the Registrar-General for Scotland (1939-1945).

importance of the uterine environment has been stressed by pathologists who have cited the high incidence of pathological embryos in ectopic pregnancies, and in association with placenta praevia where the ovum embeds in or near the lower uterine segment. It has been suggested that some deformities are produced mechanically by pressure on the foetus, but this is unlikely to explain the more common and more lethal malformations. Infections in the mother during pregnancy have also been considered since the report that a history of rubella could be elicited in a number of cases; most observations on this subject are open to the criticism that the association may be fortuitous, for as a rule the incidence of the disease in pregnant women who produce normal children is unknown.

Conclusive evidence about the influence of heredity in man is available only for the exceptional malformations in which the recorded incidence in families is in accord with the known laws of inheritance. In many other malformations an incidence higher than average is observed in the relatives of a malformed propositus, but this information does not, of course, permit us to separate environmental and genetic effects. Twin studies are few, and must be interpreted cautiously in view of the special difficulty of establishing the homozygosity of a uniovular pair.

It is an indication of our increased awareness of the difficulties that we are no longer content to examine as exclusive alternatives the possibilities of genetic or environmental causes for most observations in human beings. In this matter we are indebted particularly to Hogben (1933), who has drawn our attention to the extent to which we have

been misled by the emphasis on experience of highly standardized animal stocks, observed in the laboratory under carefully controlled conditions. On existing evidence we can neither support nor dismiss the possibility of a contribution from inheritance to the origin of most malformations, but must accommodate in our conception the interdependence of genetic and environmental variables, with the attendant difficulty of assessing the relative contribution of each. The congenital malformations have now been considered from this viewpoint (Lenart, 1941; Gruenwald, 1947; Penrose, 1948; Holt, 1948) and the question will be examined more fully in a later communication.

SOURCES OF DATA.—In collecting data on human malformations we are handicapped by the fact that there are no satisfactory sources of information about individuals for whom the malformation is not certified as the cause of death. We may conveniently consider sources of data in relation to deaths at four different periods.

(a) *Deaths in utero before the 28th Week of Gestation.*—Stillbirths are not notified in Great Britain until the 28th week of gestation,† and for information earlier than this time we rely mainly on observations of pathologists who examine the aborted foetus (for example, Mall, 1917; Hertig and Livingstone, 1944). Inevitably such reports are incomplete, since only a proportion of abortions come to medical attention. This source is occasionally supplemented by material which becomes available at operations on the pregnant uterus (Rock and Hertig, 1948).

† This date is not the same in every country.

TABLE III
INCIDENCE OF MALFORMATIONS IN HOSPITAL SERIES

Country, Author, and Date	Place	Total Numbers of Births in Series	Malformations per 1,000 Births (not necessarily fatal)	Stillbirths due to Malformations per 1,000 Total Births	Neonatal Deaths due to Malformations per 1,000 Live Births	Remarks
<i>United Kingdom</i>						
Malpas, 1937	Liverpool	13,964	21	—	—	50% of malformations were cerebrospinal.
Allen, Macaffee, and Biggart, 1943	Belfast	6,314	—	—	7.3	49% of malformations were cerebrospinal.
Baird, 1947	Aberdeen	3,296	—	4.9	5.3	Primiparae only.
Drillien, 1947	Edinburgh	7,599	—	9.3	5.4	—
<i>America</i>						
Javert and Stander, 1943	New York	27,000	29.5	—	—	Includes a number of minor malformations.
D'Esopo and Marchetti, 1942	New York	25,823	5.5	—	—	Includes only fatal malformations.
Newton and McLean, 1947	Bridgeport	15,421	8.4	—	—	65% of malformations were cerebrospinal.
Potter and Adair, 1943	Chicago	27,321	—	2.4	2.4	35% of malformations were cerebrospinal.
Potter and Dieckmann, 1948	Chicago	17,657	—	1.2	2.9	—

(b) *Deaths in utero after the 28th Week of Gestation.*—After the 28th week stillbirths are notified, and from this time national statistics record information extracted from the notification card. In England and Wales this does not include the certified cause of the stillbirth, but since 1939 the cause has been recorded by the Registrar-General for Scotland, adding greatly to the value of the data which can be extracted on malformations.

(c) *Deaths in the First Year of Life.*—In England and Wales as well as in Scotland, the cause of subsequent death is, of course, certified for live births, and the record is particularly useful in the case of the more lethal malformations which cause death in the first year of life.

(d) *Deaths after the First Year of Life.*—Information about malformed individuals who die after the first year of life is less satisfactory, since the fact of survival to this date indicates that the malformations are less serious, and therefore less likely to appear ultimately as the cause of death.

National statistics are, of course, subject to errors of diagnosis. Malformations such as anencephalus and spina bifida are unlikely to be missed, but others are not reliably diagnosed without an autopsy. On the other hand, it is probably not uncommon for the presence of an internal malformation to be inferred where it does not exist, or for deaths due to other causes to be attributed to malformations. For example, it is likely that the deaths of some infants born in a state of asphyxia livida are erroneously certified as due to congenital heart disease (Cruickshank, 1930). Yet another source of error is introduced by the incrimination of a relatively minor malformation (for example, hare-lip or cleft palate) as the cause of a stillbirth or death when the real cause is unknown.

In view of these difficulties, records of hospitals where a high proportion of cases were examined post mortem are of interest (Table III). The fact that the reported incidence of congenital malformations varied greatly from one hospital to another

TABLE IV*

STILLBIRTHS AND INFANT DEATHS DUE TO CENTRAL NERVOUS MALFORMATIONS IN SCOTLAND (1941-1945)

Year	Stillbirths			Infant Deaths		
	Due to all foetal defects	Due to anencephalus, spina bifida, and hydrocephalus	Percentage of Malformations involving Central Nervous System	Due to all Congenital Malformations	Due to spina bifida and hydrocephalus	Percentage of Malformations involving the Nervous System
1941	610	391	64	611	241	39
1942	538	472	88	646	266	41
1943	596	399	67	588	231	39
1944	588	396	67	572	215	38
1945	598	442	74	483	171	35
* Total	2,930	2,100	72	2,900	1,124	39

* Annual Reports of the Registrar-General for Scotland (1941-1945).

indicates, as might be expected, that representative statistics cannot be collected from this source. It is also possible to supplement the sources of data listed above by field enquiry. This method has been used with profit by Penrose (1934; 1946) and Murphy (1940). We have therefore chosen to collect information by field enquiry on all malformations of certain specified types notified to a large Local Authority over a period of years.

THE PRESENT ENQUIRY.—The evidence suggests that congenital malformations in man do not form a homogenous group of uniform aetiology, and this view is supported by observations of the sex ratio: the proportion of males to females in pyloric stenosis is four to one, and in anencephalus one to three; the sex ratios of other malformations lie between these extremes. Investigations are therefore more likely to be of value if restricted to one type of deformity which occurs with sufficient frequency to furnish adequate numbers, and for this reason, we have confined our attention to the malformations of the nervous system. Table IV shows that in the years 1941 to 1945 in Scotland, they accounted for at least † 72 per cent. of stillborn and 39 per cent. of live born malformations which died in the first year of life, or for 55 per cent. of the combined total (5,830). The total births in the same period were 474,959, and central nervous malformations were thus responsible for the deaths of 0·68 per cent. of all infants born.

Study of this group has the further advantage that its members are readily identified at birth from external appearances so that errors of diagnosis are

unlikely, except occasionally in hydrocephalus, where perforation of the head may be necessary to effect delivery, and in the premature infant where the relatively large head may be erroneously diagnosed as hydrocephalus. Notifications of stillbirths and infant deaths ensure the collection of all cases of anencephalus, and of almost all cases of spina bifida with occasional exceptions such as spina bifida occulta and mild examples of meningocele. The only serious statistical loss consists of those cases of hydrocephalus compatible with life for a number of years. A few deaths of infants from acquired hydrocephalus may also be erroneously attributed to congenital causes, where the history of infection is overlooked.

We were fortunate in having access to the records of the Maternity and Child Welfare Department of the City of Birmingham, which for a number of years has obtained information on all stillbirths and neonatal deaths, by means of a questionnaire completed by the doctor or midwife in charge of the case. When returned, the form is scrutinized by a medical officer of the department, and the information entered into a register. From this register, we extracted information for the eight years 1940 to 1947 about all malformations of the central nervous system which were certified as the cause of death of stillbirths or of infants in the first year of life. The data available from this source for stillbirths and neonatal deaths were:

- (1) name, address, and municipal ward;
- (2) date and place of birth;
- (3) sex, single or twin, legitimacy;
- (4) brief details of results of previous pregnancies;
- (5) details of all malformations, and other conditions contributing to death.

† Not all malformations of the nervous system are shown separately.

TABLE V

THE NUMBERS OF CENTRAL NERVOUS MALFORMATIONS OF DIFFERENT TYPES IN 930 CONSECUTIVE CASES BORN IN BIRMINGHAM (1940-1947)

Group	Sub-group**	Number of			Total
		Stillbirths	Neonatal Deaths	Later Infant Deaths	
Anencephalus	1. Anencephalus alone*	314	18	—	332
	2. Anencephalus and spina bifida ..	33	1	—	34
Spina bifida	3. Spina bifida alone*†	49	144	62	255
	4. Spina bifida and hydrocephalus ..	68	56	5	129
	5. Spina bifida and encephalocele ..	2	2	—	4
	6. Spina bifida, hydrocephalus, and encephalocele	1	—	—	1
Hydrocephalus	7. Hydrocephalus alone*	112	24	14	150
Others	8. Encephalocele alone*	2	9	—	11
	9. All other central nervous malformations†	3	6	5	14
Total Central Nervous Malformations		584	260	86	930

* Excludes the co-existence of a second central nervous malformation.

† "Spina bifida" includes spinal meningocele, meningomyelocele, and myelocele.

‡ "Other central nervous malformations" were: microcephalus—8; unspecified congenital cerebral defect—4; occipital meningocele—2.

** Numerals are referred to in Fig. 1.

For live births, the date and place of death were also recorded. The details listed above are now collected for all infant deaths in the city, but for seven of the eight years covered by the survey the only data available from central sources for deaths after the neonatal period, were the name and address, age at death, place and cause of death. In such cases there was no difficulty in completing the record in the course of the subsequent investigation.

Visits were made to the homes of all mothers of the malformed births, and of a control group of approximately equal size, obtained by selecting every two-hundredth name in the registers of live and still births for the same years (1940 to 1947). The visits were completed in the period November, 1947, to October, 1948, by a team of female investigators, most of whom had been trained as almoners or in some other branch of social work. In each case where the mother could be interviewed at her original home or elsewhere in the city a field enquiry card was completed with her assistance. Information was recorded as follows:

- (1) menstrual history (age at onset; mean length of the cycle; duration of flow);
- (2) age at marriage;

- (3) reproductive history (details of all conceptions);
- (4) history of the pregnancy resulting in the birth of the propositus (illness; work during pregnancy);
- (5) information about the father (age; occupation; blood relationship to the mother);
- (6) rent (included as an index of social circumstances);
- (7) family history of congenital malformations.

No attempt was made to trace mothers who had left the city; the proportions lost in the malformation and control series are discussed below.

OBSERVATIONS ON 930 CONSECUTIVE MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM§

CLASSIFICATION AND INCIDENCE.—In the years 1940 to 1947, malformations of the central nervous system were certified in Birmingham as the cause of death of 930 stillbirths and first year deaths. Table V (see also Fig. 1, overleaf) gives the numbers attributed to each type of malformation, which have been grouped into four main divisions: anencephalus; spina bifida; hydrocephalus; others. This is the classification suggested in the International

§ Data from Maternity and Child Welfare Department records.

TABLE VI

STILLBIRTH AND INFANT MORTALITY RATES DUE TO MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM IN BIRMINGHAM (1940-1947)

Type of Malformation	Stillbirth rate per 1,000 Total Births	Infant Mortality rate per 1,000 Live Births	Total Deaths per 1,000 Total Births
Anencephalus	2·192	0·123	2·312
Spina bifida	0·758	1·747	2·457
Hydrocephalus	0·707	0·247	0·948
Others	0·032	0·130	0·158
Total	3·689	2·247	5·875

Statistical Classification of Diseases, Injuries, and Causes of Death (1948), which does not, however, show where births with more than one malformation (for example, spina bifida with hydrocephalus) are placed. The three groups, anencephalus, spina bifida, and hydrocephalus, are also used by the Registrar-General for Scotland in his valuable statistics on stillbirths, but the fact that the precise composition of the divisions is not indicated does not permit us to identify them with our own, and he

includes all other malformations of the central nervous system with "other specified defects".

If the data are grouped, the placing of combined malformations is important in two types which are comparatively common in Birmingham records: anencephalus with spina bifida, and spina bifida with hydrocephalus. Differences in the proportion of stillbirths and in the sex ratio of each malformation suggest the need for caution in allocating to any of the three main divisions births in which two malformations are combined. We have included "anencephalus with spina bifida" in the anencephalus group, since 33 of the 34 foetuses were stillborn, and anencephalus is the more lethal malformation. "Spina bifida with hydrocephalus", is included with spina bifida; we were influenced by the fact that spina bifida is the more reliable diagnosis, although in this case the proportion of stillborn infants with the combined lesions is almost mid-way between the proportions in each of the two component groups.

During the eight years 1940 to 1947, the total number of births in Birmingham was 158,307, of which 4,290 were stillbirths and 154,017 live births. From these figures, the numbers in Table V have been converted into rates which are shown in Table VI. The total incidence of fatal malformations of the nervous system in Birmingham (0·5875

FIG. 1.—Combinations of central nervous malformations of different types.

TABLE VII

NUMBERS OF CENTRAL NERVOUS MALFORMATIONS OF DIFFERENT TYPES FOUND IN 930 CONSECUTIVE CASES IN BIRMINGHAM (1940-1947)

Type of Malformation	Number	Incidence (per 1,000 Births, Live and Stillborn)
Anencephalus ..	366	2·312
Spina bifida ..	423	2·672
Hydrocephalus ..	280	1·769
Encephalocele ..	16	0·101
Others	14	0·088
Total	1,099	6·942

per cent.) is slightly below the Scottish figure (0·68 per cent.) for 1941 to 1945, as is the stillbirth rate of 2·192 due to anencephalus compared with the Scottish rate of 2·549 for the years 1939 to 1945. As already indicated, these data are not strictly comparable, although the error in the figures here compared is probably not great.

CO-EXISTENCE OF NERVOUS MALFORMATIONS.—The comparatively high incidence of two distinct malformations of the central nervous system in one individual is not explained by their chance association. The total number of central nervous malformations of different types in the 930 affected individuals in the series are given in Table VII in which two malformations in the same foetus are entered separately. If the co-existence of malformations were entirely fortuitous, the incidence of the combination would be the product of their frequencies,

TABLE VIII

EXPECTED AND OBSERVED NUMBERS OF VARIOUS COMBINATIONS OF CENTRAL NERVOUS MALFORMATIONS

Combination	Expected Frequency per 1,000 Births	Expected Number in Universe of 158,307 Births	Observed Number in Universe of 158,307 Births
Anencephalus and spina bifida	0·006178	0·978	34
Hydrocephalus and spina bifida	0·004727	0·748	129
Encephalocele and spina bifida	0·000270	0·043	4
Hydrocephalus, encephalocele, and spina bifida ..	0·00000048	0·00008	1

TABLE IX

OTHER DEFORMITIES CO-EXISTING WITH MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM

Co-existing Deformity	Type of Central Nervous Malformation (Simplified Classification)				
	Anencephalus	Spina bifida	Hydrocephalus	Others	All
Exomphalos	9	2	—	1	12
Congenital heart	—	2	3	—	5
Hare-lip and/or cleft palate	—	3	—	1	4
Malformation of cord	1	1	—	—	2
Talipes	1	26	2	—	29
Other skeletal deformities	2	8	4	1	15
Other malformations	1	2	2	—	5
Multiple malformations	1	—	5	3	9
Total number of deformities	15	44	16	6	81
Number of individuals exhibiting these ..	14	42	16	5	77
Total number in group	366	389	150	25	930
Percentage of individuals with co-existing deformity	3·8	10·8	10·7	20·0	8·3

TABLE X
SEX INCIDENCE OF MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM IN BIRMINGHAM (1940-1947)

Type of Malformation	Number of			Sex Ratio (Number of Males per 1,000 Females)	Percentage of Males	Discrepancy between this percentage and 50% (which corresponds to a Sex Ratio of Unity)
	Males	Females	Both			
Anencephalus alone	109	223	332	489	32·83	17·17 ± 2·58
Anencephalus with spina bifida	8	26	34	308	23·53	26·47 ± 7·27
Spina bifida alone	108	146	254	740	42·52	7·48 ± 3·10
Spina bifida with hydrocephalus	59	70	129	843	45·74	4·26 ± 4·39
*Spina bifida with encephalocele	—	4	4	—	—	—
*Spina bifida with encephalocele and hydrocephalus	—	1	1	—	—	—
Hydrocephalus alone	65	85	150	765	43·33	6·67 ± 4·04
*Encephalocele alone	6	5	11	—	—	—
*Other central nervous malformations	7	7	14	—	—	—
Total	362	567	929	638	38·97	11·03 ± 1·60

* Numbers too small for calculation of sex ratio.

TABLE XI
SEX INCIDENCE OF MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM IN BIRMINGHAM (1940-1947)

Type of Malformation (Simplified Classification)	Number of			Sex Ratio (Number of Males per 1,000 Females)	Percentage of Males	Discrepancy between this percentage and 50% (which corresponds to Sex Ratio of Unity)
	Males	Females	Both			
<i>Anencephalus</i>						
Stillbirths	107	240	347	446	30·84	
Infant deaths	10	9	19	1,111	52·63	
Total	117	249	366	470	31·97	18·03 ± 2·44
<i>Spina bifida</i>						
Stillbirths	43	76	119	566	36·13	
Infant deaths	124	145	269	855	46·10	
Total	167	221	388	756	43·04	6·96 ± 2·51
<i>Hydrocephalus</i>						
Stillbirths	53	59	112	898	47·32	
Infant deaths	12	26	38	462	31·58	
Total	65	85	150	765	43·33	6·67 ± 4·04
<i>*Others</i>						
Stillbirths	2	3	5	—	—	—
Infant deaths	11	9	20	—	—	—
Total	13	12	25	—	—	—
<i>All Central Nervous Malformations</i>						
Stillbirths	205	378	583	542	35·16	14·84 ± 1·98
Infant deaths	157	189	346	831	45·38	4·62 ± 2·68
Total	362	567	929	638	38·97	11·03 ± 1·60

* Numbers too small for calculation of sex ratio.

and Table VIII (previous page) compares the expected and observed numbers. The considerable differences between these two sets of figures indicate

either that the presence of one malformation predisposes to the formation of another, or that a common factor is concerned in their aetiology.

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TABLE XII

SEX INCIDENCE OF MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM IN SCOTLAND (1939-1945)

Type of Malformation	Number of			Sex Ratio (Number of Males per 1,000 Females)	Percentage of Males	Discrepancy between this percentage and 50% (which corresponds to a Sex Ratio of Unity)
	Males	Females	Both			
<i>Anencephalus</i> Stillbirths only	446	1,222	1,668	365	26.74	23.26 ± 1.08
<i>Spina bifida</i> Stillbirths	120	182	302	659	39.74	10.26 ± 2.82
Infant deaths	534	676	1,210	790	44.13	5.87 ± 1.43
Total	654	858	1,512	762	43.25	6.75 ± 1.27
<i>Hydrocephalus</i> Stillbirths	458	428	886	1,070	51.69	-1.69 ± 1.68
Infant deaths	231	237	468	975	49.36	0.64 ± 2.31
Total	689	665	1,354	1,036	50.89	-0.89 ± 1.36
<i>Total</i> Stillbirths	1,024	1,832	2,856	559	35.85	14.15 ± 0.90
Infant deaths	765	913	1,678	838	45.59	4.41 ± 1.21
Total	1,789	2,745	4,534	652	39.46	10.54 ± 0.73

ADDITIONAL MALFORMATIONS.—Of 930 infants born with one or more central nervous malformations, 77 (8.3 per cent.) showed deformities of other organs (Table IX, p. 189). The table illustrates the well-known association between talipes and spina bifida, due presumably to a disturbance of the nervous tracts supplying the lower extremities, and also suggests an association between exomphalos and anencephalus.

SEX RATIO.—The sex incidence of 929 malformations* is given in Table X for all cases, and in Table XI for the three main divisions: anencephalus, spina bifida, hydrocephalus. Except for hydrocephalus, in which our numbers are small, the results are in reasonable agreement with the estimates calculated from Scottish data for the years 1939 to 1945 (see Table XII).

These differences are, of course, well recognized, although no satisfactory explanation is available for them. If equal numbers of both sexes are malformed in the early weeks of gestation, more males must be aborted in the period before the birth is notifiable, and when the sex is often unknown. Certainly the evidence does not suggest that males are less viable than females in the later months, for of the 929 Birmingham malformations, 43.4 per cent. of males and 33.3 per cent. of females were alive at birth. The corresponding figures for spina

bifida and hydrocephalus based on the Scottish statistics are given in Table XIII.

TABLE XIII

SEX INCIDENCE OF SPECIFIC MALFORMATIONS ALIVE AT BIRTH. SCOTLAND (1939-1945)

Malformation	Sex	Number of Cases	Percentage Live Born
Spina bifida	Male	654	81.7
	Female	858	78.8
Hydrocephalus	Male	689	33.5
	Female	665	35.6

The conclusion about the respective viability of male and female malformations would, of course, be affected if different proportions of the two sexes were alive at the end of the first year. In his report on 144 malformations of the central nervous system, Penrose (1946) records 22 male and 24 female malformations which survived the first year. Scottish data for the period 1941-1945 are also relevant (see Table XIIb, overleaf).

SECULAR TREND.—The annual numbers of malformations of the central nervous system notified in Birmingham (1940-1947) are given in Table XIII (overleaf), with the total numbers of live and still

* In one of the 930 cases, the sex was not given.

TABLE XIIb

SEX INCIDENCE OF SPECIFIC MALFORMATIONS WHICH SURVIVED FIRST YEAR. SCOTLAND (1939-45)

Malformation	Deaths after the First Year of Life		
	Males	Females	Total
Congenital hydrocephalus ..	43	25	68
Spina bifida and meningocele ..	12	21	33

births for the same years. From these figures the rates exhibited in Table XIV and Fig. 3 have been calculated. Unlike the national rates relevant to all malformations cited in Tables I and II, the Birmingham rates of anencephalus and spina bifida show an unmistakable decline in the eight-year period; the rates of hydrocephalus are fairly constant. Fig. 2 indicates that the incidence of malformations has fallen at a relatively greater rate than the incidence of stillbirths from all causes.

In accounting for this somewhat unexpected result, it is important to consider secular changes in

FIG. 2.—Annual rates for stillbirths (all causes) and for central nervous malformations (Birmingham, 1940-47).

TABLE XIII
ANNUAL NUMBERS OF MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM IN BIRMINGHAM (1940-1947)

Type of Malformation	Stillbirth or Infant Death	Year								Whole Period
		1940	1941	1942	1943	1944	1945	1946	1947	
Anencephalus	S.B.	43	37	47	53	47	42	41	37	347
	I.D.	5	2	1	—	1	3	1	6	19
	Total	48	39	48	53	48	45	42	43	366
Spina bifida	S.B.	23	13	12	14	17	10	17	14	120
	I.D.	32	25	47	39	37	28	35	26	269
	Total	55	38	59	53	54	38	52	40	389
Hydrocephalus	S.B.	11	14	12	17	13	9	21	15	112
	I.D.	5	3	4	2	4	5	6	9	38
	Total	16	17	16	19	17	14	27	24	150
Encephalocele and other Central Nervous Malformations	S.B.	—	—	1	1	—	—	—	3	5
	I.D.	3	1	3	3	4	2	3	1	20
	Total	3	1	4	4	4	2	3	4	25
All Central Nervous Malformations	S.B.	77	64	72	85	77	61	79	69	584
	I.D.	45	31	55	44	46	38	45	42	346
	Total	122	95	127	129	123	99	124	111	930
Total Live Births ..		15,882	14,063	17,657	19,376	21,720	19,185	22,134	24,000	154,017
Total Stillbirths (all Causes)		542	445	543	535	565	500	583	577	4,290
All Births, Live and Still ..		16,424	14,508	18,200	19,911	22,285	19,685	22,717	24,577	158,307

TABLE XIV

ANNUAL INCIDENCE OF MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM IN BIRMINGHAM, 1940-1947 (RATE PER 1,000 TOTAL BIRTHS)

Type of Malformation		Year								Whole Period
		1940	1941	1942	1943	1944	1945	1946	1947	
Anencephalus		2.923	2.688	2.637	2.662	2.154	2.286	1.849	1.750	2.312
Spina bifida		3.349	2.619	3.242	2.662	2.423	1.930	2.289	1.628	2.457
Hydrocephalus		0.974	1.172	0.879	0.954	0.763	0.711	1.189	0.977	0.948
Others		0.183	0.069	0.220	0.201	0.179	0.102	0.132	0.163	0.158
All Central Nervous Malformations										
	Stillbirths	4.688	4.411	3.956	4.269	3.455	3.099	3.477	2.807	3.689
	Infant Deaths	2.740	2.137	3.022	2.210	2.064	1.930	1.981	1.709	2.186
	Total	7.428	6.548	6.978	6.479	5.519	5.029	5.458	4.516	5.875
Stillbirth Rate (all Causes)		33.00	30.67	29.84	26.87	25.35	25.40	25.66	23.48	27.10

FIG. 3.—Annual incidence of central nervous malformations (Birmingham, 1940-47).

parity, since we show below that the risk of a central nervous malformation is relatively greater at the first birth rank and above the sixth. Unfortunately, information on parity is not available for all Birmingham births of these years, and although the data were recorded by field enquiry for a control group selected from all births, the fact that the percentage of women not interviewed varied from year to year considerably reduces its value. We have therefore estimated the proportions of malformations of the central nervous system notified in each year (1941 to 1947)* which are in the first birth rank or above the sixth (Table XV, overleaf). Fig. 4 (overleaf) shows that, with the exception of the year 1944, the proportions in the parities where the risks are greatest declined, as did the central nervous

malformation rate. We may interpret these observations conservatively by concluding that if the risk at different birth ranks was relatively constant, the observed reduction in the malformation rate could be explained by the changes in the parity of the mothers, and may not indicate a true reduction of the risk in the later years.

THE MALFORMATION AND CONTROL GROUPS COMPARED†

The statistics so far quoted for 930 consecutive malformations of the nervous system were available in central records, and are in consequence free from sampling errors. As indicated in the introduction, additional information in respect of the malformations, and of a control group of normal births, was

* Data for 1940 were incomplete.

† Data from field enquiry.

TABLE XV
ANNUAL PROPORTIONS OF CENTRAL NERVOUS MALFORMATIONS AT THE FIRST OR ABOVE THE SIXTH BIRTH RANKS IN BIRMINGHAM (1941-1947)

	Year							Whole Period
	1941	1942	1943	1944	1945	1946	1947	
Total Malformations	95	127	129	123	99	124	111	808
Malformations of unknown Birth Rank	1	2	1	4	—	—	—	8
Malformations of known Birth Rank ..	94	125	128	119	99	124	111	800
Number of Birth Rank 1	50	69	56	58	40	53	44	370
Number of Birth Rank 7 and over ..	5	11	7	5	2	7	4	41
Total of Birth Ranks 1 and 7+ ..	55	80	63	63	42	60	48	411
Percentage of Malformations of Birth Ranks 1 and 7+	58.5	64.0	49.2	52.9	42.4	48.4	43.2	51.4

TABLE XVI
PARTICULARS OF CONTROL SERIES SELECTED FROM REGISTERS OF LIVE BIRTHS AND STILLBIRTHS IN BIRMINGHAM (1940-1947)

	Maternities	Pairs of Twins	Infants Born
Live Births	860	16	876
Stillbirths	22	—	22
Total Live and Stillbirths	882	16	898
Less Central Nervous Malformations ..	6	—	6
Total	876	16	892

TABLE XVII
WARD GROUP DISTRIBUTION OF ALL INFANTS IN THE CONTROL SERIES COMPARED WITH ALL INFANTS BORN IN BIRMINGHAM (1940-1947)

Ward Group	Infants in Control Series		All Infants born in City	
	Number in Group	Percentage in Group	Number in Group	Percentage in Group
I	322	35.86	56,669	35.80
II	397	44.21	72,006	45.48
III	179	19.93	29,583	18.69
Not located	—	—	49	0.03
Total	898	100	158,307	100

obtained in all cases where the mother could be interviewed, and we now examine the validity of the samples on which the fuller record was completed. The selection of every two-hundredth name in the register of live and stillbirths for the years 1940-1947 gave a control group of 898 births, divided in Table XVI into live and stillborn, and single and multiple births. This sample is compared with all births in the city for the same years and shows

reasonable agreement in respect of ward group* (Table XVII), year of birth (Table XVIII, opposite), and season of birth (Table XIX, p. 196). Two adjustments are necessary and when made in Table XVI give 876 mothers in the control group for comparison with 930 in the malformation series.

* For discussion of the division of Birmingham city wards into three social groups, see Appendix A.

MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM—I

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FIG. 4.—Central nervous malformations: annual rates and proportions at birth ranks 1 and 7+ (Birmingham, 1940-47).

TABLE XVIII

ANNUAL DISTRIBUTION OF ALL INFANTS IN THE CONTROL SERIES COMPARED WITH ALL INFANTS BORN IN BIRMINGHAM (1940-1947)

Year	Infants in Control Series		All Infants born in City	
	Number	Percentage	Number	Percentage
1940	99	11.02	16,424	10.37
1941	94	10.47	14,508	9.16
1942	105	11.69	18,200	11.50
1943	113	12.58	19,911	12.58
1944	129	14.37	22,285	14.08
1945	110	12.25	19,685	12.43
1946	116	12.92	22,717	14.35
1947	132	14.70	24,577	15.52
Total	898	100	158,307	99.99

TABLE XIX
QUARTERLY DISTRIBUTION OF ALL INFANTS IN THE CONTROL SERIES COMPARED WITH ALL INFANTS BORN IN BIRMINGHAM (1940-1947)

Quarter	Infants in Control Series		All Infants born in City	
	Number	Percentage	Number	Percentage
January-March ..	215	23·94	39,383	24·88
April-June ..	231	25·72	41,036	25·92
July-September ..	228	25·39	39,017	24·65
October-December ..	224	24·94	38,871	24·55
Total	898	99·99	158,307	100

TABLE XX
RESULT OF FIELD SURVEY OF MOTHERS OF MALFORMATIONS AND CONTROLS

Result	Malformations		Controls	
	Number	Percentage	Number	Percentage
Not traced ..	91	9·78	63	7·19
Left Birmingham ..	57	6·13	55	6·28
Information refused ..	17	1·83	11	1·26
Died ..	8	0·86	4	0·46
Mental defective ..	1	0·11	1	0·11
Information unreliable ..	1	0·11	—	—
Not interviewed ..	175	18·82 ± 1·28	134	15·30 ± 1·22
Successfully interviewed ..	755	81·18	742	84·70
Total abstracted ..	930	100	876	100

TABLE XXI (see also Fig. 5)
PERCENTAGE OF MALFORMATIONS AND CONTROLS INTERVIEWED IN EACH YEAR AND WARD GROUP

Ward Group		1940	1941	1942	1943	1944	1945	1946	1947	Total
I	Malformations ..	48	75	79	75	81	74	86	92	76·4
	Controls	62	81	91	84	93	86	75	93	83·5
II	Malformations ..	80	86	84	85	81	86	89	93	85·3
	Controls	84	86	84	85	85	81	94	96	87·1
III	Malformations ..	68	67	77	82	87	71	93	100	80·8
	Controls	89	65	71	83	75	70	96	100	81·4
All	Malformations ..	65	79	81	81	82	79	89	94	81·2
	Controls	76	79	84	84	85	81	88	95	84·7

- (1) The malformations are compared with births not resulting in a central nervous malformation (not with all births); thus six malformations are excluded.
- (2) The analysis is based on the number of maternities, and not on the number of births.

Successful interviews were completed in fewer malformations (81 per cent.) than controls (85 per cent.), a difference unlikely to be due to chance (Table XX). The data given by year and ward group in Table XXI (and Fig. 5, opposite),

FIG. 5.—Percentage of malformations and controls interviewed in each year and ward group (see also Table XXI).

TABLE XXII (see also Fig. 6)

COMPARISON BETWEEN MOTHERS OF MALFORMATIONS INTERVIEWED AND NOT INTERVIEWED IN RESPECT OF AGE AND PARITY

	Interviewed		Not Interviewed	
	Number	Percentage	Number	Percentage
<i>Maternal Age Group</i>				
17-21	73	9.7	29	20.6
22-26	229	30.3	46	32.6
27-31	184	24.4	31	22.0
32-36	157	20.8	23	16.3
37-41 }	88	11.7	11	7.8
42-46 }	24	3.2	1	0.7
Total	755	100.1	141	100.0
Maternal Age not known ..	—	—	34	—
<i>Birth Rank</i>				
1	334	44.2	89	56.7
2 and 3	264	35.0	52	33.1
4, 5, and 6	109	14.4	14	8.9
7+	48	6.4	2	1.3
Total	755	100.0	157	100.0
Birth Rank not known ..	—	—	18	—

FIG. 6.—Comparison between mothers of malformations interviewed and not interviewed in respect of birth rank and maternal age.

show that the main discrepancy occurred in 1940 in ward groups I and III. In ward group I (the lowest social group) the proportion of malformations interviewed was consistently lower in the

years 1940 to 1945. In most cases where mothers were not interviewed, details of age and parity were available from central records, and are compared in Table XXII with the sample (Fig. 6.)

TABLE XXIII
SUCCESSFULLY TRACED CENTRAL NERVOUS MALFORMATIONS CLASSIFIED ACCORDING TO TYPE

Simplified Classification	Full Classification	Number Traced	Percentage of Number Notified
Anencephalus ..	alone 280	305	83·3
	with spina bifida 25		
Spina bifida	alone 204	309	79·4
	with hydrocephalus 101		
	with encephalocele 3		
	with hydrocephalus and encephalocele 1		
Hydrocephalus ..	alone 118	118	78·7
Others	encephalocele 11	23	92·0
	other central nervous malformations 12		
Total	 755	755	81·2

TABLE XXIV (see also Fig. 7)
NUMBERS OF MALFORMATIONS AND CONTROLS AT DIFFERENT BIRTH RANKS AND MATERNAL AGE GROUPS

Maternal Age Group	Birth Rank						Total	Percentage Distribution by Maternal Age
	1	2	3	4	5 and 6	7+		
<i>Malformations</i>								
17-21	66	7	—	—	—	—	73	9·669
22-26	142	51	25	7	4	—	229	30·331
27-31	72	57	31	12	11	1	184	24·371
32-36	43	45	25	16	19	9	157	20·795
37-41	10	13	9	14	18	24	88	11·656
42-46	1	—	1	4	4	14	24	3·179
Total	334	173	91	53	56	48	755	
Percentage distribution by birth rank	44·238	22·914	12·053	7·020	7·417	6·358		100·00
<i>Controls</i>								
17-21	56	9	2	—	—	—	67	9·030
22-26	107	73	29	11	2	—	222	29·919
27-31	62	78	37	17	12	—	206	27·763
32-36	20	47	32	26	24	8	157	21·159
37-41	7	12	8	14	19	9	69	9·299
42-46	—	2	3	6	4	6	21	2·830
Total	252	221	111	74	61	23	742	
Percentage distribution by birth rank	33·962	29·784	14·960	9·973	8·221	3·100		100·00

The proportion of first births, and of low maternal ages, is higher for untraced births, and may be explained by the greater mobility of small families. Malformations of the central nervous system are

more common in first than in later births (see below), and this fact may account for the higher proportion untraced. Table XXIII gives the proportion of successful interviews for different malformations.

FIG. 7.—Percentage distribution of malformations and controls at different maternal ages and birth ranks.

TABLE XXV

NUMBERS OF MALFORMATIONS AT DIFFERENT BIRTH RANKS AND MATERNAL AGES

Maternal Age (years)	Birth Rank														Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
17	2	—	—	—	—	—	—	—	—	—	—	—	—	—	2
18	3	—	—	—	—	—	—	—	—	—	—	—	—	—	3
19	11	1	—	—	—	—	—	—	—	—	—	—	—	—	12
20	24	2	—	—	—	—	—	—	—	—	—	—	—	—	26
21	26	4	—	—	—	—	—	—	—	—	—	—	—	—	30
22	40	6	2	—	—	—	—	—	—	—	—	—	—	—	48
23	21	7	1	2	—	—	—	—	—	—	—	—	—	—	31
24	29	13	4	—	—	—	—	—	—	—	—	—	—	—	46
25	22	14	11	1	2	—	—	—	—	—	—	—	—	—	50
26	30	11	7	4	2	—	—	—	—	—	—	—	—	—	54
27	17	10	7	—	1	1	1	—	—	—	—	—	—	—	37
28	21	9	10	4	—	2	—	—	—	—	—	—	—	—	46
29	14	12	6	2	—	—	—	—	—	—	—	—	—	—	34
30	12	14	3	3	1	1	—	—	—	—	—	—	—	—	34
31	8	12	5	3	3	2	—	—	—	—	—	—	—	—	33
32	21	14	7	6	2	1	—	—	1	—	—	—	—	—	52
33	9	12	—	3	3	—	—	—	1	—	—	—	—	—	28
34	8	4	6	—	5	1	—	2	3	1	—	—	—	—	30
35	2	8	4	3	1	2	1	—	—	—	—	—	—	—	21
36	3	7	8	4	3	1	—	—	—	—	—	—	—	—	26
37	—	—	2	3	5	—	1	1	2	—	—	—	—	—	14
38	5	4	1	5	2	1	2	4	—	1	—	—	—	—	25
39	1	3	3	1	—	3	—	1	1	—	—	—	—	—	13
40	1	3	2	3	1	1	2	2	1	—	—	—	1	1	18
41	3	3	1	2	1	4	1	1	—	1	—	1	—	—	18
42	—	—	1	1	—	1	—	1	—	2	2	—	—	—	8
43	1	—	—	2	1	—	2	1	—	2	—	1	—	—	10
44	—	—	—	1	1	1	—	—	—	—	—	1	—	—	4
45	—	—	—	—	—	—	—	—	—	—	—	—	—	1	1
46	—	—	—	—	—	—	—	—	—	1	—	—	—	—	1
Total	334	173	91	53	34	22	10	13	9	8	2	3	1	2	755

MATERNAL AGE AND PARITY

DATA DERIVED FROM THE SURVEY.—Our examination of the association of maternal age and parity with the risk of a central nervous malformation is based on a comparison between the malformation and control groups. Maternal age was recorded as the age of the mother at the birth of the propositus, and birth rank as one more than the number of all known previous pregnancies (that is, it was determined by the number of pregnancies, and not by the number of live births). Each birth was next allocated to the appropriate cell of a contingency table (Tables XXV and XXVI). Maternal ages and the higher birth ranks have been grouped, and percentage distributions calculated for row and column totals, in Table XXIV (see also Fig. 7). For

any age or parity the ratio of the percentage of malformations to the percentage of controls gives a measure of the relative risk of the birth of a malformation, which can be interpreted in relation to an average risk of unity for all ages and parities (Table XXIX and Fig. 8, see p. 204). The figures show that the risk is considerably increased at the first parity and above the sixth, and is correspondingly reduced between these extremes. Variations in association with maternal age are also present, but are less marked.

It is well known that the high correlation between these two variables makes it necessary to separate their effects, and in Table XXVII the risk at different birth ranks is estimated for each five-year maternal age group. The risks noted in association

TABLE XXVI
NUMBERS OF CONTROLS AT DIFFERENT BIRTH RANKS AND MATERNAL AGES

Maternal Age (years)	Birth Rank																	Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	
17	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
18	5	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	6
19	16	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	16
20	11	5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	16
21	23	3	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	28
22	23	4	6	1	—	—	—	—	—	—	—	—	—	—	—	—	—	34
23	33	19	5	1	—	—	—	—	—	—	—	—	—	—	—	—	—	58
24	15	9	3	1	—	—	—	—	—	—	—	—	—	—	—	—	—	28
25	20	21	7	4	—	—	—	—	—	—	—	—	—	—	—	—	—	52
26	16	20	8	4	2	—	—	—	—	—	—	—	—	—	—	—	—	50
27	16	15	3	5	—	—	—	—	—	—	—	—	—	—	—	—	—	39
28	11	18	6	6	2	—	—	—	—	—	—	—	—	—	—	—	—	43
29	19	16	7	2	2	1	—	—	—	—	—	—	—	—	—	—	—	47
30	9	21	12	3	1	3	—	—	—	—	—	—	—	—	—	—	—	49
31	7	8	9	1	3	—	—	—	—	—	—	—	—	—	—	—	—	28
32	6	11	8	6	—	5	2	—	—	—	—	—	—	—	—	—	—	38
33	6	10	8	6	3	1	—	—	—	—	—	—	—	—	—	—	—	34
34	3	7	7	4	2	2	1	1	—	1	—	—	—	—	—	—	—	28
35	3	13	5	5	4	3	1	—	—	—	1	—	—	—	—	—	—	35
36	2	6	4	5	3	1	—	1	—	—	—	—	—	—	—	—	—	22
37	4	3	3	4	7	1	—	—	—	—	—	—	—	—	—	—	—	22
38	2	3	2	4	1	—	2	—	—	—	—	—	—	—	—	—	—	14
39	—	3	—	3	2	1	1	—	—	—	1	—	—	—	—	—	—	11
40	—	3	2	3	—	1	—	1	—	—	—	—	—	—	—	—	—	10
41	1	—	1	—	4	2	2	1	1	—	—	—	—	—	—	—	—	12
42	—	—	2	4	1	—	1	—	—	—	—	—	—	1	—	—	—	9
43	—	—	—	1	—	2	—	—	—	—	—	—	—	—	—	—	—	3
44	—	2	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	4
45	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	1	2
46	—	—	—	—	—	1	—	—	1	—	1	—	—	—	—	—	—	3
Total	252	221	111	74	37	24	10	4	3	1	3	—	—	1	—	—	1	742

TABLE XXVII

DISTRIBUTION OF MALFORMATIONS AND CONTROLS IN THE SAME MATERNAL AGE GROUPS AT DIFFERENT BIRTH RANKS

Maternal Age Group	Birth Rank	Malformations			Controls			Difference between percentages	Standard error of difference
		No.	%	S.E.	No.	%	S.E.		
17-21	1	66	90.411	3.45	56	83.582	4.53	+ 6.83	5.69
	2	7	9.589	3.45	9	13.433	4.16	- 3.84	5.41
	3	—	—	—	2	2.985	2.08	- 2.99	2.08
	All ranks	73	100.00	—	67	100.00	—		
22-26	1	142	62.009	3.21	107	48.198	3.35	+13.81*	4.64
	2	51	22.271	2.75	73	32.883	3.15	-10.61*	4.18
	3	25	10.917	2.06	29	13.063	2.26	- 2.15*	3.06
	4	7	3.057	1.44	11	4.955	1.46	- 1.90	1.85
	5 and 6	4	1.747	0.87	2	0.901	0.63	+ 0.85	1.07
	All ranks	229	100.00	—	222	100.00	—		
27-31	1	72	39.130	3.60	62	30.097	3.20	+ 9.03	4.81
	2	57	30.978	3.41	78	37.864	3.38	- 6.89	4.80
	3	31	16.848	2.76	37	17.961	2.67	- 1.11	3.84
	4	12	6.522	1.82	17	8.252	1.92	- 1.73	2.64
	5 and 6	11	5.978	1.75	12	5.825	1.63	+ 0.15	2.39
	7+	1	0.543	0.54	—	—	—	+ 0.54	0.54
	All ranks	184	100.00	—	206	100.00	—		
32-36	1	43	27.389	3.56	20	12.739	2.66	+14.65*	4.44
	2	45	28.662	3.61	47	29.936	3.65	- 1.27	5.14
	3	25	15.924	2.92	32	20.382	3.21	- 4.46	4.34
	4	16	10.191	2.41	26	16.561	2.97	- 6.37	3.82
	5 and 6	19	12.102	2.60	24	15.287	2.87	- 3.18	3.88
	7+	9	5.732	1.86	8	5.096	1.75	+ 0.64	2.55
	All ranks	157	100.00	—	157	100.00	—		
37-41	1	10	11.364	3.38	7	10.145	3.63	+ 1.22	4.97
	2	13	14.773	3.78	12	17.391	4.56	- 2.62	5.93
	3	9	10.227	3.23	8	11.594	3.85	- 1.37	5.03
	4	14	15.909	3.90	14	20.290	4.84	- 4.38	6.22
	5 and 6	18	20.455	4.30	19	27.536	5.38	- 7.08	6.89
	7+	24	27.273	4.75	9	13.043	4.05	+14.23*	6.24
	All ranks	88	100.00	—	69	100.00	—		
42-46	1	1	4.167	4.08	—	—	—	+ 4.17	4.08
	2	—	—	—	2	9.524	6.40	- 9.52	6.40
	3	1	4.167	4.08	3	14.286	7.64	-10.12	8.66
	4	4	16.667	7.61	6	28.571	9.86	-11.90	12.45
	5 and 6	4	16.667	7.61	4	19.048	8.57	- 2.38	11.46
	7+	14	58.333	10.06	6	28.571	9.86	+29.76*	14.09
	All ranks	24	100.00	—	21	100.00	—		
All ages	1	334	44.238	1.81	252	33.962	1.74	+10.28*	2.51
	2	173	22.914	1.53	221	29.784	1.68	- 6.87*	2.27
	3	91	12.053	1.18	111	14.960	1.31	- 2.91	1.77
	4	53	7.020	0.93	74	9.973	1.10	- 2.95*	1.44
	5 and 6	56	7.417	0.95	61	8.221	1.01	- 0.80	1.39
	7+	48	6.358	0.89	23	3.100	0.64	+ 3.26*	1.09
Total all ranks		755	100.00	—	742	100.00	—		

* Difference exceeds twice its standard error.

TABLE XXVIII

DISTRIBUTION OF MALFORMATIONS AND CONTROLS IN THE SAME BIRTH RANKS AT DIFFERENT MATERNAL AGE GROUPS

Birth Rank	Maternal Age Group	Malformations			Controls			Difference between percentages	Standard error of difference
		No.	%	S.E.	No.	%	S.E.		
1	17-21	66	19.760	2.18	56	22.222	2.62	- 2.46	3.41
	22-26	142	42.515	2.70	107	42.460	3.11	+ 0.06	4.12
	27-31	72	21.557	2.25	62	24.603	2.71	- 3.05	3.52
	32-36	43	12.874	1.83	20	7.937	1.70	+ 4.94	2.50
	37-41	10	2.994	0.93	7	2.778	1.03	+ 0.22	1.39
	42-46	1	0.299	0.30	—	—	—	+ 0.30	0.30
	All groups	334	100.00	—	252	100.00	—		
2	17-21	7	4.046	1.50	9	4.072	1.33	- 0.03	2.00
	22-26	51	29.480	3.47	73	33.032	3.16	- 3.55	4.69
	27-31	57	32.948	3.57	78	35.294	3.21	- 2.35	4.81
	32-36	45	26.012	3.34	47	21.267	2.75	+ 4.74	4.32
	37-41	13	7.514	2.00	12	5.430	1.52	+ 2.08	2.52
	42-46	—	—	—	2	0.905	0.64	- 0.90	0.64
	All groups	173	100.00	—	221	100.00	—		
3	17-21	—	—	—	2	1.802	1.26	- 1.80	1.26
	22-26	25	27.473	4.68	29	26.126	4.17	+ 1.35	6.27
	27-31	31	34.066	4.97	37	33.333	4.47	+ 0.73	6.69
	32-36	25	27.473	4.68	32	28.829	4.30	- 1.36	6.35
	37-41	9	9.890	3.13	8	7.207	2.45	+ 2.68	3.98
	42-46	1	1.099	1.09	3	2.703	1.54	- 1.60	1.89
	All groups	91	100.00	—	111	100.00	—		
4	22-26	7	13.208	4.65	11	14.865	4.14	- 1.66	6.22
	27-31	12	22.642	5.75	17	22.973	4.89	- 0.33	7.55
	32-36	16	30.189	6.31	26	35.135	5.55	- 4.95	8.40
	37-41	14	26.415	6.06	14	18.919	4.55	+ 7.50	7.58
	42-46	4	7.547	3.63	6	8.108	3.17	- 0.56	4.82
	All groups	53	100.00	—	74	100.00	—		
5 and 6	22-26	4	7.143	3.44	2	3.279	2.28	+ 3.86	4.13
	27-31	11	19.643	5.32	12	19.672	5.09	- 0.03	7.35
	32-36	19	33.928	6.33	24	39.344	6.25	- 5.42	8.90
	37-41	18	32.143	6.24	19	31.148	5.93	+ 0.99	8.61
	42-46	4	7.143	3.44	4	6.557	3.17	+ 0.59	4.68
	All groups	56	100.00	—	61	100.00	—		
7+	27-31	1	2.083	2.06	—	—	—	+ 2.08	2.06
	32-36	9	18.750	5.63	8	34.783	9.93	-16.03	11.42
	37-41	24	50.000	7.22	9	39.130	10.17	+10.87	12.48
	42-46	14	29.167	6.56	6	26.087	9.16	+ 3.08	11.26
	All groups	48	100.00	—	23	100.00	—		
All birth ranks	17-21	73	9.669	1.07	67	9.030	1.05	+ 0.64	1.50
	22-26	229	30.331	1.67	222	29.919	1.68	+ 0.41	2.37
	27-31	184	24.371	1.56	206	27.763	1.64	- 3.39	2.27
	32-36	157	20.795	1.48	157	21.159	1.50	- 0.36	2.10
	37-41	88	11.656	1.17	69	9.299	1.07	+ 2.36	1.58
	42-46	24	3.179	0.64	21	2.830	0.61	+ 0.35	0.88
Total all groups		755	100.00	—	742	100.00	—		

TABLE XXIX (see also Fig. 8)

PERCENTAGE DISTRIBUTION OF MALFORMATIONS AND CONTROLS AT DIFFERENT BIRTH RANKS AND MATERNAL AGE GROUPS

	Distribution				Relative Risk of a Malformation
	Malformations		Controls		
	Number	Percentage	Number	Percentage	
<i>Birth Rank</i>					
1	334	44.24	252	33.96	1.30
2	173	22.91	221	29.78	0.77
3	91	12.05	111	14.96	0.81
4	53	7.02	74	9.97	0.70
5 and 6	56	7.42	61	8.22	0.90
7+	48	6.36	23	3.10	2.05
All birth ranks	755	100.00	742	99.99	1.00
<i>Maternal Age Group</i>					
17-21	73	9.67	67	9.03	1.07
22-26	229	30.33	222	29.92	1.01
27-31	184	24.37	206	27.76	0.88
32-36	157	20.79	157	21.16	0.98
37-41	88	11.66	69	9.30	1.25
42-46	24	3.18	21	2.83	1.12
All age groups	755	100.00	742	100.00	1.00

FIG. 8.—Relative risk of central nervous malformations at different birth ranks and maternal ages.

with parity for the whole series are fairly consistently reflected in the more detailed figures, although in some groups the numbers are small. It will be recalled that interviews were not completed for a higher proportion of mothers in the malformation series, and since first births were more common among mothers not traced, the effect of primiparity is likely to be somewhat greater than that indicated by the figures.

In Table XXVIII the same procedure is adopted in the examination of the effect of maternal age at different birth ranks; the figures demonstrate no consistent association between maternal age and the incidence of malformations, when birth rank is kept constant. Our data also enable us to examine the association of age and parity with the different types of central nervous malformation included in this study (Table XXX and Figs. 9 and 10, opposite), although the smaller numbers do not permit a separation of their effects. For anencephalus and spina bifida the results are similar to those already quoted for the whole series, but for hydrocephalus the effect of birth rank is slight when compared with the marked effect of high maternal age.

Before accepting these conclusions it is necessary to consider two possible criticisms of the validity of the method on which they are based. In the first place, if malformations were more common in families of low fertility, or if the birth of a malformation often induced parents to avoid further pregnancies, a disproportionate number of malformations would be expected in the lower birth ranks, and especially in the first birth rank. Table XXXI and Fig. 11 (p. 206) show that the malformation and control groups are reasonably comparable in respect of the mean number of pregnancies. Indeed, the figure is slightly higher for the malformations,

TABLE XXX

MALFORMATIONS OF DIFFERENT TYPES DISTRIBUTED BY BIRTH RANK AND MATERNAL AGE GROUP

		Birth Rank				Maternal Age Group			
		1	2-6	7+	Total	17-26	27-36	37-46	Total
Controls	Number	252	467	23	742	289	363	90	742
	Percentage	33.962	62.938	3.100	100	38.949	48.922	12.129	100
	Standard error	1.74	1.77	0.64		1.79	1.83	1.20	
Anencephalus	Number	142	146	17	305	126	139	40	305
	Percentage	46.557	47.869	5.574	100	41.311	45.574	13.115	100
	Standard error	2.86	2.86	1.31		2.82	2.85	1.93	
	Difference from Control	+12.59*	-15.07*	+2.47		+2.36	-3.35	+0.99	
Spina bifida	Number	140	148	21	309	130	133	46	309
	Percentage	45.307	47.897	6.796	100	42.071	43.042	14.887	100
	Standard error	2.83	2.84	1.43		2.81	2.82	2.02	
	Difference from Control	+11.34*	-15.04	+3.70		+3.12	-5.88	+2.76	
Hydrocephalus	Number	43	66	9	118	36	57	25	118
	Percentage	36.441	55.932	7.627	100	30.508	48.305	21.186	100
	Standard error	4.43	4.57	2.44		4.24	4.60	3.76	
	Difference from Control	+2.48	-7.01	+4.53		-8.44	-0.62	+9.06	
		±4.76	±4.90	±2.53		±4.60	±4.95	±3.95	

* Difference exceeds twice its standard error.

an observation which may be explained by the reduction in the period of physiological infertility resulting from the higher incidence of abortions. Secondly, incidence of first births and of malformations was higher in the earlier years of the eight-year period from which this series is drawn. Since controls were selected as a constant proportion

of all births in each year, it is possible that the sample is weighted in respect of parity against the controls. Table XXXIII (p. 207) gives the percentages of births in different birth ranks by year, and indicates that in all years except 1940 the proportions of propositi of first birth ranks and above the sixth are consistently higher in the malformation series. The exception in 1940 is explained by the high incidence of untraced first births in the malformations.

FIG. 9.—Distribution of central nervous malformations by birth rank.

FIG. 10.—Distribution of central nervous malformations by maternal age.

TABLE XXXI

MOTHERS OF THE MALFORMATION AND CONTROL BIRTHS
COMPARED IN RESPECT OF THE NUMBER OF PREGNANCIES

Number of Pregnancies	Malformations Group		Control Group	
	Number	Per- centage	Number	Per- centage
1	130	17.22	147	19.81
2	208	27.55	232	31.27
3	172	22.78	146	19.68
4	95	12.58	96	12.94
5	54	7.15	57	7.68
6	36	4.77	30	4.04
7	13	1.72	11	1.48
8	13	1.72	11	1.48
9	9	1.19	4	0.54
10	11	1.46	—	—
11	5	0.66	5	0.67
12	4	0.53	1	0.13
13	3	0.40	—	—
14	2	0.26	1	0.13
15	—	—	—	—
16	—	—	—	—
17	—	—	1	0.13
Total	755	100.0	742	100.0
Mean num- ber of preg- nancies	3.29 (S.D. 2.27)		2.96 (S.D. 1.92)	
Difference	0.33 ± 0.11			

TABLE XXXII

STILLBIRTHS WITH ANENCEPHALUS DISTRIBUTED BY
MATERNAL AGE GROUP AND BIRTH RANK IN SCOTLAND
(1939-1945)

Distribution	Number of Births	Stillbirths due to anencephalus	Stillbirth rate due to anencephalus
<i>Maternal Age Group</i>			
<20	28,593	—	—
20-24	155,520	73	2.553
25-29	182,238	359	2.308
30-34	146,609	439	2.409
35-39	87,683	405	2.762
40+	28,301	302	3.444
Not stated	2,325	93	3.286
		1	—
Total	631,269	1,672	2.649
<i>Birth Rank</i>			
1	221,943	558	2.514
2	143,031	313	2.188
3	82,286	227	2.759
4	49,390	157	3.179
5 & 6	51,671	181	3.503
7+	37,728	136	3.605
Not stated	11	—	—
Total	586,060	1,572	2.682

FIG. 11.—Mothers of malformations and control births compared in respect of the number of pregnancies.

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TABLE XXXIII
PERCENTAGE DISTRIBUTION OF PROPOSITI BY BIRTH RANK FOR EACH YEAR

Birth Rank	Year								All Years
	1940	1941	1942	1943	1944	1945	1946	1947	
<i>Malformations</i>									
1	23.8	42.1	41.7	37.2	39.0	29.3	37.1	36.9	35.9
2 and 3	24.6	17.9	24.4	29.5	29.3	35.4	28.2	37.8	28.4
4, 5 and 6	9.8	13.7	7.1	9.3	9.8	12.1	17.7	15.3	11.7
7+	6.6	5.3	7.9	5.4	4.1	2.0	5.6	3.6	5.2
Not found	35.2	21.1	18.9	18.6	17.9	21.2	11.3	6.3	18.8
Total	100	100	100	100	100	100	100	100	100.0
<i>Controls</i>									
1	29.2	31.9	36.9	33.0	23.4	21.3	25.4	30.5	28.8
2 and 3	27.1	25.3	32.0	36.7	42.7	41.7	43.9	47.3	37.9
4, 5 and 6	15.6	16.5	14.6	12.8	17.7	15.7	14.0	16.0	15.4
7+	4.2	5.5	1.0	1.8	1.6	1.9	4.4	1.5	2.6
Not found	24.0	20.9	15.5	15.6	14.5	19.4	12.3	4.6	15.3
Total	100	100	100	100	100	100	100	100	100.0
<i>Percentages of Birth Ranks 1 and 7+</i>									
In malformation series	30.4	47.4	49.6	42.6	43.1	31.3	42.7	40.5	41.1
In control series	33.4	37.4	37.9	34.8	25.0	23.2	29.8	32.0	31.4
Difference	-3.0	10.0	11.7	7.8	18.1	8.1	12.9	8.5	9.7

DATA DERIVED FROM THE REPORTS OF THE REGISTRAR-GENERAL FOR SCOTLAND (1939-1945).—The reports of the Registrar-General for Scotland since 1939 give for stillbirths the age of the mother and the number of previous children. The same information is not provided for infant deaths, and the effects of age and parity can only be examined for anencephalus which almost always results in the birth of a stillborn foetus. The figures given in Table XXXII (opposite) for the years 1939-1945 show the increased risks observed in the Birmingham data, but relatively the effects at higher ages and parities are much greater (Fig. 12). The two sets of data are not strictly comparable, for the Scottish figures are based only on legitimate births, and the Registrar-General neglects abortions in estimating parity. The higher incidence of abortions in mothers of malformations is certain to influence birth rank. Unfortunately, the Scottish data do not enable us to examine separately the effects of maternal age and parity.

DISCUSSION.—The relation of maternal age and parity to the incidence of congenital malformations has been considered by several writers, but adequate data on malformations and controls have not been available, and no evidence so far published settles the issue beyond doubt. Still (1927) first compared

a small number of malformations with an unsatisfactory control group, and concluded that risks were higher with first born, particularly in the case

FIG. 12.—Stillbirth rates due to anencephalus distributed by birth rank and maternal age (Scotland, 1939-45).

of pyloric stenosis. In the case of mongolism, however, the risk appeared to be greater at high maternal age. His results were criticized by Macklin (1929) who examined statistics on 1,000 malformations collected from the literature, and decided that primogeniture had no effect. Equally unsatisfactory are reports based on hospital records, in which the numbers are small and the populations unrepresentative. (Malpas, 1937; Potter and Adair, 1943; Drillien, 1947.)

Murphy (1940) completed a field study of malformations selected from the register of deaths in Philadelphia, and using the Greenwood-Yule method compared the malformations with the non-malformed children of the same sibships. He noted that the risk of birth of a malformation increased with both age and parity, but did not separate the two effects. In this series, many of the sibships were incomplete at the time of the investigation which was finished within six years of the first death and less than one year after the last, and the control group was therefore likely to be deficient in the higher birth ranks and maternal ages. Data published by Hindse-Nielsen (1938) on 160 cases of spina bifida in 130 families permit an examination of the association with birth rank, which shows that this malformation was slightly less frequent in the first three birth ranks. Once again there is no indication that the sibships were complete at the time the data were recorded.

The most useful contribution yet available on this subject was made by Penrose (1934; 1946). In the first of two papers he showed that the risk of mongolism increased with advancing maternal age; the effect of birth rank was less marked, but the first born and infants of high birth rank seemed predisposed to the condition. His second paper dealt with 144 malformations of the nervous system, and, using a modification of the Greenwood-Yule method, he found that their incidence increased significantly with advancing maternal age and with rising birth rank. The effect of maternal age appeared to be more marked than that of birth rank, although when the influence of maternal age was eliminated, primogeniture still seemed to increase the risk. The discrepancy between Penrose's results and our own may be explained by the higher proportion of hydrocephalics in his series (31 per cent. compared with 16 per cent.) for, as we have shown, the incidence of hydrocephalus is markedly increased at higher maternal ages.

SOCIAL STATUS

Indices of social status used are: locality of domicile; rent of house; and legitimacy. The father's occupation was also recorded, but is considered sufficiently reliable for analysis.

LOCALITY OF DOMICILE.—Appendix A describes a classification of the city wards into three social

TABLE XXXIV
MALFORMATIONS CLASSIFIED BY WARD GROUPS

Type of Malformation	Ward Group*						Unlocated	All Wards	
	I		II		III			No.	Rates per 1,000 related Births
	No.	Rates per 1,000 related Births	No.	Rates per 1,000 related Births	No.	Rates per 1,000 related Births			
Anencephalus	121	2.135	170	2.361	75	2.535	—	366	2.312
Spina bifida	136	2.400	179	2.486	73	2.468	1	389	2.457
Hydrocephalus	63	1.112	61	0.847	26	0.879	—	150	0.948
Others	6	0.106	11	0.153	8	0.270	—	25	0.158
All malformations ..	326	5.753	421	5.847	182	6.152	1	930	5.875
Calculated rate obtained by applying rates for whole city by parity to estimated parity constitution of each ward group	—	5.756	—	5.833	—	6.156	—	—	—

* Group I: Wards with the poorest houses.
Group II: Wards with houses intermediate in standard between I and III.
Group III: Wards with the best houses.

FIG. 13.—Malformation rates by ward groups (Birmingham, 1940-47).

groups, and the home address of the mother at the time of the birth was used to place each malformation in one of them. Table XXXIV gives for each group the number of malformations of the three main types, and rates have been calculated from the total births (live and stillborn) in each ward group of the city for the same period, births within the city to women normally domiciled outside being excluded. (See Fig. 13.)

TABLE XXXV
THE PROPORTION OF STILLBORN MALFORMATIONS
CLASSIFIED BY WARD GROUPS

Malformations	Ward Group			All Wards
	I	II	III	
Stillborn ..	204	262	117	583
Died in first year ..	122	159	65	346
Total	326	421	182	929
Percentage still-born	62.6	62.2	64.3	62.8

TABLE XXXVI
THE PROPORTION OF STILLBORN MALFORMATIONS
CLASSIFIED BY WARD GROUPS (ANENCEPHALUS
EXCLUDED)

Malformations	Ward Group			All Wards
	I	II	III	
Stillborn ..	90	101	45	236
Died in first year ..	115	150	62	327
Total	205	251	107	563
Percentage still-born	43.9	40.2	42.1	41.9

TABLE XXXVII
MALFORMATION AND CONTROL GROUPS COMPARED IN RELATION TO RENT OF HOUSE

Rent of House	Malformation Group		Control Group	
	Number	Percentage	Number	Percentage
Weekly Rent:				
Less than 7s. 6d. ..	25	3.31	18	2.43
7s. 6d.-9s. 11d. ..	94	12.45	106	14.29
10s.-14s. 11d. ..	227	30.07	265	35.71
		45.83		52.43
15s.-19s. 11d. ..	97	12.85	84	11.32
20s.-24s. 11d. ..	49	6.49	49	6.60
25s.-34s. 11d. ..	26	3.44	28	3.77
35s. and over ..	5	0.66	6	0.81
		23.44		22.50
Not known	11	1.46	12	1.62
		1.46		1.62
Total	534	70.73	568	76.55
No Rent Paid:				
Own house or buying it ..	123	16.29	103	13.88
Living with relatives ..	65	8.61	50	6.74
Other reasons	33	4.37	21	2.83
Total	221	29.27	174	23.45
Total	755	100.00	742	100.00

The rate for anencephalus is slightly higher in the better ward groups, but the numbers are not large enough to be more than suggestive. The proportions of malformations which were stillborn are given in Table XXXV for the three ward groups; the figure is slightly higher in the third. This group, however, contains a higher proportion of anencephalus, and when this type is excluded (Table XXXVI) there is little difference between the three groups.

Since the risk of malformation is related to birth rank, comparison between ward groups is not satisfactory unless the rates are standardized for parity. Applying the city malformation rates for each birth rank to the population of each ward group estimated from the control series, we obtained a malformation rate per ward group almost identical with the observed rate which suggests that the increased rate in the better wards is due to the increased proportion of primiparae in these wards. This result, however, must be accepted with reserve because of the rather high proportion of cases of unknown birth rank (ward group I, 16 per cent.; ward group II, 12 per cent.; ward group III, 19 per cent.).

RENT OF HOUSE.—The rent of the house was obtained in the field enquiry, and is used in Table XXXVII as the basis of a comparison between the malformation and control groups. In the malformation group the percentage in houses rented at less than 15s. per week is 6.60 (± 2.58) lower than the percentage in the control series.

LEGITIMACY.—The civil status of the malformations was obtained from Maternity and Child Welfare Department records, and Table XXXVIII compares the proportion illegitimate with the corresponding figure for all births in Birmingham of the same period. The proportion of malformations which were illegitimate is low in consequence mainly of the contribution of anencephalus. The high proportion of stillbirths characteristic of this type of malformation could account for the difference, if there were evidence of less accurate reporting of civil status for stillbirths. This possibility is examined in Table XXXIX, which gives the proportion of illegitimate births for stillborn and live born malformations of the nervous system, with anencephalus excluded. The figures do not suggest that stillbirths are less accurately reported, and the low

TABLE XXXVIII
CIVIL STATUS OF MALFORMATIONS

Type of Malformation	All Infants	Illegitimate Infants†		Difference from percentage illegitimate in all Birmingham Births (1940-47)
	Number	Number	Percentage	
Anencephalus ..	366	8	2.186 (± 0.764)	3.91*
Spina bifida ..	389	23	5.913 (± 1.196)	0.18
Hydrocephalus ..	150	8	5.333 (± 1.835)	0.76
Others ..	25	—	—	—
Total ..	930	39	4.194 (± 0.657)	1.90*

* Difference exceeds twice its standard error.

† Illegitimacy rate for live and still births for Birmingham (1940-1947): 6.096 per 100. (Registrar-General.)

TABLE XXXIX

THE PROPORTION OF ILLEGITIMATE BIRTHS FOR STILLBORN AND LIVE-BORN MALFORMATIONS (ANENCEPHALUS EXCLUDED)

Type of Malformation	Stillborn		Infant Deaths	
	Illegitimate	Legitimate and Illegitimate	Illegitimate	Legitimate and Illegitimate
Spina bifida ..	9	120	14	269
Hydrocephalus ..	6	112	2	38
Others ..	—	5	—	20
Total ..	15	237	16	327
Illegitimate as Percentage of Total ..	6.329		4.893	

TABLE XL

LEGITIMACY OF STILLBIRTHS DUE TO MALFORMATIONS OF THE NERVOUS SYSTEM AND OF INFANT DEATHS DUE TO ALL CONGENITAL MALFORMATIONS IN SCOTLAND (1939-1945)

	Legitimate and Illegitimate	Illegitimate	Percentage Illegitimate
All Live Births	631,297	44,816	7.099
All Stillbirths	24,595	2,089	8.494
Total Births	655,892	46,905	7.151
<i>Stillbirths due to:</i>			
Anencephalus	1,672	100	5.981 ± 0.580
Spina bifida	302	19	6.291 ± 1.397
Hydrocephalus	887	60	6.764 ± 0.843
Total	2,861	179	6.257 ± 0.453
Infant Deaths due to all Con- genital Malformations ..	3,975	320	8.050 ± 0.431

illegitimate rate for anencephalus appears to be independent of this factor.

The annual reports of the Registrar-General for Scotland for the years 1939-1945 record the civil status of stillbirths for anencephalus, spina bifida and hydrocephalus, and the civil status of infant deaths for all congenital malformations grouped together (Table XL). Only anencephalus can be compared with our tables, which combine stillbirths and infant deaths. Although the proportion of illegitimate births among the anencephalics in the Scottish data is considerably higher than in the Birmingham series, it is nevertheless below the proportion for all Scottish births.

DISCUSSION.—The Registrar-General (Decennial Supplement, 1921) suggested that social class had little effect on infant mortality from congenital malformations, a conclusion supported by Woolf (1946) from statistics for England and Wales (Table XLI). Murphy (1940) found a low proportion of well-to-do families among those from which 571 malformations were drawn, and noted that in a hospital for poor patients the incidence of malformations was twice as great as the rate for the whole city (Philadelphia). On this not very satisfactory evidence he concluded that mothers in poor social circumstances were exposed to an increased risk of the birth of a malformation; evidence in support of this view was provided by Baird (1947) who compared the numbers of malformations in two small series of births selected from private and hospital practice. These reports examine the relation of social class to the incidence of all malformations; the literature contains no information on its relation to the incidence of different types of malformation.

TABLE XLI

INFANT MORTALITY RATE ATTRIBUTABLE TO CONGENITAL MALFORMATIONS BY SOCIAL CLASS OF FATHER—ENGLAND AND WALES, 1930-1932. (QUOTED BY WOOLF, 1946)

Social Class ..	I	II	III	IV	V	All
Infant mortality rate per 1,000	5.0	5.4	5.6	5.7	5.4	5.5

The influence of the nutritional state of the mother on the risk of malformations has been considered in animals (Hale, 1933; Warkany, 1945, etc.). Certainly severe vitamin deficiencies do result in the occurrence of congenital malformations of a special type in a proportion of the young of selected experimental animals, though the relation of this fact to the human problem is uncertain. There is no laboratory evidence that central nervous malformations, numerically the largest group in human beings, are produced in this way. Murphy (1940) and Burke and others (1933) inspected the dietary habits of pregnant women, and concluded that poor diets were common among mothers who delivered malformed births. The conclusions in both cases are based on small numbers of observations and are influenced by the difficulties familiar to investigators of human dietary habits. Diet is, of course, only one of the variables related to social status.

MATERNAL HEALTH DURING PREGNANCY

Information about maternal health during pregnancy was obtained for the malformation and control series, by direct interrogation of the mothers. Its reliability is difficult to assess, not only because any patient's memory of her own illness is subject

TABLE XLII
DISABILITY DURING PREGNANCY

Disability	Type of Malformation										Controls (742)*	
	Anencephalus (305)*		Spina bifida (309)*		Hydrocephalus (118)*		Others (23)*		Total (755)*			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<i>First half of Pregnancy</i>												
Vomiting of pregnancy ..	28	9.2	20	6.5	3	2.5	1	4.3	52	6.9	37	5.0
Threatened abortion ..	11	3.6	6	1.9	1	0.8	1	4.3	19	2.5	8	1.1
Severe mental shock ..	3	1.0	4	1.3	—	—	—	—	7	0.9	2	0.3
Falls and minor accidents ..	4	1.3	4	1.3	1	0.8	—	—	9	1.2	—	—
Surgical operations ..	1a	0.3	1b	0.3	1c	0.8	—	—	3	0.4	1d	0.1
Other major conditions ..	1e	0.3	—	—	3f	2.5	—	—	4	0.5	1g	0.1
<i>Second half of Pregnancy</i>												
Ante-partum haemorrhage ..	—	—	—	—	—	—	—	—	—	—	—	—
Placenta praevia ..	3	1.0	—	—	—	—	—	—	3	0.4	—	—
Accidental ..	2	0.7	1	0.3	—	—	—	—	3	0.4	—	—
Unspecified ..	2	0.7	—	—	—	—	—	—	2	0.3	—	—
Toxaemia ..	15	4.9	12	3.9	10	8.5	1	4.3	38	5.0	38	5.1
Premature labour (i.e. at or before 36 weeks) ..	196	64.3	50	16.2	25	21.2	3	13.0	274	36.3	60	8.1

a Excision of skin tumour.

b Operation on toe.

c Appendicectomy.

d Uterine myomectomy.

e Pleurisy.

f Jaundice; diabetes; uterine fibroid.

g Uterine fibroid.

* No. of propositi on which percentages are based.

to error, but also because it is not unlikely that mothers readily recall details of a pregnancy which resulted in an abnormal birth, whereas details after normal deliveries are quickly forgotten. For example, falls and minor accidents were recorded nine times in association with the malformations, and not at all in the control series. With these difficulties in mind we may consider the data for both groups in Table XLII.

THREATENED ABORTION.—Threatened abortion was slightly more common in pregnancies which resulted in anencephalics than in those associated with other central nervous malformations or with normal births. With the exception of one case in which the mother admitted that she attempted to induce an abortion, we have no information about the cause, the facts being equally consistent with the threatened abortion of an abnormal embryo, or with defective implantation resulting in embryonic defect. In either case, the figures do not recommend this as a common contribution to the aetiology of central nervous malformation. The literature offers few results for comparison, but the report by Shute (1939) of 2 per cent. of deformed foetuses in 443 cases of threatened abortion treated with vitamin E or progesterone,* is consistent with this view. Kotz, Parker, and Kaufman (1941) published

details of 184 cases of threatened abortion, associated with the birth of 102 viable infants; abnormalities were recorded in five cases (4.9 per cent.) and of these only two (anencephalus and mongolism) were of a major type. In further support of this view may be cited the fact (detailed in the previous section) that illegitimate pregnancies, which almost certainly experience attempts at interference more frequently than legitimate pregnancies, do not show a greater incidence of malformations.

PLACENTA PRAEVIA.—Placenta praevia existed in three out of 305 cases of anencephalus, and in none of the other malformations or normal births. This proportion (1 per cent.) is about ten times greater than that usually given for all births (0.1 per cent.) and is unlikely to be due to chance. Even so, the majority of anencephalics have a placenta which is normally situated, and the majority of placenta praeviae are associated with normal foetuses. The association of placenta praevia with foetal deformity was first noted by Greenhill (1923), who later (1939) collected from clinic records and from the literature details of 4,446 cases of placenta praevia of which 111 were associated with deformed foetuses (2.5 per cent., as compared with 0.94 per cent. in a large series of normal deliveries). Data which confirm this association were recorded by Siegal (1934), Murphy (1940), and Potter and Adair (1943).

* A series collected from the literature.

The high incidence of foetal deformities among extra-uterine embryos is well known (Mall, 1917; Hellman and Simon, 1935; Suter and Wichser, 1948), but the relevance of this observation to the malformed foetus which develops within the uterus is in doubt. Furthermore, many of these deformities are of a minor character for which a mechanical explanation may be advanced. On present evidence it is not possible to say whether defective implantation of the ovum *per se* is or is not a factor of much importance in the aetiology of malformations of the nervous system.

DIABETES MELLITUS.—Diabetes occurred only once in the series, and was associated with the birth of a hydrocephalic infant. Skipper (1933) and White (1935) reported 3.0 per cent. and 4.2 per cent. respectively for the incidence of malformations in 169 and 166 pregnancies in diabetic women. Once again the association is noteworthy, but can scarcely be a frequent factor in the causation of malformations. It is probable that the increased incidence can be, to some extent, accounted for by the fact that diabetes is usually associated with a high stillbirth rate, thus rendering available for autopsy an unusually high proportion of foetuses. In this way minor internal malformations which may for a time be undetected in the live born are brought to notice.

TOXAEMIA.—The incidence of toxæmia is about equal in the control and malformation groups. Drillien (1947) reported a lower incidence of toxæmia in pregnancies which resulted in malformations, and certainly this condition, uncommon before the sixth month, would not be expected to influence malformations which are laid down early in pregnancy.

VIRUS INFECTIONS.—There was no history of rubella or of any other virus infection during the pregnancies resulting in 755 malformations of the nervous system; there was also no history of virus infection in the pregnancies of the controls. On this evidence we can neither confirm nor refute the suggested role of these infections in other types of malformations (which mainly exclude those of the central nervous system) but are entitled to conclude that they are not commonly associated with the malformations here investigated. The earlier observations on the association of rubella with congenital defects have been reviewed by Parsons (1946), Murphy (1947), Warkany and others (1948). Others have attempted to meet the inevitable criticism of retrospective observations on malformed foetuses by noting the incidence of malformations among the births when rubella was

recorded during pregnancy (Fox and Bortin, 1946; Ober and others, 1947; and Bradford Hill and Galloway, 1949). The numbers so far obtained in this way are small, but suggest an incidence considerably in excess of experience with normal pregnancies.

Observations on other virus infections in pregnancy have been recorded by Dogramaci and Green (1947), Fox and others (1948), and Gérard-Lefebvre and Merlen (1948), and with one exception (Gérard-Lefebvre and Merlen) gave negative results. Evans and Smith (1946) interrogated mothers who gave birth to 25 lethal malformations, and did not elicit a history of virus disease during pregnancy. Influenza has also been suggested as a causal agent, but our examination of the Registrar-General's returns since 1916 indicates that the malformation rate is not correlated with the annual death rate from influenza of the same or of the previous year.

THERAPEUTIC IRRADIATION OF THE FOETUS WITH RADIUM OR X RAYS.—Evidence assembled by Murphy (1947) strongly suggested that malformations, particularly of the nervous system, can result from irradiation of the foetus *in utero*. No history of irradiation was obtained in the pregnancies which produced the malformed births of our series.

SEVERE MENTAL SHOCK.—Popularly considered a potent factor in producing malformations, severe mental shock was recorded for seven of the malformations, and for two of the controls; for the reason stated at the beginning of this section, little attention can be paid to this slight difference in incidence. It is also worth noting that the incidence of malformations was not higher in the city during the years when air raids were most frequent.

PREMATURE LABOUR.—Premature labour is mentioned in this context, not because it has any bearing on the aetiology of malformations, but because its common occurrence when the foetus is malformed, especially in cases of anencephalus, is of interest (see Table XLII). As an index of early labour the usual definition of prematurity based on the weight of the foetus would be particularly misleading in a discussion on central nervous malformations, since the abnormal size of the head in many cases has an obvious relation to the infant's weight. Accordingly we have based our statistics on the duration of gestation estimated from the date of the last menstrual period.

Stillborn foetuses with central nervous malformations, are frequently macerated, indicating that death has taken place some time prior to labour, presumably as a result of the malformation. This accounts for a number of the cases of premature

TABLE XLIII

EMPLOYMENT OF MOTHERS OF THE CONTROL GROUP AT THE ONSET OF PREGNANCY (1940-47)*

	Year of Birth of Propositus								Total
	1940	1941	1942	1943	1944	1945	1946	1947	
Primigravidae	28 (25.0)	29 (51.7)	38 (52.6)	36 (61.1)	29 (65.5)	23 (69.6)	29 (48.3)	40 (42.5)	252 (51.6)
Multigravidae	45 (11.1)	43 (20.9)	49 (10.2)	56 (23.2)	77 (18.2)	64 (15.6)	71 (15.5)	85 (14.1)	490 (16.1)
Total	73 (16.4)	72 (33.3)	87 (28.7)	92 (38.0)	106 (31.1)	87 (29.9)	100 (25.0)	125 (23.2)	742 (28.2)
Nervous Malformation rate per 1,000 (all city births)	7.43	6.55	6.98	6.48	5.52	5.03	5.46	4.52	5.87

* The table gives the total number of women in each group, and, in brackets, the percentage of these employed in a remunerated occupation at the onset of pregnancy.

TABLE XLIV

COMPARISON BETWEEN MALFORMATION AND CONTROL GROUPS IN RESPECT OF WORK OF MOTHERS IN EARLY PREGNANCY

Work of Mother	Primigravidae				Multigravidae			
	Malformations		Controls		Malformations		Controls	
	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage
No work	8	2.40	4	1.59	9	2.15	19	3.88
Own housework with help	27	8.08	15	5.95	52	12.41	27	5.51
Own housework without help	95	28.44	104	41.27	266	63.48	365	74.49
Remunerated employment only	59	17.66	17	6.75	14	3.34	6	1.22
Remunerated employment and own housework with help	37	11.08	27	10.71	9	2.15	7	1.43
Remunerated employment and own housework without help	108	32.34	85	33.73	69	16.47	65	13.47
Total	334	100.00	252	100.00	419	100.00	490	100.00
Total engaged remuneratively	204	61.08 ± 2.67	129	51.19 ± 3.15	92	21.96 ± 2.02	79	16.12 ± 1.66
Differences between percentages (Malformations—Controls)	9.89% ± 4.13				5.84% ± 2.61			

labour. Hydramnios is a not uncommon complication of pregnancies which result in a congenital malformation, being particularly frequent in cases of anencephalus (Drillien, 1947), and no doubt many of the cases of premature labour in our series were due to the mechanical distension of the uterus from this cause.

MATERNAL OCCUPATION DURING PREGNANCY

Information was obtained in the field enquiry about the work done during pregnancy by mothers in the malformation and control groups, and the

increased proportion of mothers in remunerated employment during the war years is demonstrated separately for primigravidae and multigravidae in Table XLIII. In 1943, 38 per cent. of mothers were remuneratively employed at the onset of pregnancy, the figures being 61 per cent. and 23 per cent. for primigravidae and multigravidae respectively. The reduction in the malformation rates over these years has already been discussed, and no conspicuous association with the incidence of maternal employment is evident. This problem is further investigated in Table XLIV which shows

TABLE XLV
OCCUPATION OF MOTHERS AT THE ONSET OF PREGNANCY

Type of Occupation	Malformation Group			Control Group	
	No.	Percentage		No.	Percentage
Professional and executive	11	3.7	34.4	8	3.8
Clerical	56	18.9		28	13.5
Shop assistants and occupations of similar status	35	11.8		18	8.7
Factory work:					
Supervision	1	0.3	50.6	2	1.0
Viewing and assembling	53	17.9		27	13.0
Filing, painting, and machine work	63	21.3		51	24.5
Store-keeping and packing	6	2.0		7	3.4
Other manual work	27	9.1		32	15.4
Public house, canteen and restaurant work	13	4.4	12.2	11	5.3
Laundry and domestic work, office cleaning	16	5.4		15	7.2
Public transport—conductresses, porters	7	2.4		3	1.4
Armed Forces	4	1.4		1	0.5
Unspecified	4	1.4		5	2.4
Total	296	100.0		208	100.0

TABLE XLVI
STAGE OF PREGNANCY WHEN MOTHERS CEASED EMPLOYMENT

Duration of Gestation (weeks)	Primigravidae				Multigravidae			
	Malformations		Controls		Malformations		Controls	
	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage
Less than 12	32	15.7	14	10.8	16	17.4	9	11.4
12-15	31	15.2	33	25.6	19	20.7	8	10.1
16-19	31	15.2	14	10.8	8	8.7	5	6.3
20-23	35	17.2	21	16.3	14	15.2	16	20.3
24-27	41	20.1	20	15.5	14	15.2	13	16.5
28-31	25	12.2	13	10.1	9	9.8	10	12.7
32-35	5	2.4	9	7.0	5	5.4	5	6.3
36-39	3	1.5	4	3.1	4	4.3	10	12.7
40+	—	—	1	0.8	3	3.3	2	2.5
Unspecified	1	0.5	—	—	—	—	1	1.3
Total	204	100.0	129	100.0	92	100.0	79	100.0
Mean (weeks)	20.6		21.1		21.2		24.5	

for primigravidae and multigravidae of the malformation and control series the circumstances in respect of work in early pregnancy; the proportion of mothers remuneratively employed is higher for the malformations. Table XLV records the type of work done, and shows a slightly higher percentage of manual workers in the employed of the control group. Information obtained about the stage in pregnancy in which mothers left regular employment (Table XLVI) shows slight differences between the two groups, which could be explained by the more frequent premature onset of labour in the malformations.

The data here recorded about employment of women in pregnancy during and since the war have some intrinsic interest. It is, however, necessary to be cautious about drawing any conclusion from differences between control and malformation groups of the dimensions shown in the accompanying tables, and we limit our conclusion to the statement that there is at least no noteworthy association between the proportion of mothers remuneratively employed and the incidence of congenital malformations of the nervous system.

SUMMARY

1. In the years 1939 to 1945, congenital malformations in Scotland were responsible for 11.7 per cent. of the certified deaths of infants stillborn or dead within the first year of life. National statistics for England and Wales do not give the causes of stillbirths but, in the years 1941 to 1945, attribute to the same causes about 10 per cent. of first year deaths.

2. Scottish data (1941-45) show that malformations of the central nervous system accounted for at least 72 per cent. of stillborn and 39 per cent. of live born malformations which died in the first year of life, or for 55 per cent. of the combined total.

3. Data from Birmingham Maternity and Child Welfare Department records are examined in respect of 930 consecutive malformations of the central nervous system certified as the cause of stillbirths or of first year deaths in the city in the years 1940 to 1947. They were classified as follows: anencephalus (366); spina bifida (389); hydrocephalus (150); others (25). From this material evidence is provided of:

- (a) The frequency with which different types of malformation are associated in one individual.
- (b) The sex-ratio of the central nervous malformations.
- (c) Secular trends. The rate for hydrocephalus remained fairly constant in the 8-year period. The rates for anencephalus and spina bifida declined, and it is suggested that the observed reduction may be accounted for by the change in parity of the mothers.

4. By home visits additional information was obtained from mothers of 755 of the 930 malformations, and from mothers of 742 of 876 births not resulting in malformations, selected by taking every 200th name from the registers of live and stillbirths for the same years.

5. The association of the age and parity of the mother with the risk of birth of a central nervous malformation was examined in a comparison of the malformation and control groups, with the following results:

- (a) Considering all the central nervous malformations together, risks of the birth of a malformation are considerably increased at the first parity and above the sixth, and are correspondingly reduced between these extremes. Variations in association with maternal age are also present but are less marked.
- (b) Considering the main groups separately, results for anencephalus and spina bifida are similar to those for the whole series. In the case of hydrocephalus, the effect of birth rank is slight when compared with the marked effect of high maternal age.

6. Locality of domicile, rent of house, and legitimacy of the birth were used as indices of social

status; they do not reveal any notable differences in the incidence of central nervous malformations.

7. The incidence of maternal illness or of other maternal disability during pregnancy is recorded. There was no history of rubella or of other virus infection during the pregnancies resulting in the 755 malformations of the central nervous system.

8. Information is also recorded about maternal employment during pregnancy. There was no noteworthy association between the proportion of mothers remuneratively employed and the incidence of congenital malformations of the nervous system.

Many people assisted the work of this enquiry, and we acknowledge our indebtedness to the following: Dr. Jean Mackintosh and members of the Birmingham Maternity and Child Welfare Department who co-operated fully in making available to us the records of the department; Dr. Dorothy Tidmas, who completed a preliminary survey of the malformations of one year; Mrs. Kathleen Gibson, Miss Mary Edge, Mrs. Burgess Smith, Mrs. Leaver, Miss Day, Miss Bayes, and members of the Almoners' Department of the United Birmingham Hospitals, all of whom took part in the field work; and Miss Catherine Wall, who prepared the figures used in the text. Dr. Enid Charles and Sir Leonard Parsons read the typescript and offered useful suggestions. Finally, and in particular, we record our gratitude to Prof. Lancelot Hogben, F.R.S., who has contributed most generously to this enquiry.

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APPENDIX A

CLASSIFICATION OF BIRMINGHAM CITY WARDS INTO THREE SOCIAL GROUPS

In Birmingham certain statistics can be prepared separately for each city ward, and since alternative indices of social status are often not available, a classification of wards into social groups is of value. For many years the annual reports of the Medical Officer of Health have given statistics for central, inner and outer rings, a classification based on the wards and related broadly to social differences. This classification introduces certain anomalies: Edgbaston, for example, is in the inner ring, but having been reserved as a high-class residential area, contains few working-class dwellings; in the outer ring some wards have a high proportion of municipally-owned houses occupied by residents of the artisan class, while others have mainly privately-owned houses, many occupied by professional and business men. We have therefore re-classified the wards, using data from three sources:

- (1) The Housing Survey Report, 1946, gives for each ward the number of houses: (a) back-to-back; (b) with a bathroom; (c) with a bath; (d) municipally-owned.
- (2) The Birmingham City Statistical Office* has supplied the average rateable values for each ward.
- (3) The Town Planning Department gave the surface area of each ward, from which were calculated by wards: (a) housing densities; (b) population densities, using the ward population given in the Report of the Medical Officer of Health, 1947.

Table A and Fig. A (overleaf) give the data on which the 34 city wards were divided into three groups:

* We are indebted for this material to Dr. Enid Charles.

Group I. Fifteen wards with a high proportion of substandard houses. These include all the central wards and the more highly industrialized wards of the inner ring; it accommodates mainly the families of workers with low incomes.

Group II. Twelve wards with houses of a higher standard than Group I. The most significant feature is the high proportion of municipally-owned houses in eight wards. These houses are also occupied mainly by working-class families.

Group III. Seven wards with a high general level of housing. All except Edgbaston are in the outer ring and well removed from the industrial areas.

Infant mortality and live birth rates for the years 1946 and 1947 show considerable differences between the three ward groups. (Table B, overleaf, and Fig. B, below.)

FIG. B.—Birth rate and infant mortality rate by ward groups (Birmingham, 1946-47).

FIG. A.—Housing details by ward groups (Birmingham, 1946-47).

APPENDIX A, TABLE A
HOUSING STATISTICS OF WARD GROUPS IN BIRMINGHAM (1946)

Municipal Ward	Percentage of Dwelling Houses				Average Rateable Value (1947) £	Housing and Population Density	
	Back-to-back type	With bathroom	With bath	Municipally owned		Houses per Acre	Persons per Acre
I St. Mary's	47.2	3.9	27.1	0.0	7.61	10.7	41.6
Duddeston and Nechells	29.1	3.8	29.8	2.6	7.84	12.2	44.3
St. Bartholomew's	26.7	6.8	22.5	6.7	7.90	9.0	32.1
St. Paul's	63.8	2.0	38.3	0.0	7.93	12.8	44.0
All Saints'	29.9	2.5	45.1	0.4	8.43	15.8	52.8
Ladywood	61.0	3.2	20.9	0.6	8.45	19.0	65.0
St. Martin's	49.7	8.5	31.2	5.3	8.98	12.3	46.2
Market Hall	64.7	4.8	28.4	0.0	9.20	9.1	32.1
Aston	24.8	5.9	37.9	0.0	9.25	14.1	50.7
Saltley	1.9	29.5	49.0	13.4	11.03	6.4	24.0
Rotton Park	26.5	15.5	42.6	0.0	11.34	12.0	42.1
Lozells	21.1	5.0	31.8	0.5	11.63	19.5	70.8
Small Heath	4.4	27.9	57.6	13.7	11.70	13.3	50.4
Sparkbrook	7.5	16.7	34.4	0.0	11.75	11.4	45.2
Balsall Heath	11.0	15.9	35.4	0.0	11.95	18.1	64.2
Average for Group I	29.3	10.8	36.5	2.87	9.86	12.38	44.76
II Washwood Heath	0.8	62.7	81.8	17.4	12.94	4.9	19.1
Selly Oak	0.7	53.8	82.6	9.6	13.91	5.3	18.6
Soho	5.2	41.9	77.6	1.7	15.60	9.2	33.6
Sparkhill	0.5	52.0	67.2	2.7	16.13	7.6	27.8
Bromford	3.0	44.7	78.2	32.3	13.46	2.9	11.7
Perry Barr	0.0	86.5	99.8	35.3	13.47	6.1	25.3
Yardley	0.2	62.7	88.6	28.4	13.84	6.5	25.5
Stechford	0.0	89.7	98.7	42.4	13.89	3.1	13.1
Erdington	0.7	61.7	87.8	39.4	14.54	7.0	28.3
Acoccks Green	0.1	56.1	94.0	44.8	14.58	7.4	30.0
Northfield	0.1	82.9	95.9	38.9	14.65	2.3	8.3
Hall Green	0.0	72.8	99.5	41.6	16.37	6.3	24.8
Average for Group II	0.6	68.4	90.0	30.3	14.40	4.63	18.15
III King's Norton	0.3	73.4	82.8	11.3	16.50	3.0	11.0
Gravelly Hill	0.2	75.0	86.0	21.9	16.58	4.1	17.7
Sandwell	0.4	56.3	77.6	2.5	17.77	4.1	14.2
Harborne	0.2	76.9	86.8	15.1	18.80	4.2	14.9
Handsworth	1.7	60.1	85.4	1.4	19.16	5.6	21.2
Moseley and King's Heath	0.1	74.0	91.5	21.7	20.80	4.5	17.5
Edgbaston	5.8	75.4	88.9	0.0	34.81	2.8	11.5
Average for Group III	1.1	71.1	86.1	11.8	20.27	3.87	14.77
Whole City	10.3	49.7	71.3	17.1	—	5.56	21.08

APPENDIX A, TABLE B
VITAL STATISTICS OF WARD GROUPS IN BIRMINGHAM (1946-1947)

Vital Statistics	Ward Group			All Wards
	I	II	III	
Birth rate	25.7	21.0	19.7	22.4
Infant mortality rate	49.2	36.5	33.1	40.4