INCIDENCE OF CONGENITAL MALFORMATIONS AND THEIR RELATION TO VIRUS INFECTIONS DURING PREGNANCY

BY

W. P. D. LOGAN, M.D., B.Sc., Ph.D., D.P.H.

Chief Medical Statistician, General Register Office

Evidence is accumulating about the aetiology of congenital malformations. Reviewing this evidence, Warkany (1947) mentioned genetic, nutritional, chemical, endocrine, actinic, infectious, and mechanical factors, each of these having been recognized either from clinical observations or from animal experiments as of some causal significance. Similar reviews have been made in this country by Landtman (1948), Penrose (1951), and Carter (1951). This increasing knowledge about the causes of congenital malformations is bringing nearer the day when effective preventive action will be possible and when these malformations will cease to be the unexplainable and unavoidable misfortunes that they have been in the past.

The purpose of this paper is to review what is already known about the incidence of congenital malformations from the statistical aspect and to summarize the results of some of the investigations that have been made in various parts of the world into the effects of virus infections during pregnancy.

Information about the incidence of congenital malformations is available from national mortality statistics, Scottish stillbirth statistics, and from special studies of limited series of cases.

Mortality Statistics

During the three years 1946–8 16,324 deaths at all ages registered in England and Wales (Registrar General) were attributed to congenital malformations, and three-quarters of these were of infants under 1 year of age (Table I). Congenital malformations ranked third among the causes of infant mortality, preceded by prematurity and pneumonia. They caused 12% of all infant deaths, 14% of deaths under 4 weeks, and 11% of deaths between 4 weeks and 1 year. Of the total of 16,324 deaths 10% were of infants in their first day of life, 36% between 1 day and 4 weeks, 28% between 4 weeks and 1 year, 10% between 1 and 15 years, and 16% at higher ages.

TABLE I.—*Deaths from Congenital Malformations in England and Wales by Sex and Age, 1946–8*

A. Under 1 Year

	Under 1 Day	1–6 Days	7–13 Days	14–20 Days	21–27 Days	4 Wks–3 Mths	3–6 Mths	6–9 Mths	9–12 Mths
Males ..	863	1,712	745	404	330	1,542	721	303	157
Females	781	1,372	702	375	247	893	586	274	142
Persons	1,644	3,084	1,447	779	577	2,435	1,307	577	299

B. All Ages (Years)

	0–	1–	2–	3–	4–	5–	10–	15 and Over	All Ages
Males	6,777	281	128	63	49	182	134	1,371	8,985
Females	5,372	242	88	54	52	126	120	1,285	7,339
Persons	12 149	523	216	117	101	308	254	2,656	16,324

The infant mortality rate from congenital malformations was about 6 per 1,000 live births between 1931 and 1939, increased to over 6.5 during 1940 to 1942, but has since declined by about one-third to 4.45 per 1,000 in 1948 (Table II). This decline is identical with

TABLE II.—*Infant Mortality Rates from Congenital Malformations per 1,000 Related Live Births. England and Wales, 1931–48*

1931	..	.. 5·66	1937	..	.. 6.28	1943	..	.. 5·89
1932	..	.. 6·03	1938	..	.. 6·22	1944	..	.. 5·52
1933	..	.. 5·98	1939	..	.. 6·09	1945	..	.. 5·60
1934	..	.. 6·32	1940	..	.. 6·62	1946	..	.. 5·43
1935	..	.. 6·12	1941	..	.. 6·56	1947	..	.. 4·88
1936	..	.. 6·36	1942	..	.. 6·50	1948	..	.. 4·45

that of total infant mortality during the same period—namely, from 51 per 1,000 in 1942 to 34 in 1948. As there is no reason to believe that the *incidence* of these malformations can have substantially diminished in the last few years, the reduction in mortality means that a larger proportion of children born with malformations have been saved from dying in infancy.

During 1946–8 the neonatal mortality rate from congenital malformations was highest in the North IV region of England and Wales (Cheshire and Lancashire), where the rate was 20% above the national average, and lowest in Greater London, the East and South-east regions (Table III). These, it should be noted, were

TABLE III.—*Infant Mortality Rates from Congenital Malformations at Ages Under 4 Weeks and from 4 Weeks to 1 Year by Geographical Regions, Percentage of Rate for England and Wales, and Percentage of Infant Mortality from all Causes. Average of Rates in 1946, 1947, and 1948*

	Under 4 Weeks			4 Weeks–1 Year			Total Under 1 Year		
	Deaths from Congenital Malformation per 1,000 Related Live Births	% E. & W.	% of Infant Mortality from all Causes	Deaths from Congenital Malformation per 1,000 Related Live Births	% E. & W.	% of Infant Mortality from all Causes	Deaths from Congenital Malformation per 1,000 Related Live Births	% E. & W.	% of Infant Mortality from all Causes
England and Wales	3·04	100	14	1·88	100	11	4·92	100	12
South-east	2·77	91	15	1·66	88	13	4·43	90	14
Greater London	2·74	90	15	1·70	90	13	4·44	90	14
Remainder of South-east..	2·80	92	14	1·63	87	14	4·43	90	14
North	3·29	108	13	2·10	112	9	5·39	110	11
North I	2·95	97	12	2·00	106	8	4·95	101	10
,, II	3·08	101	13	1·71	91	9	4·79	97	11
,, III	2·96	97	13	2·07	110	11	5·03	102	12
,, IV	3·64	120	14	2·24	119	9	5·88	120	12
Midland	3·19	105	14	1·86	99	11	5·05	103	12
Midland I	3·18	105	14	1·82	97	10	5·00	102	12
,, II	3·23	106	14	1·92	102	11	5·15	105	12
East	2·77	91	14	1·70	90	13	4·47	91	13
South-west	3·12	103	14	1·74	93	15	4·86	99	14
Wales	2·89	95	12	2·41	128	12	5·30	108	12
Wales I	2·80	92	11	2·44	130	11	5·24	107	11
,, II	3·13	103	13	2·26	120	12	5·39	110	13

TABLE IV.—*Deaths from Congenital Malformations at all Ages, occurring in Each Month; and, with Correction for Varying Length of Months, Percentage of Average Monthly Deaths. England and Wales, 1946–8*

	Total	Jan.	Feb	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.-Mar. and Oct.-Dec.	April-Sept.
All congenital malformations	16,313	1,550	1,413	1,541	1,395	1,426	1,244	1,233	1,180	1,236	1,300	1,314	1,481	8,599	7,714
	100	*112*	*112*	*111*	*104*	*103*	*93*	*89*	*85*	*92*	*94*	*98*	*107*	*106*	*94*
Congenital hydrocephalus	890	78	89	92	62	82	63	77	56	76	68	76	71	474	416
	100	*103*	*129*	*122*	*85*	*109*	*86*	*102*	*74*	*104*	*90*	*104*	*94*	*107*	*93*
Spina bifida and meningocele	3,150	292	248	249	278	295	259	271	247	243	252	243	273	1,557	1,593
	100	*109*	*101*	*93*	*108*	*110*	*100*	*101*	*92*	*94*	*94*	*94*	*102*	*99*	*101*
Congenital malformation of heart	5,247	526	490	511	427	449	375	373	352	411	392	436	505	2,860	2,387
	100	*118*	*120*	*115*	*99*	*101*	*87*	*84*	*79*	*95*	*88*	*101*	*113*	*109*	*91*
Monstrosities	311	27	25	29	30	31	22	20	30	22	32	22	21	156	155
	100	*102*	*104*	*110*	*117*	*117*	*86*	*76*	*114*	*86*	*121*	*86*	*80*	*101*	*99*
Congenital pyloric stenosis	825	98	90	93	88	68	66	64	47	44	53	53	61	448	377
	100	*140*	*141*	*133*	*130*	*97*	*97*	*91*	*67*	*65*	*76*	*78*	*87*	*109*	*91*
Cleft palate, hare-lip	231	19	21	18	15	21	27	12	26	13	20	17	22	117	114
	100	*97*	*117*	*92*	*79*	*107*	*142*	*61*	*133*	*69*	*102*	*90*	*112*	*102*	*99*
Imperforate anus	143	21	9	10	16	9	14	17	6	8	11	7	15	73	70
	100	*173*	*81*	*82*	*136*	*74*	*119*	*140*	*49*	*68*	*91*	*60*	*124*	*102*	*98*
Cystic disease of kidney	671	53	58	64	61	62	66	51	58	49	46	45	58	324	347
	100	*93*	*111*	*112*	*111*	*109*	*120*	*90*	*102*	*89*	*81*	*82*	*102*	*97*	*103*
Other stated and unstated malformations*	4,845	436	383	475	418	409	352	348	358	370	426	415	455	2,590	2,255
	100	*106*	*102*	*115*	*105*	*99*	*88*	*85*	*87*	*93*	*104*	*104*	*111*	*107*	*93*

* Malformations of central nervous system 9%, of circulatory system 21%, of digestive system 44%, of genito-urinary system 9%, other 13%, unstated 4%.
NOTE: The difference in total deaths shown in Tables I and IV arises because Table I gives deaths registered, and Table IV gives deaths occurring in the periods concerned.

the regions reporting the highest and the lowest rates of neonatal mortality from all causes. The regional differences do not therefore provide definite evidence of variability in the incidence of congenital malformations in different parts of the country.

Adjustment being made for different length of months, most deaths from congenital malformations at all ages occurred in January, February, and March, and fewest in August (Table IV). Largest variations between winter and summer deaths were from congenital malformations of the heart, pyloric stenosis, hydrocephalus, and from the group of "other stated and unstated malformations."

Table V, which gives the percentage distribution of deaths at different ages by type of malformation, shows that, in infancy and childhood, mortality was greatest from malformations of the heart, but that amongst adults this group was surpassed by "other stated malformations."

TABLE V.—*Percentage Distribution of Deaths from Congenital Malformations at Various Ages by Type of Malformation. England and Wales, 1946–8*

	Under 1 Year	1–4 Years	5–14 Years	15 Years and Over	All Ages
All congenital malformations	100	100	100	100	100
Congenital hydrocephalus	5	16	10	3	5
Spina bifida, meningocele	25	10	3	1	19
Congenital malformation of heart	32	38	50	23	33
Monstrosities	3	0	—	—	2
Congenital pyloric stenosis	7	1	—	0	5
Cleft palate, hare-lip	2	3	0	—	1
Imperforate anus	1	0	0	—	1
Cystic disease of kidney	1	1	2	22	4
Other stated malformations	22	31	35	51	29
Unstated malformation	2	0	0	0	1

At all ages, deaths of males from malformations of all types exceeded deaths of females by 22%—a 26% excess of males in infancy, a 23% excess at 1–14, and a 7% excess at adult ages (Table VI). Most of the specified types of congenital malformations showed excess of male mortality, especially pyloric stenosis, but notable exceptions were spina bifida and meningocele, and monstrosities from which there were more deaths of female children than of male. Congenital malformations of the heart caused more male than female deaths in infancy and adult life but not during the years of childhood.

TABLE VI.—*Deaths of Males from Congenital Malformations as Percentage of Deaths of Females, by Age and Type of Malformation; England and Wales, 1946–8*

	Under 1 Year	1–14 Years	15 Years and Over
All congenital malformations	126	123	107
Congenital hydrocephalus	115	169	157
Spina bifida, meningocele	70	56	153
Congenital malformation of heart	142	94	114
Monstrosities	88	—	—
Congenital pyloric stenosis	396	—	—
Cleft palate, hare-lip	113	81	—
Imperforate anus	286	300	—
Cystic disease of kidney	335	300	91
Other stated malformations	154	176	107
Unstated malformation	106	100	—

Stillbirth Statistics

Since 1939 provision has been made in Scotland for the reporting of causes of stillbirth. During 1945–7, 9,995 stillbirths were registered, of which 1,706 were ascribed to congenital malformations (Registrar General for Scotland). This yields congenital malformation rates of 17.1% of all stillbirths and 5.42 per 1,000 total births, live and still.

Of the 1,706 stillbirths attributed to congenital malformations 44% were from anencephaly, 30% from hydrocephalus, 8% from spina bifida, 9% from multiple malformations, 1% from heart disease, and 8% from other stated or unstated malformations.

Special Studies of Stillbirth and Infant Deaths

In Birmingham, McKeown, Record, and MacMahon have studied consecutive cases of congenital malformations resulting in stillbirth or death in infancy during 1940–7. McKeown (unpublished data) gave the following rates per 1,000 births, live and still: anencephaly 2.3, spina bifida 2.5, hydrocephalus 0.9, other malformations of the central nervous system 0.2, congenital malformations of the heart 1.8, pyloric stenosis 0.3, mongolism 0.2, hare-lip, cleft-plate 0.2, other malformations 1.6. Altogether these yielded a total rate of stillbirths and infant deaths from congenital malformations of 10 per 1,000 births. The corresponding combined rate in Scotland in 1945 was 11.4.

Murphy (1947) examined the certified causes of stillbirths and deaths at all ages in Philadelphia during 1929–33 and estimated that there had been 47 deaths or stillbirths associated with congenital malformations per

10,000 live births during the period, or 1 to 213. Unfortunately, disregarding the fact that he was dealing only with deceased or stillborn cases, he summed up his findings as, "One malformed child was born for every 213 infants who were born alive." He used this ratio as if it measured the total incidence of congenital malformations, and this drew from Carter and Tizard (1951) the comment that this ratio of 1 in 213 was "much too low on any definition of congenital defect."

Murphy's series included 222 stillbirths from congenital malformations out of a total of 7,478 stillbirths, or 3%, a much smaller proportion than the 17.1% reported in Scotland in 1945–7.

Estimates of Total Incidence

Each of the foregoing sources has provided information about the incidence of malformations where stillbirth or death had resulted, but not about the total incidence of malformations, fatal and non-fatal. A few investigators have estimated the total incidence of malformations among series of births. They have usually dealt, however, with births in hospital, and these are perhaps not representative of births in general. Some of the difficulties in making estimates of this kind were discussed in a recent "Any Questions?" paragraph in the *British Medical Journal* (1950), and "1 in 40" was given as a reasonable estimate of the chance that any random pregnancy would end in a serious malformation.

Malpas (1937) reported on 13,964 births in the Liverpool Maternity Hospital; among these he found 294 cases of congenital malformation, or 2.1%. Of these, 149, just over 50%, were malformations of the central nervous system.

Naujoks (1938), in Cologne, found 236 malformed children (1.33%) in a series of 17,800 births. These 236 cases included 28 with hydrocephalus, 7 with anencephaly, 6 with hydrops foetalis, 15 with spina bifida or meningocele, 29 with hare-lip, cleft palate, 7 with other cranial malformations, 11 with malformations of upper limbs, 60 with malformations of lower limbs, 24 with polydactyly or syndactyly, and 39 with rare minor defects.

Javert and Stander (1943) reported that 2.95% of 27,000 infants delivered in their clinic had some abnormality, including extra digits, birth marks, undescended testicle, umbilical hernia, spina bifida, and hydrocephalus.

Tholen (1946), in Holland, found 66 children with congenital malformations out of 1,833 born during 1944–6, or 3.6%. The malformations were as follows: anencephaly 5, hydrocephalus 4, macerated foetus 18, pes valgus 1, pes varus 3, spina bifida 6, gastro-intestinal atresia 2, imperforate anus 3, hypospadias 1, epispadias 1, mongolism 6, cephalocele 1, malformation of heart 7, malformation of toes or fingers 5, congenital retro-auricular fistula 1, bilateral congenital cataract 2.

Landtman (1948) found 73 malformed children (2.0%) among 3,593 deliveries during 1945–8 at University College Hospital, London. The malformations were: anencephaly 12, spina bifida 6, hare-lip, cleft palate 5, mongolism 4, deformities of limbs 13, congenital heart disease 11, hypospadias 4, miscellaneous 18.

Greenberg *et al.* (1949), in a paper to which further reference is made below, found 30 children with congenital defects (1.37%) in a control series of 2,186 deliveries of women who had not been vaccinated against smallpox during pregnancy.

The percentages of malformed children found in these six separate series were therefore 2.1, 1.33, 2.95, 3.6, 2.0, and 1.37, giving an average 2.23. The average of these heterogeneous sets of data is of doubtful value. Nevertheless, it corresponds quite well with the estimate of 1 in 40 (2.5%) quoted by the *British Medical Journal* and based partly on the same evidence. Either may be taken as a rough indication of the total incidence of congenital malformations, or, at any rate, of those conditions that are generally recognized as such in investigations into their incidence. Clearly, however, the actual incidence found in any investigation will depend upon how widely or narrowly congenital malformations are defined for the purpose of that investigation.

Some further details about the incidence of congenital malformations, with additional references, are given in the Ministry of Health Report No. 94 (1949) on neonatal mortality and morbidity.

Influence of Virus Infections during Pregnancy

Swan (1949) has reviewed much of the work that has been done by himself and others in the investigation of the association between maternal rubella and congenital malformations, stillbirths, and abortions, an association to which attention was first drawn by Gregg (1941). Practically all of the early evidence adduced in support of this association was based on *retrospective* inquiries. Starting with the recognition of congenital malformation in the child, inquiry was made into the mother's health during pregnancy, and in a high proportion of cases a history of rubella in pregnancy was elicited. Moreover, the attack of rubella had usually occurred at some time during the first three months of pregnancy—a most important finding, as it strongly suggested that factors other than chance were involved. The double event of congenital malformation preceded by rubella early in pregnancy was found so often that there seemed little room for reasonable doubt about the existence of a causal relationship; and, as a result of inquiries of this retrospective type, it was estimated that, following an attack of rubella during the first two months of pregnancy, the chances of the child being malformed were not far short of 100% (Swan *et al.*, 1943).

It is important to realize that inquiries of this retrospective type are apt to give a misleading estimate of the degree of risk of congenital malformation following maternal rubella—first, because the cases of congenital malformation have already been selected before inquiry about the pregnancy is made; and, secondly, because the mother's recollection of events early in pregnancy may be faulty or may be influenced by the fact that she has given birth to a malformed child. It may be, therefore, that the actual risk has been greatly exaggerated. Some clinicians have adopted the policy of advising induction of abortion when rubella has occurred early in pregnancy, in the belief that otherwise the birth of a malformed child is almost certain. Before advocating such a drastic procedure as termination of pregnancy, however, they should understand that the *statistical evidence as yet available*, pointing to an almost 100% probability of malformation, is of a dubious and unsatisfactory character.

Retrospective inquiries from the abnormal child to the mother answer only the question (and, as has already been implied, do not necessarily answer it well)—"What is the probability that the mother of a malformed child had rubella during pregnancy?" The question, or rather double question, that has to be answered is: "What is the probability that rubella during pregnancy will result in the birth of a malformed child, and how does the incidence of congenital malformations following maternal rubella compare with the incidence of congenital malformations among newborn children in general?"

An answer to this double question can be obtained satisfactorily only from a *prospective* inquiry that takes the mother's health during pregnancy as the starting-point and proceeds forward from there to consider the condition of the child. This has been fully realized by a number of investigators, and results of several inquiries framed on those lines are already on record. Unfortunately, as there are considerable practical difficulties to be overcome in carrying out a satisfactory *prospective* inquiry, the results so far reported tend to be conflicting and confusing. In a number of inquiries the possible effects of diseases other than rubella have also been investigated.

Prospective Inquiries Reported in the Literature

Fox and Bortin (1946) investigated the outcome of 11 cases of maternal rubella (9 in the first three months of pregnancy) ascertained from Milwaukee Public Health Department records. One child was hydrocephalic and stillborn. Another was described as a "blue baby" with hydrocephalus; it survived, and was reported as having become normal. In each of these two cases rubella had occurred during the first three months of pregnancy. No abnormality was noted in the 10 other children (one set of twins).

Aycock and Ingalls (1946) used the Board of Health records of two Massachusetts communities to discover four cases of maternal rubella. Two had occurred in the first three months of pregnancy, and one of the resulting children was mentally retarded; the other was normal, as were the two children from the other two cases. The same authors also followed up 131 cases of poliomyelitis during pregnancy (27 in the first three months)—92 of the children born were normal; 33 pregnancies ended in abortion or stillbirth (13 where poliomyelitis had occurred during the first three months of pregnancy); three children had poliomyelitis; another child was "lame"; and two had congenital malformations. In both of these last two cases the attack of poliomyelitis had been in the first three months of pregnancy.

Ober, Horton, and Feemster (1947) sent out postal inquiries to some 3,000 Massachusetts women, aged 17–49, reported as having had rubella in 1943. Only 41% of the women replied to the inquiry, and 49 of them said they had been pregnant at the time when the attack of rubella had taken place. Five more cases were introduced into the inquiry by "supplementary methods." In 22 out of these 54 cases rubella had occurred during the first three months of pregnancy. These 22 cases resulted in 5 children born with congenital defects and 6 pregnancies terminating in stillbirth or abortion. The other 32 cases in which rubella had occurred after the third month of pregnancy produced 3 defective children and 3 abortions or stillbirths.

Grönvall and Selander (1948) reported from Sweden on the outcome of pregnancies complicated by a variety of infectious diseases. Their results can most conveniently be presented in tabular form (Table VII).

TABLE VII.—*Summary of the Results Published by Grönvall and Selander (1948)*

Type of Infectious Disease	Infection Occurring During First 3 Months of Pregnancy				Infection Occurring After First 3 Months of Pregnancy			
	Total No. of Children	Aborted or Stillborn	Live-born but with Malformation	Normal	Total No. of Children	Aborted or Stillborn	Live-born but with Malformation	Normal
Rubella ..	13	2	—	11	15	1	1	13
Measles ..	4	2	—	2	16	1	—	15
Varicella ..	4	—	—	4	9	1	—	8
Mumps ..	6	1	1	4	28	—	4	24
Acute hepatitis ..	10	1	1	8	19	3	—	16
Poliomyelitis ..	15	7	1	7	23	4	1	18
Scarlet fever ..	3	—	—	3	10	—	—	10
Herpes zoster ..	2	1	—	1	—	—	—	—

Fox, Krumbiegel, and Teresi (1948) investigated 6 cases of maternal measles (1 in the first three months of pregnancy), 23 cases of mumps (6 in the first three months), and 4 cases of chicken-pox (1 in the first three months). Only one child had a congenital malformation—hare-lip following maternal measles in the fourth month of pregnancy. A control series was also studied consisting of 665 children born to 297 women who had had one of these three infectious diseases in 1942–5 before or after but not during pregnancy. Six cases of congenital malformations were discovered in the control series.

Through the medium of a syndicated health column, Abel and Van Dellen (1949) invited readers who had had an attack of rubella during pregnancy to write and tell them about the outcome relative to the child. They received details of 82 pregnancies, resulting in the birth of 84 children. Of 54 children born to women whose attack of rubella had been in the first trimester of pregnancy, 3 were stillborn, 44 had congenital malformations, and 7 were normal. Of the other 30 children 12 had malformations and 18 were normal. The authors themselves drew attention to the obvious imperfections of their method of inquiry, but surprisingly suggested that, because of the consistency and general agreement that their results showed with the several reports in the literature, these results could not be totally disregarded.

Very different from the last-described investigation, both in method and in results, was that by Bradford Hill and Galloway (1949), the only prospective type of inquiry as yet reported from Great Britain. This inquiry was based on National Insurance records, and though it fulfilled many of the requirements of a satisfactory investigation it lacked a sufficient number of cases to yield conclusive results, and had no control series. The results are summarized in Table VIII.

Greenberg *et al.* (1949) reported that vaccination against smallpox during pregnancy had no apparent adverse effects upon the child. The children of 4,172 women vaccinated during the first three months of pregnancy included 68 with congenital defects (1.63%). A control series of 2,186 women not vaccinated during pregnancy gave birth to 30 children with congenital defects (1.37%). The authors concluded that the proportions of malformed children in the two groups were not significantly different.

TABLE VIII.—*Summary of the Results Published by Bradford Hill and Galloway (1949)*

Type of Infectious Disease	Infection Occurring During First 3 Months of Pregnancy			Infection Occurring After First 3 Months of Pregnancy		
	No. of Children Born	With Congenital Malformation	Without Congenital Malformation	No. of Children Born	With Congenital Malformation	Without Congenital Malformation
Rubella ..	5	1	4	4	—	4
Measles ..	2	—	2	4	—	4
Infectious hepatitis	—	—	—	1	—	1

Packer (1950) reviewed the literature relating to the influence of maternal measles (morbilli) on the foetus and reported the results of a postal inquiry that he conducted in South Australia into the outcome of pregnancies complicated by measles. There were seven pregnancies in which measles had occurred during the first three months of pregnancy, and these gave rise to one abortion and two live-born children with congenital malformations. The remainder were normal. Eleven other pregnancies in which measles had occurred after the first three months of pregnancy resulted in one abortion and one stillbirth, the others being normal.

Desiderata of a Successful Inquiry

The *prospective* type of inquiry is the only satisfactory approach to the problem of the effects of the virus infections during pregnancy. Nevertheless it must be evident that the various prospective inquiries described above have failed to give conclusive results. It would appear, however, that the more rigorous the technique employed in the inquiry the smaller was the proportion of malformations ascertained to have followed the maternal virus infection. In conclusion, therefore, it may be helpful to state what in my opinion are the desiderata of an inquiry that will yield statistically convincing results.

1. As has been pointed out, the inquiry should be *prospective,* directed forward from the pregnancy to the condition of the child; that is to say, knowledge of the presence or absence of abnormality in the child should not be allowed in any way to influence the selection of cases to be studied. Preferably the selection of each case should have been made before the child was born.

2. The inquiry should provide for the inclusion of cases of rubella, or of any other virus infection that it is proposed to study, occurring at all stages of pregnancy from the earliest weeks.

3. The occurrence of the virus infection should be recorded during the course of the pregnancy, no cognizance being taken of cases in which the occurrence of the infection was not recorded until after the child was born.

4. The diagnosis of the virus infection should have been made by a medical practitioner.

5. The outcome of the pregnancy should be recorded, whether the pregnancy terminated in abortion (including miscarriage), stillbirth, or live birth, and the presence of congenital malformation noted. Live-born children should be examined periodically for a number of years. The cause of abortion or stillbirth and the cause of death of a live-born child should be recorded.

6. A control series should be selected and studied in which the selected virus infections did not occur during pregnancy, precisely similar arrangements being made for ascertaining the outcome of the pregnancy as were made for cases in which virus infection did occur.

7. The medical examination of each child should be carried out, so far as is practicable, on a uniform pattern, and the examiner preferably should not know the maternal history—that is, whether the child had been born from a virus infection or a control pregnancy.

8. The number of virus infection cases and of controls should be sufficient to yield statistically significant results.

Summary

The incidence of congenital malformations is discussed utilizing evidence from mortality and stillbirth statistics and from special studies reported in the literature.

The published results of various *prospective* inquiries into the influence of virus infections during pregnancy in causing congenital malformations are reviewed, and desiderata of a successful inquiry are suggested.

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A short survey of the broad trends of psychological inquiry and the changes undergone in recent years appeared in the *Times Literary Supplement* of August 24. First comes experimental psychology. Traditionally limited to the analysis of comparatively restricted aspects of human behaviour, the study of more complicated patterns has recently been successfully carried out. Much of this work has been done at the Cambridge Psychological Laboratory, under the direction of Sir Frederic Bartlett. An important series of experiments have been carried out on pilot error. Liability to operational fatigue was studied, and much valuable information has been gained about the organization of skilled activity. Next there is medical psychology, which has had an important influence on present-day conceptions of normal behaviour. Due partly to the difficulties of psycho-analysis, and partly to the fact that physical methods of treatment are often more rapid and reliable, the value of psycho-analysis in mental disorders is relatively low. Thirdly comes social psychology, which is developing fast. Founded in 1947, the Tavistock Institute of Human Relations has been largely responsible for the wide range of empirical researches designed to throw light on the basic processes in group behaviour. Studies have been carried out on the problems of resettlement of repatriated prisoners of war, group tensions in family life, the German character structure, and so on. Lastly, there is the study of individual differences in mental capacity, known as the factorial analysis of ability.